Synthesis of Rigid Receptors Based on Triphenylene Ketals

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The synthesis of rigid receptors based on triphenylene ketals, including some improved procedures, is described in detail. Since chemical transformations are strongly influenced by the rigid character and steric bulkiness of the receptors, the construction of a subunit allowing quicker synthetic development is also reported. The preparation of these receptor structures involves an oxidative trimerization and a subsequent repeated isomerization procedure. The scope for the attachment of sterically demanding affinity groups on the receptor scaffold and the corresponding subunit is discussed, and the molecular structures and available space for molecular recognition of the chirally modified systems are outlined by some crystal structures.

Introduction

Groups of appropriate affinity in well defined orientations are key for high selectivity and association constants in artificial receptors.[1,2] Concave receptor structures with rigidly oriented or conformationally locked functional groups are therefore among the most potent systems for molecular recognition.[3–14]

Since many target molecules for sensors exhibit C_3 or *pseudo*-C_3 symmetry, complementary scaffolds with threefold symmetry are popular.[15] An unusual large and rigid backbone providing concave and convergent preorganized functional groups for supramolecular interaction was established by us recently.[16] Based on these functionalized triphenylene ketals, the first artificial caffeine receptors were developed,[17] and chirally modified receptors proved capable of the first enantiofacial discrimination of single heterocyclic guest molecules.[18] The binding modes for such highly dynamic supramolecular aggregates were studied by different spectroscopic means, providing a highly consistent picture in solution and in the solid state.[19]

The synthesis of the scaffold and some receptors have been reported in fragments as preliminary findings. We therefore present detailed procedures for the synthesis of these structures here.[16–19]

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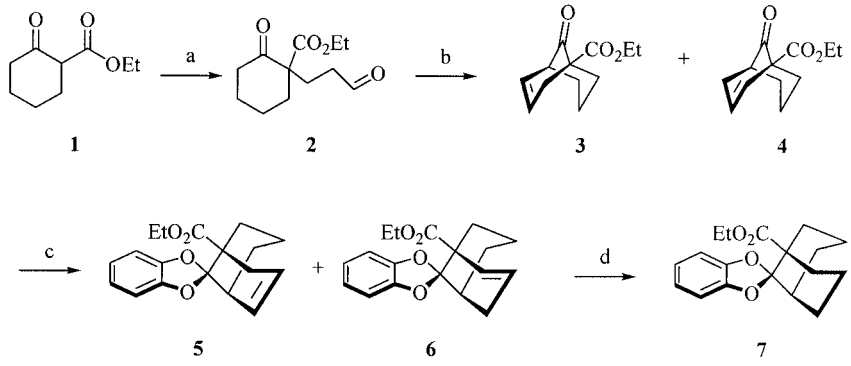
Results and Discussion

Initial investigations into the properties of functionalized triphenylene ketals revealed that the synthesis was easily performed with conformationally flexible moieties on the scaffold,[16] but that almost no preorganization was found because of the conformational freedom of these functional groups. Consequently, the separation of the two isomeric triphenylenes turned out to be challenging. Only the presence of bulky and lipophilic groups on the nonfunctionalized side of the triphenylene ketals gave access to reasonable amounts of isomerically pure scaffolds. The introduction of a bicyclic backbone into the ketal moiety of the platform should overcome several drawbacks: on the one hand the functional group would be centered and conformationally locked, which should provide excellent preorganization, be beneficial for molecular recognition, and suppresses self-aggregation. On the other hand, a defined location of the polar groups would endow the individual isomeric triphenylenes with distinct polarities, which should facilitate efforts at separation. Additionally, a more highly substituted catechol ketal would promise increased hydrolytic stability and would therefore enhance the stabilities of the receptor structures.

Several common bicyclic ketone structures were evaluated. The crucial step is the ketalization with catechol. Sterically demanding adamantane-derived systems, such as the Stetter ketone,[20] which would also give rise to functionalization on both sides of the aromatic plane, resisted all attempts at ketalization. 9-Substituted fluorenones formed catechol ketals, but these intermediates turned out to be too labile for further synthetic transformations. Bicyclo[3.3.1]-nonan-9-one moieties proved to exhibit the subtle balance between synthetic feasibility and robustness of the resulting spiroketals.



Scheme 1. Synthesis of bicyclic spiroketal **7**. a) acrolein, NEt_3, DMF, room temp., 16 h, 92%. b) H_2SO_4, –10 °C → room temp., 22 h, 77%. c) catechol, *p*TsOH, toluene, Dean–Stark trap, 22 h, 84%. d) Pd/C, H_2 (1 atm), THF, 40 h, 100%.

Table 1. Reaction conditions for addition of **1** to acrolein.

Entry	Reagents	Temperature	Reaction time	Yield	Purity (GC)
1	Na, EtOH	–78 °C → room temp.	2 h	71%	90%
2	Al_2O_3	room temp.	5 min	30% (GC)	n.d.[a]
3	NEt_3, DMF	room temp.	16 h	92%	96%

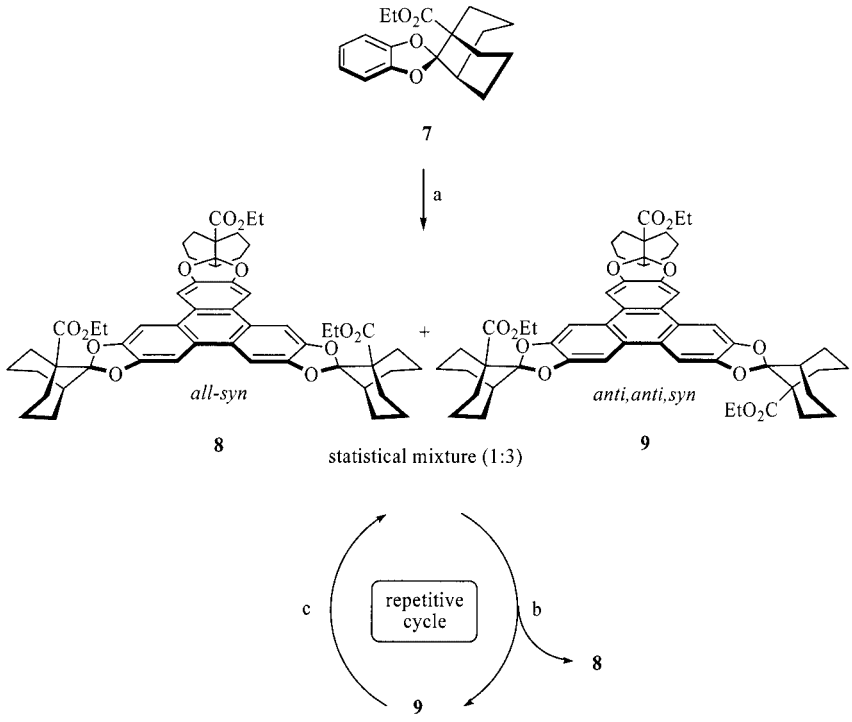
[a] Sluggish crude mixture.

The construction of the bicyclic backbone started with a Michael-type addition of commercially available ethyl 2-oxocyclohexane-1-carboxylate (**1**) to acrolein (Scheme 1).[21,22] Application of the conditions described by Cope and Synerholm,[23] with sodium ethoxide as base, turned out to be difficult due to the sensitivity of aldehyde **2**. The workup required a time-consuming purification by a short-path distillation, only applicable for small quantities (Table 1, Entry 1), so alternative procedures for the synthesis of **2** were considered (Table 1). Adsorption of β-keto ester **1** on aluminium oxide and subsequent treatment with acrolein gave only a 30% yield of the desired compound (Entry 2).[24,25] The conjugate addition method of Fujii et al., with triethylamine as catalyst in DMF, provided aldehyde **2** in excellent amounts as well as in splendid quality (Entry 3),[26] with the crude **2** exhibiting sufficient purity for the next step and the time-consuming short-path distillation therefore no longer being required.

Aldehyde **2** was then subjected to an aldol condensation reaction in concentrated sulfuric acid, resulting in an olefinic mixture. The original procedure published by Cope and Synerholm had delivered only traces of the bicyclic products,[23] but previous reports mentioned this synthetic problem and recommended the use of prolonged reaction times.[27] Best yields were obtained if the aldehyde was added dropwise to concentrated sulfuric acid that had already been chilled to –10 °C.[28] Vigorous mixing by a mechanical stirring device seemed to be essential, since the high viscosities of both reactants impedes the mixing. The reaction mixture was slowly brought to ambient temperature and stirred for a total of 20–22 h in order to provide the best yield. Construction of the catechol moiety was only achieved under acidic conditions with thermal activation. Completion of the ketalization reaction was not observed even when prolonged reaction times were applied or a large excess of catechol was employed. The isomeric catechol ketals **5** and **6** were obtained upon workup as crystalline solids. The mother liquor contained the remaining olefinic mixture **3/4**, which was collected and then exploited for further ketalization processes.

The double bond in the bicyclic moiety is fairly inaccessible. Homogeneous reduction under diverse sets of conditions was unsuccessful, but heterogeneous catalysts enabled a very slow but constantly proceeding hydrogenation reaction. Treatment under high-pressure conditions (up to 200 atm H_2) did not enhance the reaction rate. The hydrogenation process might occur only on the edges and corners of the colloidal palladium crystals, higher catalyst loading and prolonged reaction times therefore being required. Thanks to the clean and smooth reduction, the desired compound was directly obtained by crystallization.

The key step for the construction of the receptor platform is oxidative trimerization, yielding a statistical mixture of the *all-syn* (**8**) and the *anti,anti,syn* (**9**) isomers, in which the undesired less symmetric derivative **9** is the more abundant (Scheme 2). Initially, this transformation was performed by employing $MoCl_5$.[17] Detailed investigations into the stoichiometry of the trimerization indicated that the molybdenum species reacts as a single-electron oxidant and that six equivalents of $MoCl_5$ are therefore necessary for the construction of one triphenylene moiety.[29] A synthesis on large scales would consequently give significant amounts of molybdenum waste, but this might be avoidable by use of an anodic procedure.[30] Electrochemical trimerization could be performed easily even on a 20 g scale and provided the two isomeric triphenylene ketals in an almost statistical ratio. The unusually high yields for this transformation are a consequence of the low solubilities of the formed triphenylene ketals. Precipitation during the electrolysis avoids the overoxidation typical of hexamethoxy-



Scheme 2. Access to *all-syn* triester **8**: a) Pt electrodes, 20 °C, 0.1 M NBu_4BF_4 in H_3CCN, 0.45 A·cm^{-2}, 3.1 F, up to 90%. b) Crystallization from toluene/ethanol (4:1). c) 1. $ClCH_2CH_2Cl$, reflux, 2. F_3CSO_3H, reflux, 15 min., 3. NEt_3, then 0 °C.

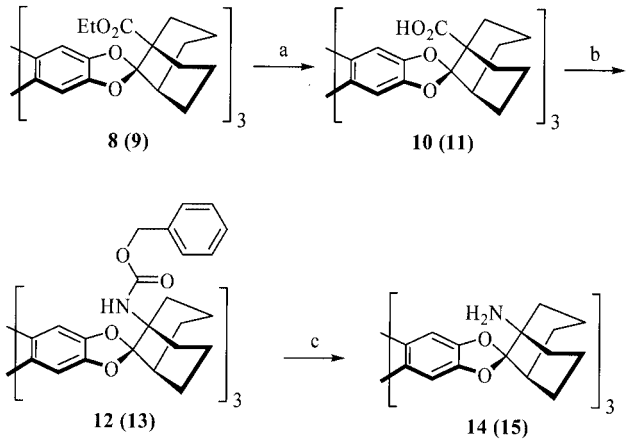
substituted triphenylenes.[31–33] Unfortunately, this limits the application of the electrochemical procedure to rigid substrates such as **7**.[34] Interestingly, the precipitation occurs mainly from solution rather than on the surfaces of the platinum electrodes. This trimerization step was performed galvanostatically under an inert atmosphere in order to prevent molecular oxygen from being incorporated as peroxide bridges and reducing product quality.[35] Addition of aqueous methanol to the electrolyte allowed an easy workup, since the crude triphenylenes could simply be filtered off.

The *all-syn* (**8**) and the *anti,anti,syn* (**9**) isomers were separated by simple crystallization from a toluene/ethanol mixture. The undesired triphenylene ketal **9** can be equilibrated to the statistical mixture of **8** and **9** under strongly acidic reaction conditions (Scheme 2). The less symmetric triphenylene ketal **9** exhibits particularly poor solubility behavior, its highest solubility being found in hot chlorinated solvents, and so only 1,2-dichloroethane was suitable. The loss of material was negligible if the isomerization was performed under strictly anhydrous conditions at elevated temperatures. Since anhydrous trifluoromethanesulfonic acid is difficult to handle, use of mixtures of the acid and its anhydride is highly recommended. Formation of the cationic triphenylene intermediate was indicated by strong coloration of the reaction mixture. The isomerization was quenched at elevated temperature by addition of base, and the repetitive sequence of isomerization of **9** to the statistical mixture, followed by the separation of these isomers, gave access to large amounts of **8**.

In the course of these investigations we also attempted to favor the *all-syn* isomer during the isomerization in order to shift the equilibrium towards the desired isomer. Unfortunately, additives that should form π–π complexes with the triphenylene core, such as 1,3,5-trinitrotoluene (TNT) or (cyclopentadienyl)iron fragments, did not succeed at all. Furthermore, a template-directed oxidative trimerization also failed, since no appropriate triple linker to promote the intramolecular oxidative coupling reaction was found.[36]

Because of the high steric hindrance of the bicyclic backbone, saponification of *all-syn* triester **8** demands hydroxide ions without solvent spheres in order to attack poorly accessible moieties (Scheme 3). These so-called naked hydroxide ions are generated in THF from potassium *tert*-butoxide with a stoichiometric amount of water, as described by Gassmann and Schenck.[37] Alternatively, potassium hydroxide dissolved in DMSO can be employed, but this is a strong oxidant and its application for electron-rich aromatic systems is limited.[38] Tricarboxylic acid **10** could be handled during workup and in solution at ambient temperature or below without decomposition. The water-containing crude triacid **10** was carefully dried at 50 °C in high vacuum. The subsequent Curtius rearrangement was performed under mild conditions by employing the nonexplosive azide-transfer reagent diphenylphosphoryl azide (DPPA), introduced to organic synthesis by Shioiri[39] and obtainable on multigram scales.[40] DPPA activates the free carboxylic acid in the presence of base. The initially formed acyl azide rearranges with the loss of nitrogen upon subsequent heating to afford the isocyanate, which was trapped in situ with benzyl alcohol. The prolonged reaction times reflect the high steric hindrance due to the bicyclic backbone. The Cbz-protected amine **12** can be purified by col-

umn chromatography and represents a stable storage form for the receptor platform. Deprotection was performed with Pearlman's catalyst under standard conditions and yielded the *all-syn* trisamine **14** as a grey, vitreous solid that should be stored under inert atmosphere with exclusion of light. The amino moieties exhibit low nucleophilicity, and transformations with highly reactive compounds such as isocyanates require prolonged transformation times, as described later on.

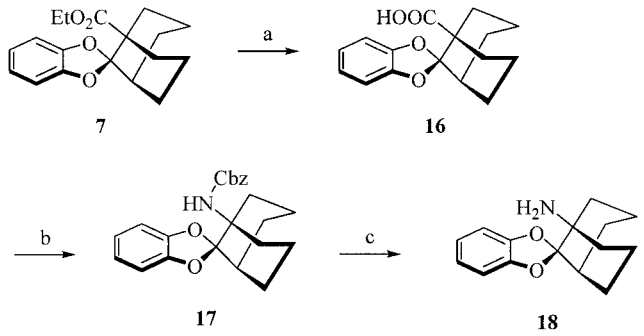


Scheme 3. Synthesis of the modified *all-syn* derivatives (*anti,anti, syn* compounds): a) 1. KO*t*Bu, THF, H_2O, 0 °C, then reflux, 16 h, 2. 0 °C, conc. HCl, **10**: 87% (**11**: 92%). b) 1. Benzene, DMF, DPPA, NEt_3, 0 °C, 30 min., then reflux, 4 h, 2. BnOH, reflux, 36 h, **12**: 81% (**13**: 85%), c) $Pd(OH)_2/C$, H_2, THF, room temp., 48 h, **14**: 99% (**15**: 99%).

These transformations can also be applied to the less symmetric *anti,anti,syn* derivatives **9**, **11**, **13**, and **15**, analogously with the reported reactions for the *all-syn* isomer. Good separation of the isomeric triphenylene compounds at the stage of the triesters **8/9** is important and advantageous, because the Cbz-protected derivatives **12/13** and subsequent isomeric compounds turned out to be chromatographically inseparable.

The corresponding subunit **18** was also prepared in order to develop the reaction conditions for the functional group transformations (Scheme 4). As expected, the yields for the individual steps were higher than those for the trimerized analogues, and furthermore, purification of these compounds was also facilitated. Since less synthetic effort is necessary for **18**, this particular subunit was exploited to elucidate optimal reaction conditions for the attachment of the corresponding hydrogen bonding donor onto the concave platform.

Urea groups on the triphenylene scaffold create good affinity systems for hydrogen bonding to heterocyclic substrates such as caffeine. The first artificial receptor for this alkaloid compound involved *n*-hexyl-substituted urea functions,[17] installation of which was accomplished by treatment of **14** with the corresponding isocyanates (Scheme 6). For the enantiofacial discrimination of single heterocyclic guest molecules α-chiral isocyanates were employed. The efficiency of the chiral interaction with the supramolecular guest is based on repulsive steric interactions.



Scheme 4. Synthesis of subunits: a) 1. KO*t*Bu, THF, H_2O, 0 °C, then reflux, 16 h, 2. 0 °C, conc. HCl, 88%. b) 1. Toluene or benzene, DMF, DPPA, NEt_3, 0 °C, 30 min., then reflux, 3 h, 2. BnOH, reflux, 24–36 h, 92%. c) $Pd(OH)_2/C$, H_2, THF, room temp., 48 h, quantitative.

Some of the employed α-chiral isocyanates in Figure 1 are either commercially available or are known from the literature, whilst full sets of analytical details are given here for compounds **21**–**23**.[41–48] Standard procedures starting from the corresponding optically pure amine included the formation of the individual ammonium chloride and subsequent phosgenation. Distillative workup provided the desired isocyanates.

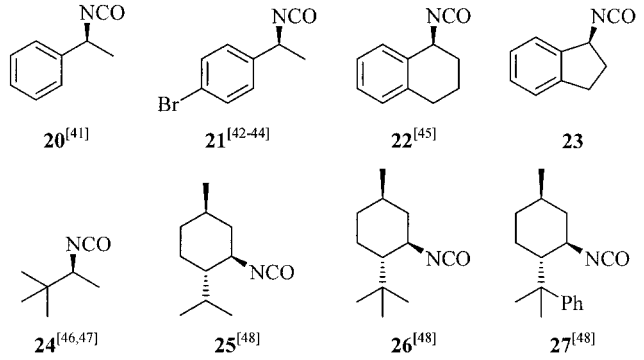
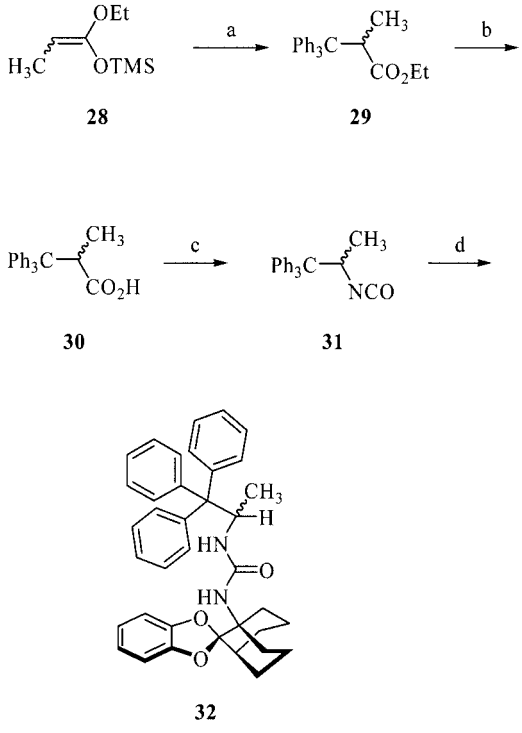


Figure 1. Synthesized optically pure isocyanates.

For further enhancement of the steric repulsion a trityl substituent was considered instead of a *tert*-butyl moiety and the corresponding α-chiral isocyanate was developed.[49] The addition of trityl bromide to diethyl ketene acetals is known.[50,51] In order to circumvent use of the mercury catalyst, trityl tetrafluoroborate[52] was used and the desired trityl ester **29** was obtained in 35% yield. Application of this transformation to the silylated ester enolate **28**,[53] however, doubled the yield of **29** (Scheme 5). Subsequent saponification and resolution of the ester has been described,[54] but procedures using quinine or other standard resolution reagents unfortunately failed in our hands, so we proceeded with the racemic mixture **30**. Curtius rearrangement under mild conditions with DPPA gave the isocyanate **31**, which was treated with the subunit **18** in situ. Despite the expected steric hindrance, **32** was obtained in excellent yield.



Scheme 5. Synthesis of trityl-substituted receptor subunit **32**: a) Et_2O, Ph_3CBF_4, 0 °C → room temp., 1 h, 60%. b) KOH, EtOH, H_2O, reflux, 64 h, 67%. c) Acetone, DPPA, 0 °C, 45 min., then toluene, reflux, 3 h. d) NEt_3, **18**, 0 °C → room temp., 14 d, 89%.

A crystal in which a water molecule was incorporated into a hydrogen bonding pattern with acetone (Figure 2) was obtained from acetone and *n*-hexane. The carbonyl moiety of another acetone molecule forms a hydrogen bond with the NH functional groups of the urea on the receptor subunit, so a mixed solvate was obtained.

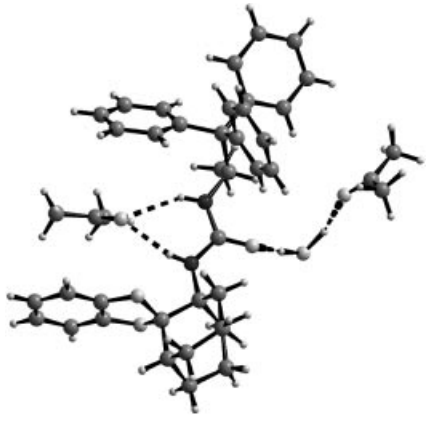
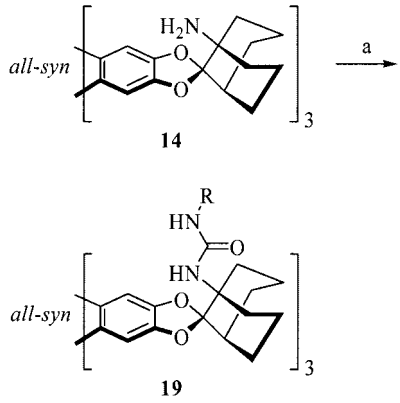


Figure 2. Crystal structure of **32**.

The trityl moieties protrude significantly into the space designed for binding the guest, and treatment of the platform **14** with **31** resulted in an isomeric mixture of receptors. Diagnostic signals in ^1H NMR spectroscopic and mass spectrometric investigations clearly indicated the anticipated structure, but molecular modeling studies indicated that the protruding trityl moieties would require more space than provided by the platform. Most probably the preferential orientation of the urea system would be strongly distorted, so the trityl-modified receptors were not investigated further.

The depicted α-chiral isocyanates (Figure 1) exhibit increasing steric demand in the vicinity of the nitrogen. The bulkiness of both reactants, isocyanate as well as scaffold, results in prolonged reaction times. The urea formation proceeded constantly without interfering side-reactions (Scheme 6).



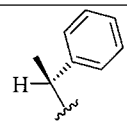
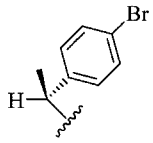
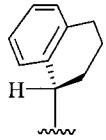
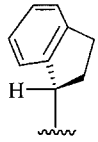
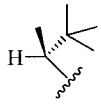
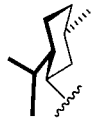
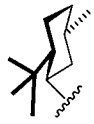
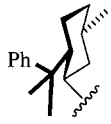
Scheme 6. Synthesis of chirally modified receptors: a) R-NCO, NEt_3, CH_2Cl_2, 0 °C → room temp.

This highly reliable transformation was applied to conversions in which both reactants featured sterically hindered functionalities (Table 2, Entries 7 and 8). The rigid character of the substituents on the urea systems might complicate the purification of the resulting receptors. Compounds **19c** and **19d** form almost capsule-like structures without rotatable side chains. The obtained receptors have poor solubilities that impede chromatographic purification, and in the case of the crude product of **19d** no solvent mixture in which to run analytical characterization in solution could be found. Mass spectrometric investigations indicated the existence of the desired receptor, but without a clear set of data revealing structure and purity, no yield can reliably be given.

The optically pure receptors based on triphenylene ketals (Table 2) were characterized by one- and two-dimensional NMR spectroscopic methods as well as by mass spectrometric investigations.[55] Correct microanalyses for the receptors without incorporated solvent molecules were obtained only in one instance, as the receptors possess not only hydrogen bonding donors in the form of the NH moieties but also a hydrogen bonding acceptor in the carbonyl function of the urea system. The solvent molecules were also detected by NMR and therefore allowed for correct microanalyses.

The α-chiral substituents on the urea moiety have preferential conformations in which the differently sized groups are positioned on opposite sides of the urea moiety. The readily available (*S*)-phenethyl system **19a** turned out not to be efficient for the enantiofacial differentiation of caf-

Table 2. Synthesized optically pure receptors based on triphenylene ketals.

Enry	Compound	R =	Reaction time	Yield
1	**19a**		30 h	79 %
2	**19b**		3 d	92 %
3	**19c**		7 d	38 %
4	**19d**		-	n. d.[a]
5	**19e**		3 d	66 %
6	**19f**		4 d	63%
7	**19g**		6 d	47%
8	**19h**		8 d	87 %

[a] Compound **19d** was obtained as powder without any means of purification.

feine. After complex formation the phenyl groups should occupy an alignment that provides maximum space to the guest, and consequently the opposite sides of the urea system would exhibit similar steric demand. Only with 1,3,5-triacetyl benzene as substrate were suitable crystals for X-ray analysis obtained. In the solid state only one form of the complex was found, in which the guest is slightly distorted (Figure 3).

Unfortunately, no caffeine complexes of **19a** afforded suitable material for crystallographic investigations, and so a *para*-bromophenethyl analogue of the receptor was constructed. The obtained caffeine complex of **19b** had a strongly disordered receptor arm, with standard deviations of binding lengths and angles twice as high as those for the other two arms. Equal binding lengths were assigned to the N–C–N bonds of the imidazole moiety of caffeine, which results in only one diastereomeric form, namely the α-form.[56] As a result of these assumptions other orientations of the bound guest cannot be excluded and might exist in solution with high probability.

The caffeine complexes of **19b** and **19c** each reveal a single orientation of the guest in the solid state. The methyl groups on the guest and the phenyl moieties of the receptors are appropriate oriented for CH/π interactions. The distances found between the methyl carbons of the caffeine and the plane of the corresponding π-system are in the range of 2.87–4.42 Å. Despite the small energy contribution and the weak nature of this attractive interaction,[57] it might explain the enantiofacial preference in the solid state. Initially, the same preference was anticipated for the 1,3,5-triacetyl benzene complexes, but the suitable orientation of the methyl protons is not possible due to the conforma-

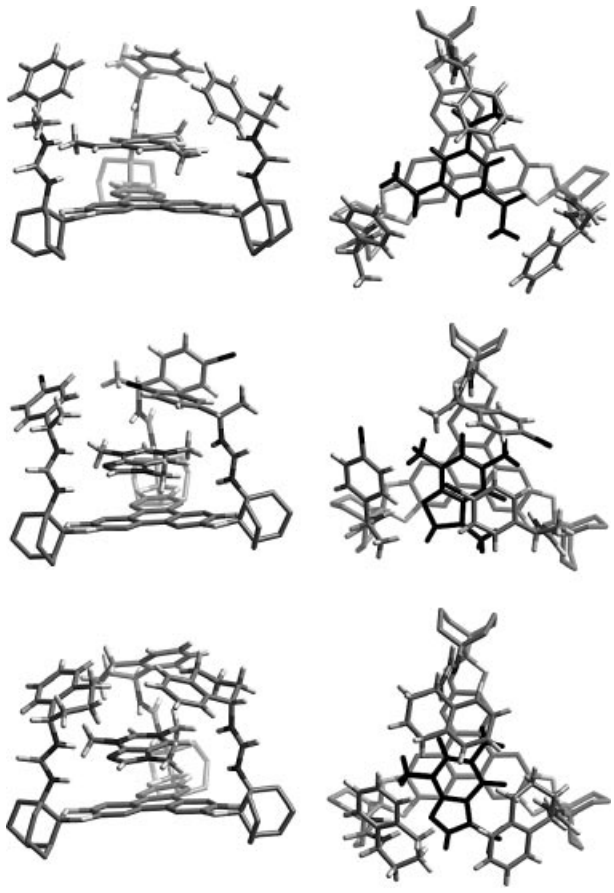


Figure 3. Molecular structures of triacetyl benzene with **19a** (top) and caffeine complexes of **19b** (middle) and **19c** (bottom). Left column: side view of the complexes. Right column: top view.

tional strain of the side chain, so that system is purely based on steric interactions. However, none of these preferences was confirmed in solution, indicating the low impact on the complex dynamic system.

Because of the annulated six-membered ring of the tetralin moiety, both the alkyl groups and the phenylene moiety are conformationally fixed relative to **19a** and **19b**, respectively. When caffeine was placed into receptor **19c** only the α-form was found in the crystal structure. This selectivity seemed to be based on packing effects, because neither molecular modeling studies nor CD-spectroscopic investigations indicated a preference for one of the two possible aggregates.[19]

Receptor **19e** was of special interest, because no aromatic moiety was located in the vicinity of the distal NHs, those further away from the triphenylene plane. Furthermore, the *tert*-butyl moieties extend further into the cavity than the phenyl group does and, indeed, the repulsive interaction between the *tert*-butyl fragments and the N-7 methyl group of the caffeine produced a distinct enantiofacial differentiation.[18] For further improvement of the discrimination we introduced α-chiral moieties reaching far into the cavity. These requirements were met by the two methyl groups of (–)-menthol-derived substructures, and the six-membered ring additionally provided higher conformational stability. However, no significant increase in the enantiofacial differentiation was observed, since the tertiary C–H parts of the isopropyl groups pointed into the coordination area for the guest. By substitution of this unit with an additional methyl group (see **19g**) excellent enantiofacial differentiation both in solution and in the solid state was observed.[18]

In **19h** the C–H unit was substituted by a phenyl group, and we assumed that the phenyl moieties would turn away and would be located outside of the receptor. The repulsive interactions between the arms of the receptor and caffeine should thus result in a further increase in the enantiofacial differentiation, since the methyl moieties should come closer to the moieties of the guest than in the case of **19g**. Surprisingly though, **19h** showed relatively poor host–guest behavior. No suitable crystals with caffeine or another guest were obtained for analytical diffraction methods. Investigations into the supramolecular properties in solution gave a less defined interaction. Subsequent simulation of **19h** by molecular dynamics indicates movements of the phenyl moieties, facilitating the extrusion of the guest and partially occupying the space in the receptor.

Conclusions

Rigid receptors based on a triphenylene core and a bicyclic moiety can be efficiently constructed. The synthesis includes oxidative trimerization of the corresponding catechol ketals, followed by a repetitive separation/isomerization sequence to provide the desired scaffold for the concave architectures. The key intermediate for all receptors is the trisamine **14**, which can be converted into trisureas with sterically very demanding chiral isocyanates. Reaction rates decrease with the steric hindrance, but still allow reliable construction of such bulky systems. With trityl-substituted benzyl or 8-phenylmenthyl moieties the available space in the receptor is not sufficient for supramolecular recognition. When rigid α-chiral groups are present, the solubility behavior becomes poor. Therefore, aliphatic moieties seem to be beneficial. With the established synthetic pathway for these receptor structures based on triphenylene ketals, novel sensors and catalysts are currently being developed and will be reported in due course.

Experimental Section

General Remarks: All reagents were used in analytical grades. Solvents were desiccated if necessary by standard methods. Column chromatography was performed on silica gel (particle size 63–200 μm, Merck, Darmstadt, Germany) with mixtures of cyclohexane or toluene and ethyl acetate as eluents. TLC was performed on silica gel (60 F_{254}) on glass (Merck, Darmstadt, Germany). Melting points were determined on a SMP3 Melting Point Apparatus (Stuart Scientific, Watford, Herts, UK) and were uncorrected. Microanalysis was performed with a Vario EL III instrument (Elementar-Analysensysteme, Hanau, Germany). NMR spectra were recorded on Bruker ARX 300 or AMX 400 machines (Analytische Messtechnik, Karlsruhe, Germany) with TMS as internal standard or $CDCl_3$ and [D_6]DMSO with δ = 7.26 ppm and δ = 2.49 ppm for

^{1}H NMR, respectively, and δ = 77.0 ppm and δ = 39.7 ppm for ^{13}C NMR, respectively. The NMR spectroscopic data are given in ppm. Mass spectra were obtained on a MAT8200 instrument (Finnigan–MAT, Bremen, Germany) for EI, on a QUATTRO LCZ instrument (Waters-Micromass, Manchester, UK) for ESI, or a LAZARUS III–DE device (built in the Institute of Organic Chemistry, Münster, Germany) for MALDI. HRMS data was recorded by the mass spectrometer MicroTof (Bruker Daltronics, Bremen, Germany). Optical rotary power was determined in a 10 cm cell on a 341 Polarimeter (Perkin–Elmer GmbH, Überlingen, Germany).

Aldehyde 2: Ethyl 2-oxo-cyclohexane-1-carboxylate (60.0 g, 352 mmol) and acrolein (29.7 g, 35.3 mL, 530 mmol) were dissolved under argon in DMF (300 mL). Triethylamine (5.3 g, 7.4 mL, 53 mmol) was added, and the reaction mixture was stirred for 16 h at ambient temperature. The mixture was diluted with diethyl ether (500 mL) and water (500 mL), and the organic phase was washed with water (3 × 250 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. The obtained yellow oil (67.3 g, 323 mmol, 92%) was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, CH_3), 1.40–2.70 (m, 12 H, CH_2), 4.20 (q, 2 H, OCH_2), 9.75 (s, 1 H, CHO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (CH_3), 22.4, 26.7, 27.3, 36.4, 39.2, 40.8 (CH_2), 59.7 (OCH_2), 61.3 (C-2), 171.6 (COO), 200.9 (CHO), 207.4 (CO) ppm. MS (EI, 70 eV): *m*/*z* (%) = 226.1 (8) $[M]^+$, 208.1 (5) $[M - H_2O]^+$, 170.1 (100) $[M - C_3H_4O]^+$, 55.0 (50) $[C_4H_7]^+$.

Olefinic Mixture 3/4: Compound **2** (56.7 g, 250 mmol) was added directly over 10 minutes to concentrated sulfuric acid that had already been chilled to –10 °C.[28] During addition the reaction mixture was vigorously stirred with a mechanical stirring device. After 2 h at 0 °C the mixture was allowed to warm to ambient temperature and stirred for 20 h. The black and viscous mixture was poured onto ice (1 kg). After extraction with diethyl ether (3 × 200 mL), the combined organic layers were washed with water (2 × 200 mL), saturated $NaHCO_3$ solution (200 mL), and brine (200 mL), dried ($MgSO_4$), and concentrated in vacuo. The olefinic mixture was purified by short-path distillation (Boiling range: 80–82 °C, 0.08 mbar) and yielded a yellow oil that crystallized upon standing (35.3 g, 170 mmol, 67%). M.p.[23] 46–47 °C. Isomeric ratio: 76:24 (GC). ^{1}H NMR (300 MHz, $CDCl_3$, olefinic mixture): δ = 1.29 (t, $^3J_{H,H}$ = 7.2 Hz, 6 H, CH_3), 1.61–1.72, 1.84–2.08, 2.30–2.95, 3.38–3.45 (4 × m, 18 H, CH_2), 4.22 (q, 4 H, OCH_2), 5.55–5.62, 5.64–5.69 (2 × m, 2 H, CH), 5.96, 6.05 (2 × dt, $^3J_{H,H}$ = 9.8, $^4J_{H,H}$ = 3.6 Hz, 2 H, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, olefinic mixture): δ = 14.0, 14.1 (CH_3), 17.5, 18.2, 33.3, 36.0, 36.7, 36.9, 39.4, 39.6 (CH_2), 45.5, 47.8 (*C*HCO), 58.9, 60.2 (C_q), 61.5, 61.6 (OCH_2), 126.6, 127.1, 129.3, 130.2 (CH), 171.7, 172.2 (CO_2Et), 210.4, 210.5 (CO) ppm. MS (EI, 70 eV): *m*/*z* (%) = 208.0 (67) $[M]^+$, 180.0 (23) $[M - CO]^+$, 162.0 (100) $[M - EtOH]^+$, 134.0 (44) $[M - EtOH - CO]^+$.

Isomeric Catechol Ketals 5/6: The olefinic mixture **3/4** (35.3 g, 167 mmol) was dissolved in toluene (300 mL). After addition of catechol (27.9 g, 253 mmol) and *p*-toluenesulfonic acid (3.0 g, 17.4 mmol), the mixture was heated under reflux, water (3.9 mL) being collected by a Dean–Stark trap. After concentration of the crude mixture under reduced pressure, the resulting oil was fractionated with diethyl ether (700 mL) and sodium hydroxide solution (3%, 200 mL). The organic layer was washed several times with water (5 × 200 mL) and brine (200 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Ethanol (100 mL) was added to the brown oil and spontaneous crystallization occurred. The obtained crystals were filtered off and washed with methanol (43.2 g, 143 mmol, 84%). We recommend recycling of the mother liquor for subsequent ketalizations. M.p. 94–95 °C. Isomeric ratio: 67:33 (GC). ^{1}H NMR (300 MHz, $CDCl_3$, olefinic mixture): δ = 0.88, 0.89 (2 × t, $^3J_{H,H}$ = 7.2 Hz, 6 H, CH_3), 1.44–1.88, 2.02–2.14, 2.22–2.44, 2.70–2.80, 3.04–3.10 (5 × m, 18 H, CH_2), 3.86, 3.88 (2 × q, 4 H, OCH_2), 5.52–5.59, 5.69–5.73 (2 × m, 2 H, CH), 5.98, 6.08 (2 × dt, $^3J_{H,H}$ = 9.9 Hz, 2 H, CH), 6.74–6.77 (br. s, 8 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, olefinic mixture): δ = 13.4 (CH_3), 16.3, 17.0, 25.9, 30.1, 30.5, 31.8, 34.1, 35.7, 36.9, 41.0 (CH_2), 48.8, 51.9 (C_q), 60.6, 60.7 (OCH_2), 107.9, 108.0, 108.1 (arom. CH), 117.9, 118.1 (OCO), 120.6, 120.8, 120.9 (arom. CH), 125.5, 125.7, 128.0, 129.2 (vinyl-CH), 147.3, 147.5, 147.6 (arom. C_q), 172.2, 173.0 (CO_2Et) ppm. MS (EI, 70 eV): *m*/*z* (%) = 300 (100) $[M]^+$, 227 (94) $[M - CO_2Et]^+$, 147 (54) [bicyclo-CO]$^+$. $C_{18}H_{20}O_4$ (300.35): calcd. C 71.98, H 6.71; found C 71.83, H 6.52.

Bicyclic Spiroketal 7: The olefinic mixture **5/6** (20 g, 66.2 mmol) was dissolved in THF (300 mL), and palladium on charcoal (10%, 3 g) was added under argon. The suspension was evacuated and treated with hydrogen (three times). After stirring for 40 h in hydrogen (1 atm) at ambient temperature the mixture was filtered through a silica gel/Celite® pad in order to remove the heterogeneous catalyst. The filter cake was washed thoroughly with dichloromethane and the filtrate was concentrated in vacuo. The remaining oil crystallized spontaneously, yielding a colorless solid (20.3 g, 66.7 mmol, 100%). M.p. 99–101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, $^3J_{H,H}$ = 7.2 Hz, 3 H, CH_3), 1.60–2.56 (m, 13 H, bicyclo-H), 3.83 (q, 2 H, OCH_2), 6.73 (s, 4 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (CH_3), 20.9, 28.7, 32.6 (bicyclo-CH_2), 38.7 (OCH_2), 49.5 (bicyclo-CH), 60.9 (bicyclo-C_q), 108.4 (arom. CH), 119.9 (OCO), 121.1 (arom. CH), 148.2 (arom. C_q), 174.1 (CO_2Et) ppm. MS (EI, 70 eV): *m*/*z* (%) = 302 (100) $[M]^+$, 229 (54) $[M - CO_2Et]^+$, 147 (40) [bicyclo-CO]$^+$. $C_{18}H_{22}O_4$ (302.36): calcd. C 71.50, H 7.33; found C 71.22, H 7.22.

***all-syn* Triester 8 and *anti,anti,syn* Triester 9:** Under an argon atmosphere, **7** (18.1 g, 60 mmol) was dissolved in tetrabutylammonium tetrafluoroborate in acetonitrile (0.1 M, 150 mL) by slightly heating and transferred into an undivided standard electrolysis cell[58] with two platinum sheets as anode and cathode. Galvanostatic electrolysis with a current density of 0.05 A·cm^{-2} was performed at 20 °C. At the beginning we observed the appearance of a green coloration that indicates the presence of radical cations. Vigorous stirring is necessary during the electrolysis; if larger crystalline aggregates of the crude products are formed, they occasionally have to be removed from the anode. After ca. 18000 C (3.1 F·mol^{-1}) had been applied the mixture was transferred into a container with dichloromethane and the solvents were evaporated to dryness. The residue was taken up in dichloromethane (250 mL), and methanol/water (9:1, 800 mL) was added slowly at 0 °C. After the mixture had been stirred for an additional 30 min the precipitate of crude *anti,anti,syn* isomer **9** was filtered off and dried in vacuo and the mother liquor contained mainly *all-syn* isomer **8**. In order to extract the remaining *all-syn* isomer of the precipitate, it was dissolved in toluene (80 mL) and heated at reflux and, after the system had been brought to ambient temperature, ethanol (20 mL) was added dropwise. Precipitation was observed, and was brought to completion by keeping the mixture for 12 h at 0 °C; pure *anti,anti,syn* isomer was filtered off. The mother liquor was concentrated to a third of its volume, and water (120 mL) was slowly added. The solid was filtered off after 10 min. and dissolved in dichloromethane (200 mL). The organic layer was dried ($CaCl_2$), concentrated, and adsorbed on silica gel. In order to circumvent cleavage of the ketal moieties the crude product was purified immediately by column chromatography (toluene to toluene/ethyl acetate, 95:5).

Compound 8: 1.44 g, 1.6 mmol, 8%. M.p. >340 °C (decomp.). R_F = 0.4 (toluene/ethyl acetate, 95:5). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.77 (t, $^3J_{H,H}$ = 6.9 Hz, 9 H, CH_3), 1.75–2.56 (m, 39 H, bicyclo-H), 3.76–3.84 (m, 6 H, OCH_2), 7.69 (br. s, 6 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 21.0, 28.9, 32.8 (bicyclo-CH_2), 39.0 (bicyclo-CH), 49.6 (OCH_2), 61.0 (bicyclo-C_q), 101.0 (arom. CH), 120.8 (bicyclo-OCO), 124.8 (arom. C_q), 148.3 (arom. ketal-C), 174.1 (CO_2Et) ppm. MS (ES+): *m*/*z* (%) = 900.6 (22), 901.6 (20), 902.6 (8), 903.6 (4) [*M* + H]$^+$, 923.6 (100), 924.6 (55), 925.6 (20), 926.6 (10) [*M* + Na]$^+$. $C_{54}H_{60}O_{12}$ (901.05): calcd. C 71.98, H 6.71; found C 71.83, H 6.73.

Compound 9: 13.9 g, 15.4 mmol, 77%. M.p. >340 °C (decomp.). R_F = 0.5 (toluene/ethyl acetate, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.76 (t, $^3J_{H,H}$ = 7.2 Hz, 9 H, CH_3), 1.70–2.55 (m, 39 H, bicyclo-H), 3.77–3.83 (m, 6 H, OCH_2), 7.69 (br. s, 6 H, arom. H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.5, 13.6 (CH_3), 20.6, 28.4, 32.4 (bicyclo-CH_2), 38.5 (bicyclo-CH), 49.2 (OCH_2), 60.6 (bicyclo-C_q), 100.6 (arom. CH), 120.4 (bicyclo-OCO), 124.3 (arom. C_q), 147.8, 147.9 (arom. ketal-C), 173.6, 173.7 (CO_2Et) ppm. MS (ES+): *m*/*z* (%) = 923.3 (100), 924.5 (60), 925.3 (20), 926.3 (5) [*M* + Na]$^+$. $(C_{54}H_{60}O_{12})_2$·EtOH (1848.16): calcd. C 71.49, H 6.87; found C 71.51, H 6.59.

Isomerization of 9: Under an argon atmosphere, **9** (10.0 g, 11.1 mmol) was completely dissolved in 1,2-dichloroethane (500 mL) by heating at reflux. Trifluoromethanesulfonic acid (0.1 mL) was added, and the mixture was heated for an additional 15 min. After quenching with triethylamine (0.4 mL), the mixture was chilled in an ice bath, and then concentrated in vacuo to recover 1,2-dichloroethane. The residue was recrystallized from toluene/ethanol (4:1, 100 mL) and kept at 0 °C for an additional 12–14 h. After removal of the solid containing pure **9** by filtration, the mother liquor was concentrated in vacuo and taken up in dichloromethane (200 mL). The organic layer was dried ($CaCl_2$) and purification was performed as described above, providing **8** (2.3 g, 2.55 mmol, 23%) as an off-white powder.

***all-syn* Tricarboxylic Acid 10:** Compound **8** (15 g, 16.7 mmol) was dissolved in THF (400 mL) with use of a mechanical stirrer, and potassium butoxide (56.1 g, 500 mmol) was added. Addition of water (4.5 mL, 4.5 g, 250 mmol) at 0 °C resulted in clouding of the reaction mixture, which was then heated at reflux for 16 h. For workup the mixture was transferred with additional water into a large flask, and THF was removed under reduced pressure. The slurry was diluted with water (500 mL) and ice (800 mL). Careful addition of concentrated hydrochloric acid brought the mixture to pH 1, and precipitation of the carboxylic acid occurred. After an additional 5 min the pH was monitored and adjusted if necessary. The aqueous layer was extracted with ethyl acetate (4 × 500 mL) and the combined organic layers were washed with water (500 mL) and brine (500 mL), dried (Na_2SO_4), and concentrated, and the resulting solid was dried in high vacuum at 50 °C for 12–14 h.

Isomer *all-syn* 10: 11.9 g, 14.5 mmol, 87%. M.p. 307 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 0.93–2.48 (m, 39 H, bicyclo-H), 7.98 (br. s, 6 H, arom. H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 19.8, 28.1, 31.9 (bicyclo-CH_2), 37.8 (bicyclo-CH), 47.8 (bicyclo-C_q), 101.2 (arom. CH), 120.3 (bicyclo-OCO), 123.9 (arom. C_q), 147.6 (arom. ketal-C), 174.3 (CO_2 H) ppm. MS (ES+): *m*/*z* (%) = 816.5 (20), 817.5 (16), 818.5 (8) [*M* + H]$^+$, 839.5 (100), 840.5 (48), 841.5 (18) [*M* + Na]$^+$. $C_{48}H_{48}O_{12}$·2THF (961.10): calcd. C 69.98, H 6.71; found C 69.94, H 6.68.

Isomer *anti,anti,syn* 11: Compound **9** was treated as for the isomer **10**: 12.6 g, 15.4 mmol, 92%. M.p. 304–308 °C. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 0.95–2.51 (m, 39 H, bicyclo-H), 7.99 (s, 6 H, arom. H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 19.9, 27.9, 31.8 (bicyclo-CH_2), 37.7 (bicyclo-CH), 47.8 (bicyclo-C_q), 101.1 (arom. CH), 120.2 (bicyclo-OCO), 123.9 (arom. C_q), 147.6 (arom. ketal-C), 174.1 (CO_2 H) ppm. MS (ES-): *m*/*z* (%) = 847.3 (1) [*M* + MeOH]$^-$, 815.8 (26), 815.3 (19) [*M* – H]$^-$. HRMS: calcd. for $C_{48}H_{48}O_{12}$ [*M* + Na]$^+$/[*M* – H]$^+$ 839.3043/815.3073; found 839.3038/815.3062.

Cbz-Protected Trisamine 12: Under argon, *all-syn* **10** (10.0 g, 12.2 mmol) was dissolved in benzene (400 mL) and DMF (100 mL). Triethylamine (5.7 g, 7.9 mL, 56.0 mmol) and diphenylphosphoryl azide (13.0 g, 10.8 mL, 47.2 mmol) were added at 0 °C. The reaction mixture was stirred for 30 min. and then heated at reflux for 4 h. After addition of benzyl alcohol (39.0 g, 37.2 mL, 360 mmol) and subsequent heating at reflux for 36 h the reaction mixture was brought to ambient temperature. Volatile components were evaporated under reduced pressure. Abundant benzyl alcohol and remaining DMF were removed by short-path distillation in high vacuum (oil bath: 80 °C, 1·10^{-2} mbar). The viscous residue was taken up in ethyl acetate (300 mL) and 0.1 M hydrochloric acid (150 mL). The organic phase was washed with water (200 mL) and brine (100 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification by column chromatography (cyclohexane/ethyl acetate, 9:1) yielded a yellow solid.

Isomer *all-syn* 12: 11.2 g, 9.9 mmol, 81%. M.p. 268 °C. R_F = 0.36 (cyclohexane/ethyl acetate, 6:4). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.77, 2.05–2.31, 2.65–2.70 (3 × m, 39 H, bicyclo-H), 4.84 (s, 6 H, OCH_2Ph), 7.04–7.08 (m, 15 H, phenyl-H), 7.76 (s, 6 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 28.2, 33.7 (bicyclo-CH_2), 38.2 (bicyclo-CH), 57.8, 57.9 (bicyclo-C_q), 65.3, 66.1 (OCH_2Ph), 101.6 (arom. CH), 121.2 (bicyclo-OCO), 124.7, 124.9, 126.9, 127.8, 128.0, 128.3, 128.5, 136.4 (arom. C_q, phenyl-CH), 140.9 (phenyl-C_q), 147.4 (arom. ketal-C), 155.0 (CO_2Bn) ppm. MS (ES+): *m*/*z* (%) = 1154.7 (100), 1155.7 (80), 1156.7 (35), 1157.7 (15) [*M* + Na]$^+$. $C_{69}H_{69}N_3O_{12}$ (1132.30): calcd. C 73.19, H 6.14, N 3.71; found C 73.08, H 6.32, N 3.38.

Isomer *anti,anti,syn* 13: This isomer was obtained by treatment of **11** as described for **12**: 11.7 g, 10.4 mmol, 85%. M.p. 265–267 °C. R_F = 0.40 (cyclohexane/ethyl acetate, 75:25). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.70–1.78, 2.06–2.33, 2.66–2.71 (3 × m, 39 H, bicyclo-H), 4.85 (s, 6 H, OCH_2Ph), 7.05–7.08 (m, 15 H, phenyl-H), 7.74 (s, 6 H, arom. H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0, 28.2, 33.0, 33.3 (bicyclo-CH_2), 38.3 (bicyclo-CH), 57.8, 58.0 (bicyclo-C_q), 65.3, 66.1 (OCH_2Ph), 101.5, 101.6, 101.6 (arom. CH), 121.1, 121.2 (bicyclo-OCO), 124.7, 124.7, 126.9, 127.6, 127.8, 128.0, 128.0, 128.2, 128.5, 136.4 (phenyl-CH), 140.9 (phenyl-C_q), 147.4, 147.5 (arom. ketal-C), 154.9 (CO_2Ph) ppm. MS (ES+) *m*/*z* (%) = 1156.6 (42), 1155.5 (37), 1154.5 (14) [*M* + Na]$^+$. $C_{69}H_{69}N_3O_{12}$ (1132.30): calcd. C 73.19, H 6.14, N 3.71; found C 73.22, H 6.02, N 3.36.

Trisamine 14: Isomer *all-syn* **12** (6.80 g, 6.00 mmol) was dissolved in THF (250 mL), and Pearlman's catalyst (20% $Pd(OH)_2$ on charcoal, 50% water) was added. The suspension was evaporated and treated with hydrogen (three times). After stirring for 48 h under hydrogen (1 atm) at ambient temperature the mixture was filtered with the aid of a Celite® pad for removing the heterogeneous catalyst. The filter cake was intensively rinsed with dichloromethane and the filtrate was concentrated in vacuo. The trisamine was obtained as an off-white solid.

Isomer *all-syn* 14: 4.37 g, 5.97 mmol, 99%. M.p. >340 °C (decomp.). R_F = 0.0 (ethyl acetate). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92–2.39 (m, 39 H, bicyclo-H), 7.70 (br. s, 6 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.4, 28.4, 36.4 (bicyclo-CH_2), 38.6 (bicyclo-CH), 54.0 (bicyclo-C_q), 100.7 (arom. CH), 122.9 (bi-

cyclo-OCO), 124.4 (arom. C_q), 148.3 (arom. ketal-C) ppm. MS (ES+): *m/z* (%) = 730.6 (100), 731.6 (50), 732.6 (14) $[M + H]^+$. $(C_{45}H_{51}N_3O_6)_2 \cdot 2HCl \cdot H_2O$ (1550.74): calcd. C 69.71, H 6.89, N 5.42; found C 69.95, H 6.92, N 5.13.

Isomer *anti,anti,syn* 15: Isomer **13** was treated as for the isomer **14**: 4.38 g, 5.97 mmol, 99%. M.p. >340 °C (decomp.). R_F = 0.0 (ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–2.42 (m, 39 H, bicyclo-H), 7.72 (s, 6 H, arom. H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 28.6, 36.8 (bicyclo-CH_2), 38.8 (bicyclo-CH), 54.1 (bicyclo-C_q), 100.7 (arom. CH), 122.9 (bicyclo-OCO), 124.4 (arom. C_q), 148.3 (arom. ketal-C) ppm. MS (ES+): *m/z* (%) = 730.5 (4) $[M]^+$. $C_{45}H_{51}N_3O_6 \cdot HCl$ (780.39): calcd. C 70.80, H 6.97, N 5.18; found C 71.15, H 7.12, N 4.77.

Carboxylic Acid 16: This compound was prepared as described for **10**, from **7** (10.0 g, 33 mmol) and potassium butoxide (37.1 g, 330 mmol) in THF (150 mL) with subsequent addition of water (3.0 g, 3.0 mL, 165 mmol). Workup and drying provided 7.3 g (26.5 mmol, 88%). M.p. 217 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60–2.60 (m, 13 H, bicyclo-H), 6.77 (br. s, 4 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.4, 28.2, 32.2 (bicyclo-CH_2), 37.4 (bicyclo-CH), 48.5 (bicyclo-C_q), 108.4 (bicyclo-OCO), 119.1, 121.0 (arom. CH), 147.4 (arom. ketal-C), 178.6 (CO_2 H) ppm. MS (EI, 70 eV): *m/z* (%) = 274 (100) $[M]^+$, 229 (19) $[M - CO_2H]^+$, 165 (16) $[M - C_6H_4O_2]^+$, 147 (51) [bicyclo-CO]$^+$, 109 (28) $[C_6H_5O_2]^+$. $C_{16}H_{16}O_4$ (274.31): calcd. C 70.06, H 6.61; found C 70.10, H 6.33.

Cbz-Protected Amine 17: This compound was prepared analogously to **12**, from **16** (8.0 g, 29.2 mmol) in benzene (200 mL), DMF (10 mL), triethylamine (6.2 mL, 4.4 g, 43.7), diphenylphosphoryl azide (10.4 g, 8.7 mL, 38.0 mmol), and benzyl alcohol (31.5 g, 30.2 mL, 292 mmol), to give **17** as a colorless, viscous oil (10.2 g, 26.9 mmol, 92%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42–1.69, 2.09–2.27, 2.69–2.73 (3×m, 13 H, bicyclo-H), 4.95 (s, 2 H, OCH_2Ph), 6.80 (s, 4 H, phenyl-H), 7.21–7.30 (m, 4 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 28.1, 28.9, 33.8 (bicyclo-CH_2), 37.7 (bicyclo-CH), 57.6 (bicyclo-C_q), 66.2 (OCH_2Ph), 108.9 (bicyclo-OCO), 121.4 (arom. CH), 128.0, 128.2, 128.5 (phenyl-CH), 137.0 (phenyl-C_q), 147.2 (arom. ketal-C), 156.7 (CO_2Bn) ppm. MS (EI, 70 eV): *m/z* (%) = 379 (27) $[M]^+$, 271 (14) $[M - C_6H_4O_2]^+$, 136 (8) $[C_9H_{14}N]^+$, 91 (100) $[PhCH_2]^+$. $C_{23}H_{25}NO_4$ (379.5): calcd. C 72.80, H 6.64, N 3.69; found C 72.81, H 6.71, N 3.76.

Amine 18: This compound was prepared analogously to **14**, from **17** (10.86 g, 28.6 mmol) and Pearlman's catalyst (0.60 g, 20% $Pd(OH)_2$ on charcoal, 50% water) in THF (250 mL) under hydrogen (1 atm). Purification of the crude product could be accomplished by sublimation in high vacuum, yielding **18** as an off-white solid (6.44 g, 26.4 mmol, 91%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.64–2.28 (m, 13 H, bicyclo-H), 6.74–6.81 (m, 4 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.9, 28.8, 36.8 (bicyclo-CH_2), 38.8 (bicyclo-CH), 54.3 (bicyclo-C_q), 108.6 (bicyclo-OCO), 121.3, 122.2 (arom. CH), 148.4 (arom. ketal-C) ppm. MS (EI, 70 eV): *m/z* (%) = 245.2 (42) $[M]^+$, 137.1 (100) $[C_9H_{15}N]^+$, 109.1 (48) $[C_6H_5O_2]^+$. $C_{15}H_{19}NO_3$ (245.3): calcd. C 73.44, H 7.81, N 5.71; found C 73.44, H 7.80, N 5.43.

Phosgenation: Phosgenation was performed according to the literature.[59] The employed optically pure amines were converted into the corresponding ammonium chlorides, which were subsequently treated with either phosgene or diphosgene in toluene. Distillative workup gave the individual isocyanates as colorless liquids.

(–)-(1*S*)-1-Phenethyl Isocyanate (20): The analytical data were in agreement with a commercial sample.

(+)-(1*S*)-1-(4-Bromophenyl)ethyl Isocyanate (21): Compound **21** (19.0 g, 84 mmol, 84%) was obtained from (–)-(1*S*)-(4-bromophenyl)ethylamine (20.0 g, 100 mmol, $[\alpha]^{20}_{589}$ = –20.9, $[\alpha]^{20}_{578}$ = –21.8, $[\alpha]^{20}_{546}$ = –24.9, $[\alpha]^{20}_{436}$ = –43.3, $[\alpha]^{20}_{365}$ = –70.3 (*c* = 2.35, MeOH)), and became solid upon standing (M.p. around room temperature). Boiling range: 123–127 °C (12 mbar). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.54 (d, $^3J_{H,H}$ = 6.9 Hz, 3 H, CH_3), 4.70 (q, 1 H, CH), 7.16–7.20, 7.43–7.48 (2×m, 4 H, arom. H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.8 (CH_3), 53.9 (CH), 121.5 (C–Br), 127.1, 131.7 (arom. CH), 141.3 (arom. C_q) ppm. MS (EI, 70 eV): *m/z* (%) = 227.0 (35), 225.0 (36) $[M]^+$, 212.0 (95), 210.0 (100) $[M - CH_3]^+$, 185.0 (14), 183.0 (15) $[BrC_6H_4CNH]^+$, 146.1 (75) $[M - Br]^+$, 77.1 (31) $[C_6H_5]^+$. $[\alpha]^{20}_{589}$ = +5.0, $[\alpha]^{20}_{578}$ = +5.3, $[\alpha]^{20}_{546}$ = +6.0, $[\alpha]^{20}_{436}$ = +10.3, $[\alpha]^{20}_{365}$ = +15.3 (*c* = 2.04, benzene). C_9H_8BrNO (226.07): calcd. C 47.82, H 3.57, N 6.20; found C 47.80, H 3.57, N 6.20.

(+)-(1*S*)-1,2,3,4-Tetrahydro-1-naphthyl Isocyanate (22): Use of (+)-(1*S*)-1,2,3,4-tetrahydronaphthylamine (15.0 g, 102 mmol, $[\alpha]^{20}_{589}$ = +29.5, $[\alpha]^{20}_{578}$ = +30.9, $[\alpha]^{20}_{546}$ = +34.9, $[\alpha]^{20}_{436}$ = +58.0, $[\alpha]^{20}_{365}$ = +87.9 (*c* = 2.55, MeOH)) yielded **22** (12.7 g, 73 mmol, 72%). B.p. 129 °C (18 mbar). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.72–1.81 (m, 1 H, 3-H), 1.88–2.05 (m, 3 H, 2-H, 3-H), 2.66–2.74 (m, 1 H, 4-H), 2.76–2.84 (m, 1 H, 4-H), 4.65 (t, $^3J_{H,H}$ = 5.2 Hz, 3 H, 1-H), 7.05–7.09 (m, 1 H, 6-H), 7.14–7.19 (m, 2 H, 7-H, 8-H), 7.29–7.34 (m, 1 H, 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2 (C-2), 28.7 (C-4), 31.8 (C-2), 53.1 (C-1), 126.2, 127.7, 128.2, 129.2 (arom. CH), 135.9, 136.1 (arom. C_q) ppm. MS (EI, 70 eV): *m/z* (%) = 173.1 (16) $[M]^+$, 145.0 (21) $[M - CO]^+$, 130.1 (100) $[M - NCO]^+$, 91.1 (16) $[C_7H_7]^+$. $[\alpha]^{20}_{589}$ = +10.7, $[\alpha]^{20}_{578}$ = +11.0, $[\alpha]^{20}_{546}$ = +12.1, $[\alpha]^{20}_{436}$ = +16.9, $[\alpha]^{20}_{365}$ = +17.9 (*c* = 1.15, benzene). $C_{11}H_{11}NO$ (173.21): calcd. C 76.28, H 6.40, N 8.09; found C 76.44, H 6.49, N 7.88.

(+)-(1*S*)-Indanyl Isocyanate (23): This compound was prepared from (+)-(1*S*)-aminoindane (15.0 g, 113 mmol, $[\alpha]^{20}_{589}$ = +18.1, $[\alpha]^{20}_{578}$ = +18.9, $[\alpha]^{20}_{546}$ = +21.0, $[\alpha]^{20}_{436}$ = +31.2, $[\alpha]^{20}_{365}$ = +37.2 (*c* = 2.15, MeOH)), providing **23** (15.5 g, 97 mmol, 86%). B.p. 116 °C (21 mbar). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.95–2.04 (m, 1 H, 2-H), 2.40–2.48 (m, 1 H, 2-H), 2.73–2.81 (m, 1 H, 3-H), 2.93–3.01 (m, 1 H, 3-H), 4.89 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, 1-H), 7.17–7.33 (m, 4 H, arom. H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.9 (C-3), 35.4 (C-2), 58.5 (C-1), 123.5, 124.8, 126.8, 128.3 (arom. CH), 142.2, 142.4 (arom. C_q) ppm. MS (EI, 70 eV): *m/z* (%) = 159.1 (84) $[M]^+$, 117.0 (100) $[M - NCO]^+$, 77.0 (27) $[C_6H_5]^+$. $[\alpha]^{20}_{589}$ = +28.7, $[\alpha]^{20}_{578}$ = +29.6 (*c* = 1.35, benzene). $C_{10}H_9NO$ (159.18): calcd. C 75.45, H 5.70, N 8.80; found C 75.30, H 5.72, N 8.75.

(+)-(2*S*)-1,2,2-Trimethylpropyl Isocyanate (24): This compound was prepared from (+)-(2*S*)-3,3-dimethylbut-2-ylamine (10.0 g, 99 mmol, $[\alpha]^{20}_{589}$ = +18.1, $[\alpha]^{20}_{578}$ = +18.9, $[\alpha]^{20}_{546}$ = +21.0, $[\alpha]^{20}_{436}$ = +31.2, $[\alpha]^{20}_{365}$ = +37.2 (*c* = 2.15, MeOH)) as a solution in toluene (8.9 g, 70 mmol, 71%). Boiling range: 108–116 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (s, 9 H, $C(CH_3)_3$), 1.22 (d, $^3J_{H,H}$ = 6.6 Hz, 3 H, CH_3), 3.31 (q, 1 H, CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.1 (CH_3), 25.9 ($C(CH_3)_3$), 60.9 (CH) ppm. MS (EI, 70 eV): *m/z* (%) = 127.0 (0.2) $[M]^+$, 112 (5) $[M - CH_3]^+$, 99.0 (5) $[M - CO]^+$, 57.0 (100) $[C_4H_9]^+$. $[\alpha]^{20}_{589}$ = +18.4, $[\alpha]^{20}_{578}$ = +19.3, $[\alpha]^{20}_{546}$ = +21.9, $[\alpha]^{20}_{436}$ = +37.7 (*c* = 11.7, toluene).

(*rac*)-1-Methyl-2,2,2-triphenylethyl Isocyanate (31): A toluene extract of the reaction mixture for **32** confirmed the existence of the isocyanate. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (d, $^3J_{H,H}$ = 6.8 Hz, 3 H, CH_3), 4.73 (q, 1 H, CH), 7.03–7.27 (m, 15 H, phenyl) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.3 (CH_3), 58.7 (CH), 70.6 (C_q), 126.5, 127.6, 129.6 (phenyl-CH), 144.5 (phenyl-

C_q). GC-MS (EI+): *m/z* (%) = 298 (55) $[M - CH_3]^+$, 270 (100) $[M - HNCO]^+$, 243 (36) $[Ph_3C]^+$.

Trityl-Modified Subunit 32: 2-Methyl-3,3,3-triphenylpropionic acid (**30**, 486 mg, 1.53 mmol) was dissolved in toluene (10 mL), concentrated under reduced pressure (3×), and then well dried in vacuo. The anhydrous acid was dissolved in toluene (20 mL) by gentle warming. After addition of triethylamine (0.32 mL, 233 mg, 2.30 mmol) and diphenylphosphoryl azide (507 mg, 1.84 mmol) at ambient temperature and stirring for 15 min., the mixture was heated at reflux until gas evaporation was no longer observed (2–3 h) and was then allowed to cool to ambient temperature before being chilled to 0 °C. Compound **18** (250 mg, 1.02 mmol), and afterwards triethylamine (0.14 mL, 103 mg, 1.02 mmol), were added, and the mixture was stirred for 14 d at ambient temperature. After fractionation between ethyl acetate (50 mL) and water (75 mL) the aqueous phase was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Purification was performed by column chromatography (toluene/ethyl acetate, 9:1 → 8:2), yielding a colorless solid (510 mg, 0.91 mmol, 89%). M.p. 107 °C (decomp.). R_F = 0.58 (toluene/ethyl acetate, 8:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (d, $^3J_{H,H}$ = 6.4 Hz, 3 H, CH_3), 1.49–1.54, 1.60–1.66, 1.91–2.14 (3 × m, 11 H, bicyclo-CH_2), 2.20 (br. s, 1 H, bicyclo-CH), 2.38–2.41 (m, 1 H, bicyclo-CH_2), 4.14 (br. s, 1 H, NH_{prox}), 4.52 (d, $^3J_{H,H}$ = 10.0 Hz, 1 H, NH_{dist}), 5.54–5.58 (m, 1 H, CH), 6.25 (d (b), $^3J_{H,H}$ = 7.6 Hz, 1 H, catechol-CH); 6.62–6.75 (m, 3 H, catechol-CH); 7.21–7.35 (m, 15 H, trityl-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.6 (CH_3), 21.1, 21.1, 27.9, 28.0, 32.9, 36.0 (bicyclo-CH_2); 38.3 (bicyclo-CH), 48.0 (CH), 57.7 (bicyclo-C_q), 61.7 (CPh_3), 108.6, 108.6 (catechol-CH), 120.7 (bicyclo-OCO), 120.9, 121.5 (catechol-CH), 126.0, 126.0, 127.8 (trityl-C), 146.4, 147.3 (catechol-C_q), 156.7 (CO) ppm. MS (MALDI, DHB matrix): *m/z* = 559, 560 $[M + H]^+$, 581, 582 $[M + Na]^+$, 597, 598 $[M + K]^+$. $(C_{37}H_{38}N_2O_3)_2{\cdot}H_2O$ (1135.43): calcd. C 78.28, H 6.92, N 4.83; found C 78.23, H 7.18, N 4.40. HRMS: calcd. for $[C_{37}H_{38}N_2O_3 + H^+/Na^+]$ 559.2961/581.2780; found 559.2964/581.2790.

General Procedure for Synthesis of Optically Pure Receptors (19a–19h): The *all-syn* trisamine **14** (1 equiv.) was dissolved in dichloromethane (20 mL) and chilled to 0 °C. After addition of triethylamine (3 equiv.) and *α*-chiral isocyanate (6 equiv.) the reaction mixture was allowed to warm to ambient temperature, stirred for the given time, and then diluted with ethyl acetate (50 mL) and hydrochloric acid (0.2 M, 75 mL). The aqueous phase was extracted with ethyl acetate (3 × 75 mL) and the combined organic layers were washed with brine (2 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product was purified by column chromatography or by crystallization from methanol or ethanol and subsequently dried in high vacuum.

Compounds **19a**, **19e**, **19f**, and **19g** are partially known, so their complete sets of data are given in the Supporting Information (for Supporting Information see also the footnote on the first page of this article).

(+)-(1*S*)-4-Bromophenethyl-Substituted Receptor 19b: Compound **19b** was obtained as a gray solid (348 mg, 0.25 mmol, 92%) from *all-syn* trisamine **14** (200 mg, 0.27 mmol), triethylamine (0.12 mL, 83 mg, 0.82 mmol), and (+)-(1*S*)-1-(4-bromophenyl)ethyl isocyanate (**21**, 372 mg, 1.64 mmol) after stirring for 3 d and purification by column chromatography (toluene/ethyl acetate, 6:4). M.p. 185 °C (decomp.). R_F = 0.16 (toluene/ethyl acetate, 6:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (d, $^3J_{H,H}$ = 6.8 Hz, 9 H, CH_3), 1.66–1.71, 1.98–2.29, 2.86–2.91 (3 × m, 39 H, bicyclo-H), 4.36–4.39 (m, 3 H, CH), 4.58 (br. s, 3 H, NH_{prox}), 4.66 (d, $^3J_{NH,H}$ = 5.6 Hz, 3 H, NH_{dist}), 6.76, 7.05 (2 × d, $^3J_{12,13}$ = 8.4 Hz, 6 H, phenyl-H), 7.69, 7.85 (2 × s, 2 × 3 H, triphenylene-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 21.0 (bicyclo-CH_2), 23.5 (CH_3), 28.2, 28.3, 34.1, 34.2 (bicyclo-CH_2), 38.2 (bicyclo-CH), 50.1 (CH), 57.9 (bicyclo-C_q), 101.8, 102.0 (triphenylene-CH), 120.5 (C–Br), 121.9 (bicyclo-OCO), 124.5, 124.6 (triphenylene-C_q), 127.3, 131.5 (phenyl-CH), 143.2 (phenyl-C_q), 147.4, 147.6 (triphenylene-CO), 156.7 (CO) ppm. MS (ES+): *m/z* (int.) = 1407.4 (11), 1408.4 (9), 1409.4 (11), 1410.4 (9), 1411.4 (5) $[M + H]^+$, 1427.4 (25), 1428.4 (22), 1429.4 (85), 1430.4 (66), 1431.4 (100), 1432.4 (58), 1433.4 (48), 1434.4 (31), 1435.4 (11) $[M + Na]^+$, 1443.4 (16), 1444.4 (11), 1445.4 (51), 1446.4 (40), 1447.4 (65), 1448.4 (43), 1449.4 (38), 1450.4 (20), 1451.4 (8) $[M + K]^+$. $[\alpha]^{20}_{589}$ = +44.1, $[\alpha]^{20}_{578}$ = +46.9, $[\alpha]^{20}_{546}$ = +53.8, $[\alpha]^{20}_{436}$ = +96.5 (*c* = 0.54, CH_2Cl_2). $C_{72}H_{75}Br_3N_6O_9{\cdot}2EtOAc{\cdot}PhCH_3$ (1676.46): calcd. C 62.33, H 5.95, N 5.01; found C 62.35, H 5.91, N 5.21.

(+)-Tetralyl-Substituted Receptor 19c: The compound was obtained as a gray solid (262 mg, 0.21 mmol, 38%) from *all-syn* trisamine **14** (400 mg, 0.55 mmol), triethylamine (0.23 mL, 167 mg, 1.65 mmol), and (+)-(1*S*)-1,2,3,4-tetrahydronaphthyl isocyanate (**22**, 372 mg, 1.64 mmol), stirring for 7 d and purification by column chromatography (cyclohexane/ethyl acetate, 8.2 → 6:4). M.p. 240 °C (decomp.). R_F = 0.20 (cyclohexane/ethyl acetate, 8:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.37 (br. s, 12 H, tetralin-CH_2), 1.65–1.67, 2.00–2.24 (m, 33 H, bicyclo-H), 2.33 (br. s, 6 H, tetralin-CH_2), 2.84 (br. s, 6 H, bicyclo-H), 4.36–4.54 (m, 9 H, tetralin-C*H*NH and N*H*), 6.61 (d, $^3J_{H,H}$ = 7.6 Hz, 3 H, tetralin-C_{ar}H), 6.66, 6.79 (2 × t, $^3J_{H,H}$ = 7.2, $^3J_{H,H}$ = 7.6 Hz, 2 × 3 H, tetralin-C_{ar}H), 6.85 (d, $^3J_{H,H}$ = 7.6 Hz, 3 H, tetralin-C_{ar}H), 7.63 (br. s, 6 H, triphenylene-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.8 (tetralin-CH_2), 21.1, 28.3 (bicyclo-CH_2), 29.1, 30.4 (tetralin-CH_2), 34.5, 34.6 (bicyclo-CH_2), 38.3 (bicyclo-CH), 48.0 (tetralin-CHNH), 58.0 (bicyclo-C_q), 101.6, 101.6 (triphenylene-CH), 121.9 (bicyclo-OCO), 124.6 (triphenylene-C_q), 125.7, 126.6, 128.5, 128.7 (tetralin-CH_{arom}), 137.1, 137.3 (tetralin-C_q), 147.4, 147.4 (triphenylene-CO), 156.9 (CO) ppm. MS (ES+): *m/z* (int.) = 1271.8 (100), 1272.8 (93), 1273.8 (40), 1274.8 (15), 1275.7 (5) $[M + Na]^+$, 1287.8 (5), 1288.8 (5) $[M + K]^+$. $[\alpha]^{20}_{589}$ = +40.2, $[\alpha]^{20}_{578}$ = +42.8, $[\alpha]^{20}_{546}$ = +49.8, $[\alpha]^{20}_{436}$ = +104.9 (*c* = 0.22, CH_2Cl_2). $(C_{78}H_{84}N_6O_9)_2{\cdot}2EtOAc{\cdot}H_2O$ (2693.30): calcd. C 73.14, H 6.96, N 6.24; found C 73.06, H 6.69, N 6.12.

(+)-(1*R*,3*R*,4*S*)-8-Phenylmenthyl-Substituted Receptor 19h: This compound was obtained as a light yellow solid (895 mg, 0.60 mmol, 87%) from *all-syn* trisamine **14** (500 mg, 0.69 mmol), triethylamine (0.30 mL, 208 mg, 2.06 mmol), and (–)-(1*R*,3*R*,4*S*)-8-phenylmenthyl isocyanate (**27**) (1.06 g, 4.11 mmol), stirring for 8 d, and purification by column chromatography (cyclohexane/ethyl acetate, 9:1 → 6:4). M.p. 225 °C (decomp.). R_F = 0.27 (cyclohexane/ethyl acetate, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.40–0.49 (m, 3 H, 14-H_a), 0.68 (d, $^3J_{15,13}$ = 6.4 Hz, 9 H, 15-H,), 0.73–0.83 (m, 3 H, 12-H_a), 0.99 (s, 9 H, 21-/22-H), 1.04–1.08 (m, 3 H, 11-H_a), 1.14 (s, 9 H, 21-/22-H), 1.27–1.36 (m, 3 H, 13-H_a), 1.51–1.65 (m, 18 H, of which 12 H: bicyclo-CH_2 and 6H: 10-H_a, 12-H_e), 1.77–1.83 (m, 6 H, 11-H_e, 14-H_e), 1.96–2.23 (m, 21 H, bicyclo-H), 2.67–2.69 (m, 3 H, 9-H_a), 2.91–2.93 (m, 6 H, bicyclo-CH_2), 3.33–3.38 (m, 6 H, N*H*), 6.49 (t, $^3J_{20,19}$ = 7.2 Hz, 3 H, 20-H), 6.98 (t, $^3J_{19,18/20}$ = 7.6 Hz, 6 H, 19-H), 7.11 (d, $^3J_{18,19}$ = 7.6 Hz, 6 H, 18-H), 7.84, 7.89 (2 × s, 2 × 3 H, triphenylene-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5 (C-21/-22), 20.9, 21.1 (bicyclo-CH_2), 21.8 (C-15), 27.1 (C-11), 28.4, 28.5 (bicyclo-CH_2), 31.0 (C-13), 31.6 (C-21/-22), 34.0 (bicyclo-CH_2), 34.8 (C-12), 35.2 (bicyclo-CH_2), 37.8 (bicyclo-CH), 39.4 (C-16), 44.7 (C-14), 51.4 (C-10), 51.8 (C-9), 57.1 (bicyclo-C_q), 101.9, 102.0 (triphenylene-CH), 121.9 (bicyclo-

OCO), 124.7 (C-20), 124.7 (triphenylene-C_q), 125.2 (C-18), 128.2 (C-19), 147.5, 147.6 (triphenylene-CO), 153.2 (phenyl-C_q), 155.6 (CO) ppm. MS (ES+): *m/z* (int.) = 1502.2 (78), 1503.2 (70), 1504.2 (46), 1505.2 (18) $[M + H]^+$, 1524.1 (91), 1525.1 (100), 1526.1 (53), 1527.1 (20) $[M + Na]^+$, 1540.0 (18), 1541.0 (15), 1542.0 (8) $[M + K]^+$. $[\alpha]_{589}^{20}$ = +278.0, $[\alpha]_{578}^{20}$ = +292.2, $[\alpha]_{546}^{20}$ = +340.3, $[\alpha]_{436}^{20}$ = +684.5 (*c* = 0.54, CH_2Cl_2). $C_{96}H_{120}N_6O_9$·EtOAc (1590.12): calcd. C 75.53, H 8.11, N 5.29; found C 75.35, H 8.03, N 5.25.

X-ray Crystallographic Study: Data sets were collected with Enraf Nonius CAD4 and Nonius KappaCCD diffractometers, in case of Mo-radiation equipped with a rotating anode generator. Programs used: data collection EXPRESS (Nonius B.V., 1994) and COLLECT (Nonius B.V., 1998), data reduction MolEN (K. Fair, Enraf–Nonius B.V., 1990) and Denzo-SMN,[60] absorption correction for CCD data SORTAV[61,62] and Denzo,[63] structure solution SHELXS-97,[64] structure refinement SHELXL-97,[65] graphics SCHAKAL-97 (E. Keller, 1997) and DIAMOND.[66]

X-ray Crystal Structure Analysis for 32: formula $C_{37}H_{38}N_2O_3$·$2C_3H_6O$·H_2O, *M* = 692.87, colorless crystal 0.30 × 0.25 × 0.18 mm, *a* = 13.233(1), *b* = 13.129(1), *c* = 21.811(1) Å, *β* = 97.78(1)°, *V* = 3754.5(4) Å^3, ρ_{calc} = 1.226 g·cm^{-3}, μ = 0.81 cm^{-1}, empirical absorption correction (0.976 *T* ≤ 0.986), *Z* = 4, monoclinic, space group $P2_1/n$ (No. 14), λ = 0.71073 Å, *T* = 198 K, ω and φ scans, 14468 reflections collected (±*h*, ±*k*, ±*l*), $[(\sin\theta)/\lambda]$ = 0.62Å^{-1}, 7624 independent (R_{int} = 0.034) and 5004 observed reflections [$I \geq 2\ \sigma(I)$], 477 refined parameters, *R* = 0.053, wR_2 = 0.133, max. residual electron density 0.34 (–0.32) e·Å^{-3}, hydrogen atoms at nitrogen atoms and water from difference Fourier calculations, other calculated and refined as riding atoms.

X-ray Crystal Structure Analysis for 19a with 1,3,5-Triacetylbenzene: formula $C_{72}H_{78}N_6O_9$·$C_{12}H_{12}O_3$·$1.5CH_2Cl_2$·$2CH_3OH$, *M* = 1567.09, yellow crystal 0.35 × 0.25 × 0.1 mm, *a* = 15.347(2), *b* = 22.926(2), *c* = 24.639(2) Å, *V* = 8669.1(15) Å^3, ρ_{calc} = 1.201 g·cm^{-3}, μ = 14.74 cm^{-1}, empirical absorption correction via ψ scan data (0.627 ≤ *T* ≤ 0.809), *Z* = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, *T* = 223 K, $\omega/2\theta$ scans, 9617 reflections collected (+*h*, –*k*, +*l*), $[(\sin\theta)/\lambda]$ = 0.62Å^{-1}, 9617 independent and 4351 observed reflections [$I \geq 2\ \sigma(I)$], 974 refined parameters, *R* = 0.086, wR_2 = 0.226, max. residual electron density 0.65 (–0.39) e·Å^{-3}, hydrogen atoms at nitrogen atoms from difference Fourier calculations, other calculated and refined as riding atoms, one phenyl group (C62–C67) refined with geometrical constraints and isotropic thermal displacement parameters, one methanol refined with split positions, due to the disorder the accuracy of the analysis is poor.

X-ray Crystal Structure Analysis for 19b with Caffeine: formula $C_{72}H_{75}Br_3N_6O_9$·$C_8H_{10}N_4O_2$·$3C_7H_8$, *M* = 1878.71, colorless crystal 0.45 × 0.30 × 0.10 mm, *a* = 18.464(1), *b* = 22.110(1), *c* = 22.449(1) Å, *V* = 9164.6(8) Å^3, ρ_{calc} = 1.362 g·cm^{-3}, μ = 21.66 cm^{-1}, empirical absorption correction (0.442 ≤ *T* ≤ 0.813), *Z* = 4, orthorhombic, space group $P2_12_12_1$ (No. 19), λ = 1.54178 Å, *T* = 223 K, ω and φ scans, 40740 reflections collected (±*h*, ±*k*, ±*l*), $[(\sin\theta)/\lambda]$ = 0.59 Å^{-1}, 14381 independent (R_{int} = 0.039) and 12443 observed reflections [$I \geq 2\ \sigma(I)$], 1029 refined parameters, *R* = 0.080, wR_2 = 0.226, max. residual electron density 1.11 (–0.67) e·Å^{-3}, hydrogen atoms at nitrogen atoms from difference Fourier calculations, other calculated and refined as riding atoms, caffeine was refined with geometrical constraints and isotropic thermal displacement parameters, one toluene with anisotropic thermal parameters, one with isotropic ones, and the third with a common isotropic one, the last two also with geometrical constraints; due to the disorder the accuracy of the analysis is poor.

X-ray Crystal Structure Analysis for 19c with Caffeine: formula $C_{78}H_{84}N_6O_9$·$C_8H_{10}N_4O_2$, *M* = 1443.71, colorless crystal 0.45 × 0.20 × 0.20 mm, *a* = 11.243(1), *b* = 14.238(1), *c* = 23.644(1) Å, *β* = 90.87(1)°, *V* = 3784.4(5) Å^3, ρ_{calc} = 1.267 g·cm^{-3}, μ = 0.85 cm^{-1}, empirical absorption correction (0.963 ≤ *T* ≤ 0.983), *Z* = 2, monoclinic, space group $P2_1$ (No. 4), λ = 0.71073 Å, *T* = 198 K, ω and φ scans, 30634 reflections collected (±*h*, ±*k*, ±*l*), $[(\sin\theta)/\lambda]$ = 0.66 Å^{-1}, 16570 independent (R_{int} = 0.047) and 12402 observed reflections [$I \geq 2\ \sigma(I)$], 991 refined parameters, *R* = 0.051, wR_2 = 0.119, max. residual electron density 0.43 (–0.23) e·Å^{-3}, hydrogen atoms at nitrogen atoms from difference Fourier calculations, other calculated and refined as riding atoms.

CCDC-261423 (for **32**), -261424 (for **19a** with 1,3,5-triacetylbenzene), -261425 (for **19b** with caffeine), and -261426 (for **19c** with caffeine) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(1223)336-033, E-mail: deposit@ccdc.cam.ac.uk].

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