

Synthesis and Biological Evaluation of Potent Bisubstrate Inhibitors of the Enzyme Catechol *O*-Methyltransferase (COMT) Lacking a Nitro Group

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Inhibition of the enzyme catechol *O*-methyltransferase (COMT) represents a viable strategy for regulation of the catabolism of catecholamine neurotransmitters or their precursors, and is of considerable interest in the therapy of *Parkinson's* disease. Herein, we report the development of a new generation of potent bisubstrate inhibitors of COMT derived from nitro-substituted ligand **1** ($K_i = 28$ nM, *Table 1*), which achieve high biological activity despite the lack of a NO₂ substituent on the catechol moiety. Their synthesis takes advantage of a convergent approach, in which a series of functionalized catechol intermediates is prepared (*Schemes 2–7*) and coupled to a common adenosine-derived allylic amine building block (*Scheme 8*). Biological activities of the newly synthesized inhibitors, determined by *in vitro* enzymatic assay and kinetic studies, clearly demonstrate that high inhibitory potency of the bisubstrate inhibitors is not correlated with the p*K_a* of the catechol OH groups. Aromatic residues, connected to the catechol *via* a biaryl-type linkage, were found to maximally benefit from additional favorable hydrophobic interactions with the enzyme and thus to be preferred replacements of the NO₂ group in **1**. A competitive kinetic inhibition mechanism (*Fig. 2*) with respect to the cofactor binding site was confirmed in all cases, supporting a bisubstrate inhibition mode for inhibitors **2–19**.

1. Introduction. – Catechol *O*-methyltransferase (COMT) is an important enzyme involved in catecholamine catabolism, which, in the presence of Mg²⁺ ions, catalyzes the *O*-methylation of biologically active catechols such as dopamine or its precursor L-Dopa [1] (for a crystal structure of COMT, see [1d]). Thus, inhibition of COMT allows for regulation of catechol-based neurotransmitter levels and offers an important therapeutic approach to the treatment of central nervous system (CNS) disorders such as *Parkinson's* disease [2] and possibly schizophrenia [2d][3] and depression [4]. Nitro-substituted catechols are potent COMT inhibitors, and two of them (tolcapone (*Tasmar*[®]) [5] and entacapone (*Comtan*[®]) [6]) have been developed as therapeutic adjuncts to the L-Dopa-based treatment of *Parkinson's* disease, reducing the peripheral metabolic degradation and significantly prolonging the beneficial effects of L-Dopa. However, adverse effects of hepatotoxicity¹⁾ associated in rare cases with the use of tolcapone [7] have been related to the NO₂ substituent of the catechol (= benzene-1,2-diol) structural unit [8]. Therefore, the development of potent COMT inhibitors lacking this functional group is desirable. Such an endeavor faces the challenge of replacing

¹⁾ For a controversial discussion on entacapone-induced hepatotoxicity, see [7b]; however, hepatotoxicity is believed not to be a class effect of nitrocatechols [7d].

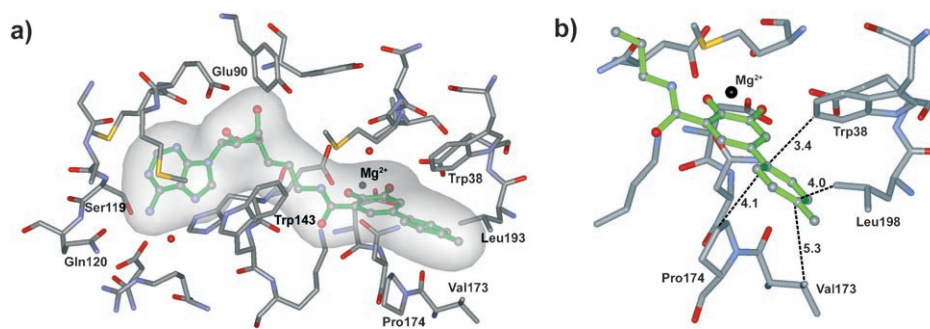


Fig. 1. a) Computer model (MOLOC) of bisubstrate inhibitor **3** complexed in the active site of COMT in the presence of a Mg^{2+} ion. The Connolly surface of the inhibitor is shown. b) Detailed view of the catechol binding site. Inhibitor skeleton: green, C-atoms: gray, O-atoms: red, N-atoms: blue, S-atoms: yellow, Mg-atom: black. Distances are given in Å.

a structural element, which, by its electron-withdrawing effect, ensures both high binding affinity and reduced *O*-methylation of the respective inhibitors. In fact, the NO_2 group has been regarded key element for tight and reversible binding to the substrate pocket of the active site [5a].

Recently, we described the synthesis of potent bisubstrate inhibitor **1** (Table 1; $\text{IC}_{50} = 9 \text{ nM}$; IC_{50} = concentration of inhibitor at which 50% maximal initial velocity is observed) and demonstrated its ability to block both the SAM and catechol binding sites of COMT by kinetic studies and X-ray crystal structure analysis [9] (for modifications of the ribose unit of **1**, see [9c,d]). Guided by molecular modeling results²⁾, we designed compounds **2–19** (Table 1) to take advantage of a hydrophobic cleft at the enzyme surface [2c] [11], located in proximity of the NO_2 group of **1**. We hypothesized that bisubstrate inhibitors featuring suitable substituents connected to position 5 of the catechol could undergo favorable apolar interactions with the lipophilic side chains of the amino acid residues Trp38, Leu198, Val173, and Pro174 of COMT (Fig. 1). Here, we report the synthesis and biological evaluation of this new generation of highly active bisubstrate inhibitors that eliminate the need for NO_2 substitution of the catechol structural unit (for a preliminary communication of parts of this work, see [12]).

2. Results and Discussion. – 2.1. *Synthesis.* In analogy to the synthesis of **1** [9a,b], we envisioned bisubstrate inhibitors **2–19** arising in a highly convergent manner from amide coupling of previously described allylic amine **20** [9a,b] with adequately functionalized catechol *N*-hydroxysuccinimide esters, derived from the corresponding carboxylic acids **21–38** (Scheme 1). To this end, diphenylmethyldioxy or bis(4-methoxyphenyl)methyldioxy moieties were chosen to mask the catechol OH functionalities, enabling the final one-pot acid-catalyzed deprotection of both catechol and ribose moieties.

²⁾ Computer simulations were performed using the molecular modeling package MOLOC [10].

Table 1. Structures of Inhibitors **1–19** and Catechol Carboxylic Acid Intermediates **21–38**

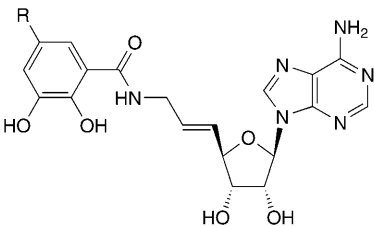
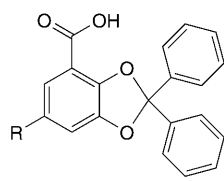
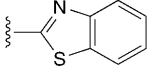
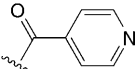
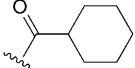
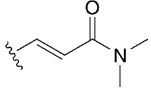
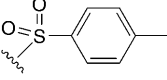
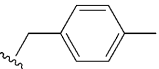
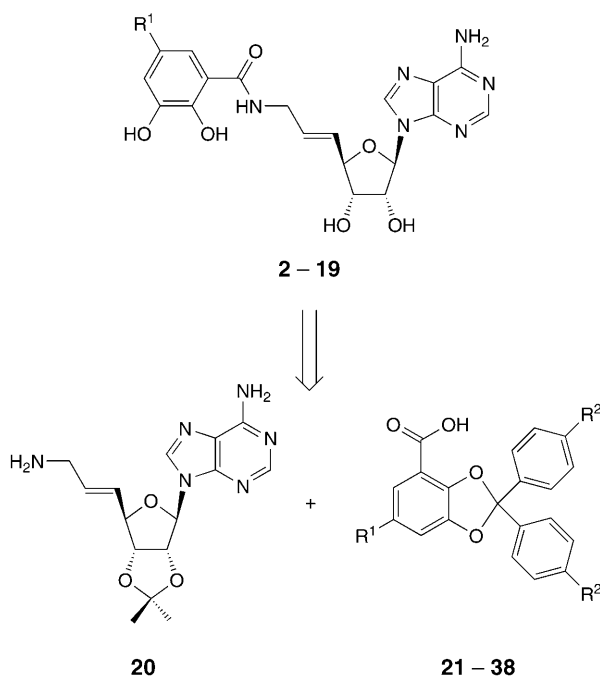
 1 – 19  21 – 38		
R	Inhibitor	Catechol intermediate
	1	–
	2	21
	3	22
	4	23
	5	24
	6	25
	7	26
	8	27
	9	28
	10	29
	11	30
	12	31
	13	32
	14	33
	15	34
	16	35
	17	36

Table 1 (cont.)

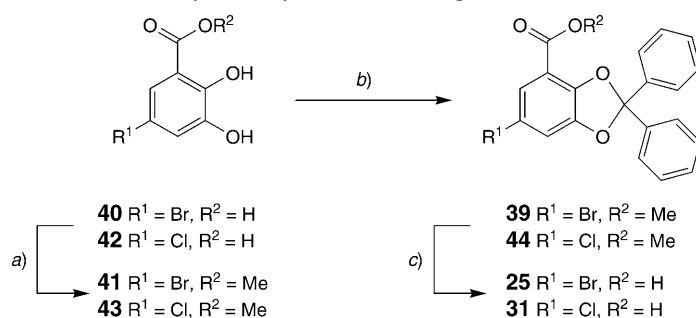
R	Inhibitor	Catechol intermediate
	18	37
H	19	38

Scheme 1. Retrosynthetic Analysis of Inhibitors **2–19**. $R^2 = \text{H}$ or MeO. For an explicit description of the catechol substituents R^1 , see Table 1.

Key building block for the synthesis of protected catechol derivatives is 5-bromo intermediate **39**, obtained from 5-bromo-2,3-dihydroxybenzoic acid (**40**) by esterification to give **41** (88%; Scheme 2) and protection with dichloro(diphenyl)methane (76%).

Analogously, conversion of the known carboxylic acid **42** [13] to the corresponding methyl ester **43**, followed by ketal formation, yielded 5-Cl-substituted building block **44** in 42% overall yield. The ester functionalities of **39** and **44** were subsequently hydrolyzed under standard basic conditions to provide the corresponding carboxylic acids **25** and **31** in high yields (91 and 82%, resp.).

The 5-Br substituent of intermediates **39** and **25** additionally served as a handle for further functionalization. Thus, generation of the dianion of **25** by sequential deproto-

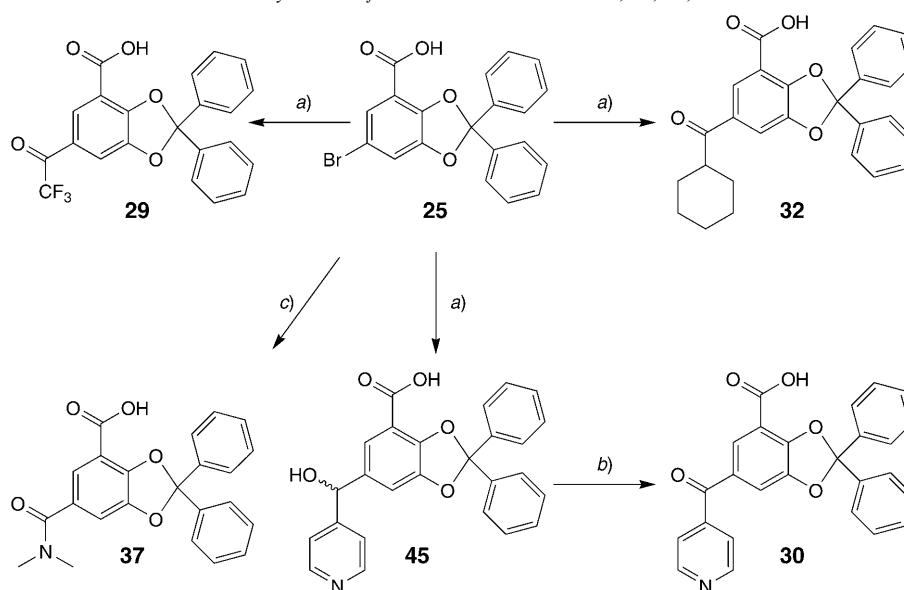
Scheme 2. Synthesis of Catechol Building Blocks **25** and **31**

a) SOCl_2 , MeOH, Δ , 12 h; 80–88%. b) Ph_2CCl_2 (neat), 160° , 40 min; 52–76%. c) LiOH, THF/ H_2O 1:1, Δ , 4 h; 82–91%.

nation with MeOLi/MeOH and careful drying of the resulting lithium carboxylate under high vacuum, followed by Br/Li exchange (*t*-BuLi/THF) and subsequent quenching with the appropriate electrophile, gave rise to acylated building blocks **29** and **32**, and secondary alcohol **45** in moderate yields (25–38%; *Scheme 3*). Intermediate **45** was easily oxidized to give (pyridin-4-yl)carbonyl derivative **30** by treatment with *ortho*-iodoxybenzoic acid (IBX; 95%). Alternatively, deprotonation of **25** with LiH/THF, followed by Br/Li exchange (*t*-BuLi/THF), avoided the change of the solvent medium, furnishing carbamoyl derivative **37** upon quenching with *N,N*-dimethylcarbamoyl chloride (21%). Interestingly, attempts to generate the respective dianionic intermediate by treatment of **25** with 2 equiv. or an excess of alkyl lithium reagent led to exclusive formation of the corresponding 5-unfunctionalized catechol **38** (replacement of Br by H) upon reaction with electrophiles and aqueous workup.

Starting from intermediate **39**, a variety of catechol building blocks could be accessed using Pd^0 -catalyzed cross-coupling reactions. Thus, *Suzuki* cross-coupling of **39** with (4-fluorophenyl)- or (4-methylphenyl)boronic acid furnished the corresponding biaryl carboxylates **46** and **47** (78 and 79%, resp.; *Scheme 4*), which, after hydrolysis, provided carboxylic acids **21** and **22** in high yields (89 and 93%, resp.). Heterocyclic and benzylic residues could be introduced by one-pot Pd^0 -catalyzed conversion of Br derivative **39** to the corresponding boronate, followed by *Suzuki* cross-coupling with the desired aryl or benzyl (Bn) bromide to give biaryls **48–50** and 5-Bn carboxylate **51** (40–80% overall). Again, the methyl esters of these intermediates were subjected to basic hydrolysis to furnish the corresponding carboxylic acids **23**, **24**, **26**, and **35** (92–99%). Furthermore, (*N,N*-dimethylcarbamoyl)ethenyl-substituted intermediate **52** was obtained by *Heck* cross-coupling of **39** with *N,N*-dimethylacrylamide, using Ph_3P as Pd ligand (44%). Addition of Bu_4NBr to the reaction mixture significantly accelerated the conversion of **39** to **52**. Subsequent hydrolysis provided carboxylic acid **33** (77%).

Cross-coupling methodology was also used for the synthesis of 5-CN-functionalized catechol building blocks **27** and **53** starting from 5-Br intermediates **39** and **54**, respectively [9d]. In this case, protection of the catechol OH groups as the corresponding bis(4-methoxyphenyl)methyldioxy moieties was introduced to improve the outcome

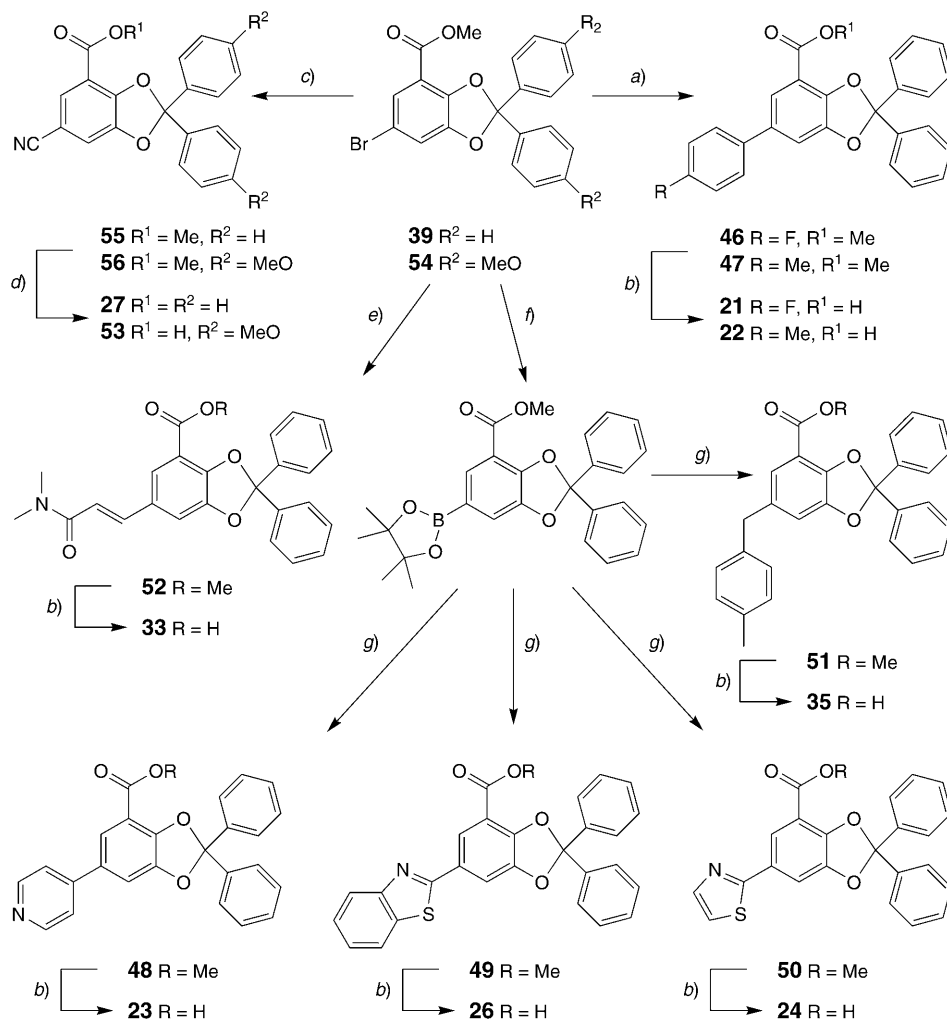
Scheme 3. Synthesis of Catechol Intermediates **29**, **30**, **32**, and **37**

a) 1. MeOLi, MeOH, 20°, 10 min; 2. *t*-BuLi, THF, -78°, 30 min; 3. ethyl trifluoroacetate ($\rightarrow$ **29**) or *N*-methyl-*N*-(methoxy)cyclohexanecarboxamide ($\rightarrow$ **32**) or pyridine-4-carbaldehyde ($\rightarrow$ **45**), -78°, 30 min, then 20°, 2 h; 25–38%. b) *ortho*-Iodoxybenzoic acid (IBX), acetone/Me₂SO 3:1, 50°, 3 h; 95%. c) 1. LiH, THF, 20°, 10 min; 2. *t*-BuLi, THF, -78°, 30 min; 3. *N,N*-Dimethylcarbamoyl chloride, -78°, 30 min, then 20°, 2 h; 21%.

of the final acid-catalyzed ketal hydrolysis (*vide infra*). Thus, Pd⁰-catalyzed reaction of **39** or **54** with KCN in benzene (or toluene)/DMF (3:1) in the presence of 18-crown-6 provided intermediates **55** and **56** in moderate to good yields (76 and 48%, resp.). Interestingly, the composition of the solvent mixture plays a decisive role in the outcome of this transformation. Whereas an increase of the proportion of the aromatic solvent component leads to a significant increase in reaction times and low conversions, extensive decomposition of the starting 5-bromocatechol is observed when the proportion of the polar solvent component is increased. Saponification of the methyl esters of **55** and **56**, carried out under mild conditions to prevent hydrolysis of the newly introduced CN group (LiOH/MeOH at ambient temperature), furnished carboxylic acids **27** and **53** in high yields (92 and 93%, resp.).

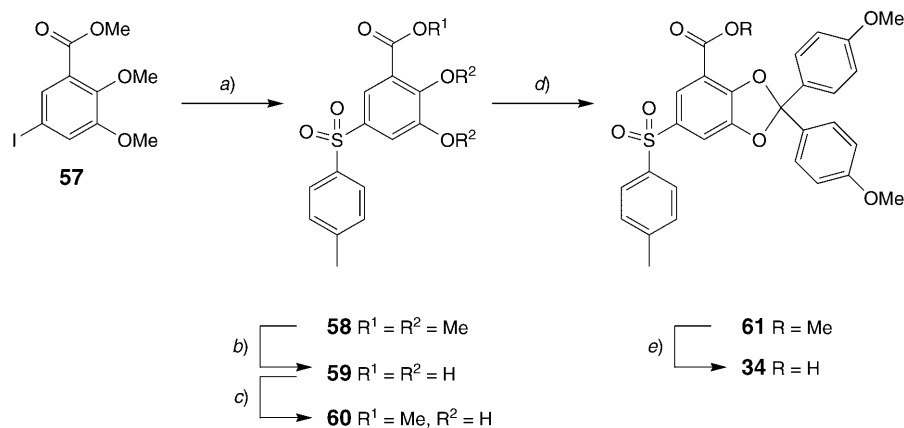
The synthesis of (4-methylphenyl)sulfonyl-substituted catechol building block **34** started from known methyl 5-iodo-2,3-dimethoxybenzenecarboxylate (**57**) [14], which was converted to sulfonyl derivative **58** by CuI-mediated coupling with sodium *p*-toluenesulfinate (Scheme 5; 58%). Cleavage of methyl ester and ethers under harsh acidic conditions ($\rightarrow$ **59**), followed by re-esterification ($\rightarrow$ **60**) and ketal formation, furnished methyl catechol-carboxylate **61**, which was subjected to basic ester hydrolysis to give intermediate **34** (26% overall).

In contrast to the usual functionalization route of 5-Br-catechol intermediates, building blocks **36** and **28** were obtained by carboxylation of a corresponding 4-substi-

Scheme 4. Synthesis of Catechol Building Blocks **21–24**, **26**, **27**, **33**, **35**, and **53**

a) (4-Fluorophenyl)- or (4-methylphenyl)boronic acid, $[\text{Pd}(\text{PPh}_3)_4]$, Na_2CO_3 , benzene/EtOH/ H_2O , Δ , 12 h; 78–79%. b) LiOH, THF/ H_2O 1:1, Δ , 4 h; 77–99%. c) KCN, $[\text{Pd}(\text{PPh}_3)_4]$, 18-crown-6, toluene/DMF 3:1, 100°, 16 h; 48–76%. d) LiOH, MeOH, 20°, 16 h; 92–93%. e) *N,N*-Dimethylacrylamide, $\text{Pd}(\text{OAc})_2$, Na_2CO_3 , Bu_4NBr , $\text{P}(\text{OPh})_3$, *N,N*-dimethylacetamide (DMA), 140°, 72 h; 44%. f) 'Pinacol diboron', $[\text{Pd}(\text{PPh}_3)_4]$, AcOK, toluene, Δ ; 4 h. g) Aryl or benzyl bromide, $[\text{Pd}(\text{PPh}_3)_4]$, Na_2CO_3 , toluene/EtOH/ H_2O , Δ , 16 h; 40–80% (2 steps).

tuted catechol intermediate. Thus, 5-*i*Pr-substituted **36** was derived from known protected 4-acetylcatechol **62** [15] by Wittig methenylation of the carbonyl group ($\rightarrow$ **63**, 86%; Scheme 6) and catalytic hydrogenation of the disubstituted C=C bond ($\rightarrow$ **64**, 94%), followed by *ortho*-lithiation and trapping of the aryllithium nucleophile with methyl chloroformate to give methyl ester **65** (51%). The hydroxy functionalities of

Scheme 5. Synthesis of Catechol Intermediate **34**

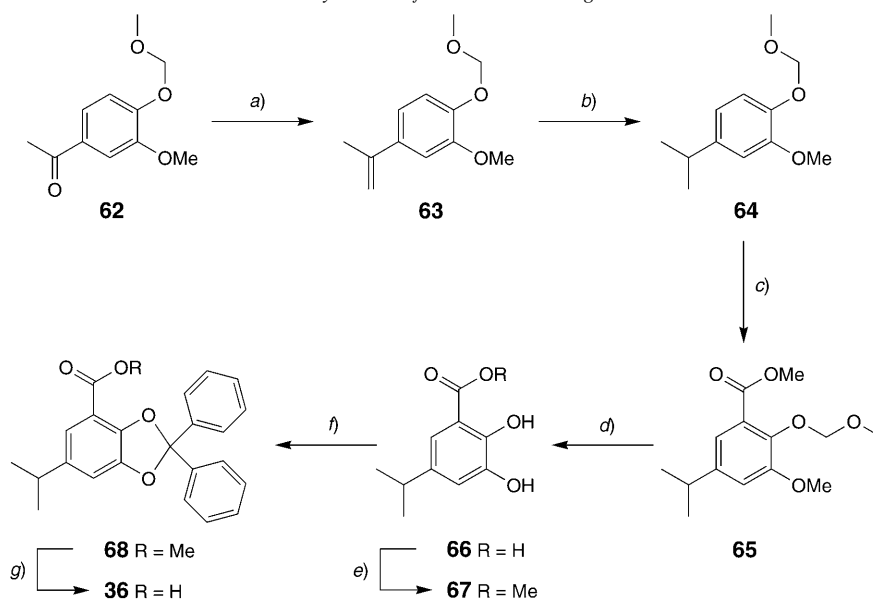
a) Sodium *p*-toluenesulfonate hydrate, CuI, DMF, 110°, 14 h; 58%. b) HBr, Bu₄NBr, AcOH, 140°, 20 h; 45%. c) SOCl₂, MeOH, Δ, 12 h; 75%. d) 1. (COCl)₂, 4,4'-dimethoxybenzophenone, 60°, 30 min; 2. **60**, 160°, 40 min; 77%. e) LiOH, THF/H₂O 1:1, reflux, 4 h, 99%.

intermediate **65** were subsequently unmasked in a two-step protocol calling for initial reaction with BBr₃, followed by acid-catalyzed deprotection of the remaining methyl ether with HBr/AcOH (→ **66**, 41%). Additional protecting-group transformations furnished ⁱPr-containing building block **36** in 58% overall yield (via **67** and **68**).

Similarly, the synthesis of the CF₃-substituted catechol building block **28** started from 4-(trifluoromethyl)benzene-1,2-diol, obtained from 4-(trifluoromethyl)phenol according to a modified literature protocol [16] (Scheme 7). Regioselective bromination (→ **70**, 74%), followed by Bn-protection of the OH groups (→ **71**, 87%), allowed for installation of the methyl ester functionality by Br/Li exchange and interception of the lithium arylate with methyl chloroformate (→ **72**, 52%). Removal of the Bn groups by hydrogenolysis, followed by the usual installation of the desired protective group pattern, gave access to the carboxylic acid intermediate **28** (via **73** and **74**; 57% overall yield).

For completion of the synthesis, catechol-carboxylic acids **21–38** were converted to the corresponding *N*-hydroxysuccinimide esters and coupled by a one-pot procedure with allylic amine **20** to give amides **75–92** (Scheme 8; 40–81% overall yield). Inhibitors **2–19** were finally unmasked by careful treatment with acid (CF₃COOH(TFA)/H₂O, 1:1) in yields ranging from 48 to 99%, and purified by reversed-phase HPLC. Low deprotection yields could, in some cases, be dramatically improved by use of bis(4-methoxyphenyl)methyldioxy rather than unfunctionalized diphenylmethyldioxy moiety as the catechol-protecting-group, which ensured rapid deprotection using shorter reaction times and milder conditions, thus avoiding substrate decomposition by depurination side-reactions (e.g., deprotection yields for CN-functionalized diphenylmethyldioxy-protected **81** and the corresponding bis(4-methoxyphenyl)methyldioxy-protected derivative **93** (not shown) were 42 and 99%, resp.).

2.2. Biological Activity. Biological activities (*IC*₅₀ values; Table 2) of the newly synthesized bisubstrate inhibitors towards COMT were determined with pre-incubation

Scheme 6. Synthesis of Catechol Building Block **36**

a) MePPh_3Br , BuLi , THF, -78° , 15 min, then 20° , 12 h; 86%. b) H_2 , Pd/C , MeOH , 20° , 16 h; 94%. c) 1. BuLi , THF, 0° , 2.5 h; 2. ClCO_2CH_3 , 20° , 12 h; 51%. d) 1. BBr_3 , CH_2Cl_2 , -78° , 30 min; then 20° , 1 h; 2. HBr , AcOH , 120° , 5 h; 41%. e) SOCl_2 , MeOH , Δ , 12 h; 83%. f) Ph_2CCl_2 , 160° , 40 min; 74%. g) LiOH , $\text{THF}/\text{H}_2\text{O}$ 1:1, Δ , 4 h; 95%.

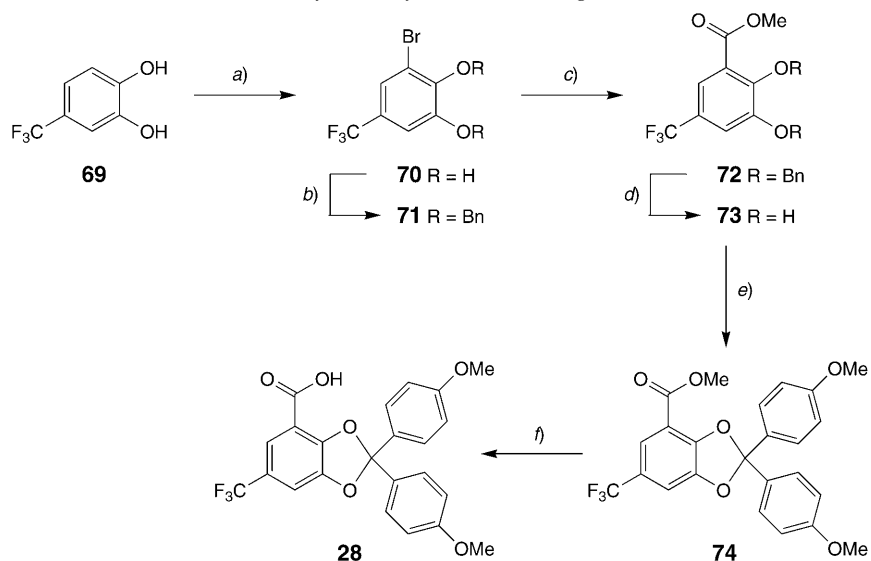
using a radiochemical assay described, in full detail, in [17]. To assess the electronic effects of the newly introduced substituents in position 5 of the catechol, $\text{p}K_{\text{a}}$ values were measured and are given in Table 2 for the most acidic catechol OH group along with the Hammett constants σ_{p} [18] for the respective substituents. In addition, kinetic studies were carried out to determine the inhibition mechanism of ligands **2–19** with respect to the cofactor binding site. Initial velocities, obtained without pre-incubation by varying the cofactor concentration for a series of different inhibitor concentrations, were globally fitted to Eqns. 1, 2, and 3, describing the cases of competitive, mixed competitive, and uncompetitive inhibition, respectively, to obtain kinetic parameters (K_{i} values, Table 2).

$$v = V[S]/(K_{\text{m}}(1 + [I]/K_{\text{ic}}) + [S]) \quad (1)$$

$$v = V[S]/(K_{\text{m}}(1 + [I]/K_{\text{ic}}) + [S](1 + [I]/K_{\text{iu}})) \quad (2)$$

$$v = V[S]/(K_{\text{m}} + [S](1 + [I]/K_{\text{iu}})) \quad (3)$$

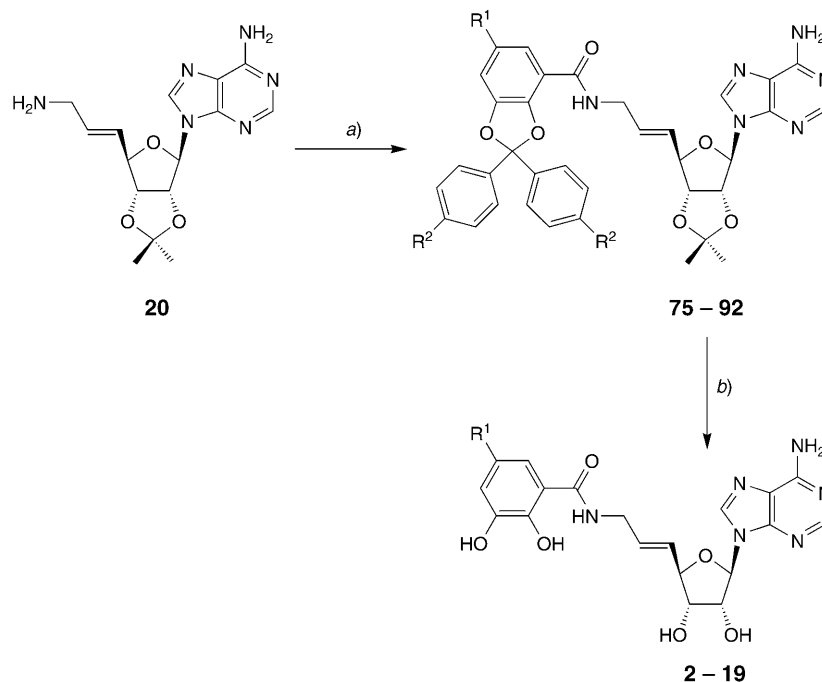
In the Eqns., competitive and uncompetitive inhibition constants are given by K_{ic} and K_{iu} , respectively, whereas $[S]$ and $[I]$ denote cofactor and inhibitor concentrations, respectively. V is the maximal and v the initial velocity of the enzymatic reaction. In all cases, best fit was obtained by using the competitive inhibition model (Eqn. 1), as exem-

Scheme 7. Synthesis of Catechol Building Block **28**

a) Br_2 , CCl_4 , 20° , 1 h; 74%. b) BnBr , K_2CO_3 , acetone, Δ , 4 h; 87%. c) 1. BuLi , THF, -90° , 15 min; 2. ClCO_2CH_3 , $-90^\circ \rightarrow 20^\circ$, 1 h; 52%. d) H_2 , Pd/C , MeOH , 20° , 16 h; 99%. e) 1. $(\text{COCl})_2$, 4,4'-dimethoxybenzophenone, 60° , 30 min; 2. **73**, 160° , 40 min; 63%. f) LiOH , THF/ H_2O 1:1, Δ , 4 h; 91%.

plified graphically for inhibitor **2** by intersection of the lines for different inhibitor concentrations on the $1/v$ axis of the respective *Lineweaver–Burk* plots (Fig. 2).

We were delighted to find that, in the majority of cases, replacement of the NO_2 substituent leads to potent bisubstrate inhibitors with inhibitory activities towards COMT in the low (double-digit) nanomolar range. This data not only provides an impressive validation of the bisubstrate inhibition approach, but also establishes the absence of linear free-energy relationships (LFERs) between the free enthalpy of inhibition ($-\Delta G_{\text{inh}}$) and $\text{p}K_{\text{a}}$ values or *Hammett* parameters. This finding stands in sharp contrast to the interdependence of biological activities and catechol $\text{p}K_{\text{a}}$ values in the case of inhibitors blocking only the (catechol) substrate binding site [5a]. On the contrary, numerous examples of bisubstrate inhibitors in the series **2–19**, exhibiting high $\text{p}K_{\text{a}}$ values of the catechol OH group and, at the same time, having remarkably high inhibitory activities, demonstrate the efficiency of favorable apolar interactions with the hydrophobic cleft at the enzyme surface (e.g., biaryl-functionalized inhibitors **2** and **3** with $\text{p}K_{\text{a}}$ values 6.87 and 7.06, IC_{50} values of 21 and 23 nM, and K_{i} value of 55 nM, resp.). These lipophilic interactions clearly compensate for the fall in binding free enthalpy as a consequence of increased $\text{p}K_{\text{a}}$ values of the catechol OH groups observed in the absence of suitable lipophilic residues R (e.g., **19**, $\text{R} = \text{H}$, $\text{p}K_{\text{a}} = 7.37$, $\text{IC}_{50} = 2600$ nM, $K_{\text{i}} = 1644$ nM). As a result, aromatic groups connected to position 5 of the catechol in a biaryl-type fashion offer an optimal balance of electron-withdrawing ability and hydrophobic contact area, and represent preferred replacements of the NO_2 group. On the other hand, binding affinity deteriorates when polar residues such as the

Scheme 8. Synthesis of the Bisubstrate Inhibitors **2–19**

a) 1. Catechol carboxylic acid, *N*-[3-(dimethylamino)propyl]-*N'*-ethylcarbodiimide (EDC)·HCl, *N*-hydroxysuccinimide, CH_2Cl_2 , 20° , 1 h; 2. **20**, Et_3N , CH_2Cl_2 , 20° , 16 h; 40–81%. *b*) $\text{TFA}/\text{H}_2\text{O}$ 1:1, 0° , 20–60 min, 42–99%. $R^2 = \text{H}$ or MeO. For an explicit description of the catechol substituents R^1 , see Table 1.

N,N-dimethylcarbamoyl group of **18** are placed into the hydrophobic environment ($\text{IC}_{50} = 2000 \text{ nM}$, $K_i = 511 \text{ nM}$).

Furthermore, good biological activities can also be achieved by a combination of acceptor capacity and hydrophobic character of the catechol substituent (*e.g.*, inhibitors **9–11**). Not surprisingly, substitution of the catechol with small but strong σ acceptors also leads to potent bisubstrate inhibitors (*e.g.*, **8**).

3. Conclusions. – A new series of bisubstrate inhibitors of COMT featuring a variety of replacements of the NO_2 group as a catechol substituent have been synthesized by a highly convergent approach. Potent inhibition could, for the first time, be achieved despite the lack of NO_2 substituent on the catechol moiety by exploitation of favorable apolar interactions with a hydrophobic cleft near the enzyme surface, impressively validating the bisubstrate inhibition approach. Further optimization of the pharmacokinetic properties of the new inhibitors, *e.g.*, by modifications of the ribose and the nucleobase moieties are underway, and could in the future lead to the development of new therapeutic entities for the treatment of CNS disorders. In addition, efforts to further validate the proposed binding mode by X-ray crystal-structure analysis of enzyme–inhibitor complexes are ongoing.

Table 2. In vitro *Biological Activities* (IC_{50} [nM] (uncertainties $\pm 5\%$), K_i , and ΔG_{inh} values (310 K) [kJ mol $^{-1}$]), Hammett *Substituent Constants* σ_p [18] of *Residues R*, pK_a Values, and *Calculated Partitioning Coefficients* ($c \log P$) of *Inhibitors 1–19*. K_i Data refer to the inhibition of the SAM binding site. Partitioning coefficients were calculated using the corresponding software from ACDLabs.

Compound	σ_p	IC_{50} [nM]	K_i [nM]	$-\Delta G_{inh}$ [kJ mol $^{-1}$]	pK_a	$c \log P$
1	0.78	9	28 ± 2	44.8 ± 0.2	4.42	2.05
2	0.06	21	55 ± 5	43.1 ± 0.2	6.87	2.70
3	−0.03	23	55 ± 3	43.1 ± 0.1	7.06	3.23
4	0.23	23	55 ± 2	43.1 ± 0.1	6.89	1.38
5	−	27	60 ± 5	42.9 ± 0.2	6.15	3.12
6	0.23	28	80 ± 5	42.1 ± 0.2	6.54	2.70
7	0.29	29	41 ± 3	43.8 ± 0.2	6.18	4.14
8	0.66	29	124 ± 3	41.0 ± 0.3	5.18	2.14
9	0.54	35	69 ± 11	42.5 ± 0.4	6.22	3.78
10	0.80	39	52 ± 7	43.2 ± 0.3	5.74	2.22
11	−	42	71 ± 6	42.4 ± 0.2	6.95	1.82
12	0.23	44	169 ± 21	40.2 ± 0.3	6.65	2.58
13	−	83	88 ± 6	41.9 ± 0.2	5.46	3.80
14	0.05	97	151 ± 17	40.5 ± 0.3	6.34	0.73
15	−	213	96 ± 3	41.7 ± 0.1	5.07	2.31
16	−0.09	608	211 ± 4	39.6 ± 0.1	7.56	3.51
17	−0.15	1370	546 ± 9	37.6 ± 0.1	7.63	2.40
18	0.36	2000	511 ± 36	37.3 ± 0.2	6.25	0.31
19	0	2600	1644 ± 144	34.3 ± 0.2	7.37	1.06

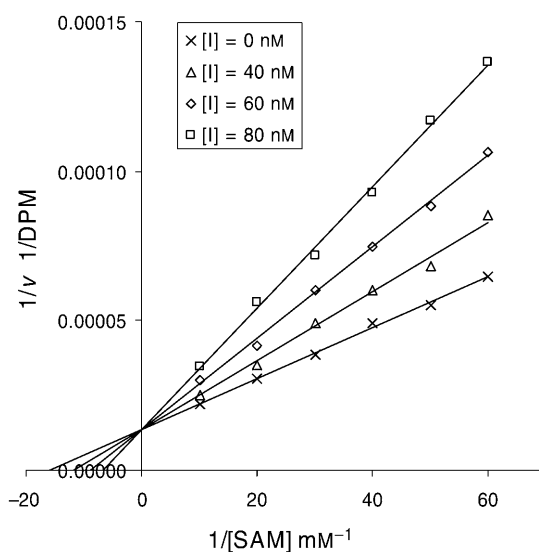


Fig. 2. Exemplary Lineweaver–Burk plot of reciprocal enzymatic activity vs. reciprocal concentration of the cofactor (SAM) for varying concentrations of inhibitor **2** at saturating benzene-1,2-diol concentrations. DPM = decays per min.

Experimental Part

General. Solvents and reagents were purchased reagent-grade and used without further purification. Solvents for extractions and chromatography were of technical grade and were distilled prior to usage. All reactions were carried out under an Ar atmosphere unless otherwise stated. THF was distilled from sodium benzophenone ketyl, and CH_2Cl_2 from CaH_2 . Anhyd. Me_2SO , DMF, and pyridine, stored over molecular sieves, were purchased from Fluka. All products were dried under high vacuum (10^{-2} Torr) before anal. characterization. The preparation of the following compounds has been reported in the literature: **38** [19], **41** [20], **57** [14], **62** [21], **69** [22], *N*-methoxy-*N*-methylcyclohexanecarboxamide [23]. The synthesis of intermediates **20** [9a,b] and **54** [9d] has been described previously. TLC: aluminum-backed sheets coated with SiO_2 60 F_{254} from Macherey-Nagel. Column chromatography (CC): Fluka SiO_2 60 (230–400 mesh, 0.040–0.063 mm). Anal. reversed-phase (RP) HPLC: Merck LiChrospher® 100 C-18 column (250 × 4 mm, 5 μm , 100 Å), eluted with a linear gradient (5–55%) of MeCN in H_2O containing 0.1% TFA during 20 min, with a flow rate of $1\text{ cm}^3\text{ min}^{-1}$, and UV detection at 254 nm. Prep. RP-HPLC: Merck LiChrosorb® C-18 column (250 × 25 mm, 7 μm), eluted with a linear gradient of MeCN in H_2O containing 0.1% TFA, with a flow rate of $10\text{ cm}^3\text{ min}^{-1}$, and UV detection at 254 nm. M.p.: Büchi B-540 apparatus; uncorrected. Optical rotations: Perkin-Elmer 241 polarimeter at $\lambda = 589$ nm. IR Spectra: Perkin-Elmer 1600-FT-IR spectrometer or a Perkin-Elmer Spectrum BX II. ^1H - and ^{13}C -NMR spectra: Varian Gemini 300, Varian Mercury 300, or Bruker AMX-500 spectrometers; chemical shifts (δ) are reported in ppm downfield of Me_4Si , using the residual signal of the solvent as an internal reference; coupling constants (J) are given in Hz. MALDI Mass spectra: IonSpec Ultima instrument with 2,5-dihydroxybenzoic acid or 2,4,5-trihydroxyacetophenone/diammonium citrate 2:1 as a matrix. Elemental analyses were performed by the Mikrolabor at the Laboratorium für Organische Chemie, ETH Zürich. The nomenclature was generated using the computer program ACD-Name (ACD/Labs).

General Procedure 1 (GP 1) for the Synthesis of Methyl 2,3-Dihydroxybenzoate Derivatives from the Corresponding 2,3-Dihydroxybenzoic Acids. To a soln. of the 2,3-dihydroxybenzoic acid derivative (1 equiv.) in MeOH, SOCl_2 (3 equiv.) was slowly added, and the mixture was heated to reflux for 12–16 h. After evaporation of the solvent under reduced pressure, the resulting grayish solid was redissolved in AcOEt and washed twice with sat. aq. K_2CO_3 soln., and sat. aq. NaCl soln., before drying (MgSO_4), and evaporated *in vacuo*. Drying under high vacuum yielded the product as a grayish solid.

General Procedure 2 (GP 2) for the Protection of Catechols as Diarylmethylketals. GP 2.1. **Protection as Diphenylmethylketal.** A suspension of the corresponding methyl 2,3-dihydroxybenzoate derivative (1 equiv.) in dichloro(diphenyl)methane (1.5 equiv.) was stirred at 160° for 40 min.

Workup Method A. After cooling to ca. 50° , MeOH (30 ml) was added to the viscous brown oil, leading to the formation of a precipitate. The precipitate was filtered, washed with MeOH (3 × 20 ml), and dried under high vacuum to yield the desired compound as a colorless solid.

Workup Method B. After cooling to 20° , AcOEt was added to the viscous mixture, and the soln. was washed with sat. aq. NaCl soln., dried (MgSO_4), and evaporated under reduced pressure. The crude product was purified by CC (SiO_2 ; hexane/ Et_2O 10:1) to yield the desired compound as a colorless solid.

GP 2.2. **Protection as Bis(4-methoxyphenyl)methylketal.** 4,4'-Dimethoxybenzophenone (1.5 equiv.) and oxalyl chloride (8 equiv.) were stirred at 60° for 30 min, then the temp. was raised to 110° to remove the excess oxalyl chloride, and the corresponding methyl 2,3-dihydroxybenzoate derivative (1 equiv.) was added to the mixture. The dark red soln. was stirred at 160° for 40 min. After cooling, AcOEt was added to the viscous mixture, and the soln. was washed with sat. aq. NaCl soln., dried (MgSO_4), and evaporated under reduced pressure. The crude product was purified by CC (SiO_2 ; hexane/ Et_2O 10:1 or hexane/AcOEt 20:1).

General Procedure 3 (GP 3) for the Hydrolysis of Catechol-carboxylates to the Corresponding Carboxylic Acids. A soln. of $\text{LiOH}\cdot\text{H}_2\text{O}$ (3 equiv.) in H_2O (5 ml) was added to a soln. of the methyl catechol-carboxylate derivative (1 equiv.) in THF (5 ml), and the biphasic mixture was heated to reflux for 4 h. After cooling to 20° , the mixture was acidified by addition of 10% aq. AcOH soln. (4 ml) or sat. aq. NH_4Cl soln. (10 ml), and partitioned between H_2O (50 ml) and AcOEt (50 ml). The aq. phase was extracted twice with AcOEt (20 ml). The combined org. fractions were washed twice with sat. aq. NaCl soln., dried (MgSO_4), and evaporated *in vacuo* to yield the desired compound as a colorless solid.

General Procedure 4 (GP 4) for the Synthesis of Functionalized Catechol-carboxylic Acids Starting from 6-Bromo-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (25). Deprotonation Method A. To a suspension of **25** (1 equiv.) in MeOH (3 ml), MeOLi (2 equiv.) was added, and the now clear soln. was stirred 20 min at 20°. Volatiles were removed *in vacuo*, and the resulting white foam was dried overnight under high vacuum (ca. 10^{-6} Torr). The residue was redissolved in dry THF (10 ml) and cooled to –78°.

Deprotonation Method B. To a soln. of **25** (1 equiv.) in dry THF (8 ml), LiH (2 equiv.) was added. The mixture was stirred 15 min at 20°, and then cooled to –78°.

Br/Li Exchange and Quenching with Electrophile. *t*-BuLi (2.5 equiv.) was added dropwise to the soln. via a syringe, and the resulting dark yellow mixture was stirred 30 min at –78°. The desired electrophile was added, and stirring was continued for 30 min at –78°. The cooling bath was removed, and the mixture was stirred another 2 h at 20°, followed by acidification with 10% aq. AcOH soln. and extraction with AcOEt (2 × 30 ml). The org. fractions were combined, dried (MgSO₄), and evaporated *in vacuo*. The residue was purified using CC (SiO₂; hexane/AcOEt/AcOH) to yield the desired compound as a yellowish to colorless solid.

General Procedure 5 (GP 5) for the Synthesis of (Diarylmethyldioxy)-catechol-carboxylates via Suzuki Reaction. Method A. To a soln. of **39** (1 equiv.) and [Pd(PPh₃)₄] (0.05 equiv.) in toluene (10 ml), a soln. of the desired arylboronic acid (4 equiv.) in EtOH (1.5 ml), and a soln. of K₂CO₃ (6 equiv.) in H₂O (1 ml) were added. This mixture was heated to reflux for 4 h. After cooling to 20°, the mixture was partitioned between AcOEt and H₂O. The org. phase was washed twice with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo*. The residue was purified by CC (SiO₂; hexane/AcOEt 20:1 → 5:1) to afford the desired compound as a colorless solid.

Method B. To a soln. of **39** (1 equiv.) in dry toluene (20 ml), [Pd(PPh₃)₄] (0.05 equiv.), bis(pinacolato)diboron (1.3 equiv.), and AcOK (1.5 equiv.) were added, and the mixture was heated to reflux for 4 h. After cooling to 20°, the mixture was filtered over Celite. [Pd(PPh₃)₄] (0.05 equiv.), the desired aryl or benzyl bromide (1.2 equiv.), and a soln. of K₂CO₃ (5 equiv.) in H₂O (3 ml) were added to the yellowish soln., and the mixture was heated to reflux for 16 h. After cooling to 20°, the mixture was partitioned between H₂O and AcOEt, and the org. phase was washed twice with sat. aq. NaCl soln. (20 ml), dried (MgSO₄), and evaporated under reduced pressure. The residue was purified by CC (SiO₂; hexane/AcOEt 20:1 → 9:1) to yield the desired compound as a colorless solid.

General Procedure 6 (GP 6) for the Amide Coupling of Catechol-carboxylic Acid Building Blocks with Primary Amine 20. To a soln. of the corresponding carboxylic acid building block (1 equiv.) in CH₂Cl₂ (5 ml), EDC·HCl (1.5 equiv.) and *N*-hydroxysuccinimide (1.3 equiv.) were added, and the mixture was stirred 1 h at 20°. After the addition of amine **20** (0.7–1 equiv.) and Et₃N (0.1 ml), stirring was continued for 16 h at 20°. The mixture was partitioned between CH₂Cl₂ and H₂O, and the org. phase was washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo*. The residue was purified by CC (SiO₂; CH₂Cl₂/MeOH 20:1) to yield the desired compound as a colorless foam.

General Procedure 7 (GP 7) for the Acid-Catalyzed Deprotection of Acetonide and Diarylmethylketal Protecting Groups. The protected precursor was treated with a mixture of TFA/H₂O 1:1 (3 ml) at 0° for 20–60 min. Volatiles were removed under high vacuum at ambient temp. The residue was redissolved in Me₂SO (2–3 ml) and purified by prep. RP-HPLC. The combined product fractions were evaporated to dryness by lyophilization.

Methyl 6-Bromo-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (39). Compound **41** (3 g, 12.87 mmol) [20] was reacted with dichloro(diphenyl)methane (3.7 ml, 4.58 g, 19.31 mmol) according to GP 2.1, Workup Method A, to afford **39** (4 g, 76%). Colorless solid. M.p. 146–148°. IR (KBr): 3079w, 2950w, 1718s, 1467s, 1355s, 1238s, 1204s, 1043s, 1013s, 944m, 867m, 780s. ¹H-NMR (300 MHz, CDCl₃): 3.94 (s, 3 H); 7.14 (d, *J* = 1.9, 1 H); 7.38–7.41 (m, 6 H); 7.55–7.59 (m, 5 H). ¹³C-NMR (75 MHz, CDCl₃): 52.4; 112.6; 113.7; 115.6; 119.1; 125.0; 126.2; 128.3; 129.4; 139.0; 147.5; 149.1; 163.7. HR-MALDI-MS: 411.0220 ([*M* + H]⁺, C₂₁H₁₆BrO₄⁺; calc. 411.0231).

6-Bromo-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (25). Compound **39** (0.5 g, 1.216 mmol) and LiOH·H₂O (204 mg, 4.86 mmol) were reacted according to GP 3 to afford **25** (437 mg, 91%). Colorless solid. M.p. 215°. IR (KBr): 3063m, 2873m (br.), 2538m, 1695s, 1598w, 1468s, 1406m, 1350m, 1287s, 1234s, 1202s, 1045s, 1023s, 949m, 858m, 784m, 698s. ¹H-NMR (300 MHz, CDCl₃): 7.19 (d, *J* = 2.1, 1 H);

7.40–7.42 (*m*, 6 H); 7.58–7.62 (*m*, 5 H). ^{13}C -NMR (75 MHz, CDCl_3): 112.7; 112.8; 116.4; 119.5; 125.4; 126.3; 128.4; 129.5; 138.9; 148.3; 149.3; 167.9. HR-MALDI-MS: 397.0078 ($[M+H]^+$, $\text{C}_{20}\text{H}_{14}\text{BrO}_4^+$; calc. 397.0075). Anal. calc. for $\text{C}_{20}\text{H}_{13}\text{BrO}_4$ (396.00): C 60.47, H 3.30; found C 60.40, H 3.35.

Methyl 5-Chloro-2,3-dihydroxybenzoate (**43**). Compound **42** (290 mg, 1.54 mmol) and SOCl_2 (550 mg, 4.61 mmol) were reacted according to *GP 1* to yield **43** (250 mg, 80%). Grayish solid. M.p. 108–110°. IR (KBr): 3453s, 3096m, 2960m, 1700s, 1673s, 1471s, 1437s, 1316s, 1233s, 1202s, 1152s, 1013m, 932m, 863m, 788m, 723m. ^1H -NMR (300 MHz, CDCl_3): 3.96 (*s*, 3 H); 5.73 (*br. s*, 1 H); 7.10 (*d*, $J=2.1$, 1 H); 7.35 (*d*, $J=2.1$); 10.84 (*s*, 1 H). ^{13}C -NMR (75 MHz, CDCl_3): 52.8; 112.7; 119.7; 120.0; 124.1; 145.7; 147.6; 169.7. HR-EI-MS: 201.9774 (M^+ , $\text{C}_8\text{H}_7\text{ClO}_4^+$; calc. 202.0033).

Methyl 6-Chloro-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (**44**). Compound **43** (330 mg, 1.63 mmol) and dichloro(diphenyl)methane (470 mg, 1.96 mmol) were reacted according to *GP 2.1, Workup Method B*, to afford **44** (310 mg, 52%). Colorless solid. M.p. 151–152°. IR (KBr): 3086w, 2947w, 1719s, 1595w, 1468s, 1445m, 1360m, 1277m, 1245s, 1202s, 1166m, 1042m, 1014m, 905w, 866w, 806m, 781m, 762m, 696m. ^1H -NMR (300 MHz, CDCl_3): 3.94 (*s*, 3 H); 7.00 (*d*, $J=2.1$, 1 H); 7.38–7.40 (*m*, 6 H); 7.56–7.59 (*m*, 4 H). ^{13}C -NMR (75 MHz, CDCl_3): 52.6; 111.1; 113.3; 119.4; 122.3; 126.3; 126.6; 128.6; 129.7; 139.4; 147.4; 149.3; 164.2. HR-MALDI-MS: 367.0731 ($[M+H]^+$, $\text{C}_{21}\text{H}_{16}\text{ClO}_4^+$; calc. 367.0737). Anal. calc. for $\text{C}_{21}\text{H}_{15}\text{ClO}_4$ (366.07): C 68.77, H 4.12; found C 68.64, H 4.29.

6-Chloro-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (**31**). Compound **44** (150 mg, 0.408 mmol) and $\text{LiOH}\cdot\text{H}_2\text{O}$ (52 mg, 1.23 mmol) were reacted according to *GP 3* to yield **31** (117 mg, 82%). Colorless solid. M.p. 206–207°. IR (KBr): 3071m, 2868m, 2616w, 1704s, 1599w, 1469s, 1450m, 1407w, 1350w, 1284m, 1267m, 1238s, 1200s, 1044m, 1022m, 949w, 908w, 859w, 799m, 761m, 698m, 642w. ^1H -NMR (300 MHz, CDCl_3): 7.05 (*d*, $J=2.1$, 1 H); 7.39–7.42 (*m*, 6 H); 7.46 (*d*, $J=2.1$, 1 H); 7.58–7.61 (*m*, 4 H). ^{13}C -NMR (75 MHz, CDCl_3): 112.3; 114.1; 119.9; 122.6; 126.5; 126.6; 128.7; 129.8; 139.2; 148.1; 149.5; 168.5. HR-MALDI-MS: 353.0576 ($[M+H]^+$, $\text{C}_{20}\text{H}_{14}\text{ClO}_4^+$; calc. 353.0581).

2,2-Diphenyl-6-(trifluoroacetyl)-1,3-benzodioxole-4-carboxylic Acid (**29**). Compound **25** (200 mg, 0.503 mmol), MeOLi (40 mg, 1 mmol), and CF_3COOEt (0.6 ml, 5.03 mmol) as the electrophile were reacted according to *GP 4, Deprotonation Method A*. The crude product was purified by CC (SiO_2 ; hexane/ AcOEt/AcOH 77:20:3) to afford **29** (79 mg, 38%). Yellowish solid. M.p. 187°. IR (KBr): 2925m, 2555m, 1692s, 1635m, 1482s, 1254s, 1213s, 1131s, 1048m, 1013m, 987m, 945m, 802m, 760s, 699s. ^1H -NMR (300 MHz, CDCl_3): 7.40–7.44 (*m*, 6 H); 7.59–7.62 (*m*, 4 H); 7.74 (*d*, $J=1.2$, 1 H); 8.35 (*m*, 1 H). ^{13}C -NMR (75 MHz, CDCl_3): 111.7; 112.4; 116.5 (*q*, $J=289$); 121.0; 124.0; 126.2; 128.5; 128.9; 129.8; 138.3; 149.6; 154.3; 167.7; 178.1 (*q*, $J=35.2$). ^{19}F -NMR (282 MHz, CDCl_3): –70.7 (*s*). HR-MALDI-MS: 415.0784 ($[M+H]^+$, $\text{C}_{22}\text{H}_{14}\text{F}_3\text{O}_5^+$; calc. 415.0793). Anal. calc. for $\text{C}_{22}\text{H}_{13}\text{F}_3\text{O}_5$ (414.07): C 63.77, H 3.16; found C 63.81, H 3.29.

6-(Cyclohexylcarbonyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (**32**). Compound **25** (1.26 g, 3.16 mmol), MeOLi (240 mg, 6.32 mmol) and *N*-methoxy-*N*-methylcyclohexanecarboxamide (650 mg, 3.8 mmol) as the electrophile were reacted according to *GP 4, Deprotonation Method A*. The crude product was purified by CC (SiO_2 ; hexane/ $\text{Et}_2\text{O}/\text{AcOH}$ 5:1:0.1), and subsequent recrystallization from CH_2Cl_2 /hexane afforded **32** (338 mg, 25%). Yellowish solid. M.p. 212–214°. IR (KBr): 3062w, 2932m, 2854m, 1693s, 1628w, 1448s, 1250s, 1205s, 1155m, 1042m, 1020m, 988m, 948m, 875w, 752m, 695s. ^1H -NMR (300 MHz, CDCl_3): 1.26–1.52 (*m*, 6 H); 1.72–1.86 (*m*, 4 H); 3.24 (*m*, 1 H); 7.38–7.45 (*m*, 6 H); 7.59–7.65 (*m*, 4 H); 7.70 (*d*, $J=1.7$, 1 H); 8.16 (*d*, $J=1.7$, 1 H). ^{13}C -NMR (75 MHz, CDCl_3): 25.9; 26.0; 29.7; 45.4; 110.9; 112.1; 119.8; 125.4; 126.3; 128.4; 129.6; 130.7; 138.8; 149.3; 152.4; 168.8; 201.2. HR-MALDI-MS: 429.1693 ($[M+H]^+$, $\text{C}_{27}\text{H}_{25}\text{O}_5^+$; calc. 429.1702).

6-[Hydroxy(pyridine-4-yl)methyl]-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (**45**). Compound **25** (1 g, 2.52 mmol), MeOLi (192 mg, 5.04 mmol), and pyridine-4-carbaldehyde (0.48 ml, 5.03 mmol) as the electrophile were reacted according to *GP 4, Deprotonation Method A*. The crude product was purified by CC (SiO_2 ; CH_2Cl_2 /MeOH 92:8 $\rightarrow$ 80:20) to yield **45** (350 mg, 33%). Yellowish solid. M.p. 213–217° (dec.). IR (KBr): 3381s (*br.*), 1565s, 1473m, 1410s, 1257s, 1205s, 1047s, 1026m, 948w, 806w, 777m, 698m, 642m. ^1H -NMR (300 MHz, $(\text{CD}_3)_2\text{SO}$): 5.63 (*s*, 1 H); 6.11 (*br. s*, 1 H); 7.04 (*s*, 1 H); 7.36 (*d*, $J=5.7$, 2 H); 7.40–7.42 (*m*, 7 H); 7.50–7.54 (*m*, 4 H); 8.46 (*d*, $J=5.7$, 1 H). ^{13}C -NMR (75 MHz, $(\text{CD}_3)_2\text{SO}$): 62.6; 108.2; 116.1; 120.9; 121.4; 125.7; 128.2; 129.1; 137.3; 139.5; 139.6; 145.3; 147.0; 149.2; 153.6; 189.8. HR-MALDI-MS: 426.1332 ($[M+H]^+$, $\text{C}_{26}\text{H}_{20}\text{NO}_5^+$; calc. 426.1341).

2,2-Diphenyl-6-[(pyridine-4-yl)carbonyl]-1,3-benzodioxole-4-carboxylic Acid (30). To a soln. of **45** (128 mg, 0.324 mmol) in Me₂CO/Me₂SO 3 : 1 (12 ml), IBX (273 mg, 0.973 mmol) was added, and the mixture was stirred for 3 h at 50°. The mixture was partitioned between H₂O and AcOEt, and the org. phase washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated under reduced pressure to yield **30** (130 mg, 95%). Yellowish solid. M.p. 256–257°. IR (KBr): 3447w (br.), 3062w, 2426w, 1709m, 1669m, 1624m, 1475m, 1440s, 1408w, 1323w, 1270s, 1211s, 1048s, 1017m, 910w, 801w, 759m, 698m, 642m. ¹H-NMR (300 MHz, (CD₃)₂SO): 7.45–7.48 (m, 7 H); 7.54–7.58 (m, 6 H); 7.73 (s, 1 H); 8.77 (d, *J* = 4.5, 2 H). ¹³C-NMR (75 MHz, (CD₃)₂SO): 111.8; 112.9; 118.9; 122.4; 125.8; 127.9; 128.6; 129.5; 129.8; 138.2; 144.2; 148.4; 149.8; 151.1; 163.9; 192.1. HR-MALDI-MS: 425.1254 ([*M* + 2 H]⁺, C₂₆H₁₉NO₅⁺; calc. 425.1263).

6-[(Dimethylamino)carbonyl]-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (37). Compound **25** (200 mg, 0.486 mmol), LiH (10 mg, 0.97 mmol), and *N,N*-dimethylcarbamoyl chloride (0.18 ml, 1.94 mmol) as the electrophile were reacted according to GP 4, *Deprotonation Method B*. The crude product was purified by CC (SiO₂; hexane/AcOEt/AcOH 67:30:3) to yield **37** (40 mg, 21%). Colorless solid. M.p. 207–208°. IR (KBr): 3417w, 2935w, 1718s, 1635m, 1607s, 1448s, 1415m, 1247s, 1207s, 1075w, 1041s, 1023s, 949m, 881m, 788m, 765m, 701s, 643m. ¹H-NMR (300 MHz, CDCl₃): 3.06 (br. s, 6 H); 7.20 (d, *J* = 1.5, 1 H); 7.37–7.41 (m, 6 H); 7.56 (d, *J* = 1.5, 1 H); 7.58–7.62 (m, 4 H). ¹³C-NMR (75 MHz, CDCl₃): 35.8; 40.0; 111.2; 112.4; 119.3; 122.7; 126.4; 128.4; 129.4; 129.5; 139.1; 148.8; 149.8; 168.5; 170.1. HR-MALDI-MS: 390.1340 ([*M* + H]⁺, C₂₃H₂₀NO₄⁺; calc. 390.1341).

Methyl 6-(4-Fluorophenyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (46). Compound **39** (100 mg, 0.243 mmol), [Pd(PPh₃)₄] (15 mg, 0.012 mmol), (4-fluorophenyl)boronic acid (135 mg, 0.972 mmol), and K₂CO₃ (202 g, 1.46 mmol) were reacted according to GP 5, *Method A*, to afford **46** (80 mg, 78%). Colorless solid. M.p. 125–127°. IR (KBr): 3061m, 2950m, 1723s, 1634w, 1603m, 1517m, 1472s, 1364m, 1257s, 1215s, 1053s, 947m, 833s, 780m, 698s, 640m. ¹H-NMR (300 MHz, CDCl₃): 3.97 (s, 3 H); 7.10 (tt, *J* = 8.7, 2.0, 2 H); 7.20 (d, *J* = 2.0, 1 H); 7.39–7.42 (m, 6 H); 7.45–7.50 (m, 2 H); 7.59 (d, *J* = 2.0, 1 H); 7.62–7.65 (m, 4 H). ¹³C-NMR (75 MHz, CDCl₃): 52.2; 111.1; 112.7; 115.6 (d, *J* = 21.2); 118.4; 121.1; 126.3; 128.2; 128.3; 129.2; 134.0; 136.0; 139.4; 147.4; 148.8; 162.2 (d, *J* = 244.7); 164.8. ¹⁹F-NMR (282 MHz, CDCl₃): –115.9 (tt, *J* = 9.6, 5.4). HR-MALDI-MS: 426.1258 (*M*⁺, C₂₇H₁₉FO₄⁺; calc. 426.1267).

6-(4-Fluorophenyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (21). Compound **46** (250 mg, 0.586 mmol) and LiOH·H₂O (74 mg, 1.76 mmol) were reacted according to GP 3 to yield **21** (214 mg, 89%). Colorless solid. M.p. 215–217°. IR (KBr): 3032m, 2625w, 1687s, 1635w, 1604m, 1519m, 1473s, 1422m, 1355w, 1281s, 1219s, 1179m, 1055s, 1022s, 948m, 918w, 832s, 784m, 756m, 699s, 641m. ¹H-NMR (300 MHz, CDCl₃): 7.10 (t, *J* = 8.7, 2 H); 7.26 (d, *J* = 1.0, 1 H); 7.39–7.43 (m, 6 H); 7.46–7.51 (m, 2 H); 7.63–7.66 (m, 5 H). ¹³C-NMR (75 MHz, CDCl₃): 111.7; 112.0; 115.7 (d, *J* = 21.2); 118.9; 121.6; 126.3; 128.3; 128.4; 129.4; 134.3; 135.9 (d, *J* = 3.1); 139.3; 148.1; 149.0; 162.3 (d, *J* = 245); 169.0. ¹⁹F-NMR (282 MHz, CDCl₃): –115.7 (tt, *J* = 8.5, 5.4). HR-MALDI-MS: 435.1000 ([*M* + Na]⁺, C₂₇H₁₉FNaO₄⁺; calc. 435.1009).

Methyl 6-(4-Methylphenyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (47). Compound **39** (500 mg, 1.215 mmol), [Pd(PPh₃)₄] (70 mg, 0.06 mmol), (4-methylphenyl)boronic acid (330 mg, 2.43 mmol), and K₂CO₃ (1 g, 7.29 mmol) were reacted according to GP 5, *Method A*, to yield **46** (403 mg, 79%). Colorless solid. M.p. 159–160°. IR (KBr): 3034w, 2941w, 1719s, 1470s, 1450s, 1429m, 1363w, 1255s, 1209s, 1161m, 1053s, 1028s, 944w, 817m, 775m, 702s, 640m. ¹H-NMR (300 MHz, CDCl₃): 2.38 (s, 3 H); 3.97 (s, 3 H); 7.22 (d, *J* = 7.8, 2 H); 7.26 (d, *J* = 1.8, 1 H); 7.38–7.44 (m, 8 H); 7.62–7.66 (m, 5 H). ¹³C-NMR (75 MHz, CDCl₃): 21.2; 52.2; 111.1; 112.7; 118.2; 121.0; 126.3; 126.6; 128.2; 129.2; 129.4; 135.0; 136.9; 137.0; 139.6; 147.3; 148.7; 164.9. HR-MALDI-MS: 445.1406 ([*M* + Na]⁺, C₂₈H₂₂NaO₄⁺; calc. 445.1416).

6-(4-Methylphenyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (22). Compound **46** (280 mg, 0.662 mmol) and LiOH·H₂O (84 mg, 2 mmol) were reacted according to GP 3 to afford **22** (251 mg, 93%). Colorless solid. M.p. 223–224°. IR (KBr): 3030m, 2624m, 1684s, 1634m, 1602w, 1473s, 1421m, 1355w, 1282s, 1213s, 1055s, 1023s, 947m, 918w, 871w, 814m, 784m, 758m, 699s, 640m. ¹H-NMR (300 MHz, CDCl₃): 2.39 (s, 3 H); 7.23 (d, *J* = 7.8, 2 H); 7.31 (d, *J* = 1.8, 1 H); 7.39–7.45 (m, 8 H); 7.64–7.67 (m, 4 H); 7.71 (d, *J* = 1.8). ¹³C-NMR (75 MHz, CDCl₃): 21.1; 111.8; 112.0; 118.7; 121.5; 126.4; 126.7; 128.4; 129.4; 129.5; 135.3; 136.9; 137.2; 139.5; 148.0; 149.0; 169.4. HR-MALDI-MS: 431.1259 ([*M* + Na]⁺, C₂₇H₂₀NaO₄⁺; calc. 431.1259).

Methyl 6-Cyano-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (55). To a soln. of **39** (800 mg, 1.95 mmol) in benzene/DMF 3:1 (20 ml), [Pd(PPh₃)₄] (225 mg, 0.195 mmol), KCN (127 mg, 1.95 mmol), and 18-crown-6 (415 mg, 1.56 mmol) were added, and the mixture was stirred for 16 h at 100°. The mixture was partitioned between AcOEt (50 ml) and H₂O (50 ml), and the aq. phase was extracted with AcOEt (2×20 ml). The combined org. phases were washed with H₂O and sat. aq. NaCl soln., dried (MgSO₄), and evaporated under reduced pressure. CC (SiO₂; hexane/AcOEt 20:1 → 9:1) afforded **55** (530 mg, 76%). Colorless solid. M.p. 141°. IR (KBr): 3051w, 2951w, 2228m, 1713s, 1470s, 1375m, 1264s, 1225s, 1045s, 917m, 786s. ¹H-NMR (300 MHz, CDCl₃): 3.97 (s, 3 H); 7.20 (d, *J*=1.9, 1 H); 7.39–7.43 (m, 6 H); 7.55–7.58 (m, 4 H); 7.82 (d, *J*=1.9, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 52.7; 104.8; 113.4; 113.9; 118.0; 120.4; 126.2; 128.4; 129.2; 129.7; 138.4; 148.9; 151.5; 163.1. HR-MALDI-MS: 358.1071 ([*M*+H]⁺, C₂₂H₁₆NO₄⁺; calc. 358.1079).

6-Cyano-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (27). A soln. of LiOH·H₂O (21 mg, 0.5 mmol) in H₂O (3 ml) was added to a soln. of **55** (60 mg, 0.168 mmol) in MeOH/CH₂Cl₂ (6:1, 3.5 ml), and the mixture was vigorously stirred for 16 h at 20°. Sat. aq. NH₄Cl soln. (10 ml) was added, and the mixture was partitioned between H₂O (40 ml) and AcOEt (40 ml). The aq. phase was extracted with AcOEt (3×20 ml), and the combined org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo* to afford **27** (53 mg, 92%). Colorless solid. M.p. 221°. IR (KBr): 2925m, 2229m, 1696s, 1449s, 1267s, 1213s, 1048s, 949m, 922m, 756m, 694s, 641m, 617w. ¹H-NMR (300 MHz, CDCl₃): 7.25 (d, *J*=1.7, 1 H); 7.41 (m, 6 H); 7.58 (m, 4 H); 7.87 (d, *J*=1.7, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 105.0; 112.6; 114.4; 117.8; 120.7; 126.1; 128.5; 129.6; 129.8; 138.2; 149.0; 152.1; 167.1. HR-MALDI-MS: 344.0910 ([*M*+H]⁺, C₂₁H₁₄NO₄⁺; calc. 344.0923).

Methyl 6-Cyano-2,2-bis(4-methoxyphenyl)-1,3-benzodioxole-4-carboxylate (56). A soln. of **54** (600 mg, 1.27 mmol), [Pd(PPh₃)₄] (150 mg, 0.127 mmol), KCN (170 mg, 2.55 mmol), and 18-crown-6 (530 mg, 2.0 mmol) in toluene/DMF (3:1, 20 ml) was stirred at 100° for 16 h. After cooling to 20°, the mixture was partitioned between H₂O (50 ml) and AcOEt (50 ml), and the aq. phase was extracted with AcOEt (2×50 ml). The pooled org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo*. CC (SiO₂; hexane/AcOEt 20:1 → 9:1) afforded **56** (265 mg, 48%). Colorless solid. M.p. 159–160°. IR (KBr): 3414w, 2946w, 2836w, 2222m, 1719s, 1611m, 1581w, 1513m, 1464s, 1417w, 1375w, 1309w, 1282m, 1254s, 1207m, 1171s, 1032m, 1004m, 953w, 939w, 836m, 817m, 782m, 617w. ¹H-NMR (300 MHz, CDCl₃): 3.81 (s, 6 H); 3.95 (s, 3 H); 6.90 (d, *J*=8.9, 4 H); 7.17 (d, *J*=1.7, 1 H); 7.45 (d, *J*=8.9, 4 H); 7.80 (d, *J*=1.7, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 52.5; 55.3; 104.6; 113.3; 113.7; 113.8; 118.1; 120.9; 128.0; 129.1; 130.6; 149.1; 151.8; 160.7; 163.3. HR-MALDI-MS: 418.1290 ([*M*+H]⁺, C₂₄H₂₀NO₆⁺; calc. 418.1285). Anal. calc. for C₂₄H₁₉NO₆ (417.12): C 69.09, H 4.59; found C 69.10, H 4.77.

6-Cyano-2,2-bis(4-methoxyphenyl)-1,3-benzodioxole-4-carboxylic Acid (53). A soln. of LiOH·H₂O (60 mg, 1.43 mmol) in H₂O (5 ml) was added to a soln. of **56** (200 mg, 0.479 mmol) in MeOH/CH₂Cl₂ 6:1 (7 ml), and the mixture was vigorously stirred for 16 h at 20°. Sat. aq. NH₄Cl soln. (15 ml) was added, and the mixture was partitioned between H₂O (40 ml) and AcOEt (40 ml). The aq. phase was extracted with AcOEt (3×20 ml), and the combined org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo* to afford **53** (179 mg, 93%). Colorless solid. M.p. 100–102°. IR (KBr): 3446w (br.), 2934w, 2837w, 2228m, 1685w, 1610s, 1513m, 1466s, 1414m, 1308m, 1254s, 1210m, 1175s, 1032m, 1004m, 931w, 832m, 617w. ¹H-NMR (300 MHz, (CD₃)₂SO): 3.74 (br. s, 6 H); 6.97 (br. s, 4 H); 7.38 (m, 5 H); 7.54 (br. s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 55.3; 103.2; 113.8; 118.6; 119.0; 127.9; 129.7; 130.0; 130.5; 131.9; 148.1; 150.4; 160.2; 162.5. HR-MALDI-MS: 404.1134 ([*M*+H]⁺, C₂₃H₁₈NO₆⁺; calc. 404.1129).

Methyl 6-[(E)-3-(Dimethylamino)-3-oxoprop-1-enyl]-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (52). A soln. of **39** (130 mg, 0.32 mmol), *N,N*-dimethylacrylamide (47 mg, 0.47 mmol), P(OPh)₃ (980 mg, 3.16 mmol), Bu₄NBr (20 mg, 0.06 mmol), Na₂CO₃ (40 mg, 0.38 mmol), and Pd(OAc)₂ (10 mg, 0.03 mmol) in DMA (10 ml) was stirred at 140° for 72 h. After cooling to 20°, the mixture was partitioned between AcOEt (50 ml) and H₂O (50 ml). The org. phase was washed with sat. aq. NaCl soln. (2×30 ml), dried (MgSO₄), and evaporated *in vacuo*. CC (SiO₂; hexane/AcOEt 5:1 → 3:2) afforded **52** (60 mg, 44%). Colorless, viscous oil. IR (KBr): 3059w, 2927w, 1721s, 1652s, 1607m, 1481m, 1447s, 1396m, 1300m, 1256s, 1203s, 1046m, 1017m, 970w, 779w, 699m, 641w. ¹H-NMR (300 MHz, CDCl₃): 3.11 (br. s, 6 H); 3.96 (s, 3 H); 6.75 (d, *J*=15.6, 1 H); 7.20 (d, *J*=1.8, 1 H); 7.36–7.41 (m, 6 H); 7.55–7.61 (m, 6

H). ^{13}C -NMR (75 MHz, CDCl_3): 36.2; 37.7; 52.5; 110.5; 113.0; 116.8; 119.1; 124.1; 126.6; 128.6; 129.6; 129.7; 139.6; 141.5; 149.2; 149.5; 164.9; 166.7. HR-MALDI-MS: 452.1473 ($[M+\text{Na}]^+$, $\text{C}_{26}\text{H}_{23}\text{NNaO}_5^+$; calc. 452.1474).

6-[(E)-3-(Dimethylamino)-3-oxoprop-1-enyl]-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (**33**). Compound **52** (170 mg, 0.4 mmol) and $\text{LiOH}\cdot\text{H}_2\text{O}$ (50 mg, 1.19 mmol) were reacted according to *GP 3* to afford **33** (126 mg, 77%). Colorless solid. M.p. 230–231°. IR (KBr): 3431w, 3058w, 1710s, 1653m, 1596m, 1467m, 1445m, 1404w, 1249s, 1212m, 1176m, 1050m, 1027w, 975w, 843w, 784w, 697w, 641w. ^1H -NMR (300 MHz, CDCl_3): 3.07 (s, 3 H); 3.16 (s, 3 H); 6.75 (d, $J=15.3$, 1 H); 7.24 (d, $J=1.5$, 1 H); 7.35–7.40 (m, 6 H); 7.59–7.62 (m, 5 H); 7.67 (d, $J=1.5$, 1 H). ^{13}C -NMR (75 MHz, CDCl_3): 36.1; 37.5; 110.6; 112.3; 116.4; 119.2; 124.6; 126.3; 128.4; 129.4; 129.5; 139.2; 141.5; 149.1; 149.8; 166.8; 167.8. HR-MALDI-MS: 416.1498 ($[M+\text{H}]^+$, $\text{C}_{25}\text{H}_{22}\text{NO}_5^+$; calc. 416.1498).

Methyl 6-[(4-Methylphenyl)methyl]-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (**51**). Compound **39** (200 mg, 1.486 mmol), $[\text{Pd}(\text{PPh}_3)_4]$ (57 mg, 0.049 mmol), bis(pinacolato)diboron (160 mg, 0.632 mmol), and AcOK (72 mg, 0.73 mmol), then $[\text{Pd}(\text{PPh}_3)_4]$ (57 mg, 0.049 mmol), 1-(bromomethyl)-4-methylbenzene (117 mg, 0.63 mmol), and K_2CO_3 (336 mg, 2.43 mmol) were reacted according to *GP 5*, *Method B*, to yield **51** (197 mg, 80%). Colorless, very viscous oil. IR (neat): 3030w, 2950w, 1722s, 1636w, 1603w, 1477s, 1449s, 1381w, 1251s, 1202s, 1047s, 1019m, 948w, 918w, 829w, 782m, 763m, 699m, 642m. ^1H -NMR (300 MHz, CDCl_3): 2.32 (s, 3 H); 3.85 (s, 2 H); 3.93 (s, 3 H); 6.83 (d, $J=1.8$, 1 H); 7.06 (d, $J=8.6$, 2 H); 7.10 (d, $J=8.6$, 1 H); 7.29 (d, $J=1.8$, 1 H); 7.35–7.38 (m, 6 H); 7.57–7.60 (m, 4 H). ^{13}C -NMR (75 MHz, CDCl_3): 21.0; 41.1; 52.0; 112.2; 113.1; 117.9; 122.3; 126.3; 128.2; 128.7; 129.1; 129.2; 134.9; 135.8; 137.5; 139.8; 146.6; 148.5; 165.2. HR-MALDI-MS: 459.1573 ($[M+\text{Na}]^+$, $\text{C}_{29}\text{H}_{24}\text{NaO}_4^+$; calc. 459.1572).

6-[(4-Methylphenyl)methyl]-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (**35**). Compound **51** (300 mg, 0.69 mmol) and $\text{LiOH}\cdot\text{H}_2\text{O}$ (87 mg, 2.06 mmol) were reacted according to *GP 3* to afford **35** (287 mg, 99%). Colorless solid. M.p. 211–213°. IR (KBr): 3434w (br.), 2904w, 2571w, 1685m, 1638w, 1604w, 1479m, 1464m, 1304m, 1252m, 1209s, 1050m, 1027m, 947w, 921w, 828w, 784m, 750w, 797m, 641w. ^1H -NMR (300 MHz, CDCl_3): 2.32 (s, 3 H); 3.86 (s, 2 H); 6.88 (d, $J=1.2$, 1 H); 7.07 (d, $J=8.4$, 2 H); 7.11 (d, $J=8.4$, 2 H); 7.34–7.40 (m, 7 H); 7.58–7.62 (m, 4 H). ^{13}C -NMR (75 MHz, CDCl_3): 21.0; 41.1; 111.3; 113.9; 118.4; 122.7; 126.4; 128.3; 128.7; 129.3; 135.2; 135.9; 137.4; 139.6; 147.3; 148.6; 169.7. HR-MALDI-MS: 445.1415 ($[M+\text{Na}]^+$, $\text{C}_{28}\text{H}_{22}\text{NaO}_4^+$; calc. 445.1416).

Methyl 2,2-Diphenyl-6-(1,3-thiazol-2-yl)-1,3-benzodioxole-4-carboxylate (**50**). Compound **39** (250 mg, 0.608 mmol), $[\text{Pd}(\text{PPh}_3)_4]$ (70 mg, 0.06 mmol), bis(pinacolato)diboron (200 mg, 0.79 mmol), and AcOK (90 mg, 0.912 mmol), then $[\text{Pd}(\text{PPh}_3)_4]$ (70 mg, 0.06 mmol), 2-bromothiazole (110 mg, 0.67 mmol), and K_2CO_3 (420 mg, 3.04 mmol) were reacted according to *GP 5*, *Method B*, to afford **50** (166 mg, 66%). Colorless solid. M.p. 154–155°. IR (KBr): 3054w, 2947w, 1712s, 1627w, 1497w, 1468s, 1447s, 1359m, 1321w, 1286m, 1254s, 1212s, 1047s, 1017s, 944w, 929w, 883w, 801m, 781m, 760m, 699s, 641m. ^1H -NMR (300 MHz, CDCl_3): 3.97 (s, 3 H); 7.28 (d, $J=3.2$, 1 H); 7.37–7.42 (m, 6 H); 7.60–7.63 (m, 4 H); 7.71 (d, $J=2.3$, 1 H); 7.81 (d, $J=3.2$, 1 H); 8.01 (d, $J=2.3$, 1 H). ^{13}C -NMR (75 MHz, CDCl_3): 52.5; 110.4; 113.1; 118.9; 119.4; 122.2; 126.6; 127.8; 128.6; 129.7; 139.5; 143.5; 149.4; 149.9; 164.6; 167.4. HR-MALDI-MS: 416.0947 ($[M+\text{H}]^+$, $\text{C}_{24}\text{H}_{18}\text{NO}_4\text{S}^+$; calc. 416.0957).

2,2-Diphenyl-6-(1,3-thiazol-2-yl)-1,3-benzodioxole-4-carboxylic Acid (**24**). Compound **50** (300 mg, 0.722 mmol) and $\text{LiOH}\cdot\text{H}_2\text{O}$ (91 mg, 2.17 mmol) were reacted according to *GP 3* to afford **24** (290 mg, 96%). Colorless solid. M.p. 226–227°. IR (KBr): 3122w, 2924w, 1702m, 1629w, 1477s, 1446s, 1319w, 1266s, 1235m, 1213s, 1133s, 1048m, 1018m, 948w, 909w, 851w, 792m, 762w, 720w, 699m, 641w. ^1H -NMR (300 MHz, $(\text{CD}_3)_2\text{SO}$): 7.46–7.50 (m, 6 H); 7.34–7.57 (m, 4 H); 7.76 (d, $J=3.0$, 1 H); 7.78 (d, $J=1.8$, 1 H); 7.89 (d, $J=3.0$, 1 H); 7.92 (d, $J=1.8$, 1 H). ^{13}C -NMR (75 MHz, $(\text{CD}_3)_2\text{SO}$): 109.7; 113.8; 118.3; 120.4; 121.3; 125.9; 127.3; 128.7; 129.7; 138.7; 143.7; 148.4; 148.5; 164.4; 165.7. HR-MALDI-MS: 402.0794 ($[M+\text{H}]^+$, $\text{C}_{23}\text{H}_{16}\text{NO}_4\text{S}^+$; calc. 402.0800).

Methyl 6-(1,3-Benzothiazol-2-yl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (**49**). Compound **39** (600 mg, 1.459 mmol), $[\text{Pd}(\text{PPh}_3)_4]$ (85 mg, 0.073 mmol), bis(pinacolato)diboron (480 mg, 1.9 mmol), and AcOK (216 mg, 2.2 mmol), then $[\text{Pd}(\text{PPh}_3)_4]$ (85 mg, 0.073 mmol), 2-bromo-1,3-benzothiazole (375 mg, 1.75 mmol), and K_2CO_3 (1 g, 7.3 mmol) were reacted according to *GP 5*, *Method B*, to afford **49** (271 mg, 40%). Colorless solid. M.p. 184–185°. IR (KBr): 3055w, 2950w, 1718s, 1635w, 1502w, 1446s,

1368*m*, 1297*m*, 1239*s*, 1212*s*, 1163*m*, 1047*s*, 1015*s*, 945*m*, 921*m*, 874*m*, 795*m*, 776*s*, 759*s*, 723*w*, 701*s*, 640*m*. ¹H-NMR (300 MHz, CDCl₃): 4.00 (s, 3 H); 7.38–7.51 (*m*, 8 H); 7.62–7.64 (*m*, 4 H); 7.86 (*d*, *J* = 1.7, 1 H); 7.88 (*d*, *J* = 9.3, 1 H); 8.04 (*d*, *J* = 9.3, 1 H); 8.13 (*d*, *J* = 1.7, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 52.4; 110.6; 112.8; 119.3; 121.5; 122.9; 123.2; 125.1; 126.3; 127.5; 128.3; 129.4; 134.8; 139.1; 149.1; 150.2; 153.7; 164.1; 166.5. HR-MALDI-MS: 466.1113 ([*M* + H]⁺, C₂₈H₂₀NO₄S⁺; calc. 466.1113). Anal. calc. for C₂₈H₁₉NO₄S (465.10): C 72.24, H 4.11, N 3.01; found C 72.15, H 4.03, N 3.19.

6-(1,3-Benzothiazol-2-yl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (**26**). Compound **49** (210 mg, 0.451 mmol) and LiOH·H₂O (57 mg, 1.35 mmol) were reacted according to *GP* 3 to afford **26** (201 mg, 99%). Colorless solid. M.p. 227°. IR (KBr): 3437*w*, 2965*w*, 2610*w*, 1738*m*, 1688*s*, 1634*w*, 1460*s*, 1427*m*, 1360*w*, 1256*s*, 1237*s*, 1211*s*, 1047*s*, 1048*m*, 1015*m*, 999*m*, 928*w*, 878*w*, 788*m*, 760*m*, 726*w*, 699*m*, 641*w*. ¹H-NMR (300 MHz, CDCl₃): 7.36–7.44 (*m*, 7 H); 7.46–7.53 (*m*, 1 H); 7.53–7.67 (*m*, 4 H); 7.88 (*d*, *J* = 1.8, 1 H); 7.89 (*d*, *J* = 8.7, 1 H); 8.15 (*d*, *J* = 8.7, 1 H); 8.28 (*d*, *J* = 1.8, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 111.4; 112.2; 119.7; 121.5; 123.1; 123.7; 125.2; 126.3; 126.4; 127.5; 128.3; 129.5; 134.6; 138.9; 149.3; 150.9; 153.6; 166.6; 167.8. HR-MALDI-MS: 452.0955 ([*M* + H]⁺, C₂₇H₁₈NO₄S⁺; calc. 452.0957).

Methyl 2,2-Diphenyl-6-(pyridin-4-yl)-1,3-benzodioxole-4-carboxylate (**48**). Compound **39** (400 mg, 0.973 mmol), [Pd(PPh₃)₄] (100 mg, 0.087 mmol), bis(pinacolato)diboron (320 mg, 1.26 mmol), and AcOK (150 mg, 1.5 mmol), then [Pd(PPh₃)₄] (112 mg, 0.097 mmol), 2-bromopyridine hydrochloride (265 mg, 1.36 mmol), and K₂CO₃ (680 mg, 4.9 mmol) were reacted according to *GP* 5, *Method B*, to yield **48** (264 mg, 67%). Colorless solid. M.p. 151–152°. IR (KBr): 3030*w*, 2954*w*, 1718*s*, 1635*w*, 1594*m*, 1475*s*, 1439*s*, 1418*m*, 1325*m*, 1291*m*, 1269*s*, 1225*s*, 1180*m*, 1054*s*, 1038*m*, 1018*m*, 947*w*, 927*w*, 886*w*, 815*m*, 782*m*, 753*w*, 703*m*, 693*m*, 641*m*. ¹H-NMR (300 MHz, CDCl₃): 3.98 (s, 3 H); 7.31 (*d*, *J* = 1.8, 1 H); 7.39–7.41 (*m*, 6 H); 7.48 (*dd*, *J* = 4.7, 1.8, 1 H); 7.61–7.64 (*m*, 4 H); 7.75 (*d*, *J* = 1.7, 1 H); 8.63 (*dd*, *J* = 4.7, 1.8, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 52.6; 110.9; 113.4; 119.4; 121.6; 122.3; 126.6; 128.6; 129.8; 131.7; 139.5; 148.0; 149.4; 149.7; 149.8; 164.9. HR-MALDI-MS: 410.1383 ([*M* + H]⁺, C₂₆H₂₀NO₄⁺; calc. 410.1392).

2,2-Diphenyl-6-(pyridin-4-yl)-1,3-benzodioxole-4-carboxylic Acid (**23**). Compound **48** (250 mg, 0.61 mmol) and LiOH·H₂O (80 mg, 1.84 mmol) were reacted according to *GP* 3 to afford **23** (220 mg, 92%). Grayish solid. M.p. 266° (dec.). IR (KBr): 3446*w* (br.), 3061*w*, 2447*w* (br.), 1696*m*, 1632*w*, 1603*m*, 1469*s*, 1440*m*, 1373*w*, 1326*w*, 1273*s*, 1213*s*, 1182*m*, 1054*s*, 1015*m*, 949*w*, 921*w*, 906*w*, 832*m*, 789*w*, 777*w*, 765*m*, 701*m*, 640*w*. ¹H-NMR (300 MHz, (CD₃)₂SO): 7.46–7.48 (*m*, 6 H); 7.52–7.58 (*m*, 4 H); 7.67 (*d*, *J* = 4.4, 2 H); 7.73 (*m*, 2 H); 8.59 (*d*, *J* = 4.4, 2 H). ¹³C-NMR (75 MHz, (CD₃)₂SO): 110.7; 113.9; 117.9; 120.8; 121.6; 125.8; 128.6; 129.6; 131.1; 138.7; 145.6; 147.8; 148.5; 150.0; 164.6. HR-MALDI-MS: 396.1234 ([*M* + H]⁺, C₂₅H₁₈NO₄⁺; calc. 396.1236).

Methyl 2,3-Dimethoxy-5-[(4-methylphenyl)sulfonyl]benzoate (**58**). To a soln. of **57** (2.25 g, 7.0 mmol) in DMF (20 ml), sodium *p*-toluenesulfonate hydrate (2.21 g, 11.26 mmol) and CuI (2.22 g, 11.6 mmol) were added, and the light green soln. was stirred at 110° for 14 h. The mixture was partitioned between H₂O (80 ml) and AcOEt (50 ml), and the aq. phase was extracted with AcOEt (2 × 40 ml). The combined org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated under reduced pressure. CC (SiO₂; hexane/AcOEt 8:2 → 3:2) afforded **58** (1.41 g, 58%). Colorless solid. M.p. 114°. IR (KBr): 3081*w*, 2945*w*, 1731*s*, 1594*w*, 1482*m*, 1426*w*, 1317*s*, 1273*s*, 1146*s*, 1104*m*, 994*w*, 872*w*, 811*w*, 713*w*, 665*m*, 585*m*, 535*w*. ¹H-NMR (300 MHz, CDCl₃): 2.40 (s, 3 H); 3.90 (s, 3 H); 3.92 (s, 3 H); 3.92 (s, 3 H); 7.31 (*d*, *J* = 8.1, 2 H); 7.54 (*d*, *J* = 2.1, 1 H); 7.82 (*d*, *J* = 8.1, 2 H); 7.87 (*d*, *J* = 2.1, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 21.7; 52.6; 56.5; 61.7; 113.4; 122.0; 126.4; 127.5; 129.9; 136.8; 138.2; 144.2; 152.7; 153.8; 164.9. HR-MALDI-MS: 373.0714 ([*M* + Na]⁺, C₁₇H₁₈NaO₆S⁺; calc. 373.0722). Anal. calc. for C₁₇H₁₈O₆S (350.08): C 58.27, H 5.18; found C 58.38, H 5.36.

2,3-Dihydroxy-5-[(4-methylphenyl)sulfonyl]benzoic Acid (**59**). To a soln. of **58** (1.3 g, 4.036 mmol) in AcOH (5 ml), HBr (33% in AcOH, 15 ml) and Bu₄NBr (1.1 g, 3.4 mmol) were added, and the mixture was stirred at 140° for 20 h. H₂O (20 ml) was added, and the mixture was extracted with AcOEt (3 × 30 ml). The combined org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo*. CC (SiO₂; hexane/AcOEt/AcOH 3:2:0.2 → 1:3:0.2) afforded **59** (560 mg, 45%). Orange solid. M.p. 223–225° (dec.). IR (KBr): 3165*m* (br.), 1692*m*, 1597*w*, 1467*m*, 1403*w*, 1282*s*, 1214*w*, 1141*s*, 1094*m*, 967*w*, 893*w*, 799*w*, 743*w*, 709*m*, 665*m*. ¹H-NMR (300 MHz, (CD₃)₂SO): 2.35 (s, 3

H); 4.42 (br. s, 1 H); 7.28 (*d*, *J* = 2.1, 1 H); 7.39 (*d*, *J* = 8.1, 2 H); 7.75 (*m*, 3 H); 9.86 (br. s, 1 H). ¹³C-NMR (75 MHz, (CD₃)₂SO): 21.0; 114.7; 115.6; 120.0; 126.8; 128.7; 130.0; 138.9; 143.6; 147.1; 156.4; 170.5. HR-MALDI-MS: 331.0246 ([*M* + Na]⁺, C₁₄H₁₂NaO₆S⁺; calc. 331.0252).

Methyl 2,3-Dihydroxy-5-[(4-methylphenyl)sulfonyl]benzoate (60). Compound **59** (410 mg, 1.33 mmol) and SOCl₂ (790 mg, 6.65 mmol) were reacted according to *GP 1* to afford **60** (321 mg, 75%). Colorless solid. M.p. 168–170° (dec.). IR (KBr): 3362*m* (br.), 2956*w*, 1695*s*, 1596*m*, 1494*m*, 1447*m*, 1284*s*, 1243*s*, 1146*s*, 1094*s*, 1018*m*, 937*w*, 883*m*, 810*m*, 736*w*, 700*w*, 666*s*. ¹H-NMR (300 MHz, CDCl₃): 2.39 (*s*, 3 H); 4.00 (*s*, 3 H); 5.91 (br. s, 1 H); 7.29 (*d*, *J* = 7.8, 2 H); 7.55 (*d*, *J* = 1.2, 1 H); 7.83 (*d*, *J* = 7.8, 2 H); 8.05 (*d*, *J* = 1.2, 1 H); 11.43 (br. s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 21.7; 53.1; 112.2; 117.8; 120.9; 127.4; 129.8; 132.8; 138.5; 144.1; 145.6; 152.5; 169.6. HR-MALDI-MS: 345.0402 ([*M* + Na]⁺, C₁₅H₁₄NaO₆S⁺; calc. 345.0409).

Methyl 2,2-Bis(4-methoxyphenyl)-6-[(4-methylphenyl)sulfonyl]-1,3-benzodioxole-4-carboxylate (61). Compound **60** (200 mg, 0.62 mmol), 4,4'-dimethoxybenzophenone (225 mg, 0.93 mmol), and oxalyl chloride (944 mg, 7.44 mmol) were reacted according to *GP 2.2*. CC (SiO₂; hexane/AcOEt 20:1 → 9:1) afforded **61** (260 mg, 77%). Colorless solid. M.p. 79–82°. IR (KBr): 2951*w*, 2832*w*, 1727*m*, 1610*m*, 1512*m*, 1464*s*, 1320*m*, 1285*m*, 1248*s*, 1210*m*, 1175*s*, 1150*s*, 1090*m*, 1042*m*, 1004*w*, 885*w*, 832*w*, 739*w*, 663*w*, 616*w*. ¹H-NMR (300 MHz, CDCl₃): 2.39 (*s*, 3 H); 3.80 (*s*, 6 H); 3.93 (*s*, 3 H); 6.88 (*dt*, *J* = 8.7, 2.5, 4 H); 7.29 (*d*, *J* = 8.1, 2 H); 7.43 (*m*, 5 H); 7.81 (*d*, *J* = 8.7, 2 H); 8.09 (*d*, *J* = 1.8, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 21.7; 52.5; 55.4; 110.1; 112.5; 113.6; 120.9; 124.0; 127.5; 127.9; 129.9; 130.7; 134.9; 138.4; 144.1; 149.2; 151.9; 160.4; 163.4. HR-MALDI-MS: 547.1428 ([*M* + H]⁺, C₃₀H₂₇O₈S⁺; calc. 547.1427). Anal. calc. for C₃₀H₂₆O₈S (546.13): C 65.65, H 4.87; found C 65.92, H 4.79.

2,2-Bis(4-methoxyphenyl)-6-[(4-methylphenyl)sulfonyl]-1,3-benzodioxole-4-carboxylic Acid (34). Compound **61** (205 mg, 0.375 mmol) and LiOH·H₂O (79 mg, 1.88 mmol) were reacted according to *GP 3* to afford **34** (197 mg, 99%). Colorless solid. M.p. 109–110°. IR (KBr): 3423*w* (br.), 2961*w*, 2837*w*, 1649*w*, 1611*m*, 1514*m*, 1443*m*, 1313*s*, 1254*s*, 1175*s*, 1119*m*, 1030*s*, 931*w*, 903*w*, 832*m*, 675*w*. ¹H-NMR (300 MHz, CD₃OD): 2.32 (*s*, 3 H); 3.73 (*s*, 6 H); 6.85 (*d*, *J* = 8.7, 4 H); 7.27 (*d*, *J* = 8.1, 2 H); 7.38 (*d*, *J* = 8.7, 4 H); 7.43 (*d*, *J* = 1.8, 1 H); 7.74 (*d*, *J* = 8.1, 2 H); 8.03 (*d*, *J* = 1.8, 1 H). ¹³C-NMR (75 MHz, CD₃OD): 21.5; 55.8; 110.1; 114.0; 114.5; 125.4; 128.1; 128.4; 129.1; 130.8; 131.0; 132.0; 133.2; 135.9; 139.1; 145.7; 150.5; 162.0. HR-MALDI-MS: 533.1274 ([*M* + H]⁺, C₂₉H₂₅O₈S⁺; calc. 533.1270).

2-Methoxy-1-[(methoxy)methyl]oxy-4-(1-methylethyl)benzene (63). A suspension of methyl(triphenyl)phosphonium bromide (1.1 g, 3.09 mmol) in dry THF (5 ml) was cooled to –78° and slowly treated with BuLi (1.6*M* in hexane, 1.94 ml). To this yellow suspension, a soln. of **62** (500 mg, 2.38 mmol) in dry THF (5 ml) was added, and the mixture was stirred at 20° for 12 h. The suspension was filtered, and the solvent was evaporated *in vacuo*. CC (SiO₂; hexane/AcOEt 6:1) afforded **63** (424 mg, 86%). Colorless oil. IR (neat): 3085*w*, 2952*m*, 2827*w*, 1627*w*, 1602*w*, 1580*m*, 1513*s*, 1463*m*, 1413*m*, 1300*m*, 1248*s*, 1224*m*, 1157*s*, 1139*s*, 1077*s*, 997*s*, 922*m*, 885*m*, 855*m*, 817*w*, 765*w*. ¹H-NMR (300 MHz, CDCl₃): 2.14 (*s*, 3 H); 3.52 (*s*, 3 H); 3.91 (*s*, 3 H); 5.03 (*d*, *J* = 1.5, 1 H); 5.23 (*s*, 2 H); 5.29 (*d*, *J* = 1.5, 1 H); 6.99 (*dd*, *J* = 8.4, 2.1, 1 H); 7.02 (*dd*, *J* = 6.9, 2.1, 1 H); 7.11 (*d*, *J* = 8.4, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 21.9; 55.8; 56.2; 95.4; 109.2; 111.4; 115.9; 118.1; 135.9; 142.9; 146.0; 149.3. HR-EI-MS: 208.1097 (*M*⁺, C₁₂H₁₆O₃⁺; calc. 208.1099).

2-Methoxy-1-[(methoxy)methyl]oxy-4-(1-methylethyl)benzene (64). To a soln. of **63** (3.5 g, 16.81 mmol) in MeOH (20 ml), Pd/C (10%, 350 mg) was added, and the mixture was stirred 16 h under an H₂ atmosphere. The mixture was filtered over *Celite*, evaporated *in vacuo*, and briefly dried at *ca.* 10 Torr to yield **64** (3.31 g, 94%). Colorless oil. IR (neat): 2959*s*, 2827*w*, 1592*w*, 1516*s*, 1464*s*, 1419*m*, 1297*w*, 1266*s*, 1228*s*, 1198*m*, 1156*s*, 1079*s*, 1037*w*, 1004*s*, 923*m*, 852*w*, 815*w*, 763*w*, 653*w*. ¹H-NMR (300 MHz, CDCl₃): 1.24 (*d*, *J* = 7.0, 6 H); 2.86 (*sept.*, *J* = 7.0, 1 H); 3.52 (*s*, 3 H); 3.88 (*s*, 3 H); 5.20 (*s*, 2 H); 6.75 (*dd*, *J* = 8.2, 2.2, 1 H); 6.77 (*dd*, *J* = 3.5, 2.2, 1 H); 7.07 (*d*, *J* = 8.2, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 24.1; 33.8; 55.8; 56.1; 110.3; 116.5; 118.2; 143.5; 144.4; 149.5. HR-EI-MS: 210.1246 (*M*⁺, C₁₂H₁₈O₃⁺; calc. 210.1256).

Methyl 3-Methoxy-2-[(methoxy)methyl]oxy-5-(1-methylethyl)benzoate (65). To a soln. of **64** (2.0 g, 9.51 mmol) in dry THF (35 ml) cooled to 0°, BuLi (1.6*M* in hexane, 9 ml) was added dropwise, and the mixture was stirred for 2.5 h at 0°. This soln. was then slowly added to a soln. of methyl chloroformate (9 g, 95.1 mmol) in dry THF (10 ml) cooled to 0°. The mixture was stirred 12 h at 20° and then partitioned

between sat. aq. KHCO_3 soln. (60 ml) and AcOEt (60 ml). The org. phase was washed with sat. aq. NaCl soln. (2×40 ml), dried (MgSO_4), and evaporated *in vacuo*. CC (SiO_2 ; hexane/AcOEt 9:1 $\rightarrow$ 6:1) afforded **65** (1.3 g, 51%). Colorless oil. IR (neat): 2960m, 2841w, 1769m, 1729s, 1586w, 1487m, 1464m, 1439m, 1339m, 1263s, 1207s, 1157m, 1063s, 961s, 860w, 797w, 656w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.24 (d, $J=6.9$, 6 H); 2.88 (sept., $J=6.9$, 1 H); 3.57 (s, 3 H); 3.86 (s, 3 H); 3.90 (s, 3 H); 5.10 (s, 2 H); 6.91 (d, $J=2.1$, 1 H); 7.18 (d, $J=2.1$, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 24.0; 34.0; 52.2; 56.2; 75.4; 99.4; 114.4; 119.8; 126.0; 143.3; 144.9; 152.8; 166.8. HR-EI-MS: 268.1300 (M^+ , $\text{C}_{14}\text{H}_{20}\text{O}_5^+$; calc. 268.1311).

2,3-Dihydroxy-5-(1-methylethyl)benzoic Acid (66). To a soln. of **65** (900 mg, 3.35 mmol) in dry CH_2Cl_2 (5 ml) cooled to -80° , BBr_3 (1M in CH_2Cl_2 , 3.4 ml) was added dropwise, and the mixture was stirred 30 min at -78° , then 1 h at 20° . The reaction was quenched by addition of H_2O (10 ml), and the resulting mixture was extracted with CH_2Cl_2 (2×30 ml). The combined org. phases were dried (MgSO_4) and evaporated *in vacuo*. The residue was redissolved in AcOH (1 ml), and HBr (33% in AcOH, 2.5 ml) was added. The mixture was stirred at 120° for 5 h, then H_2O (10 ml) was slowly added, and the mixture was extracted with AcOEt (2×40 ml). The combined org. phases were washed with sat. aq. NaCl soln., dried (MgSO_4), and evaporated *in vacuo* to yield **66** (270 mg, 41%). Brownish solid. M.p. $151-152^\circ$. IR (KBr): 3311m, 2958s, 1675s, 1613w, 1483s, 1384w, 1276s, 1161s, 986w, 872w, 796w, 778w, 728w, 703w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.22 (d, $J=7.1$, 6 H); 2.84 (sept., $J=7.1$, 1 H); 5.64 (br. s, 1 H); 7.09 (d, $J=2.4$, 1 H); 7.30 (d, $J=2.4$, 1 H); 10.29 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 23.9; 33.5; 110.8; 118.7; 119.7; 140.5; 144.8; 147.4; 174.8. HR-EI-MS: 196.0720 (M^+ , $\text{C}_{10}\text{H}_{10}\text{O}_5^+$; calc. 196.0736).

Methyl 2,3-Dihydroxy-5-(1-methylethyl)benzoate (67). Compound **66** (140 mg, 0.71 mmol) and SOCl_2 (430 mg, 3.6 mmol) were reacted according to *GP 1* to afford **67** (125 mg, 83%). Colorless solid. M.p. $66-67^\circ$. IR (KBr): 3425s, 2955m, 1688s, 1485s, 1438s, 1338s, 1276s, 1231m, 1159m, 1112w, 1018m, 964w, 893w, 785m, 693w, 641w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.21 (d, $J=6.9$, 6 H); 2.82 (sept., $J=6.9$, 1 H); 3.95 (s, 3 H); 5.61 (s, 1 H); 7.02 (d, $J=2.0$, 1 H); 7.21 (d, $J=2.0$, 1 H); 10.69 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 23.9; 33.5; 52.3; 111.8; 117.7; 118.4; 140.1; 144.7; 146.9; 170.8. HR-EI-MS: 210.0892 (M^+ , $\text{C}_{11}\text{H}_{14}\text{O}_4^+$; calc. 210.0892).

Methyl 6-(1-Methylethyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylate (68). Compound **67** (85 mg, 0.4 mmol) and Ph_2CCl_2 (125 mg, 0.53 mmol) were reacted according to *GP 2.1, Workup Method B*, to afford **68** (112 mg, 74%). Colorless solid. M.p. $108-110^\circ$. IR (KBr): 2959w, 1714s, 1478s, 1447s, 1385w, 1285m, 1045m, 1017m, 915w, 868w, 807m, 782m, 701s, 641m. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.21 (d, $J=6.8$, 6 H); 2.85 (sept., $J=6.8$, 1 H); 3.94 (s, 3 H); 6.92 (d, $J=1.9$, 1 H); 7.26 (d, $J=1.9$, 1 H); 7.35–7.41 (m, 6 H); 7.60–7.65 (m, 4 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 24.0; 33.9; 52.0; 111.0; 112.1; 117.7; 119.9; 126.4; 128.2; 129.2; 140.0; 142.5; 146.3; 148.3; 165.4. HR-MALDI-MS: 397.1414 ($[M+\text{Na}]^+$, $\text{C}_{24}\text{H}_{22}\text{NaO}_4^+$; calc. 397.1416).

6-(1-Methylethyl)-2,2-diphenyl-1,3-benzodioxole-4-carboxylic Acid (36). Compound **68** (100 mg, 0.267 mmol) and $\text{LiOH}\cdot\text{H}_2\text{O}$ (45 mg, 1.07 mmol) were reacted according to *GP 3* to afford **36** (91 mg, 95%). Colorless solid. M.p. $155-156^\circ$. IR (KBr): 2958m, 2630w, 1683s, 1478s, 1450s, 1254s, 1207s, 1044m, 1023m, 947w, 864w, 760w, 697m, 641w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.21 (d, $J=6.9$, 6 H); 2.86 (sept., $J=6.9$, 1 H); 6.97 (d, $J=1.8$, 1 H); 7.31 (d, $J=1.8$, 1 H); 7.35–7.42 (m, 6 H); 7.61–7.64 (m, 4 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 24.0; 33.8; 111.2; 111.9; 118.2; 120.3; 126.4; 128.3; 129.3; 139.8; 142.7; 146.9; 148.4; 169.6. HR-MALDI-MS: 383.1250 ($[M+\text{Na}]^+$, $\text{C}_{23}\text{H}_{20}\text{NaO}_4^+$; calc. 383.1259).

3-Bromo-5-(trifluoromethyl)benzene-1,2-diol (70). To a soln. of **69** (870 mg, 4.8 mmol) in CCl_4 (20 ml), Br_2 (770 mg, 4.8 mmol) was added, and the mixture was stirred at 20° for 1 h. The solvent was removed *in vacuo*, and the residue was purified by CC (SiO_2 ; hexane/AcOEt 4:1 $\rightarrow$ 3:2) to yield **70** (910 mg, 74%). Yellowish oil. IR (neat): 3048w (br.), 1599w, 1502w, 1433w, 1312s, 1234m, 1168m, 1115s, 934m, 866w, 838w, 767w, 726w, 670m. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 5.68 (br. s, 1 H); 5.81 (br. s, 1 H); 7.14 (dd, $J=2.3$, 0.6, 1 H); 7.32 (dd, $J=2.3$, 0.6, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CD_3OD): 110.2; 111.6 (q, $J=3.4$); 121.4 (q, $J=4.2$); 123.1 (q, $J=33.0$); 125.0 (q, $J=270$); 147.4; 147.7. $^{19}\text{F-NMR}$ (282 MHz, CDCl_3): -61.6 (s). HR-EI-MS: 255.9348 (M^+ , $\text{C}_7\text{H}_4\text{BrF}_3\text{O}_2^+$; calc. 255.9347).

1-Bromo-2,3-bis(phenylmethoxy)-5-(trifluoromethyl)benzene (71). To a soln. of **70** (510 mg, 1.98 mmol) in acetone (10 ml), K_2CO_3 (2.74 g, 19.84 mmol) and BnBr (1.02 g, 5.95 mmol) were added, and the mixture was heated to reflux for 4 h. After cooling to 20° , the mixture was partitioned between H_2O (20 ml) and AcOEt (20 ml), and the aq. phase was extracted with AcOEt (2×20 ml). The combined

org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo*. CC (SiO₂; hexane/AcOEt 10:1) afforded **71** (750 mg, 87%). Colorless solid. M.p. 79–80°. IR (KBr): 3032w, 2935w, 2884w, 1576w, 1499w, 1485w, 1455w, 1424m, 1382w, 1335s, 1290m, 1230m, 1164s, 1120s, 1011m, 957m, 919w, 859w, 751m, 698m. ¹H-NMR (300 MHz, CDCl₃): 5.09 (s, 2 H); 5.15 (s, 2 H); 5.97 (s, 1 H); 7.18 (d, *J* = 1.5, 1 H); 7.32–7.47 (m, 11 H). ¹³C-NMR (75 MHz, CDCl₃): 71.5; 75.0; 110.3 (*q*, *J* = 3.9); 118.4; 122.5 (*q*, *J* = 3.9); 123.1 (*q*, *J* = 271); 127.0 (*q*, *J* = 33.6); 127.6; 128.2; 128.3; 128.4; 128.5; 128.6; 135.5; 136.3; 148.4; 152.8. ¹⁹F-NMR (282 MHz, CDCl₃): –62.6 (s). HR-MALDI-MS: 459.0169 ([*M*+Na]⁺, C₂₁H₁₆BrF₃NaO₂⁺; calc. 459.0183). Anal. calc. for C₂₁H₁₆O₂F₃Br (436.03): C 57.69, H 3.69; found C 57.45, H 3.82.

Methyl 2,3-Bis(phenylmethoxy)-5-(trifluoromethyl)benzoate (72). To a soln. of **71** (750 mg, 1.76 mmol) in dry THF (10 ml) cooled to –90°, BuLi (1.6M in hexane, 3.3 ml, 5.28 mmol) was slowly added, and the yellow soln. was stirred at –90° for 15 min. Methyl chloroformate (1.66 g, 17.6 mmol) was added, and the mixture was allowed to warm to 20° and stirred at this temp. for 1 h. H₂O (10 ml) was added, and the mixture was extracted with AcOEt (2 × 30 ml). The combined org. phases were washed with sat. aq. NaCl soln., dried (MgSO₄), and evaporated *in vacuo*. CC (SiO₂; hexane/AcOEt 10:1) afforded **72** (383 mg, 52%). Colorless solid. M.p. 78–79°. IR (KBr): 3033w, 2950w, 1733s, 1610w, 1486w, 1430m, 1363s, 1299m, 1250s, 1199m, 1151m, 1121s, 1045s, 956w, 935w, 909w, 867w, 750w, 698m. ¹H-NMR (300 MHz, CDCl₃): 3.87 (s, 3 H); 5.14 (s, 2 H); 5.17 (s, 2 H); 7.30–7.45 (m, 11 H); 7.65 (dd, *J* = 1.8, 1.2, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 52.5; 71.6; 75.8; 113.9 (*q*, *J* = 3.3); 118.0; 119.9 (*q*, *J* = 3.3); 123.4 (*q*, *J* = 270); 126.0 (*q*, *J* = 33.6); 127.0; 127.6; 128.1; 128.3; 128.4; 128.5; 128.6; 135.5; 136.6; 150.7; 153.0; 165.4. ¹⁹F-NMR (282 MHz, CDCl₃): –62.7 (s). HR-MALDI-MS: 439.1132 ([*M*+Na]⁺, C₂₃H₁₉F₃NaO₂⁺; calc. 439.1133). Anal. calc. for C₂₃H₁₉O₄F₃ (416.12): C 66.34, H 4.60; found C 66.16, H 4.78.

Methyl 2,3-Dihydroxy-5-(trifluoromethyl)benzoate (73). To a soln. of **72** (280 mg, 0.67 mmol) in MeOH (10 ml), Pd/C (10%, 30 mg) was added, and the mixture was stirred 16 h under an H₂ atmosphere. The mixture was then filtered over *Celite* and evaporated *in vacuo* to yield **73** (148 mg, 99%). Grayish solid. M.p. 94–95°. IR (KBr): 3462m, 3132w, 2961w, 1676m, 1494m, 1447m, 1338s, 1245s, 1199m, 1120s, 1014w, 936w, 887w, 793m, 679m. ¹H-NMR (300 MHz, CD₃OD): 3.97 (s, 3 H); 7.17 (s, 1 H); 7.58 (s, 1 H). ¹³C-NMR (75 MHz, CD₃OD): 53.2; 113.6; 116.9; 118.0; 121.8 (*q*, *J* = 32.8); 125.3 (*q*, *J* = 268); 148.6; 154.6; 170.9. ¹⁹F-NMR (282 MHz, CD₃OD): –62.0 (s). HR-EI-MS: 236.0295 (*M*⁺, C₉H₇F₃O₄⁺; calc. 236.0296).

Methyl 2,2-Bis(4-methoxyphenyl)-6-(trifluoromethyl)-1,3-benzodioxole-4-carboxylate (74). 4,4'-Dimethoxybenzophenone (213 mg, 0.88 mmol), oxalyl chloride (900 mg, 7.1 mmol), and **73** (130 mg, 0.59 mmol) were reacted according to *GP 2.2*. CC (SiO₂; hexane/Et₂O 10:1) afforded **74** (170 mg, 63%). Colorless, very viscous oil. IR (neat): 3003w, 2956w, 2839w, 1727s, 1642w, 1612s, 1585w, 1514s, 1486m, 1445s, 1324s, 1268s, 1234s, 1175s, 1123m, 1042s, 1005m, 935w, 832m, 783w, 674w. ¹H-NMR (300 MHz, CDCl₃): 3.81 (s, 6 H); 3.95 (s, 3 H); 6.90 (dd, *J* = 6.7, 2.3, 4 H); 7.18 (d, *J* = 1.5, 1 H); 7.47 (dd, *J* = 6.7, 2.3, 4 H); 7.74 (d, *J* = 1.5, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 52.4; 55.4; 108.6 (*q*, *J* = 3.1); 112.3; 113.7; 120.2; 120.8 (*q*, *J* = 4.3); 123.5 (*q*, *J* = 270); 123.6 (*q*, *J* = 33.4); 128.0; 131.0; 148.9; 150.7; 160.4; 163.8. ¹⁹F-NMR (282 MHz, CDCl₃): –61.8 (s). HR-MALDI-MS: 461.1202 ([*M*+H]⁺, C₂₄H₂₀F₃O₆⁺; calc. 461.1212). Anal. calc. for C₂₄H₁₉O₆F₃ (460.11): C 62.61, H 4.16; found C 62.52, H 4.26.

2,2-Bis(4-methoxyphenyl)-6-(trifluoromethyl)-1,3-benzodioxole-4-carboxylic Acid (28). Compound **74** (60 mg, 0.13 mmol) and LiOH·H₂O (28 mg, 0.65 mmol) were reacted according to *GP 3* to afford **28** (53 mg, 91%). Colorless solid. M.p. 114–116°. IR (KBr): 3441w (br.), 2936w, 2837w, 1687w, 1611s, 1513s, 1442m, 1364m, 1312s, 1253s, 1175s, 1121m, 1031s, 1005m, 952w, 931w, 831m, 676w. ¹H-NMR (300 MHz, CDCl₃): 3.79 (s, 6 H); 6.94 (dd, *J* = 6.9, 2.1, 4 H); 7.30 (d, *J* = 1.5, 1 H); 7.46 (dd, *J* = 6.9, 2.1, 4 H); 7.70 (d, *J* = 1.5, 1 H). ¹⁹F-NMR (282 MHz, CDCl₃): –63.7 (s). HR-MALDI-MS: 447.1059 ([*M*+H]⁺, C₂₃H₁₈F₃O₆⁺; calc. 447.1055).

9-[(E)-5,6,7-Trideoxy-7-({[6-(4-fluorophenyl)-2,2-diphenyl-1,3-benzodioxol-4-yl]carbonyl}amino)-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (75). Compound **21** (130 mg, 0.315 mmol), EDC·HCl (91 mg, 0.473 mmol), *N*-hydroxysuccinimide (48 mg, 0.409 mmol), **20** (90 mg, 0.271 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to *GP 6*. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **75** (130 mg, 66%). Colorless foam. [*α*]_D²⁰ = +4.5 (*c* = 1.2, CHCl₃). IR (KBr): 3425m,

3175w, 2987w, 1636s, 1598m, 1517m, 1469s, 1373w, 1274m, 1213s, 1158w, 1082m, 1052m, 1016w, 867w, 834w, 777w, 699m. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.38 (s, 3 H); 1.62 (s, 3 H); 4.08 (m, 2 H); 4.71 (m, 1 H); 4.95 (dd, $J=6.6$, 3.6, 1 H); 5.44 (dd, $J=6.6$, 2.3, 1 H); 5.87 (m, 2 H); 5.93 (br. s, 2 H); 6.09 (d, $J=2.3$, 1 H); 7.10 (tt, $J=8.7$, 2.1, 2 H); 7.12 (t, $J=5.6$, 1 H); 7.22 (d, $J=1.8$, 1 H); 7.37–7.41 (m, 6 H); 7.47–7.56 (m, 6 H); 7.77 (d, $J=1.8$); 7.87 (s, 1 H); 8.19 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 25.5; 27.3; 40.9; 84.1; 84.5; 87.1; 90.3; 110.6; 114.7; 115.3; 115.6 (d, $J=21.2$); 118.8; 120.1; 121.0; 126.4; 128.2; 128.4; 128.5; 129.7; 130.7; 135.0; 136.1; 138.7; 139.9; 144.1; 147.8; 149.2; 152.0; 154.8; 162.3 (d, $J=244.7$); 163.1. $^{19}\text{F-NMR}$ (282 MHz, CDCl_3): –115.9 (tt, $J=8.5$, 5.4). HR-MALDI-MS: 749.2501 ($[M+\text{Na}]^+$, $\text{C}_{41}\text{H}_{35}\text{FN}_6\text{NaO}_6^+$; calc. 749.2500).

9-[(E)-5,6,7-Trideoxy-2,3-O-(1-methylethylidene)-7-([6-(4-methylphenyl)-2,2-diphenyl-1,3-benzodioxol-4-yl]carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**76**). Compound **22** (164 mg, 0.4 mmol), EDC-HCl (115 mg, 0.6 mmol), *N*-hydroxysuccinimide (60 mg, 0.52 mmol), **20** (90 mg, 0.271 mmol), and Et_3N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO_2 ; $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **76** (111 mg, 57%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +1.7$ ($c=0.95$, CHCl_3). IR (KBr): 3423m, 3176m, 2986w, 1638s, 1597s, 1531m, 1469s, 1434m, 1373w, 1329w, 1276s, 1207s, 1156w, 1081m, 1052s, 1016m, 970w, 867m, 818m, 777m, 699m, 641m. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.38 (s, 3 H); 1.62 (s, 3 H); 2.37 (s, 3 H); 4.09 (m, 2 H); 4.71 (m, 1 H); 4.94 (dd, $J=6.5$, 3.6, 1 H); 5.42 (dd, $J=6.5$, 2.6, 1 H); 5.86 (m, 2 H); 6.06 (br. s, 2 H); 6.09 (d, $J=2.6$, 1 H); 7.17 (t, $J=5.6$, 1 H); 7.21 (d, $J=8.3$, 2 H); 7.26 (d, $J=1.8$, 1 H); 7.36–7.42 (m, 6 H); 7.46 (d, $J=8.3$, 2 H); 7.51–7.56 (m, 4 H); 7.82 (d, $J=1.8$, 1 H); 7.88 (s, 1 H); 8.19 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 25.2; 25.5; 27.2; 40.8; 84.1; 84.4; 87.1; 90.3; 110.5; 114.7; 115.2; 118.6; 120.0; 120.8; 126.4; 126.6; 128.0; 128.3; 129.4; 129.6; 130.8; 135.9; 136.0; 137.0; 138.8; 140.0; 143.8; 147.7; 149.1; 151.5; 154.6; 163.2. HR-MALDI-MS: 745.2750 ($[M+\text{Na}]^+$, $\text{C}_{42}\text{H}_{38}\text{N}_6\text{NaO}_6^+$; calc. 745.2751). Anal. calc. for $\text{C}_{42}\text{H}_{38}\text{N}_6\text{O}_6$ (722.29): C 69.79, H 5.30, N 11.63; found C 69.61, H 5.56, N 11.93.

9-[(E)-5,6,7-Trideoxy-7-([2,2-diphenyl-6-(pyridine-4-yl)-1,3-benzodioxol-4-yl]carbonyl)amino)-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**77**). Compound **23** (160 mg, 0.405 mmol), EDC-HCl (117 mg, 0.608 mmol), *N*-hydroxysuccinimide (61 mg, 0.527 mmol), **20** (100 mg, 0.3 mmol), and Et_3N (0.1 ml, 0.68 mmol) were reacted in $\text{CH}_2\text{Cl}_2/\text{DMF}$ (1:1, 5 ml) according to GP 6. CC (SiO_2 ; $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **77** (95 mg, 45%). Yellowish foam. $[\alpha]_{\text{D}}^{20} = +2.5$ ($c=0.4$, CHCl_3). IR (neat): 3321w (br.), 2963m, 1696m, 1645m, 1597m, 1530w, 1468s, 1435w, 1374w, 1261s, 1213s, 1053s, 867w, 799m, 699m, 642w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.37 (s, 3 H); 1.61 (s, 3 H); 4.08 (m, 2 H); 4.70 (m, 1 H); 4.96 (dd, $J=6.3$, 3.9, 1 H); 5.45 (dd, $J=6.3$, 2.3, 1 H); 5.86 (m, 2 H); 5.98 (br. s, 2 H); 6.08 (d, $J=2.3$, 1 H); 7.16 (t, $J=5.7$, 1 H); 7.31 (d, $J=1.7$, 1 H); 7.36–7.42 (m, 6 H); 7.47–7.55 (m, 6 H); 7.86 (s, 1 H); 7.92 (d, $J=1.7$, 1 H); 8.18 (s, 1 H); 8.61 (d, $J=6.3$, 2 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 25.6; 27.4; 41.1; 84.3; 84.7; 87.4; 90.5; 110.4; 114.9; 116.0; 119.7; 120.4; 121.6; 122.0; 126.2; 126.7; 128.8; 130.2; 130.8; 132.8; 138.8; 140.1; 145.9; 147.6; 148.6; 149.6; 150.2; 153.0; 155.6; 163.1. HR-MALDI-MS: 732.2549 ($[M+\text{Na}]^+$, $\text{C}_{40}\text{H}_{35}\text{N}_7\text{NaO}_6^+$; calc. 732.2547).

9-[(E)-5,6,7-Trideoxy-7-([2,2-diphenyl-6-(1,3-thiazole-2-yl)-1,3-benzodioxol-4-yl]carbonyl)amino)-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**78**). Compound **24** (170 mg, 0.38 mmol), EDC-HCl (110 mg, 0.565 mmol), *N*-hydroxysuccinimide (57 mg, 0.49 mmol), **20** (100 mg, 0.3 mmol), and Et_3N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO_2 ; $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **78** (158 mg, 73%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +3.5$ ($c=0.63$, CHCl_3). IR (KBr): 3424m, 3199w, 2987w, 1639s, 1598m, 1532m, 1471m, 1440m, 1374w, 1329w, 1263m, 1212s, 1156w, 1081m, 1050m, 1015m, 867w, 779w, 700m, 643w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.39 (s, 3 H); 1.62 (s, 3 H); 4.08 (m, 2 H); 4.76 (m, 1 H); 4.93 (dd, $J=6.2$, 3.0, 1 H); 5.42 (dd, $J=6.2$, 2.0, 1 H); 5.82 (m, 2 H); 6.10 (d, $J=2.0$, 1 H); 6.63 (br. s, 2 H); 7.12 (t, $J=5.7$, 1 H); 7.30 (d, $J=3.5$, 1 H); 7.37–7.43 (m, 6 H); 7.50–7.54 (m, 4 H); 7.73 (d, $J=1.7$, 1 H); 7.81 (d, $J=3.5$, 1 H); 7.92 (s, 1 H); 8.14 (d, $J=1.7$, 1 H); 8.20 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 25.4; 27.1; 40.9; 84.3; 84.4; 87.3; 90.7; 109.7; 114.6; 115.4; 119.0; 119.3; 119.9; 121.9; 126.4; 127.9; 128.4; 128.6; 129.8; 130.8; 138.4; 140.5; 143.3; 145.9; 148.0; 148.9; 149.5; 153.8; 162.6; 167.2. HR-MALDI-MS: 738.2095 ($[M+\text{Na}]^+$, $\text{C}_{38}\text{H}_{33}\text{N}_7\text{NaO}_6\text{S}^+$; calc. 738.2111). Anal. calc. for $\text{C}_{42}\text{H}_{38}\text{N}_6\text{O}_6$ (722.29): C 63.76, H 4.65, N 13.70; found C 63.55, H 4.70, N 13.68.

9-[(E)-7-[(6-Bromo-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl]amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**79**). Compound **25** (200 mg, 0.503

mmol), EDC·HCl (145 mg, 0.755 mmol), *N*-hydroxysuccinimide (76 mg, 0.654 mmol), **20** (120 mg, 0.361 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to GP 7. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **79** (166 mg, 65%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +9.3$ ($c = 0.6$, CHCl₃). IR (KBr): 3424m, 3170w (br.), 2985w, 1636s, 1594s, 1531m, 1495s, 1423w, 1373w, 1236s, 1207s, 1156w, 1082s, 1016m, 867w, 778w, 698m. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 4.04 (m, 2 H); 4.69 (m, 1 H); 4.95 (dd, $J = 6.3$, 3.6, 1 H); 5.45 (dd, $J = 6.3$, 2.3, 1 H); 5.84 (m, 2 H); 5.96 (br. s, 2 H); 6.09 (d, $J = 2.3$, 1 H); 7.05 (t, $J = 5.6$, 1 H); 7.15 (d, $J = 2.0$, 1 H); 7.35–7.40 (m, 6 H); 7.44–7.50 (m, 4 H); 7.72 (d, $J = 2.0$, 1 H); 7.87 (s, 1 H); 8.20 (s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.5; 27.3; 40.9; 84.1; 84.5; 87.1; 90.3; 114.0; 114.7; 115.2; 116.3; 119.5; 120.1; 125.0; 126.3; 128.4; 129.8; 130.5; 138.3; 140.1; 144.1; 148.1; 149.2; 151.7; 154.7; 162.0. HR-MALDI-MS: 711.1553 ($[M + H]^+$, C₃₅H₃₂BrN₆O₆⁺; calc. 711.1567). Anal. calc. for C₃₅H₃₁BrN₆O₆ (710.15): C 59.08, H 4.39, N 11.81; found C 59.06, H 4.54, N 11.62.

9-[(E)-7-([6-(1,3-Benzothiazol-2-yl)-2,2-diphenyl-1,3-benzodioxol-4-yl]carbonyl)amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**80**). Compound **26** (170 mg, 0.38 mmol), EDC·HCl (110 mg, 0.565 mmol), *N*-hydroxysuccinimide (57 mg, 0.49 mmol), **20** (100 mg, 0.3 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **80** (151 mg, 66%). Colorless foam. $[\alpha]_{\text{D}}^{20} = -1.7$ ($c = 0.9$, CHCl₃). IR (KBr): 3424m, 2982w, 1635s, 1596m, 1533m, 1463m, 1436s, 1373w, 1259m, 1208s, 1155w, 1081m, 1048m, 1011m, 867w, 759w, 699w, 641w. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 4.07 (m, 2 H); 4.72 (m, 1 H); 4.95 (dd, $J = 6.3$, 3.6, 1 H); 5.44 (dd, $J = 6.3$, 2.3, 1 H); 5.85 (m, 2 H); 6.09 (d, $J = 2.3$, 1 H); 6.17 (br. s, 2 H); 7.13 (t, $J = 5.7$, 1 H); 7.34–7.49 (m, 8 H); 7.49–7.55 (m, 4 H); 7.87 (s, 1 H); 7.88 (d, $J = 7.8$, 1 H); 7.91 (d, $J = 1.9$, 1 H); 7.81 (d, $J = 7.8$, 1 H); 8.20 (s, 1 H); 8.22 (d, $J = 1.9$, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.4; 27.2; 40.9; 84.1; 84.4; 87.2; 90.3; 110.1; 114.6; 115.4; 119.5; 120.0; 121.5; 122.9; 123.2; 125.1; 126.2; 126.4; 128.3; 128.4; 128.6; 129.8; 130.5; 135.0; 138.3; 140.0; 146.7; 148.1; 149.1; 151.5; 153.7; 154.7; 162.4; 166.7. HR-MALDI-MS: 788.2266 ($[M + Na]^+$, C₄₂H₃₅N₇NaO₆S⁺; calc. 788.2267).

9-[(E)-7-([6-(2-Cyano-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl)amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**81**). Compound **27** (80 mg, 0.23 mmol), EDC·HCl (73 mg, 0.38 mmol), **20** (50 mg, 0.15 mmol), and Et₃N (0.05 ml, 0.34 mmol) were reacted according to GP 6. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **81** (201 mg, 68%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +12.5$ ($c = 0.4$, CHCl₃). IR (KBr): 3428s, 3171w, 2986w, 2227w, 1635s, 1597m, 1528m, 1466s, 1374m, 1262s, 1209s, 1082m, 1017m, 867w, 762w, 699m, 641w. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 4.05 (m, 2 H); 4.70 (m, 1 H); 4.96 (dd, $J = 6.3$, 3.9, 1 H); 5.46 (dd, $J = 6.3$, 2.0, 1 H); 5.79 (br. s, 2 H); 5.83 (m, 2 H); 6.08 (d, $J = 2.0$, 1 H); 7.00 (t, $J = 5.7$, 1 H); 7.22 (d, $J = 1.7$, 1 H); 7.38–7.49 (m, 10 H); 7.86 (s, 1 H); 7.99 (d, $J = 1.7$, 1 H); 8.19 (s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.5; 27.3; 41.0; 84.1; 84.5; 87.2; 90.3; 105.9; 113.7; 114.7; 116.1; 118.0; 120.2; 120.7; 126.3; 128.6; 128.8; 129.1; 130.1; 130.2; 137.6; 140.0; 147.8; 148.0; 149.2; 152.3; 155.0; 161.2. HR-MALDI-MS: 658.2403 ($[M + H]^+$, C₃₆H₃₂N₇O₆⁺; calc. 658.2414).

9-[(E)-7-([2,2-Bis(4-methoxyphenyl)-6-cyano-1,3-benzodioxol-4-yl]carbonyl)amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**93**). Compound **53** (100 mg, 0.248 mmol), EDC·HCl (71 mg, 0.372 mmol), *N*-hydroxysuccinimide (37 mg, 0.322 mmol), **20** (83 mg, 0.248 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **93** (122 mg, 69%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +11.2$ ($c = 1.0$, CHCl₃). IR (KBr): 3424m, 3176w, 2934w, 2226w, 1635s, 1610s, 1514s, 1465s, 1440m, 1373m, 1254s, 1209s, 1174s, 1082m, 1025m, 1004w, 867w, 832m, 649w. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 3.81 (s, 6 H); 4.03 (m, 2 H); 4.68 (dd, $J = 5.7$, 3.6, 1 H); 4.96 (dd, $J = 6.3$, 3.6, 1 H); 5.47 (dd, $J = 6.3$, 2.1, 1 H); 5.72 (br. s, 2 H); 5.81 (m, 2 H); 6.08 (d, $J = 2.1$, 1 H); 6.90 (dd, $J = 9.0$, 1.5, 4 H); 7.01 (t, $J = 5.7$, 1 H); 7.18 (d, $J = 1.5$, 1 H); 7.37 (m, 4 H); 7.85 (s, 1 H); 7.97 (d, $J = 1.5$, 1 H); 8.20 (s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.3; 27.1; 40.9; 55.4; 84.1; 84.5; 87.2; 90.3; 105.7; 113.6; 113.7; 114.6; 116.0; 118.2; 120.2; 121.4; 128.2; 128.8; 129.0; 129.8; 130.1; 139.9; 148.1; 148.3; 149.4; 152.9; 155.3; 161.0; 161.5. HR-MALDI-MS: 718.2631 ($[M + H]^+$, C₃₈H₃₆N₇O₈⁺; calc. 718.2625).

9-[(E)-7-([2,2-Bis(4-methoxyphenyl)-6-(trifluoromethyl)-1,3-benzodioxol-4-yl]carbonyl)amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**82**). Compound **28** (90 mg, 0.2 mmol), EDC·HCl (58 mg, 0.3 mmol), *N*-hydroxysuccinimide (31 mg, 0.26 mmol),

20 (70 mg, 0.2 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to *GP 6*. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **82** (119 mg, 77%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +10.4$ ($c = 1.5$, CHCl₃). IR (KBr): 3426m, 3178w, 2935w, 2837w, 1640s, 1607s, 1514m, 1443w, 1375w, 1317s, 1254s, 1210m, 1175s, 1121m, 1025m, 1004w, 867w, 732m. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 3.81 (s, 6 H); 4.04 (m, 2 H); 4.68 (m, 1 H); 4.95 (dd, $J = 6.6, 3.6$, 1 H); 5.45 (dd, $J = 6.6, 2.1$, 1 H); 5.81 (m, 4 H); 6.08 (d, $J = 2.1$, 1 H); 6.88–6.92 (m, 4 H); 7.09 (t, $J = 5.7$, 1 H); 7.19 (d, $J = 2.1$, 1 H); 7.36–7.42 (m, 4 H); 7.85 (s, 1 H); 7.91 (d, $J = 2.1$, 1 H); 8.22 (s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.4; 27.2; 40.9; 55.4; 84.1; 84.5; 87.1; 90.2; 108.3; 113.7; 114.6; 115.1; 120.1; 120.6; 120.7; 123.54 ($q, J = 270$); 124.6 ($q, J = 33.5$); 128.1; 128.5; 130.1; 130.3; 139.8; 147.2; 147.9; 149.2; 152.3; 155.1; 160.7; 162.0. ¹⁹F-NMR (282 MHz, CDCl₃): –61.7 (s). HR-MALDI-MS: 759.2535 ($[M + H]^+$, C₃₈H₃₆F₃N₆O₈⁺; calc. 761.2547).

9-[(E)-5,6,7-Trideoxy-7-([2,2-diphenyl-6-(trifluoroacetyl)-1,3-benzodioxol-4-yl]carbonyl)amino]-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**83**). Compound **29** (250 mg, 0.603 mmol), EDC·HCl (175 mg, 0.91 mmol), *N*-hydroxysuccinimide (90 mg, 0.784 mmol), **20** (120 mg, 0.361 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to *GP 6*. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **83** (174 mg, 66%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +9.6$ ($c = 0.55$, CHCl₃). IR (KBr): 3426m, 3199m, 2986w, 2227w, 1644s, 1599m, 1534m, 1476m, 1442m, 1378w, 1253s, 1207s, 1151m, 1082m, 1017w, 866w, 761w, 699m, 642w. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 4.07 (m, 2 H); 4.68 (m, 1 H); 4.97 (dd, $J = 6.3, 3.6$, 1 H); 5.47 (dd, $J = 6.3, 2.1$, 1 H); 5.85 (m, 4 H); 6.08 (d, $J = 2.1$, 1 H); 7.03 (t, $J = 5.7$, 1 H); 7.38–7.45 (m, 6 H); 7.47–7.52 (m, 4 H); 7.69 (d, $J = 1.7$, 1 H); 7.86 (s, 1 H); 8.21 (s, 1 H); 8.43 (d, $J = 1.7$, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.5; 27.3; 41.1; 84.1; 84.5; 87.1; 90.2; 111.5; 114.7; 115.5; 116.6 ($q, J = 281.0$); 120.1; 120.9; 124.8; 126.3; 128.2; 128.6; 128.8; 130.2; 137.6; 137.7; 139.9; 148.4; 149.2; 150.2; 152.3; 155.0; 161.6; 178.5 ($q, J = 35.5$). ¹⁹F-NMR (282 MHz, CDCl₃): –71.24 (s). HR-MALDI-MS: 729.2291 ($[M + H]^+$, C₃₇H₃₂F₃N₆O₈⁺; calc. 729.2285).

9-[(E)-5,6,7-Trideoxy-7-([2,2-diphenyl-6-(pyridine-4-yl)carbonyl]-1,3-benzodioxol-4-yl)carbonyl)-amino]-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**84**). Compound **30** (100 mg, 0.236 mmol), EDC·HCl (68 mg, 0.354 mmol), *N*-hydroxysuccinimide (36 mg, 0.307 mmol), **20** (72 mg, 0.215 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to *GP 6*. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **84** (98 mg, 62%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +9.4$ ($c = 0.2$, CHCl₃). IR (KBr): 3427m, 1661s, 1596m, 1528m, 1472m, 1435m, 1374w, 1266s, 1208s, 1019w, 867w, 780w, 759w, 700w, 647w. ¹H-NMR (300 MHz, CDCl₃): 1.38 (s, 3 H); 1.62 (s, 3 H); 4.07 (m, 2 H); 4.72 (m, 1 H); 4.93 (dd, $J = 6.3, 3.6$, 1 H); 5.40 (dd, $J = 6.3, 2.0$, 1 H); 5.83 (m, 2 H); 6.10 (d, $J = 2.0$, 1 H); 6.55 (br. s, 2 H); 7.10 (t, $J = 5.4$, 1 H); 7.39–7.45 (m, 6 H); 7.51–7.55 (m, 6 H); 7.65 (d, $J = 1.8$, 1 H); 7.92 (s, 1 H); 8.03 (d, $J = 1.8$); 8.29 (s, 1 H); 8.79 (dd, $J = 4.5, 1.8$, 2 H). ¹³C-NMR (75 MHz, CDCl₃): 25.5; 27.2; 41.0; 84.2; 84.4; 87.2; 90.4; 111.8; 114.6; 114.7; 120.0; 120.4; 122.6; 126.3; 128.0; 128.6; 130.1; 130.3; 130.8; 137.9; 138.0; 140.2; 144.3; 148.4; 148.9; 149.1; 150.3; 151.0; 154.4; 162.1; 193.0. HR-MALDI-MS: 738.2677 ($[M + H]^+$, C₄₁H₃₆N₇O₇⁺; calc. 738.2676).

9-[(E)-7-[(6-Chloro-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl]amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**85**). Compound **31** (90 mg, 0.255 mmol), EDC·HCl (75 mg, 0.383 mmol), *N*-hydroxysuccinimide (40 mg, 0.332 mmol), **20** (85 mg, 0.255 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to *GP 6*. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **85** (123 mg, 73%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +10.6$ ($c = 1.7$, CHCl₃). IR (KBr): 3424m, 3176m, 2986m, 1638s, 1595s, 1530m, 1462s, 1374m, 1329m, 1240s, 1208s, 1156w, 1083m, 1047m, 1017m, 971w, 867w, 778w, 698m. ¹H-NMR (300 MHz, CDCl₃): 1.37 (s, 3 H); 1.61 (s, 3 H); 4.04 (m, 2 H); 4.69 (m, 1 H); 4.94 (dd, $J = 6.3, 3.6$, 1 H); 5.44 (dd, $J = 6.3, 2.1$, 1 H); 5.83 (m, 2 H); 6.05 (br. s, 2 H); 6.08 (d, $J = 2.1$, 1 H); 7.00 (d, $J = 2.1$, 1 H); 7.06 (t, $J = 5.7$, 1 H); 7.35–7.40 (m, 6 H); 7.44–7.50 (m, 4 H); 7.56 (d, $J = 2.1$, 1 H); 7.87 (s, 1 H); 8.19 (s, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.6; 27.4; 41.0; 84.4; 84.7; 87.4; 90.5; 112.8; 115.0; 116.1; 119.8; 120.2; 122.3; 126.6; 127.6; 128.6; 128.8; 130.2; 130.8; 138.7; 140.4; 143.9; 148.3; 149.5; 152.2; 155.1; 162.5. HR-MALDI-MS: 667.2065 ($[M + H]^+$, C₃₅H₃₂ClN₆O₆⁺; calc. 667.2072).

9-[(E)-7-[(6-(Cyclohexylcarbonyl)-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl]amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**86**). Compound **32** (197 mg, 0.46 mmol), EDC·HCl (133 mg, 0.69 mmol), *N*-hydroxysuccinimide (70 mg, 0.6 mmol), **20** (130 mg, 0.391 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to *GP 6*. CC (SiO₂;

$\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **86** (145 mg, 50%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +7.4$ ($c=0.45$, CHCl_3). IR (KBr): 3428m (br.), 2931m, 2853w, 1667s, 1636s, 1596m, 1529m, 1473m, 1433m, 1376w, 1252s, 1209s, 1154w, 1082m, 1049m, 1018w, 867w, 777w, 699w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.24–1.52 (m, 9 H); 1.62 (s, 3 H); 1.70–1.86 (m, 4 H); 3.70 (m, 1 H); 4.07 (m, 2 H); 4.70 (m, 1 H); 4.96 (dd, $J=6.5$, 3.9, 1 H); 5.45 (dd, $J=6.5$, 2.1, 1 H); 5.86 (m, 2 H); 5.92 (br. s, 2 H); 6.09 (d, $J=2.1$, 1 H); 7.11 (t, $J=5.4$, 1 H); 7.36–7.41 (m, 6 H); 7.48–7.52 (m, 4 H); 7.65 (d, $J=1.5$, 1 H); 7.87 (s, 1 H); 8.22 (s, 1 H); 8.24 (d, $J=1.5$, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 25.4; 25.8; 26.0; 27.2; 29.6; 40.9; 45.3; 84.1; 84.4; 87.1; 90.2; 110.9; 114.4; 114.7; 119.7; 120.1; 124.6; 126.3; 128.4; 129.8; 130.4; 131.5; 138.1; 138.2; 139.9; 148.0; 148.1; 149.2; 152.0; 154.8; 162.5; 201.8. HR-MALDI-MS: 743.3195 ($[M+H]^+$, $\text{C}_{42}\text{H}_{42}\text{N}_6\text{O}_5^+$; calc. 743.3193). Anal. calc. for $\text{C}_{42}\text{H}_{42}\text{N}_6\text{O}_5$ (710.32): C 67.91, H 5.70, N 11.31; found C 67.77, H 5.85, N 11.05.

9-[(E)-5,6,7-Trideoxy-7-[(6-[(E)-3-(dimethylamino)-3-oxoprop-1-enyl]-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl)amino]-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**87**). Compound **33** (90 mg, 0.22 mmol), EDC·HCl (63 mg, 0.33 mmol), *N*-hydroxysuccinimide (33 mg, 0.28 mmol), **20** (72 mg, 0.22 mmol), and Et_3N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO_2 ; $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **87** (63 mg, 40%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +3.9$ ($c=0.1$, CHCl_3). IR (KBr): 3424m, 2931w, 1653s, 1598s, 1528m, 1474m, 1437m, 1374w, 1259m, 1207m, 1154w, 1081m, 1049m, 1019m, 973w, 867w, 776w, 699w, 642w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.37 (s, 3 H); 1.61 (s, 3 H); 3.05 (s, 3 H); 3.14 (s, 3 H); 4.05 (m, 2 H); 4.69 (m, 1 H); 4.96 (dd, $J=6.6$, 3.9, 1 H); 5.46 (dd, $J=6.6$, 2.1, 1 H); 5.70 (br. s, 2 H); 5.84 (m, 2 H); 6.08 (d, $J=2.1$, 1 H); 6.82 (d, $J=15.5$, 1 H); 7.07 (t, $J=6.0$, 1 H); 7.17 (d, $J=1.7$, 1 H); 7.35–7.42 (m, 6 H); 7.47–7.52 (m, 4 H); 7.60 (d, $J=15.5$, 1 H); 7.80 (d, $J=1.7$, 1 H); 7.84 (s, 1 H); 8.19 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 25.4; 27.1; 35.9; 37.4; 40.7; 84.1; 84.5; 87.2; 90.3; 110.6; 114.6; 115.4; 117.0; 119.2; 120.2; 122.8; 126.4; 128.5; 129.8; 130.3; 130.5; 138.5; 138.6; 139.8; 141.2; 145.6; 147.9; 149.4; 153.0; 155.3; 162.9; 166.5. HR-MALDI-MS: 730.2993 ($[M+H]^+$, $\text{C}_{40}\text{H}_{40}\text{N}_7\text{O}_7^+$; calc. 730.2989).

9-[(E)-7-[(2,2-Bis(4-methoxyphenyl)-6-[(4-methylphenyl)sulfonyl]-1,3-benzodioxol-4-yl)carbonyl)amino]-5,6,7-trideoxy-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**88**). Compound **34** (160 mg, 0.3 mmol), EDC·HCl (86 mg, 0.45 mmol), *N*-hydroxysuccinimide (46 mg, 0.39 mmol), **20** (100 mg, 0.31 mmol), and Et_3N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO_2 ; $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **88** (146 mg, 62%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +6.9$ ($c=1.53$, CHCl_3). IR (KBr): 3424m, 2930w, 1640s, 1638s, 1607s, 1514s, 1458s, 1374w, 1315m, 1249s, 1209m, 1175s, 1184s, 1090s, 1004m, 833m, 664m, 616w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.38 (s, 3 H); 1.61 (s, 3 H); 2.38 (s, 3 H); 3.80 (s, 6 H); 4.01 (m, 2 H); 4.69 (m, 1 H); 4.94 (dd, $J=6.5$, 3.6, 1 H); 5.45 (dd, $J=6.5$, 2.1, 1 H); 5.77 (m, 2 H); 5.83 (br. s, 2 H); 6.09 (d, $J=2.1$, 1 H); 6.88 (dt, $J=8.7$, 1.8, 4 H); 6.99 (t, $J=5.7$, 1 H); 7.27 (d, $J=7.8$, 2 H); 7.31–7.38 (m, 4 H); 7.48 (d, $J=1.8$, 1 H); 7.83 (d, $J=7.8$, 2 H); 7.84 (s, 1 H); 8.21 (s, 1 H); 8.22 (d, $J=1.8$, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 21.7; 25.4; 27.2; 40.9; 55.4; 84.2; 84.5; 87.2; 90.3; 109.8; 113.7; 114.5; 115.4; 120.1; 121.2; 124.0; 127.7; 128.1; 128.5; 129.8; 130.2; 136.1; 138.2; 139.8; 144.1; 148.1; 148.3; 149.2; 152.4; 155.0; 160.7; 161.6. HR-MALDI-MS: 847.2747 ($[M+H]^+$, $\text{C}_{44}\text{H}_{43}\text{N}_6\text{O}_{10}\text{S}^+$; calc. 847.2761). Anal. calc. for $\text{C}_{44}\text{H}_{42}\text{N}_6\text{O}_{10}\text{S}$ (846.27): C 62.40, H 5.00, N 9.92; found C 62.16, H 5.21, N 9.81.

9-[(E)-5,6,7-Trideoxy-2,3-O-(1-methylethylidene)-7-[(6-[(4-methylphenyl)methyl]-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl)amino]- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**89**). Compound **35** (165 mg, 0.39 mmol), EDC·HCl (115 mg, 0.59 mmol), *N*-hydroxysuccinimide (57 mg, 0.49 mmol), **20** (100 mg, 0.3 mmol), and Et_3N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO_2 ; $\text{CH}_2\text{Cl}_2/\text{MeOH}$ 19:1) afforded **89** (172 mg, 78%). Colorless foam. $[\alpha]_{\text{D}}^{20} = +2.4$ ($c=0.4$, CHCl_3). IR (KBr): 3426m, 3176w, 2986w, 1636s, 1597s, 1529m, 1474s, 1440m, 1374w, 1328w, 1254s, 1207s, 1156w, 1082m, 1049m, 1020m, 868w, 776w, 699m, 642w. $^1\text{H-NMR}$ (300 MHz, CDCl_3): 1.38 (s, 3 H); 1.62 (s, 3 H); 2.29 (s, 3 H); 3.87 (s, 2 H); 4.05 (m, 2 H); 4.71 (m, 1 H); 4.91 (dd, $J=6.4$, 3.6, 1 H); 5.38 (dd, $J=6.4$, 2.4, 1 H); 5.83 (m, 2 H); 6.09 (d, $J=2.4$, 1 H); 6.40 (br. s, 2 H); 6.83 (d, $J=1.8$, 1 H); 7.07 (s, 4 H); 7.14 (t, $J=5.7$, 1 H); 7.33–7.38 (m, 6 H); 7.45–7.49 (m, 5 H); 7.91 (s, 1 H); 8.16 (s, 1 H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): 21.1; 25.4; 27.2; 40.7; 41.3; 84.2; 84.4; 87.1; 90.4; 112.5; 114.7; 114.8; 118.2; 119.9; 122.1; 126.3; 127.7; 128.3; 128.6; 129.1; 129.5; 131.0; 135.7; 136.0; 137.5; 138.9; 140.5; 143.0; 147.3; 148.9; 149.8; 153.8; 163.4. HR-MALDI-MS: 759.2909 ($[M+\text{Na}]^+$, $\text{C}_{43}\text{H}_{40}\text{N}_6\text{NaO}_6^+$; calc. 759.2907). Anal. calc. for $\text{C}_{43}\text{H}_{40}\text{N}_6\text{O}_6$ (736.30): C 70.09, H 5.47, N 11.41; found C 69.89, H 5.60, N 11.33.

9-((E)-5,6,7-Trideoxy-7-((6-(1-methylethyl)-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl)amino)-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**90**). Compound **36** (80 mg, 0.22 mmol), EDC-HCl (64 mg, 0.33 mmol), *N*-hydroxysuccinimide (34 mg, 0.29 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **90** (89 mg, 59%). Colorless foam. $[\alpha]_D^{20} = +5.0$ ($c=0.3$, CHCl₃). IR (KBr): 3424m, 3179w, 2960w, 1645s, 1598s, 1530m, 1475s, 1449m, 1330w, 1255s, 1208s, 1156w, 1081m, 1047m, 1018m, 949w, 867w, 779w, 699w, 642w. ¹H-NMR (300 MHz, CDCl₃): 1.21 (*d*, $J=6.9$, 6 H); 1.37 (*s*, 3 H); 1.62 (*s*, 3 H); 2.88 (*sept.*, $J=6.9$, 1 H); 4.05 (*m*, 2 H); 4.68 (*m*, 1 H); 4.93 (*dd*, $J=6.6$, 3.9, 1 H); 5.44 (*dd*, $J=6.6$, 2.4, 1 H); 5.79 (*br. s*, 2 H); 5.86 (*m*, 2 H); 6.08 (*d*, $J=2.4$, 1 H); 6.92 (*d*, $J=1.5$, 1 H); 7.14 (*t*, $J=5.4$, 1 H); 7.35–7.39 (*m*, 6 H); 7.43 (*d*, $J=1.5$, 1 H); 7.48–7.53 (*m*, 4 H); 7.86 (*s*, 1 H); 8.23 (*s*, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 24.1; 25.5; 27.2; 34.1; 40.7; 84.0; 84.4; 87.0; 90.1; 110.3; 114.7; 118.0; 119.7; 120.1; 126.3; 128.0; 128.3; 128.4; 129.5; 130.8; 139.1; 139.8; 142.7; 143.4; 147.1; 149.3; 152.5; 155.0; 163.5. HR-MALDI-MS: 675.2947 ($[M+H]^+$, C₃₈H₃₉N₆O₆⁺; calc. 675.2931).

9-((E)-5,6,7-Trideoxy-7-((6-((dimethylamino)carbonyl)-2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl)amino)-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**91**). Compound **37** (120 mg, 0.31 mmol), EDC-HCl (90 mg, 0.46 mmol), *N*-hydroxysuccinimide (46 mg, 0.4 mmol), **20** (93 mg, 0.28 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **91** (160 mg, 81%). Colorless foam. $[\alpha]_D^{20} = +7.6$ ($c=0.5$, CHCl₃). IR (KBr): 3425m, 3193w, 2932w, 1639s, 1528m, 1471m, 1449m, 1396w, 1329w, 1263m, 1208s, 1157w, 1082m, 1048m, 1018m, 867w, 781w, 700m, 643w. ¹H-NMR (300 MHz, CDCl₃): 1.38 (*s*, 3 H); 1.61 (*s*, 3 H); 3.02 (*br. s*, 3 H); 3.07 (*br. s*, 3 H); 4.05 (*m*, 2 H); 4.74 (*dd*, $J=7.2$, 3.3, 1 H); 4.91 (*dd*, $J=6.5$, 3.3, 1 H); 5.43 (*dd*, $J=6.5$, 2.0, 1 H); 5.79 (*m*, 2 H); 6.08 (*d*, $J=2.0$, 1 H); 6.18 (*br. s*, 2 H); 7.08 (*t*, $J=5.7$, 1 H); 7.16 (*d*, $J=1.8$, 1 H); 7.35–7.42 (*m*, 6 H); 7.46–7.51 (*m*, 4 H); 7.69 (*d*, $J=1.8$, 1 H); 7.82 (*s*, 1 H); 8.17 (*s*, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.3; 27.0; 35.5; 39.8; 40.6; 84.4; 84.6; 87.5; 90.7; 111.2; 114.5; 114.6; 119.3; 120.1; 122.2; 126.4; 128.0; 128.5; 129.8; 130.3; 130.8; 138.5; 139.9; 145.6; 147.5; 149.1; 151.6; 154.8; 162.7; 170.3. HR-MALDI-MS: 704.2834 ($[M+H]^+$, C₃₈H₃₈N₆O₆⁺; calc. 704.2833).

9-((E)-5,6,7-Trideoxy-7-((2,2-diphenyl-1,3-benzodioxol-4-yl)carbonyl)amino)-2,3-O-(1-methylethylidene)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**92**). Compound **38** (50 mg, 0.157 mmol), EDC-HCl (47 mg, 0.240 mmol), *N*-hydroxysuccinimide (24 mg, 0.210 mmol), **20** (50 mg, 0.150 mmol), and Et₃N (0.1 ml, 0.68 mmol) were reacted according to GP 6. CC (SiO₂; CH₂Cl₂/MeOH 19:1) afforded **92** (69 mg, 73%). Colorless foam. $[\alpha]_D^{20} = -14.3$ ($c=1.0$, CH₃OH). IR (KBr): 3424m, 3175m, 2987w, 1651s, 1532s, 1455s, 1373m, 1246s, 1082s, 867m, 748m. ¹H-NMR (300 MHz, CDCl₃): 1.37 (*s*, 3 H); 1.62 (*s*, 3 H); 4.05 (*m*, 2 H); 4.69 (*m*, 1 H); 4.95 (*dd*, $J=6.5$, 3.7, 1 H); 5.46 (*dd*, $J=6.5$, 2.2, 1 H); 5.61 (*br. s*, 2 H); 5.86 (*m*, 2 H); 6.08 (*d*, $J=2.2$, 1 H); 6.95 (*t*, $J=8.1$, 1 H); 7.02 (*dd*, $J=8.1$, 1.2, 1 H); 7.14 (*t*, $J=5.6$, 1 H); 7.37 (*m*, 6 H); 7.51 (*m*, 4 H); 7.58 (*dd*, $J=8.7$, 1.2, 1 H); 7.84 (*s*, 1 H); 8.20 (*s*, 1 H). ¹³C-NMR (75 MHz, CDCl₃): 25.5; 27.2; 40.7; 84.0; 84.5; 87.1; 90.2; 111.8; 114.6; 115.5; 118.1; 120.1; 122.0; 122.4; 126.3; 128.2; 128.3; 129.5; 130.6; 138.8; 139.6; 144.5; 147.0; 149.3; 153.0; 155.3; 163.2. HR-MALDI-MS: 633.2442 ($[M+H]^+$, C₃₅H₃₃N₆O₆⁺; calc. 633.2461).

9-((E)-5,6,7-Trideoxy-7-((4'-fluoro-4,5-dihydroxy-1,1'-biphenyl-3-yl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**2**). Deprotection of **75** (70 mg, 96 μ mol) according to GP 7 afforded **2** (28 mg, 56%). Colorless solid. t_R 17.8 min. M.p. 144–147°. $[\alpha]_D^{20} = +2.5$ ($c=0.16$, (CH₃)₂SO). IR (KBr): 3407s (*br.*), 1700s, 1641m, 1542w, 1479w, 1314w, 1204s, 1137m, 1050w, 835w, 801w, 725w. ¹H-NMR (500 MHz, CD₃OD): 4.07 (*m*, 2 H); 4.24 (*t*, $J=5.3$, 1 H); 4.52 (*t*, $J=5.3$, 1 H); 4.73 (*t*, $J=4.8$, 1 H); 5.96 (*br. d*, $J=3.3$, 2 H); 6.05 (*d*, $J=4.8$, 1 H); 7.13 (*t*, $J=8.8$, 2 H); 7.20 (*d*, $J=2.0$, 1 H); 7.51 (*d*, $J=2.0$, 1 H); 7.58 (*dd*, $J=8.8$, 5.4, 2 H); 8.23 (*s*, 1 H); 8.37 (*s*, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 41.7; 75.2; 75.6; 86.1; 90.5; 116.4 (*d*, $J=21.3$); 117.0; 117.1; 118.2; 129.3; 129.4; 130.3; 131.0; 132.3; 138.1; 143.0; 147.8; 149.0; 152.6; 149.8; 163.6 (*d*, $J=242.5$); 171.2. HR-MALDI-MS: 523.1731 ($[M+H]^+$, C₂₅H₂₄FN₆O₆⁺; calc. 523.1741).

9-((E)-5,6,7-Trideoxy-7-((4,5-dihydroxy-4'-methyl-1,1'-biphenyl-3-yl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**3**). Deprotection of **76** (70 mg, 97 μ mol) according to GP 7 afforded **3** (28 mg, 56%). Colorless solid. t_R 18.3 min. $[\alpha]_D^{20} = +7.4$ ($c=0.3$, (CH₃)₂SO). IR (KBr): 3397s (*br.*), 1700s, 1640m, 1541w, 1478w, 1430w, 1319w, 1203s, 1137m, 1050w, 973w, 799w, 725w. ¹H-NMR (500 MHz, (CD₃)₂SO): 3.97 (*m*, 2 H); 4.10 (*t*, $J=4.9$, 1 H); 4.37 (*t*, $J=4.9$, 1 H); 4.64 (*t*, $J=5.1$, 1 H);

5.83–5.90 (*m*, 2 H); 5.91 (*d*, *J* = 5.1, 1 H); 7.20 (*d*, *J* = 1.9, 1 H); 7.22 (*d*, *J* = 8.0, 1 H); 7.51 (*d*, *J* = 8.0, 1 H); 7.63 (*d*, *J* = 1.9, 1 H); 8.12 (*br. s*, 1 H); 8.23 (*s*, 1 H); 8.47 (*s*, 1 H); 9.16 (*t*, *J* = 5.5, 1 H); 12.79 (*br. s*, 1 H). ¹³C-NMR (125 MHz, (CD₃)₂SO): 20.6; 40.1; 73.0; 73.9; 84.2; 87.7; 114.8; 114.9; 116.8; 119.0; 125.9; 129.3; 129.5; 130.1; 136.0; 136.7; 141.0; 146.5; 148.9; 149.2; 153.5; 169.6. HR-MALDI-MS: 541.1810 ([*M* + Na]⁺, C₂₆H₂₆N₆NaO₆⁺; calc. 541.1812).

9-[(E)-5,6,7-Trideoxy-7-([2,3-dihydroxy-5-(pyridin-4-yl)phenyl]carbonyl)amino]-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**4**). Deprotection of **77** (35 mg, 49 μmol) according to *GP* 7 afforded **4** (15 mg, 61%). Yellowish solid. *t*_R 10.6 min. [*α*]_D²⁰ = −1.9 (*c* = 0.1, (CH₃)₂SO). IR (KBr): 3384s (*br.*), 1684s, 1633m, 1474w, 1431m, 1321m, 1202s, 1134m, 832w, 723w. ¹H-NMR (500 MHz, (CD₃)₂SO): 4.02 (*m*, 2 H); 4.11 (*t*, *J* = 4.8, 1 H); 4.37 (*m*, 1 H); 4.67 (*t*, *J* = 5.1, 1 H); 5.82–5.94 (*m*, 2 H); 5.91 (*d*, *J* = 5.1, 1 H); 7.52 (*d*, *J* = 1.8, 1 H); 7.85 (*br. s*, 1 H); 8.01 (*d*, *J* = 1.8, 1 H); 8.08 (*d*, *J* = 5.2, 1 H); 8.17 (*s*, 1 H); 8.42 (*s*, 1 H); 8.79 (*d*, *J* = 5.2, 1 H); 9.23 (*t*, *J* = 5.5, 1 H); 9.69 (*br. s*, 1 H); 13.35 (*br. s*, 1 H). ¹³C-NMR (125 MHz, (CD₃)₂SO): 40.1; 72.9; 73.9; 84.1; 87.7; 115.2; 117.0; 117.2; 119.1; 121.8; 124.8; 129.1; 129.6; 140.7; 144.9; 147.3; 149.0; 150.3; 152.6; 154.2; 169.2. HR-MALDI-MS: 528.1607 ([*M* + Na]⁺, C₂₄H₂₃N₇NaO₆⁺; calc. 528.1608).

9-[(E)-5,6,7-Trideoxy-7-([2,3-dihydroxy-5-(1,3-thiazol-2-yl)phenyl]carbonyl)amino]-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**5**). Deprotection of **78** (80 mg, 112 μmol) according to *GP* 7 afforded **5** (43 mg, 75%). Colorless solid. *t*_R 13.1 min. [*α*]_D²⁰ = −10.3 (*c* = 0.1, (CH₃)₂SO). IR (KBr): 3402s (*br.*), 1700s, 1642m, 1597m, 1552w, 1428w, 1318w, 1293w, 1200s, 1136m, 1050w, 837w, 800w, 723m. ¹H-NMR (500 MHz, (CD₃)₂SO): 3.97 (*m*, 2 H); 4.10 (*t*, *J* = 4.9, 1 H); 4.37 (*dd*, *J* = 5.0, 4.9, 1 H); 4.63 (*t*, *J* = 5.0, 1 H); 5.82–5.91 (*m*, 2 H); 5.92 (*d*, *J* = 5.0, 1 H); 7.53 (*d*, *J* = 1.7, 1 H); 7.68 (*d*, *J* = 3.3, 1 H); 7.83 (*d*, *J* = 3.3, 1 H); 7.92 (*d*, *J* = 1.7, 1 H); 8.52 (*s*, 1 H); 8.56 (*br. s*, 1 H); 9.27 (*t*, *J* = 5.7, 1 H); 9.71 (*s*, 1 H); 12.98 (*br. s*, 1 H). ¹³C-NMR (125 MHz, (CD₃)₂SO): 40.1; 73.2; 73.9; 84.3; 87.8; 115.5; 115.8; 115.9; 119.0; 119.6; 123.8; 129.3; 129.6; 141.4; 143.4; 146.8; 148.4; 148.8; 151.5; 152.7; 167.0; 168.9. HR-MALDI-MS: 534.1173 ([*M* + Na]⁺, C₂₂H₂₁N₇NaO₆S⁺; calc. 534.1172).

9-[(E)-7-[(5-Bromo-2,3-dihydroxyphenyl)carbonyl]amino]-5,6,7-trideoxy-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**6**). Deprotection of **79** (50 mg, 70 μmol) according to *GP* 7 afforded **6** (18 mg, 52%). Colorless solid. *t*_R 13.4 min. [*α*]_D²⁰ = −6.7 (*c* = 0.13, (CH₃)₂SO). IR (KBr): 3396m (*br.*), 1699s, 1637m, 1467w, 1426w, 1325w, 1203s, 1135m, 1050w. ¹H-NMR (500 MHz, CD₃OD): 4.03 (*m*, 2 H); 4.23 (*t*, *J* = 5.0, 1 H); 4.52 (*m*, 1 H); 4.72 (*t*, *J* = 4.8, 1 H); 5.92–5.94 (*m*, 2 H); 6.06 (*d*, *J* = 4.8, 1 H); 7.05 (*d*, *J* = 2.3, 1 H); 7.43 (*d*, *J* = 2.3, 1 H); 8.27 (*s*, 1 H); 8.39 (*s*, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 41.6; 75.2; 75.6; 86.1; 90.6; 111.2; 118.2; 120.7; 121.3; 122.3; 130.3; 130.9; 143.4; 147.8; 148.8; 149.6; 150.2; 153.5; 169.9. HR-MALDI-MS: 507.0628 ([*M* + H]⁺, C₁₉H₂₀BrN₆O₆⁺; calc. 507.0627).

9-[(E)-7-[(5-(1,3-Benzothiazol-2-yl)-2,3-dihydroxyphenyl)carbonyl]amino]-5,6,7-trideoxy-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**7**). Deprotection of **80** (83 mg, 108 μmol) according to *GP* 7 afforded **7** (38 mg, 64%). Colorless solid. *t*_R 17.7 min. [*α*]_D²⁰ = +4.0 (*c* = 0.8, (CD₃)₂SO). IR (KBr): 3377s (*br.*), 1685s, 1645m, 1544w, 1436m, 1303m, 1202s, 1137m, 834w, 800w, 759w, 724w. ¹H-NMR (500 MHz, (CD₃)₂SO): 4.01 (*m*, 2 H); 4.13 (*t*, *J* = 4.9, 1 H); 4.39 (*dd*, *J* = 6.7, 4.9, 1 H); 4.66 (*t*, *J* = 5.0, 1 H); 5.80–5.96 (*m*, 2 H); 5.93 (*d*, *J* = 5.0, 1 H); 7.43 (*t*, *J* = 8.0, 1 H); 7.53 (*t*, *J* = 8.0, 1 H); 7.68 (*d*, *J* = 2.0, 1 H); 8.00 (*d*, *J* = 8.0, 1 H); 8.09 (*d*, *J* = 2.0, 1 H); 8.12 (*d*, *J* = 8.0, 1 H); 8.27 (*s*, 1 H); 9.37 (*t*, *J* = 5.3, 1 H); 9.86 (*s*, 1 H); 13.19 (*br. s*, 1 H). ¹³C-NMR (125 MHz, (CD₃)₂SO): 40.7; 73.1; 73.9; 84.2; 87.7; 115.6; 116.4; 117.2; 119.0; 122.2; 122.4; 123.3; 125.1; 126.5; 129.4; 129.5; 134.3; 141.2; 146.9; 148.8; 152.5; 153.1; 153.5; 167.0; 168.7. HR-MALDI-MS: 584.1330 ([*M* + Na]⁺, C₂₆H₂₃N₇NaO₆S⁺; calc. 584.1328).

9-[(E)-7-[(5-Cyano-2,3-dihydroxyphenyl)carbonyl]amino]-5,6,7-trideoxy-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**8**). Deprotection of **93** (51 mg, 70 μmol) according to *GP* 7 afforded **8** (32 mg, 99%). Colorless solid. *t*_R 9.0 min. [*α*]_D²⁰ = −3.0 (*c* = 0.23, Me₂SO). IR (KBr): 3396s (*br.*), 2233w, 1703s, 1639s, 1477w, 1441w, 1303m, 1195s, 1137m, 1050w. ¹H-NMR (500 MHz, CD₃OD): 4.06 (*d*, *J* = 3.7, 2 H); 4.24 (*t*, *J* = 4.9, 1 H); 4.51 (*t*, *J* = 4.9, 1 H); 4.73 (*t*, *J* = 4.6, 1 H); 5.94 (*m*, 2 H); 6.04 (*d*, *J* = 4.6, 1 H); 7.17 (*d*, *J* = 1.8, 1 H); 7.70 (*d*, *J* = 1.8, 1 H); 8.23 (*s*, 1 H); 8.33 (*s*, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 41.7; 75.1; 75.6; 85.9; 90.4; 102.8; 117.6; 119.8; 121.1; 124.4; 130.6; 130.7; 142.5; 148.6; 150.4; 153.5; 154.8; 169.6. HR-MALDI-MS: 454.1466 ([*M* + H]⁺, C₂₀H₂₀N₇O₆⁺; calc. 454.1475).

9-[(E)-5,6,7-Trideoxy-7-([2,3-dihydroxy-5-(trifluoromethyl)phenyl]carbonyl)amino]-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**9**). Deprotection of **82** (75 mg, 100 μmol) according to *GP* 7 afforded **9** (49 mg, 99%). Colorless solid. *t*_R 14.7 min. [*α*]_D²⁰ = −9.2 (*c* = 0.1, (CD₃)₂SO). IR (KBr): 3409s (*br.*), 1670s,

1649m, 1607m, 1545w, 1398w, 1327m, 1194m, 1124m, 1049w, 801w, 725w. ¹H-NMR (500 MHz, CD₃OD): 4.06 (m, 2 H); 4.24 (t, *J* = 5.1, 1 H); 4.52 (m, 1 H); 4.71 (t, *J* = 4.8, 1 H); 5.95 (m, 2 H); 6.06 (d, *J* = 4.8, 1 H); 7.15 (d, *J* = 1.2, 1 H); 7.64 (d, *J* = 1.2, 1 H); 8.29 (s, 1 H); 8.39 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 41.8; 75.3; 75.6; 86.1; 90.6; 115.5 (*q*, *J* = 2.5); 116.4 (*q*, *J* = 5.0); 116.9; 120.8; 121.9 (*q*, *J* = 32.5); 125.7 (*q*, *J* = 269); 130.5; 130.9; 143.4; 147.8; 148.3; 150.3; 153.3; 153.6; 170.1. ¹⁹F-NMR (282 MHz, CD₃OD): –61.6 (s). HR-MALDI-MS: 497.1401 ([*M* + *H*]⁺, C₂₀H₂₀F₃N₆O₆⁺; calc. 497.1396).

9-[(E)-5,6,7-Trideoxy-7-([2,3-dihydroxy-5-(trifluoroacetyl)phenyl]carbonyl)amino]-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**10**). Deprotection of **83** (100 mg, 137 μmol) according to GP 7 afforded **10** (40 mg, 56%). Colorless solid. *t*_R 11.1 min. [*α*]_D²⁰ = +3.3 (*c* = 0.27, Me₂SO). IR (KBr): 3370s (br.), 1699s, 1640s, 1545w, 1439w, 1326m, 1283m, 1202s, 1142s, 1052w, 724w. ¹H-NMR (500 MHz, CD₃OD): 4.05 (d, *J* = 2.2, 2 H); 4.23 (t, *J* = 5.0, 1 H); 4.52 (m, 1 H); 4.72 (t, *J* = 4.9, 1 H); 5.94 (m, 2 H); 6.05 (d, *J* = 4.9, 1 H); 7.18 (s, 1 H); 7.57 (m, 1 H); 8.26 (d, *J* = 4.2, 1 H); 8.38 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 41.6; 75.2; 75.6; 86.1; 90.5; 116.4; 119.2; 119.3; 120.7; 124.4 (*q*, *J* = 286); 126.4; 130.2; 131.1; 143.1; 147.2; 148.6; 150.3; 151.0; 154.0; 170.9. HR-MALDI-MS: 525.1345 ([*M* + *H*]⁺, C₂₁H₂₀F₃N₆O₇⁺; calc. 525.1346).

9-[(E)-5,6,7-Trideoxy-7-([2,3-dihydroxy-5-(pyridin-4-yl)carbonyl]phenyl)carbonyl)amino]-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**11**). Deprotection of **84** (50 mg, 68 μmol) according to GP 7 afforded **11** (18 mg, 50%). Yellowish solid. *t*_R 10.9 min. [*α*]_D²⁰ = +2.9 (*c* = 0.14, (CH₃)₂SO). IR (KBr): 3385s (br.), 1678s, 1637s, 1432w, 1307m, 1201s, 1132m, 1051w, 835w, 723w. ¹H-NMR (500 MHz, CD₃OD): 3.94 (d, *J* = 3.7, 2 H); 4.13 (t, *J* = 5.3, 1 H); 4.39 (t, *J* = 5.3, 1 H); 4.64 (t, *J* = 4.8, 1 H); 5.82 (m, 2 H); 5.93 (d, *J* = 4.8, 1 H); 7.37 (d, *J* = 2.1, 1 H); 7.57 (dd, *J* = 4.6, 1.6, 2 H); 7.71 (d, *J* = 2.1, 1 H); 8.12 (s, 1 H); 8.22 (s, 1 H); 8.65 (dd, *J* = 4.6, 1.6, 2 H). ¹³C-NMR (125 MHz, CD₃OD): 41.7; 75.1; 75.6; 85.9; 90.5; 116.7; 119.6; 120.7; 123.5; 124.5; 127.9; 130.5; 130.7; 142.5; 147.7; 148.1; 150.3; 150.4; 150.5; 155.1; 155.7; 170.2; 194.7. HR-MALDI-MS: 534.1729 ([*M* + *H*]⁺, C₂₅H₂₄N₇O₇⁺; calc. 534.1737).

9-[(E)-7-[(5-Chloro-2,3-dihydroxyphenyl)carbonyl]amino]-5,6,7-trideoxy-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**12**). Deprotection of **85** (70 mg, 105 μmol) according to GP 7 afforded **12** (35 mg, 73%). Colorless solid. *t*_R 13.1 min. [*α*]_D²⁰ = –5.2 (*c* = 0.1, (CH₃)₂SO). IR (KBr): 3396s (br.), 1700s, 1636m, 1542w, 1469w, 1429w, 1326w, 1203s, 1135m, 1050w, 972w, 800w, 725w. ¹H-NMR (500 MHz, (CD₃)₂SO): 3.93 (m, 2 H); 4.09 (t, *J* = 4.9, 1 H); 4.35 (m, 1 H); 4.64 (t, *J* = 5.1, 1 H); 5.78–5.89 (m, 2 H); 5.91 (d, *J* = 5.1, 1 H); 6.92 (d, *J* = 2.5, 1 H); 7.41 (d, *J* = 2.5, 1 H); 8.12 (br. s, 1 H); 8.23 (s, 1 H); 8.46 (s, 1 H); 9.02 (t, *J* = 5.4, 1 H); 12.62 (br. s, 1 H). ¹³C-NMR (125 MHz, (CD₃)₂SO): 40.1; 73.0; 73.9; 84.3; 87.8; 115.7; 116.5; 118.3; 119.1; 121.7; 129.3; 129.4; 141.1; 147.6; 148.8; 148.9; 149.3; 153.4; 168.3. HR-MALDI-MS: 463.1133 ([*M* + *H*]⁺, C₁₉H₂₀ClN₆O₆⁺; calc. 463.1132).

9-[(E)-7-[(5-(Cyclohexylcarbonyl)-2,3-dihydroxyphenyl)carbonyl]amino]-5,6,7-trideoxy-β-D-ribo-5-enofuranosyl]-9H-purin-6-amine (**13**). Deprotection of **86** (60 mg, 81 μmol) according to GP 7 afforded **13** (25 mg, 59%). Colorless solid. *t*_R 14.5 min. [*α*]_D²⁰ = –3.5 (*c* = 0.12, (CH₃)₂SO). IR (KBr): 3388s (br.), 2933m, 1700s, 1638s, 1543w, 1430w, 1326m, 1295m, 1202s, 1130m, 1048w, 837w, 801w, 724w. ¹H-NMR (500 MHz, CD₃OD): 1.23–1.50 (m, 5 H); 1.72–1.83 (m, 5 H); 3.35 (t, *J* = 1.6, 1 H); 4.08 (d, *J* = 3.3, 2 H); 4.25 (t, *J* = 5.0, 1 H); 4.52 (t, *J* = 5.0, 1 H); 4.74 (t, *J* = 4.7, 1 H); 5.96 (m, 2 H); 6.04 (d, *J* = 4.7, 1 H); 7.53 (d, *J* = 2.0, 1 H); 8.02 (d, *J* = 2.0, 1 H); 8.23 (s, 1 H); 8.34 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 26.8; 27.1; 30.8; 41.7; 46.0; 75.1; 75.6; 86.0; 90.5; 116.4; 118.5; 120.7; 128.6; 130.5; 130.9; 142.8; 147.8; 149.7; 150.3; 154.7; 154.9; 170.7; 204.6. HR-MALDI-MS: 539.2244 ([*M* + *H*]⁺, C₂₆H₃₁N₆O₇⁺; calc. 539.2254).

9-[(E)-5,6,7-Trideoxy-7-[(5-[(E)-3-(dimethylamino)-3-oxoprop-1-enyl]-2,3-dihydroxyphenyl)carbonyl]amino]-β-D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**14**). Deprotection of **87** (35 mg, 48 μmol) according to GP 7 afforded **14** (12 mg, 48%). Colorless solid. *t*_R 9.7 min. [*α*]_D²⁰ = –14.2 (*c* = 0.1, Me₂SO). IR (KBr): 3373s (br.), 1696s, 1642s, 1591s, 1499w, 1419w, 1307w, 1264w, 1201m, 1138w, 1052w, 977w, 840w, 800w, 723w, 642w. ¹H-NMR (500 MHz, CD₃OD): 3.05 (s, 3 H); 3.22 (s, 3 H); 4.07 (m, 2 H); 4.24 (t, *J* = 5.0, 1 H); 4.53 (m, 1 H); 4.74 (t, *J* = 4.8, 1 H); 5.95 (m, 2 H); 6.06 (d, *J* = 4.8, 1 H); 6.96 (d, *J* = 15.4, 1 H); 7.25 (d, *J* = 1.8, 1 H); 7.46 (d, *J* = 15.4, 1 H); 7.53 (d, *J* = 1.8, 1 H); 8.26 (s, 1 H); 8.40 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 36.3; 37.9; 41.7; 75.3; 75.8; 86.2; 90.7; 116.5; 116.6; 117.9; 199.9; 120.8; 127.5; 130.4; 131.0; 143.5; 143.6; 147.5; 148.0; 150.2; 152.4; 153.3; 169.3; 171.0. HR-MALDI-MS: 548.1859 ([*M* + Na]⁺, C₂₄H₂₇N₇NaO₇⁺; calc. 548.1864).

9-((E)-5,6,7-Trideoxy-7-((2,3-dihydroxy-5-((4-methylphenyl)sulfonyl)phenyl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**15**). Deprotection of **88** (90 mg, 106 μ mol) according to *GP 7* afforded **15** (61 mg, 98%). Colorless solid. t_R 13.9 min. $[\alpha]_D^{20} = +6.6$ ($c=0.26$, Me₂SO). IR (KBr): 3375s (br.), 1695s, 1639m, 1597m, 1548w, 1467w, 1430w, 1286m, 1201s, 1144s, 1098w, 1051w, 973w, 799w, 723w, 666m. ¹H-NMR (500 MHz, CD₃OD): 2.37 (s, 3 H); 4.05 (m, 2 H); 4.23 (t, $J=4.9$, 1 H); 4.51 (t, $J=4.9$, 1 H); 4.72 (t, $J=4.8$, 1 H); 5.94 (m, 2 H); 6.05 (d, $J=4.8$, 1 H); 7.33 (d, $J=8.2$, 2 H); 7.35 (d, $J=2.2$, 1 H); 7.78 (d, $J=8.2$, 2 H); 7.95 (d, $J=2.2$, 1 H); 8.25 (s, 1 H); 8.38 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 21.51; 41.8; 75.3; 75.6; 86.1; 90.7; 117.0; 117.2; 119.5; 120.8; 128.5; 130.5; 130.8; 131.1; 133.0; 140.5; 143.5; 145.7; 147.7; 148.6; 150.2; 153.5; 154.7; 169.8. HR-MALDI-MS: 583.1600 ($[M+H]^+$, C₂₆H₂₇N₆O₆S⁺; calc. 583.1611).

9-((E)-5,6,7-Trideoxy-7-((2,3-dihydroxy-5-((4-methylphenyl)methyl)phenyl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**16**). Deprotection of **89** (90 mg, 117 μ mol) according to *GP 7* afforded **16** (62 mg, 97%). Colorless solid. t_R 15.8 min. M.p. 119–120°. $[\alpha]_D^{20} = -3.4$ ($c=0.1$, Me₂SO). IR (KBr): 3384s (br.), 1700s, 1640m, 1596m, 1534w, 1513w, 1484w, 1437m, 1324m, 1290w, 1205s, 1133m, 1048w, 972w, 836w, 799w, 725w. ¹H-NMR (500 MHz, CD₃OD): 2.25 (s, 3 H); 3.79 (s, 2 H); 4.03 (m, 2 H); 4.22 (t, $J=5.0$, 1 H); 4.51 (m, 1 H); 4.73 (t, $J=4.9$, 1 H); 5.93 (m, 2 H); 6.05 (d, $J=4.9$, 1 H); 6.76 (d, $J=2.1$, 1 H); 7.04 (s, 4 H); 7.14 (d, $J=2.1$, 1 H); 8.17 (s, 1 H); 8.39 (s, 1 H). ¹³C-NMR (75 MHz, CD₃OD): 21.1; 41.6; 41.9; 75.3; 75.7; 86.2; 90.7; 116.5; 118.8; 120.6; 120.8; 129.7; 130.1; 130.2; 131.2; 133.6; 136.7; 139.7; 143.5; 147.3; 147.6; 148.5; 150.2; 153.4; 171.3. HR-MALDI-MS: 555.1957 ($[M+Na]^+$, C₂₇H₂₈N₆NaO₆⁺; calc. 555.1968).

9-((E)-5,6,7-Trideoxy-7-((2,3-dihydroxy-5-(1-methylethyl)phenyl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**17**). Deprotection of **90** (50 mg, 74 μ mol) according to *GP 7* afforded **17** (29 mg, 85%). Colorless solid. t_R 12.2 min. $[\alpha]_D^{20} = +22.7$ ($c=0.1$, Me₂SO). IR (KBr): 3378s (br.), 2962m, 1700s, 1641m, 1594m, 1542m, 1484w, 1430w, 1323w, 1201s, 1137m, 1049w, 970w, 836w, 800w, 724w, 642w. ¹H-NMR (500 MHz, CD₃OD): 1.21 (d, $J=6.8$, 6 H); 2.79 (sept., $J=6.8$, 1 H); 4.03 (m, 2 H); 4.23 (t, $J=4.9$, 1 H); 4.51 (m, 1 H); 4.73 (t, $J=4.8$, 1 H); 5.94 (m, 2 H); 6.03 (d, $J=4.8$, 1 H); 6.85 (d, $J=2.0$, 1 H); 7.12 (d, $J=2.0$, 1 H); 8.22 (s, 1 H); 8.37 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 24.5; 35.0; 41.6; 75.2; 75.6; 86.1; 90.6; 116.2; 116.3; 118.2; 120.8; 130.2; 131.2; 140.7; 143.2; 147.1; 148.2; 148.7; 150.3; 154.1; 171.5. HR-MALDI-MS: 471.1981 ($[M+H]^+$, C₂₂H₂₇N₆O₆⁺; calc. 471.1992).

9-((E)-5,6,7-Trideoxy-7-((5-((dimethylamino)carbonyl)-2,3-dihydroxyphenyl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**18**). Deprotection of **91** (90 mg, 128 μ mol) according to *GP 7* afforded **18** (54 mg, 86%). Colorless solid. t_R 7.3 min. $[\alpha]_D^{20} = -5.4$ ($c=0.11$, Me₂SO). IR (KBr): 3385s (br.), 1700s, 1605s, 1548w, 1509w, 1478w, 1416w, 1326w, 1296m, 1253w, 1202s, 1137m, 1048w, 972w, 838w, 801w, 725w. ¹H-NMR (500 MHz, CD₃OD): 2.96 (br. s, 6 H); 3.95 (m, 2 H); 4.14 (t, $J=4.9$, 1 H); 4.42 (t, $J=4.9$, 1 H); 4.66 (t, $J=4.8$, 1 H); 5.83 (m, 2 H); 5.96 (d, $J=4.8$, 1 H); 6.92 (d, $J=2.0$, 1 H); 7.29 (d, $J=2.0$, 1 H); 8.15 (s, 1 H); 8.31 (s, 1 H). ¹³C-NMR (125 MHz, CD₃OD): 34.4; 38.8; 40.1; 73.7; 74.2; 84.8; 89.3; 115.1; 116.7; 116.8; 119.3; 126.0; 128.7; 129.4; 142.4; 145.4; 146.1; 148.6; 150.3; 151.5; 169.0; 171.8. HR-MALDI-MS: 500.1894 ($[M+H]^+$, C₂₂H₂₆N₇O₇⁺; calc. 500.1894).

9-((E)-5,6,7-Trideoxy-7-((2,3-dihydroxyphenyl)carbonyl)amino)- β -D-ribo-hept-5-enofuranosyl]-9H-purin-6-amine (**19**). Deprotection of **92** (120 mg, 190 μ mol) according to *GP 7* afforded **19** (60 mg, 74%). Colorless solid. t_R 10.9 min. $[\alpha]_D^{20} = -6.1$ ($c=0.2$, Me₂SO). IR (KBr): 3424s (br.), 1641s, 1604s, 1460w, 1420w, 1340w, 1278m, 1129w, 1050w. ¹H-NMR (500 MHz, (CD₃)₂SO): 3.95 (m, 2 H); 4.11 (t, $J=4.8$, 1 H); 4.37 (m, 1 H); 4.65 (t, $J=5.1$, 1 H); 5.82–5.93 (m, 2 H); 5.93 (d, $J=5.1$, 1 H); 6.69 (t, $J=7.9$, 1 H); 6.92 (dd, $J=7.9$, 1.1, 1 H); 7.31 (dd, $J=7.9$, 1.1, 1 H); 8.23 (s, 1 H); 8.49 (s, 1 H); 8.97 (t, $J=5.4$, 1 H); 12.64 (br. s, 1 H). ¹³C-NMR (125 MHz, (CD₃)₂SO): 40.1; 73.1; 73.9; 84.3; 87.8; 115.0; 117.2; 118.0; 118.9; 119.1; 129.2; 129.6; 141.3; 146.2; 148.9; 149.0; 149.6; 153.2; 169.5. HR-MALDI-MS: 429.1513 ($[M+H]^+$, C₁₉H₂₁N₆O₆⁺; calc. 429.1522).

We thank *F. Hoffmann-La Roche AG*, Basel, for generous support of this work. We are grateful to Dr. *B. Wagner* and Dr. *M. Kansy* for the measurement of pK_a values.

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Received May 11, 2006