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Intramolecular [2+2] Photocycloaddition Reactions as an Entry to the 2-Oxatricyclo[4.2.1.0^{4,9}]nonan-3-one Skeleton of Lactiflorin

Ping Lu, Eberhardt Herdtweck, and Thorsten Bach*[a]

Abstract: Two [2+2] photocycloaddition routes were evaluated as possible ways to access the tricyclic core structure found in the terpene monoglycoside lactiflorin. While the first route via γ-substituted cyclopentenones was quickly discarded, the reactions of racemic (5*R**)-3-benzyloxy-5-but-3′-enyl-4-methoxycarbonylfuran-2(5*H*)-ones proceeded in high yields and with perfect diastereoselectivity. However, it turned out that the regioselectivity was strongly dependent on the substitution pattern within the but-3′-enyl chain, which connects the terminal olefinic double bond to the photoexcited butenolide chromophor. If the chain was unsubstituted or if a *tert*-butyldimethylsilyloxy group was placed at the 2′ position in a *syn*-relationship to the existing stereogenic center (5*R**,2′*S**), the crossed product prevailed with regioselectivities of 89:11 to 69:31. If the *tert*-butyldimethylsilyloxy group was positioned at 2′ in an *anti*-relationship to the existing stereogenic center (5*R**,2′*R**), the desired straight products were obtained in regioselectivities of 74:24 to 55:45 (61–83% yield). Following this route, the aglycon part of lactiflorin was obtained by an intramolecular [2+2] photocycloaddition and a subsequent hydrogenolysis in 53% yield. Its further conversion into the natural product after glycosylation included a methyl addition to the lactone carbonyl group, which was optimized to give the desired key intermediate in a yield of 70%. The further conversion to lactiflorin was achieved in four steps and with an overall yield of 49%.

Keywords: cycloaddition · glycosylation · photochemistry · regioselectivity · total synthesis

Introduction

Terpenoid natural products frequently display a cyclobutane ring as part of their structure, the formation of which occurs biosynthetically by olefinic attack at a cationic carbon center.[1] Synthetic access to cyclobutanes has been achieved in many total syntheses by inter- and intramolecular [2+2] photocycloaddition reactions of cyclic α,β-unsaturated carbonyl compounds.[2,3] Intermolecular [2+2] photocycloaddition reactions offer more versatility in the choice of potential substrates but they lack the regioselectivity, which is commonly associated with intramolecular [2+2] photocycloaddition reactions.[4] For the latter reactions, the formation of five-membered rings seems to be generally favored[5] as a consequence of a fast ring closure from an intermediate excited triplet species.[6] Exceptions to this 'rule of five' are known,[7] although it is difficult to predict when to expect these exceptions.

The unique structure of (+)-lactiflorin (**1**) as proposed by Liang et al.[8] made this monoterpene glycoside an intriguing target for total synthetic studies. The fact that two additional alternative structures could be found in the literature for this compound[9] added further zest to the synthetic efforts, which we recently completed successfully.[10] The structure of the natural product, as it was eventually proven by synthesis, is depicted in Figure 1.

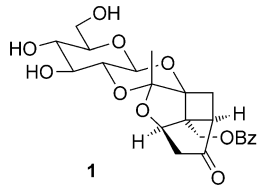

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Figure 1. Absolute and relative configuration of (+)-lactiflorin (**1**) as established by total synthesis.

Regarding the synthesis of lactiflorin it is apparent that the molecule can be dissected into a glycosidic part, which is derived from D-glucose, and an aglycon, which bears an interesting 2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one skeleton. Retrosynthetically, a further disconnection of the tricyclic skeleton invites the use of intramolecular [2+2] photocycloaddition reactions. The core structure **A**, as depicted in Scheme 1, can be disconnected horizontally to provide precursors of type **B** or vertically to lactones of type **C**. In both cases the stereogenic center within the five-membered ring was expected to provide a high facial diastereoselectivity. In addition, the previously mentioned 'rule of five'[5] appeared

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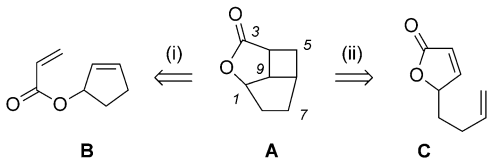
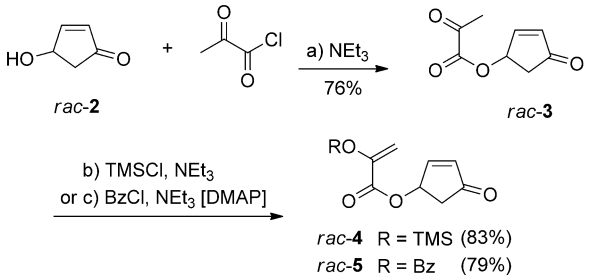


Scheme 1. Retrosynthetic disconnection of the 2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one core (**A**) related to the lactiflorin aglycon.



Scheme 2. Preparation of substrates *rac*-**4** and *rac*-**5** for an intramolecular [2+2] photocycloaddition according to disconnection (i) (Scheme 1). Exact reaction conditions: a) NEt_3 (1.5 equiv), $CH_3COCOCl$ (2 equiv), CH_2Cl_2, 0 °C→rt, overnight, 76 %; b) TMSCl (1.3 equiv), NEt_3 (1.5 equiv), CH_2Cl_2, 0 °C→rt, overnight, 83 %; c) BzCl (2 equiv), NEt_3 (3 equiv), DMAP (0.5 equiv), CH_2Cl_2, 79 %. Bz = benzoyl, DMAP = 4-dimethylaminopyridine, TMS = trimethylsilyl.

to make the formation of the desired regioisomer likely. The simple diastereoselectivity in [2+2] photocycloaddition reactions is determined by the geometric restrictions of the cyclobutane ring and five-membered rings are normally found to be *cis*-anellated to the four-membered ring.[2,11]

Further considerations concerned the introduction of the functional group at C-7. In compounds of type **B** it seemed reasonable to introduce the keto group from the very beginning because cyclopentenones are known to be excellent substrates for [2+2] photocycloaddition reactions.[2] In compounds of type **C** the introduction of a vinyl ketone at an early stage was discouraged due to its sensitivity to nucleophilic attack and due to its undesired, long-wavelength absorption. It seemed therefore sensible to introduce the functional group at C-7 as protected hydroxy group.

In this manuscript we describe in detail our photosynthetic studies towards the core of lactiflorin. It turned out that the disconnection according to (i) in Scheme 1 was not feasible and, even more surprisingly, that the disconnection according to (ii) led to severe regioselectivity issues in the [2+2] photocycloaddition. In addition, we discuss the final stages of our enantioselective lactiflorin synthesis complementing our previous communication[10] on this topic.

Results and Discussion

Access to Precursors of Type B

The syntheses of γ-substituted cyclopentenones of type **B** commenced with the known enone 4-hydroxy-2-cyclopenten-1-one (*rac*-**2**)[12] (Scheme 2). Esterification with pyruvic acid chloride afforded *rac*-**3**, which was exposed to TMSCl or BzCl under basic conditions furnishing the corresponding enol derivatives *rac*-**4** or *rac*-**5** in high yields.

Pyruvate-derived silyl enol ethers have been shown to be reliable olefin components in intermolecular [2+2] photocycloaddition reactions with quinolone or cyclohexenone.[13] The intramolecular reaction of *rac*-**4** or *rac*-**5** was not feasible, however. The irradiation of *rac*-**4** at $\lambda = 254$ nm or $\lambda = 300$ nm led exclusively to its decomposition. We initally assumed that the low chemoselectivity may be attributable to the labile trimethylsilyl group. Disappointingly, precursor *rac*-**5**, in which the trimethylsilyl group was replaced by a more stable benzoyl group, did not give any isolable cycloaddition products either. For both substrates the irradiation conditions (solvent, wavelength, and sensitizer) were broadly varied. The most likely reason for the failure of the reaction appears to be the limited conformational freedom of the carboxylate linkage, which prevents a proper positioning of the acrylate double bond to the photoexcited enone. Indeed, there is no precedent for this type of ring closure in the literature.

Preliminary Experiments with Substrates of Type C

The intramolecular reaction of substrates of type **C** was slightly better precedented. In our own work on tetronate [2+2] photocycloadditon chemistry, we had successfully employed a γ-butenyl-substituted tetronate that produced a diastereomerically pure product in good yield (75 %).[14] The regioselectivity was in line with the 'rule of five' and only a straight [2+2] photoproduct could be detected. Support for a successful [2+2] photocycloaddition was also found by previous [2+2] photocycloaddition reactions of other γ-butenyl-substituted α,β-unsaturated γ-lactones (butenolides)[15] and by a related intramolecular allene [2+2] photocycloaddition.[16] In the work of Figueredo, Font et al. three γ-substituted α,β-unsaturated butenolides were studied. The [2+2] photocycloaddition proceeded with high diastereoselectivity and with a clear preference for the straight product.[15c]

α,β,γ-Trisubstituted α,β-unsaturated lactones *rac*-**8** and *rac*-**10**, unsubstituted at the allylic position, were chosen as initial model substrates of type **C**. The syntheses began with the known β-hydroxy ester methyl 3-hydroxyhept-6-enoate (*rac*-**6**)[17] (Scheme 3). Cyclization of an in situ generated 1,3-bis(silyloxy)alk-1-ene with oxalyl chloride provided butenolide **7**.[18] The latter was subsequently *O*-benzylated, giving lactone *rac*-**8** in 71 % yield. Butenolide *rac*-**10** was obtained in a three-step sequence involving saponification, reduction to primary alcohol,[19] and benzoylation in 47 % overall yield.

Irradiation of *rac*-**8** smoothly afforded [2+2] photocycloaddition products at $\lambda = 300$ nm in moderate to excellent yields (entries 1–6, Table 1). Various solvents were screened and the reaction provided the best yield when acetonitrile was used as solvent together with acetone as sensitizer

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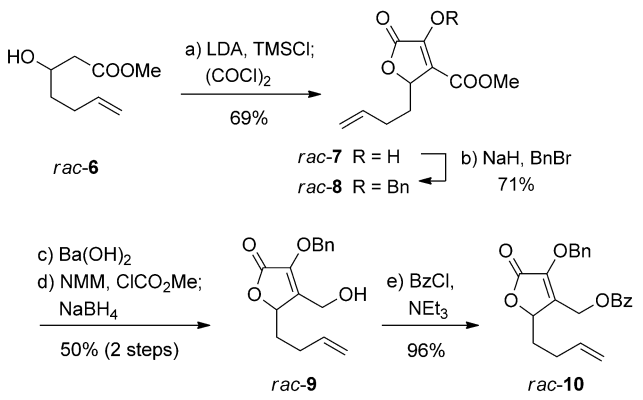
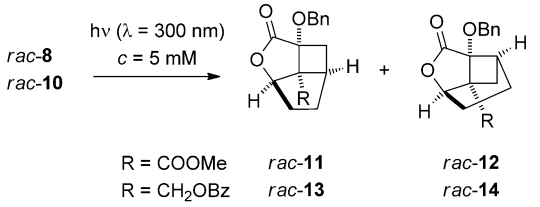


Scheme 3. Preparation of [2+2] photocycloaddition substrates from β-hydroxyketoester *rac*-**6**. Exact reaction conditions: a) LDA (2.2 equiv), TMSCl (2.5 equiv), THF, −78 °C→rt, 19 h; then $(COCl)_2$ (1 equiv), CH_2Cl_2, −78 °C→rt, 21 h, 69 %; b) NaH (2 equiv), BnBr (2 equiv), DMF, rt, 21 h, 71 %; c) $Ba(OH)_2{\cdot}8H_2O$ (5 equiv), THF/H_2O, 48 h, 74 %; d) NMM (1 equiv), $ClCO_2Me$ (1 equiv), THF, −10 °C, 0.5 h; then $NaBH_4$ (3 equiv), MeOH, 0 °C, 0.5 h, 68 %; e) BzCl (1.5 equiv), DMAP (0.2 equiv), NEt_3 (2 equiv), CH_2Cl_2, 0 °C → rt, 1 h, 96 %. Bn = benzyl, LDA = lithium diisopropylamide, NMM = *N*-methylmorpholine.

Table 1. Preliminary [2+2] photocycloaddition experiments with substrates *rac*-**8** (R = COOMe) and *rac*-**10** (R = CH_2OBz).

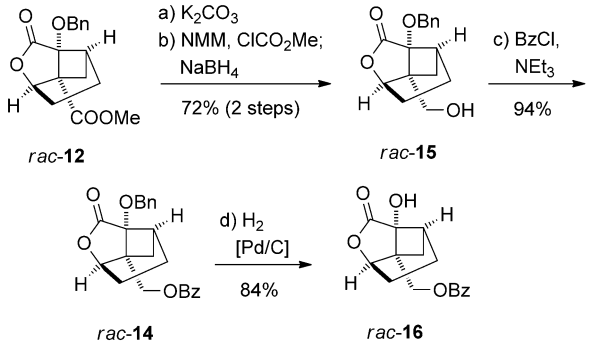


Entry[a]	Substrate	Solvent(s)	*t* [h][b]	Product [*rac*-]	Yield [%][c]	r.r.[d]
1	*rac*-**8**	Et_2O	3	**11**:**12**	53	19:81
2	*rac*-**8**	toluene	3	**11**:**12**	75	25:75
3	*rac*-**8**	MeOH	3	**11**:**12**	46	26:74
4	*rac*-**8**	CH_2Cl_2	3	**11**:**12**	86	26:74
5	*rac*-**8**	ac	0.5	**11**:**12**	92	15:85
6	*rac*-**8**	MeCN/ac	1.5	**11**:**12**	97[e]	18:82
7	*rac*-**10**	CH_2Cl_2	22	**13**:**14**	70	31:69
8	*rac*-**10**	CH_2Cl_2/ac	8	**13**:**14**	70	33:67
9	*rac*-**10**	MeCN/ac	2	**13**:**14**	78[f]	33:67
10	*rac*-**10**	MeCN/ac[g]	2	**13**:**14**	63	35:65

[a] All reactions were conducted using a RPR-100 reactor with 16 Rayonet RPR-3000 Å lamps (Duran filter) as the irradiation source in deaerated solvent ($c = 5$ mM). Solvent mixtures included acetonitrile/acetone (11:1) or dichloromethane/acetone (1:1). [b] Elapsed reaction time to achieve 100 % conversion of the starting material. [c] The product yield was determined by crude NMR using mesitylene as internal standard. [d] The regioisomeric ratio (r.r.) of the crude product was determined by ^1H NMR spectroscopy. [e] 91 % Yield in a preparative run. [f] 70 % Yield in a preparative run. [g] The reaction was performed in quartz but not in Duran tubes.

(ratio 11:1; entry 6, Table 1). In contrast to the above-mentioned literature precedent,[14–16] the main product in these reactions was found to be the crossed product *rac*-**12** (see below). The regioisomeric ratio (r.r. = *rac*-**11**:*rac*-**12**) varied minimally ranging from 26:74 in MeOH and CH_2Cl_2 (entries 3 and 4, Table 1) to 15:85 in acetone (entry 5, Table 1). The reaction was much slower without acetone as sensitizer but the sensitization did not significantly change the regioselectively. Sensitization also helped to increase the reaction rate in the [2+2] photocycloaddition of the benzoyloxymethyl-substituted substrate *rac*-**10** (entries 7–10, Table 1). The relative ratio of straight-to-crossed isomer (*rac*-**13**:*rac*-**14**) was slightly enhanced compared with *rac*-**8** but still remained unfavorable in view of the intended application. These preliminary experiments were performed only on analytical scale but it was shown for the best examples (entries 6 and 9, Table 1) that yields of isolated products are in the same range as the NMR yields.

The separation of the regioisomers was facile and the products could be obtained as spectroscopically homogenous compounds. Since there were some contradictory signals in the HMBC (heteronuclear multiple bond correlation) spectra of the photocycloaddition products and no obvious conclusions could be drawn from NOE (nuclear Overhauser effect) experiments, we sought to prove the constitution and configuration of the products by single-crystal X-ray crystallography. The assignment was based on alcohol *rac*-**16** (Scheme 4), which was prepared from product *rac*-**14**



Scheme 4. Structure proof of [2+2] photocycloaddition products *rac*-**12** and *rac*-**14** by conversion to alcohol *rac*-**16**. Exact reaction conditions: a) K_2CO_3 (5 equiv), MeOH, rt, 16 h, 87 %; b) NMM (1 equiv), $ClCO_2Me$ (1 equiv), THF, −10 °C, 0.5 h; then $NaBH_4$ (3 equiv), MeOH, 0 °C, 0.5 h, 83 %; c) BzCl (1.5 equiv), DMAP (0.2 equiv), NEt_3 (2 equiv), CH_2Cl_2, 0 °C→rt, 1 h, 94 %; d) 10 % Pd/C (0.5 equiv), H_2, EtOH, 2 h, 84 %.

by hydrogenolysis. In turn, compound *rac*-**12** could be easily transformed to *rac*-**14** in a three-step sequence (saponification, reduction, and benzoylation)[19] via primary alcohol *rac*-**15** (68 % overall yield), thus establishing an immediate correlation between the two major regioisomers of the [2+2] photocycloaddition.

Tertiary alcohol *rac*-**16** turned out to be a crystalline solid and its core structure was shown to be the 9-oxatricyclo[4.3.0.$0^{4,7}$]nonan-8-one skeleton of a crossed photocycloaddition product by single-crystal X-ray crystallography. In addition, the crystal structure confirmed unambiguously the relative configuration (Figure 2).

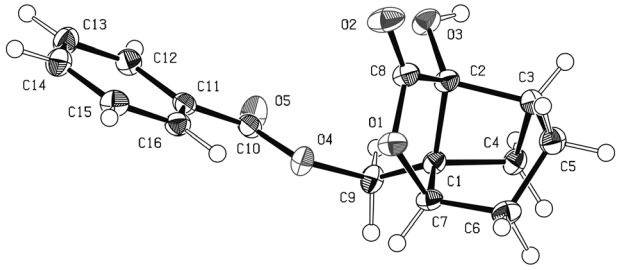
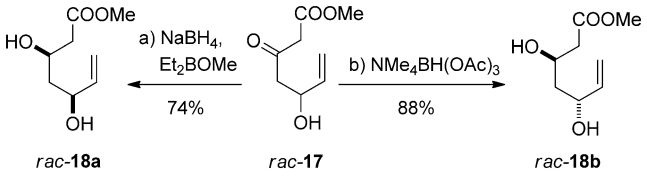


Figure 2. Structure of alcohol *rac*-**16** in the crystal (ORTEP drawing with 50% ellipsoids).

[2+2] Photocycloaddition Reactions to 7-Substituted 2-Oxatricyclo[4.2.1.0^{4,9}]nonan-3-ones

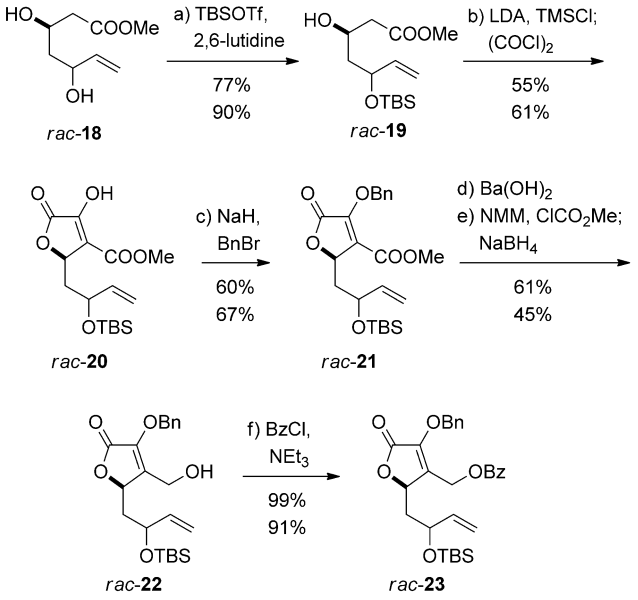
Since the regioselectivity of the [2+2] photocycloaddition can depend on minimal changes in the substitution pattern of the substrate and although the photocycloaddition reaction of butenolides *rac*-**8** and *rac*-**10** had favored crossed products, we performed a more comprehensive study with substrates that already bear the oxygen functionality at C-7 of the desired skeleton (Scheme 1). Along these lines, lactones *rac*-**21** and *rac*-**23**, which show an opposite 1,3-diol-type relationship to the stereogenic center at the lactone, were synthesized.

Selective *syn*-reduction of the known methyl 5-hydroxy-3-oxo-6-heptenoate (*rac*-**17**)[20] to product *rac*-**18a** could be easily realized with $Et_2B(OMe)/NaBH_4$,[21] and reduction with $NMe_4BH(OAc)_3$ led *anti*-selectively to 1,3-diol *rac*-**18b** (Scheme 5).[22] The syntheses of *syn*- and *anti*-photocycloaddition precursors followed an identical synthetic scheme starting from the corresponding diols (Scheme 6). Selective mono-TBS protection[23] of the 1,3-diols *rac*-**18** led to β-hydroxy esters *rac*-**19** in good yield. Treatment of compounds *rac*-**19** with LDA and TMSCl generated 1,3-bis(silyloxy)alk-1-enes, which were cyclized with oxalyl chloride[18] to provide butenolides *rac*-**20**. Subsequent *O*-benzylation produced lactones *rac*-**21** in moderate yields. The photocycloaddition precursors *rac*-**23** were subsequently obtained in a three-step sequence[19] in good overall yields.



Scheme 5. Preparation of the *syn*-diol *rac*-**18a** and the *anti*-diol *rac*-**18b** from β-hydroxyketone *rac*-**17**. Exact reaction conditions: a) $NaBH_4$ (1.05 equiv), Et_2BOMe (1.05 equiv), THF/MeOH, −78°C, 74%; b) $Me_4NHB(OAc)_3$ (5 equiv), CH_3CN/HOAc, −35°C, 44 h, 88%.

In close analogy to the above-mentioned model studies, the reaction of *syn*-substrates *rac*-**21a** and *rac*-**23a** favored the corresponding crossed products *rac*-**25a** and *rac*-**27a** (entries 1–5, Table 2). Without sensitization (entries 1, 3, and 4, Table 2) the photocycloaddition was — under identical conditions — much slower than with the unsubstituted precursors. Specifically, in the case of *rac*-**23a** the reaction did not go to completion (entries 3 and 4, Table 2). Sensitization improved the performance of the reactions and product formation was complete within two (entry 2, Table 2) or two and a half hours (entry 5, Table 2). The preference in favor of the crossed products was even more pronounced than observed with the unsubstituted substrates *rac*-**8** and *rac*-**10**.

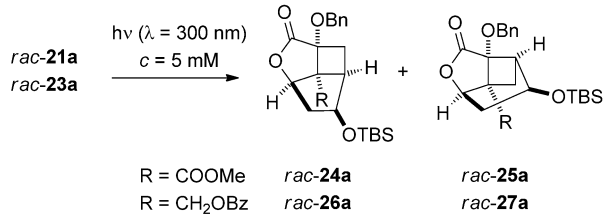


Scheme 6. Preparation of [2+2] photocycloaddition substrates from *syn*-diol *rac*-**18a** and *anti*-diol *rac*-**18b**. Yields on top refer to the *syn*-series, yields on the bottom to the *anti*-series. Exact reaction conditions: a) TBSOTf (1.05 equiv), 2,6-lutidine (3 equiv), CH_2Cl_2, −78°C, 4 h, 77% (*rac*-**19a**) or 90% (*rac*-**19b**); b) LDA (2.2 equiv), TMSCl (2.5 equiv), THF, −78°C→rt, 19 h; then $(COCl)_2$ (1 equiv), CH_2Cl_2, −78°C→rt, 21 h, 55% (*rac*-**20a**) or 61% (*rac*-**20b**); c) NaH (2 equiv), BnBr (2 equiv), DMF, rt, 21 h, 60% (*rac*-**21a**) or 67% (*rac*-**21b**); d) $Ba(OH)_2 \cdot 8H_2O$ (5 equiv), THF/H_2O, 60 h; e) NMM (1 equiv), $ClCO_2Me$ (1 equiv), THF, −10°C, 0.5 h; then $NaBH_4$ (3 equiv), MeOH, 0°C, 0.5 h, 61% (*rac*-**22a** from *rac*-**21a**) or 45% (*rac*-**22b** from *rac*-**21b**); f) BzCl (1.5 equiv), DMAP (0.2 equiv), NEt_3 (2 equiv), CH_2Cl_2, 0°C→rt, 1 h, 99% (*rac*-**23a**) or 91% (*rac*-**23b**). TBSOTf = *tert*-butyldimethylsilyl trifluoromethanesulfonate.

The NOE analysis of crossed product *rac*-**25a** or *rac*-**27a** showed a characteristic signal (see below) between two hydrogen atoms at each of the two methylene groups. The HMBC spectra, however, led to considerable ambiguities. Thus, further transformations were conducted to confirm the product structures.

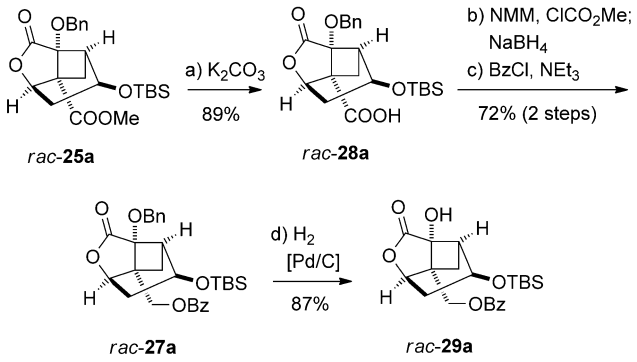
The conversion of *rac*-**25a** into *rac*-**27a** was achieved in high yield following a procedure (Scheme 7) similar to that depicted in Scheme 4. Saponification of ester *rac*-**25a** delivered the free carboxylic acid *rac*-**28a**, which was reduced after activation via the respective anhydride to a primary alcohol,[19] which in turn was *O*-benzoylated to compound *rac*-**27a**. Upon hydrogenolysis, the liberated tertiary alcohol *rac*-**29a** could be obtained in 87% yield.

Table 2. Diastereoselective [2+2] photocycloaddition of *syn*-substrates *rac*-**21a** (R = COOMe) and *rac*-**23a** (R = CH_2OBz).



Entry[a]	Substrate	Solvent(s)	t [h][b]	Product [*rac*-]	Yield [%][c]	r.r.[d]
1	*rac*-**21a**	CH_2Cl_2	9	**24a**:**25a**	66	26:74
2	*rac*-**21a**	MeCN/ac	2	**24a**:**25a**	64	19:81
3	*rac*-**23a**	CH_2Cl_2	24	**26a**:**27a**	45[e]	21:79
4	*rac*-**23a**	CH_2Cl_2	46	**26a**:**27a**	53[f]	11:89
5	*rac*-**23a**	MeCN/ac	2.5	**26a**:**27a**	66	15:85

[a] All reactions were conducted using a RPR-100 reactor with sixteen Rayonet RPR-3000 Å lamps (Duran filter) as the irradiation source in deaerated dichloromethane or acetonitrile/acetone (11:1) as the solvent (c = 5 mM). [b] Elapsed reaction time to achieve 100% conversion of the starting material. [c] Yield of isolated product. [d] The regioisomeric ratio (r.r.) of the crude product was determined by ^{1}H NMR spectroscopy. [e] Incomplete reaction; 34% of the starting material was recovered. [f] Incomplete reaction; 11% of the starting material was recovered.



Scheme 7. Structural proof of [2+2] photocycloaddition products *rac*-**25a** and *rac*-**27a** by conversion into alcohol *rac*-**29a**. Exact reaction conditions: a) K_2CO_3 (7 equiv), MeOH, 60 °C, 9 h, 89%; b) NMM (1 equiv), $ClCO_2Me$ (1 equiv), THF, −10 °C, 0.5 h; then $NaBH_4$ (3 equiv), MeOH, 0 °C, 0.5 h; c) BzCl (1.5 eq), DMAP (0.2 eq), NEt_3 (2 equiv), CH_2Cl_2, 0 °C→rt, 1 h, 72% (over two steps); d) 10% Pd/C, H_2, EtOH, 87%.

Compound *rac*-**29a** turned out to be a crystalline solid. Its constitution and relative configuration was unambiguously proven by single-crystal X-ray crystallography (see the Supporting Information). In addition, the structure of straight product *rac*-**30a**, which was obtained upon treatment of *rac*-**26a** with Pd/C under 1 atm of hydrogen (99%), was confirmed by single-crystal X-ray crystallography (Figure 3).

Gratifyingly, the reaction of *anti*-precursors *rac*-**21b**–*rac*-**23b** largely enhanced the ratio of straight relative to crossed products (entries 1–5, Table 3). As in the previous cases, a significant rate increase was observed when acetone was used as a sensitizing co-solvent. The reaction of *rac*-**21b** afforded a 1:1 mixture of regioisomers in good yield (entries 1 and 2, Table 3). The straight product *rac*-**27b** dominated the

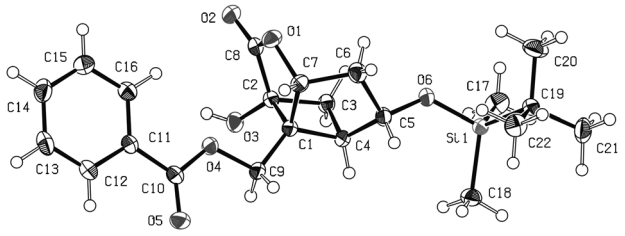
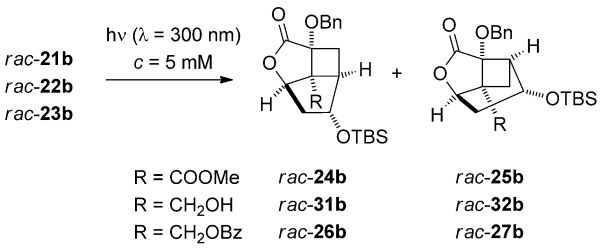


Figure 3. Structure of alcohol *rac*-**30a** in the crystal (ORTEP drawing with 50% ellipsoids).

Table 3. Diastereoselective [2+2] photocycloaddition of *anti*-substrates *rac*-**21b** (R = COOMe), *rac*-**22b** (R = CH_2OH), and *rac*-**23b** (R = CH_2OBz).



Entry[a]	Substrate	Solvent(s)	t [h][b]	Product [*rac*-]	Yield [%][c]	r.r.[d]
1	*rac*-**21b**	CH_2Cl_2	9	**24b**:**25b**	75	49:51
2	*rac*-**21b**	MeCN/ac	2	**24b**:**25b**	67	55:45
3	*rac*-**22b**	MeCN/ac	2	**31b**:**32b**	61	66:34
4	*rac*-**23b**	CH_2Cl_2	22	**26b**:**27b**	80	70:30
5	*rac*-**23b**	MeCN/ac	2	**26b**:**27b**	83	72:28

[a] All reactions were conducted using a RPR-100 reactor with 16 Rayonet RPR-3000 Å lamps (Duran filter) as the irradiation source in deaerated dichloromethane or acetonitrile/acetone (11:1) as the solvent (c = 5 mM). [b] Elapsed reaction time to achieve 100% conversion of the starting material. [c] Yield of isolated product. [d] The regioisomeric ratio (r.r.) of the crude product was determined by ^{1}H NMR spectroscopy.

reaction of *rac*-**23b** in different solvents with or without acetone as sensitizer (entries 4 and 5, Table 3). The reaction of debenzoylated alcohol *rac*-**22b** gave a similar regioselectivity, but the product yield was lower (entry 3, Table 3).

NOE experiments of crossed product *rac*-**25b** also showed a characteristic signal (see below) between two hydrogen atoms at the two methylene groups. The structure was further unambiguously confirmed by single-crystal X-ray crystallography (Figure 4).

However, the photocycloaddition products *rac*-**26b** and *rac*-**27b** were inseparable at this stage. It has to be stressed that this was the only instance in all cases studied, in which the regioisomers were not separable. Therefore, the subsequent hydrogenolysis of the product mixture was performed with the expectation that the tertiary alcohols might be better separable. Indeed, this turned out to be feasible and further optimization studies were performed aiming at a convenient two-step access to diastereomerically pure alcohol *rac*-**33b** (Table 4). The ratio of regioisomers varied slightly but there was no apparent trend to be observed (entries 1–4, Table 4). The higher reaction rate observed with acetone as co-solvent (entry 5, Table 4) and the satisfactory regioselec-

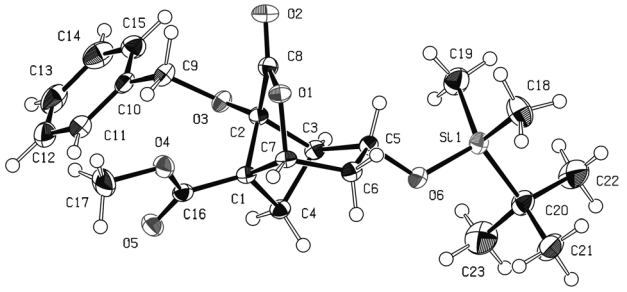
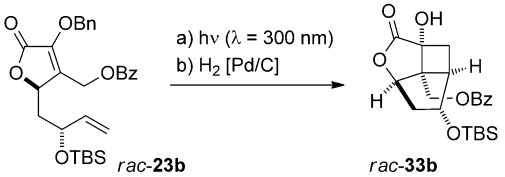


Figure 4. Structure of alcohol *rac*-**25b** in the crystal (ORTEP drawing with 50% ellipsoids).

tivity made these conditions the conditions of choice. Eventually, the reaction delivered aglycon *rac*-**33b** as a single diastereomer in 53% yield over two steps.

Despite the fact that NMR experiments suggested the constitution and relative configuration of tertiary alcohol *rac*-**33b** it was — given its importance for the progress of the total synthesis — extremely useful that this compound

Table 4. Conversion of substrate *rac*-**23b** into diastereomerically pure alcohol *rac*-**33b** by [2+2] photocycloaddition and subsequent hydrogenolysis.



Entry[a]	Solvent(s)	t [h][b]	r.r.[c]	Yield [%][d]
1	CH_2Cl_2	22	74:26	40
2	CH_2Cl_2	8.5[e]	72:28	36
3	MeCN	15.5	69:31	45
4	CH_2Cl_2/hex	14	74:26	40
5	MeCN/ac	2	71:29	53
6	MeCN/ac	1[e]	72:28	43

[a] All photochemcial reactions were conducted using a RPR-100 reactor with 16 Rayonet RPR-3000 Å lamps (Duran filter) as the irradiation source in deaerated solvent (c = 5 mM). Solvent mixtures included acetonitrile/acetone (11:1) or dichloromethane/hexane (1:1). [b] Elapsed reaction time to achieve 100% conversion of the starting material in the [2+2] photocycloaddition. [c] The regioisomeric ratio (r.r.) of the crude product mixture (*rac*-**33b**/*rac*-**34b**) was determined by ^{1}H NMR spectroscopy. [d] Yield of isolated product *rac*-**33b**. [e] The reaction was performed in quartz but not in Duran tubes.

turned out to be a crystalline solid, the relative configuration of which was unambiguously proven by single-crystal X-ray crystallography (Figure 5).

Structure and Mechanistic Discussion

All cycloaddition products could be safely assigned based on crystallographic data and based on synthetic transformations connecting the individual products. With these data in hand, it was possible to analyze in retrospective the NMR data of the cyclobutane products in more detail. For exam-

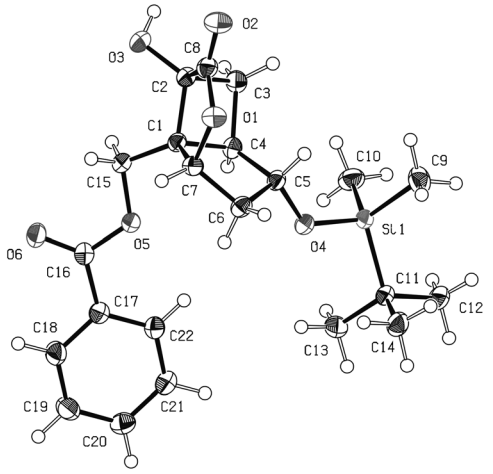


Figure 5. Structure of alcohol *rac*-**33b** in the crystal (ORTEP drawing with 50% ellipsoids).

ple, it was observed that the ^2J coupling constant of protons H-5 within the cyclobutane ring provides clear evidence of the product constitution (straight or crossed). All straight products **D** (Figure 6) display a geminal coupling constant of ^2J = 12.5–14.0 Hz, while crossed products **E** exhibit a cou-

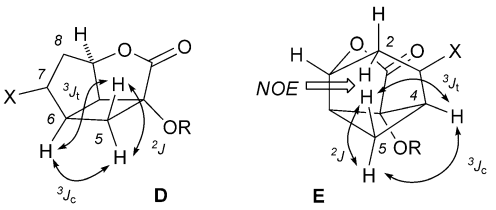
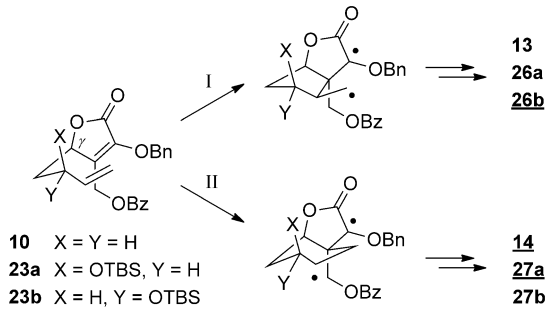


Figure 6. Three-dimensional representation of the 2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one skeleton **D** and of the 9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one skeleton **E** formed in the intramolecular [2+2] photocycloaddition. Characteristic J_{HH} couplings and the characteristic NOE contact between H-2 and H-5 in crossed skeleton **E** are marked. The CH_2OBz/COOMe group was omitted for clarity.

pling constant of ^2J = 10.1–10.5 Hz (see the Supporting Information for further details). Further coupling constants of hydrogen atoms H-5 proved that proton H-6 and its adjacent *cis*-proton at C-5 are almost synperiplanar in structure **D**. The coupling constant ^3J_c varies between 10.5 Hz and 11.1 Hz. The *trans* coupling constant in the straight products **D** is clearly detectable at $^3J_t \cong 4$ Hz, whereas the coupling is not observed for the *trans*-protons H-5 and H-4 in compound **E**. The dihedral angle between the respective C–H bonds appears to be close to 90°. The *cis* coupling for H-4 and the respective proton H-5 was found to be ^3J_c = 6.1–6.8 Hz in structure **E**. The coupling constant of H-6 and H-7 is relatively large ($^3J \cong 7$ Hz) for straight products **D** derived from *syn*-diol *rac*-**18a** and smaller ($^3J \cong 3.5$ Hz) for straight products derived from *anti*-diol *rac*-**18b.** A similar trend was observed for the coupling of H-4 to the vicinal proton H-3 in structure **E**.

COSY (correlation spectroscopy) data allowed us to distinguish the methylene protons at C-8 in structure **D** and at C-2 in structure **E**. In a similar fashion the methylene protons at C-5 could be distinguished in both structures (see above). The characteristic NOE contact between H-2 and H-5, which was mentioned previously, is depicted in structure **E**. A more extensive discussion of relevant NOESY signals can be found in the Supporting Information.

The efficient sensitization with acetone as a co-solvent strongly suggests that the [2+2] photocycloaddition occurs via an excited triplet state intermediate, which is best described by a $\pi\pi^*$ state located at the α,β-unsaturated lactone double bond. Further product formation should occur via 1,4-biradicals to the respective cyclobutanes.[24] When analyzing the different regioselectivities in the photocycloaddition of β-benzoyloxymethyl-substituted substrates **10**, **23a**, and **23b**, it is evident that a chair-like conformation is feasible, in which the internal carbon atom of the olefin and the β-carbon atom of the lactone are ideally positioned to form a 1,4-biradical by five-membered ring closure (path I in Scheme 8). Biradicals of this type lead to the respective straight products **13**, **26a**, and **26b**. A distortion of the conformation that brings the terminal carbon atom of the olefin closer to the β-carbon atom of the lactone can lead to the alternative crossed 1,4-biradical, which should be thermodynamically favored (secondary vs. primary radical). It appears that the required conformation in favor of path I is best enforced in compound **23b** because the TBSO group is equatorially positioned. In the absence of this enforcing effect and, most severely, in a situation in which the TBSO group suffers severe 1,3-diaxial interactions with the C_γ-oxygen bond of the lactone, as for substrate **23a**, the internal carbon atom moves away from the β-carbon atom of the lactone and path II is preferred. The relative high stability of the radical center in α-position to the lactone may increase this preference because it allows for the correction of a disfavored 1,4-biradical formation by retrocleavage.

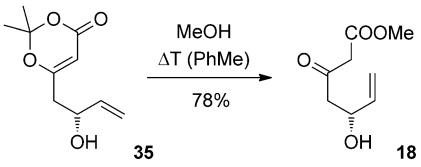


Scheme 8. Conformations of substrates **10** and **23** and putative 1,4-biradicals en route to straight products **13** and **26** and crossed products **14** and **27**. Major products are underlined.

The fact that the benzyloxy group at the α-carbon atom of the butenolide partially deteriorates the expected 'rule of five' selectivity is in line with the findings of Figueredo, Font et al., who detected a similar but less pronounced effect with a methyl substituent at the α-carbon atom.[15c]

Enantioselective Preparation of Starting Materials, Lactol Formation, and Completion of the Synthesis

The synthesis of enantiopure aglycon **33b** commenced with known (2′*R*)-2,2-dimethyl-6-(2′-hydroxybut-3-enyl)-1,3-dioxin-4-one (**35**)[25] (Scheme 9). Refluxing of dioxinone **35** and methanol in toluene provided ketoester **18** in 78% yield. The further conversion of compound **18** into product **33b** was performed as depicted for the racemic compound in Scheme 6 and Table 4.

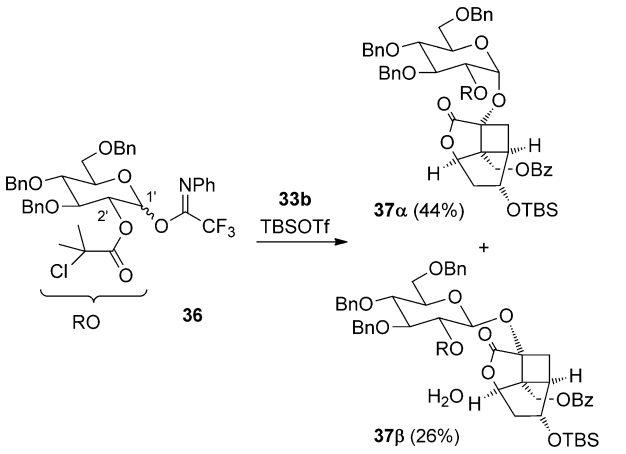


Scheme 9. Preparation of enantiomerically pure alcohol **18** from literature-known[25] 1,3-dioxin-4-one **35.** Exact reaction conditions: Methanol (2.8 equiv), toluene, reflux, 3 h, 78%.

Glucosylation attempts were extensively surveyed with various glycosyl donors bearing different leaving groups (at C-1′) and neighboring groups (at C-2′) derived from D-glucose. Glucosyl donor **36** with *N*-phenyltrifluoroacetimidate (PTFAI)[26] as leaving group at C-1′ and the 2-chloro-2-methylpropanoyl group[27] as protecting group for the alcohol at C-2′ delivered the highest yield of β-glucoside **37β** (26%) together with α-anomer **37α** (Scheme 10), which was obtained in 44% yield.

The lactone moiety in **37β** was supposed to be strained and was expected to react most readily with methyl lithium.[28] It was found, however, that the benzoate group in **37β** was much more easily removed under addition conditions. Exposure to four equivalents of methyl lithium gave three products in varying amounts (Figure 7): diol **38** with the lactone ring intact, lactol **39** with the C-2′ ester group intact, and the completely deacylated lactol **40**. Lactol **40** could be smoothly cyclized to the single diastereomer **41** under mild acidic conditions in quantitive yield.

Even in $CDCl_3$ solution, a rapid conversion of lactol **40** into product **41** was observed and no lactol signal was detected in the ^{1}H NMR spectrum. Lactol **39** could be transformed to acetal **41** after removal of the 2-chloro-2-methylpropanoyl group (K_2CO_3, MeOH/THF) via lactol **40**. The best way to convert compound **37β** into the pentacyclic product **41** was found to be the successive treatment of the former compound with an excess of methyl lithium (13 equiv) at −78 °C in THF and then with pyridinium *para*-toluenesulfonate (PPTS) in CH_2Cl_2. By this means, acetal **41** could be obtained in 70% yield. Methyl addition to the intermediate lactol or its open aldehyde form was not observed under these conditions.



Scheme 10. Glycosylation of alcohol with glucosyl donor **36** to form β-anomer **37β** together with α-anomer **37α**. Exact reaction conditions: **36** (3 equiv), TBSOTf (0.4 equiv), 4 Å MS, hexane/CH_2Cl_2, 0 °C, 12 h, 26% for **37β**, and 44% for **37α**.

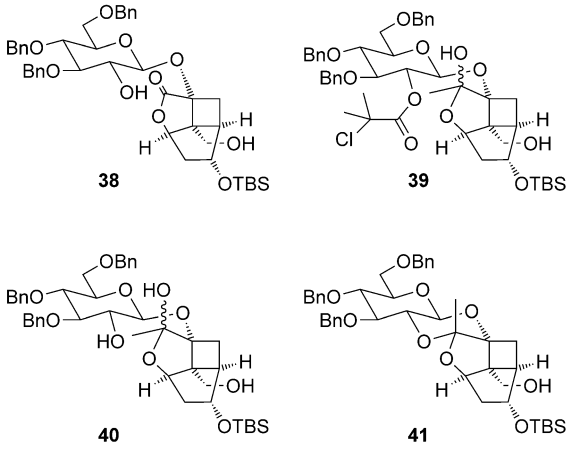


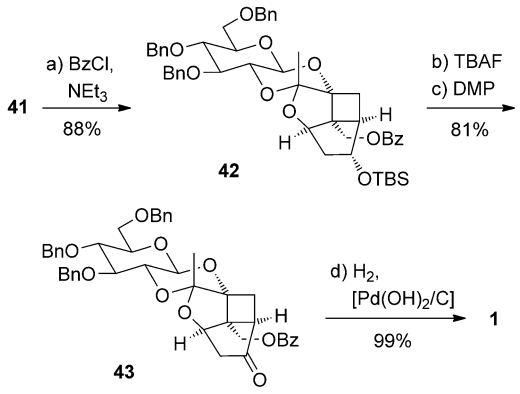
Figure 7. Possible products **38**–**41** in the reaction of glucoside **37β** with methyl lithium.

Benzoylation of the primary alcohol **41** followed by liberation of the secondary alcohol at C-7 and oxidation with Dess–Martin periodinane (DMP)[29] smoothly gave the triply benzylated ketone **43** (Scheme 11). Global debenzylation with Pearlman's catalyst[30] gave lactiflorin **1**.

The structure of lactiflorin was finally confirmed by comparison with the reported spectra.[10] The assignment was further corroborated by the preparation of lactiflorin triacetate, which was obtained upon treatment of triol **1** with acetic anhydride in pyridine (59% yield).

Conclusions

In summary, the present study has shown the subtle differences that can influence the outcome of an intramolecular [2+2] photocycloaddition. Conformational factors, which disfavor five-membered ring closure, together with stabilizing substituents at the putative 1,4-biradical intermediates



Scheme 11. Completion of the total synthesis of (+)-lactiflorin (**1**) in four steps, starting from primary alcohol **41**. Exact reaction conditions: a) NEt_3 (5 equiv), DMAP (1 equiv), BzCl (5 equiv), CH_2Cl_2, 18 h, 88%; b) TBAF (3.4 equiv), THF, rt, 2 h; c) DMP (3 equiv), $NaHCO_3$ (8 equiv), CH_2Cl_2, rt, 4 h, 81%; d) $Pd(OH)_2/C$, H_2, EtOH, rt, 4 h, 99%. TBAF = tetra-*n*-butylammonium fluoride, DMP = Dess–Martin periodinane.

can significantly alter the regioselectivity of a [2+2] photocycloaddition. In our specific example, model studies with unsubstituted substrates such as *rac*-**8** and *rac*-**10** had hinted clearly at an undesired regiochemical outcome and might have led to a premature change in synthetic strategy. Thus, the need for substrates that are not only close to the real target molecules but are indeed intermediates in a projected total synthesis has been — once again — manifested and seems to be particular important for photocycloaddition reactions as key steps in natural product synthesis. With the appropriately substituted [2+2] photocycloaddition precursor **23b**, it was possible to establish the desired 2-oxatricyclo[4.2.1.$0^{4,9}$]nonan-3-one skeleton en route to lactiflorin. The three stereogenic centers at the cyclobutane core of the natural product were all established with perfect diastereoselectivity in the [2+2] photocycloaddition step. The efficient synthesis of the aglycon (nine steps from known compound **35**; 6% overall yield) makes this approach very attractive, in particular if the biological activity of aglycon is to be studied separately. The yield in the further conversion into (+)-lactiflorin was hampered by the unsatisfactory glucosylation reaction, which could not be improved. The further transformation could be optimized, however, and enabled the synthesis to be completed in five steps from glycoside **37β** and in an overall yield of 49%.

Experimental Section

General

All reactions involving moisture-sensitive chemicals were carried out in flame-dried glassware in dried solvents with magnetic stirring under argon. Tetrahydrofuran (THF), diethyl ether (Et_2O), and dichloromethane (CH_2Cl_2) were purified by using a SPS-800 solvent purification system (M. Braun). Diisopropylamine was distilled over calcium hydride. All other chemicals were used as received. TLC was performed on silica-coated glass plates (silica gel 60 F_{254}) with detection by UV light (254 nm) or ceric ammonium molybdate (CAM) with subsequent heat-

ing. Flash chromatography was performed on silica gel 60 (Merck, 230–400 mesh) with the indicated eluent. All solvents for chromatography were distilled prior to use. Compounds *rac*-**2**,[12] *rac*-**6**,[17] *rac*-**17**,[20] *rac*-**18a**[21], and **35**[25] are literature-known. The preparation and analytical data of all new compounds are reported below or in the Supporting Information. IR spectra were recorded on a JASCO IR-4100 spectrometer (ATR) and MS/HRMS measurements were performed on a Finnigan MAT 8200 (EI), a Finnigan MAT 95S (HR-EI), a Finnigan LCQ classic (ESI), or a Thermo Finnigan LTQ FT mass spectrometer (HRMS-ESI), respectively. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 303 K, either on a Bruker AV-360 or a Bruker AV-500 spectrometer. The chemical shifts are reported relative to $CHCl_3$ ($\delta = 7.26$ ppm) or C_6H_6 ($\delta = 7.16$ ppm). Apparent multiplets that occur as a result of the accidental equality of coupling constants to those of magnetically nonequivalent protons are marked as virtual (*virt*). If clearly visible, virtual doublets in *para*-substituted arenes were also assigned and marked as virtual (*virt*). The multiplicities of ^{13}C NMR signals were determined by DEPT experiments, and assignments are based on COSY, HMBC, and HSQC experiments. Melting points were measured on a Koffler Thermopan and are uncorrected.

Single-crystal X-ray Structure Determinations

rac-**16**: colorless fragment, $C_{16}H_{16}O_5$, $M_r = 288.29$; orthorhombic, space group *Pbcn* (No. 60), $a = 23.5346(6)$, $b = 9.4007(2)$, $c = 12.5110(3)$ Å, $V = 2767.96(11)$ Å^3, $Z = 8$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $\mu = 0.103$ mm^{-1}, $\rho_{calcd} = 1.384$ gcm^{-3}, $T = 123(1)$ K, $F(000) = 1216$, θ_{max}: 25.35°, $R1 = 0.0321$ (2462 observed data), $wR2 = 0.0801$ (all 2528 data), $GOF = 1.054$, 255 parameters, $\Delta\rho_{max/min} = 0.32/-0.20$ e Å^{-3}.

rac-**25b**: colorless fragment, $C_{23}H_{32}O_6Si$, $M_r = 432.58$; monoclinic, space group $P2_1/n$ (No. 14), $a = 14.7334(4)$, $b = 7.8565(2)$, $c = 20.5340(5)$ Å, $\beta = 92.7607(10)$°, $V = 2374.11(11)$ Å^3, $Z = 4$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $\mu = 0.133$ mm^{-1}, $\rho_{calcd} = 1.210$ gcm^{-3}, $T = 123(1)$ K, $F(000) = 928$, θ_{max}: 25.35°, $R1 = 0.0315$ (4167 observed data), $wR2 = 0.0856$ (all 4335 data), $GOF = 1.060$, 399 parameters, $\Delta\rho_{max/min} = 0.32/-0.28$ e Å^{-3}.

rac-**29a**: colorless plate, $C_{22}H_{30}O_6Si$, $M_r = 418.55$; monoclinic, space group $P2_1/c$ (No. 14), $a = 28.4443(8)$, $b = 12.4627(4)$, $c = 12.6023(4)$ Å, $\beta = 97.6806(14)$°, $V = 4427.3(2)$ Å^3, $Z = 8$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $\mu = 0.140$ mm^{-1}, $\rho_{calcd} = 1.256$ gcm^{-3}, $T = 123(1)$ K, $F(000) = 1792$, θ_{max}: 25.37°, $R1 = 0.0313$ (7434 observed data), $wR2 = 0.0847$ (all 8116 data), $GOF = 1.051$, 763 parameters, $\Delta\rho_{max/min} = 0.34/-0.25$ e Å^{-3}.

rac-**30a**: colorless plate, $C_{22}H_{30}O_6Si$, $M_r = 418.55$; monoclinic, space group $P2_1/c$ (No. 14), $a = 17.6456(14)$, $b = 10.5766(8)$, $c = 11.8548(9)$ Å, $\beta = 93.124(4)$°, $V = 2209.2(3)$ Å^3, $Z = 4$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $\mu = 0.141$ mm^{-1}, $\rho_{calcd} = 1.258$ gcm^{-3}, $T = 123(1)$ K, $F(000) = 896$, θ_{max}: 25.37°, $R1 = 0.0300$ (3797 observed data), $wR2 = 0.0790$ (all 4049 data), $GOF = 1.052$, 382 parameters, $\Delta\rho_{max/min} = 0.33/-0.28$ e Å^{-3}.

rac-**33b**: colorless fragment, $C_{22}H_{30}O_6Si$, $M_r = 418.55$; triclinic, space group $P\bar{1}$ (No. 2), $a = 10.2014(4)$, $b = 10.4234(4)$, $c = 11.5998(4)$ Å, $\alpha = 82.6260(15)$°, $\beta = 78.5574(16)$°, $\gamma = 65.7693(15)$°, $V = 1100.90(7)$ Å^3, $Z = 2$, $\lambda(Mo_{K\alpha}) = 0.71073$ Å, $\mu = 0.141$ mm^{-1}, $\rho_{calcd} = 1.263$ gcm^{-3}, $T = 123(1)$ K, $F(000) = 448$, θ_{max}: 25.44°, $R1 = 0.0338$ (3899 observed data), $wR2 = 0.0917$ (all 4043 data), $GOF = 1.027$, 382 parameters, $\Delta\rho_{max/min} = 0.37/-0.27$ e Å^{-3}.

CCDC 870803 (*rac*-**16**), CCDC 870804 (*rac*-**25b**), CCDC 870805 (*rac*-**29a**), CCDC 870807 (*rac*-**30a**), and CCDC 870806 (*rac*-**33b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Photocycloaddition Reactions

A deaerated solution of butenolide (5 mM) was irradiated in a Rayonet RPR 100 merry-go-round reactor, equipped with 16 Rayonet RPR 3000 Å lamps (Duran filter unless otherwise stated, $\lambda = 300$ nm), at room temperature. Unless otherwise stated, the reaction was stopped when the starting material was fully consumed according to TLC analysis. Subsequently, the reaction mixture was concentrated in vacuo to afford the residue, which was purified by flash chromatography (eluent: pentane/EtOAc) on silica gel to afford the cycloaddition products.

Intramolecular photocycloaddition reaction of butenolide *rac*-8: The reaction of butenolide *rac*-**8** (20.0 mg, 0.0662 mmol) in CH_3CN/acetone (11:1, 13 mL) afforded straight product *rac*-**11** (3.2 mg, 16%) and crossed product *rac*-**12** (15.0 mg, 75%) after flash chromatography (eluent: pentane/EtOAc = 7:1).

(1*R**,4*R**,6*R**,9*R**)-4-Benzyloxy-9-methoxycarbonyl-2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one (*rac*-**11**): $R_f = 0.22$ (Pentane/EtOAc = 7:1, CAM); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.35$–7.27 (m, 5H, CH_2*Ph*), 5.38 (d, $J = 3.6$ Hz, 1H, H-*1*), 4.58 (d, $J = 10.8$ Hz, 1H, *CH*HPh), 4.52 (d, $J = 10.8$ Hz, 1H, *CH*HPh), 3.73 (s, 3H, CO_2*Me*), 3.10 (*virt.* tdd, $J \cong 9.7$, 6.9, 2.8 Hz, 1H, H-*6*), 2.84 (dd, $J = 12.8$, 10.5 Hz, 1H, *H*H-*5*), 2.35–2.21 (m, 2H, *H*H-*7*, *H*H-*8*), 2.13 (dd, $J = 12.8$, 2.8 Hz, 1H, H*H*-*5*), 1.80 (dddd, $J = 14.3$, 12.1, 8.3, 3.6 Hz, 1H, H*H*-*8*), 1.68–1.58 ppm (m, 1H, H*H*-*7*); ^{13}C NMR (91 MHz, $CDCl_3$): $\delta = 175.2$ (C-*3*), 169.0 (CO_2Me), 136.8 (*Ph*), 128.3 (*Ph*), 127.9 (*Ph*), 127.6 (*Ph*), 85.0 (C-*1*), 79.7 (C-*4*), 68.0 (CH_2Ph), 63.4 (C-*9*), 52.6 (CO_2*Me*), 36.6 (C-*8*), 35.4 (C-*5*), 33.2 (C-*6*), 29.9 ppm (C-*7*); IR (ATR): $\tilde{\nu} = 2951$, 2941, 2878, 1770, 1725, 1497, 1435 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 302 (0.8) [M^+], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{17}H_{18}O_5$ [M^+] calcd. 302.1149, found 302.1150.

(1*R**,4*S**,6*R**,7*R**)-7-Benzyloxy-6-methoxycarbonyl-9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one (*rac*-**12**): $R_f = 0.11$ (Pentane/EtOAc = 7:1, CAM); ^{1}H NMR (500 MHz, C_6D_6): $\delta = 7.51$ (d, $J = 7.4$ Hz, 2H, CH_2*Ph*), 7.27 (t, $J = 7.4$ Hz, 2H, CH_2*Ph*), 7.18 (t, $J = 7.4$ Hz, 1H, CH_2*Ph*), 4.95 (d, $J = 11.2$ Hz, 1H, C*H*HPh), 4.91 (s, 1H, H-*1*), 4.83 (d, $J = 11.2$ Hz, 1H, CH*H*Ph), 3.37 (s, 3H, CO_2*Me*), 2.91 (dd, $J = 10.3$, 6.7 Hz, 1H, *H*H-*5*), 2.42 (*virt.* t, $J \cong 5.6$ Hz, 1H, H-*4*), 1.68 (ddd, $J = 14.2$, 10.6, 7.0 Hz, 1H, *H*H-*3*), 1.55 (ddd, $J = 14.2$, 7.0, 1.1 Hz, 1H, *H*H-*2*), 1.45 (dd, $J = 10.3$, 1.0 Hz, 1H, H*H*-*5*), 1.44–1.37 (m, 1H, H*H*-*3*), 1.34–1.23 ppm (m, 1H, H*H*-*2*); ^{13}C NMR (91 MHz, C_6D_6): $\delta = 172.0$ (C-*8*), 169.7 (CO_2Me), 138.2 (*Ph*), 128.6 (*Ph*), 128.1 (*Ph*), 128.0 (*Ph*), 90.0 (C-*7*), 81.1 (C-*1*), 69.0 (CH_2Ph), 54.5 (C-*6*), 51.9 (CO_2*Me*), 39.3 (C-*4*), 24.4 (C-*5*), 23.3 (C-*2*), 22.1 ppm (C-*3*); IR (ATR): $\tilde{\nu} = 2953$, 2873, 1770, 1728, 1497, 1455, 1436 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 302 (0.66) [M^+], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{17}H_{18}O_5$ [M^+] calcd. 302.1149, found 302.1136.

Intramolecular photocycloaddition reaction of butenolide *rac*-10: The reaction of *rac*-**10** (22.0 mg, 68.1 μmol) in CH_3CN/acetone (11:1, 12 mL) afforded straight product *rac*-**13** (5.3 mg, 24%) and crossed product *rac*-**14** (10.2 mg, 46%) after flash chromatography (eluent: pentane/EtOAc = 9:1).

(1*R**,4*R**,6*R**,9*R**)-9-Benzoyloxymethyl-4-benzyloxy-2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one (*rac*-**13**): $R_f = 0.50$ (Pentane/EtOAc = 6:1, CAM); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.00$ (d, $J = 8.2$ Hz, 2H, CO*Ph*), 7.61 (t, $J = 7.4$ Hz, 1H, CO*Ph*), 7.46 (*virt.* t, $J \cong 7.8$ Hz, 2H, CO*Ph*), 7.36–7.27 (m, 5H, CH_2*Ph*), 5.01 (d, $J = 3.7$ Hz, 1H, H-*1*), 4.90 (d, $J = 11.3$ Hz, 1H, C*H*HPh), 4.69 (d, $J = 11.3$ Hz, 1H, CH*H*Ph), 4.67 (d, $J = 11.9$ Hz, 1H, C*H*HOCO), 4.63 (d, $J = 11.9$ Hz, 1H, CH*H*OCO), 2.78–2.63 (m, 2H, *H*H-*5*, H-*6*), 2.35–2.27 (m, 2H, *H*H-*7*, *H*H-*8*), 2.22–2.10 (m, 1H, H*H*-*5*), 1.91 (dddd, $J = 14.2$, 12.1, 8.4, 3.7 Hz, 1H, H*H*-*8*), 1.77–1.58 ppm (m, 1H, H*H*-*7*); ^{13}C NMR (91 MHz, $CDCl_3$): $\delta = 176.7$ (C-*3*), 166.2 (*C*OPh), 137.4 (*Ph*), 133.3 (*Ph*), 129.49 (*Ph*), 128.51 (*Ph*), 128.3 (*Ph*), 127.7 (*Ph*), 127.4 (*Ph*), 86.2 (C-*1*), 77.4 (C-*4*), 67.7 (CH_2Ph), 62.0 (CH_2OCO), 58.5 (C-*9*), 36.3 (C-*8*), 34.0 (C-*5*), 32.1 (C-*6*), 30.2 ppm (C-*7*); IR (ATR): $\tilde{\nu} = 3033$, 2963, 2877, 1767, 1717, 1452, 1267 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 378 (1) [M^+], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{23}H_{22}O_5$ [M^+] calcd. 378.1462, found 378.1466; $C_{16}H_{15}O_5$ [M^+-91] calcd. 287.0914, found 287.0913.

(1*R**,4*S**,6*R**,7*R**)-6-Benzoyloxymethyl-7-benzyloxy-9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one (*rac*-**14**): $R_f = 0.34$ (Pentane/EtOAc = 6:1, CAM); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.03$ (d, $J = 8.4$ Hz, 2H, CO*Ph*), 7.59 (t, $J = 7.4$ Hz, 1H, CO*Ph*), 7.47 (*virt.* t, $J \cong 8.0$ Hz, 2H, CO*Ph*), 7.42 (d, $J = 7.2$ Hz, 2H, CH_2*Ph*), 7.36 (t, $J = 7.2$ Hz, 2H, CH_2*Ph*), 7.31 (t, $J = 7.2$ Hz, 1H, CH_2*Ph*), 5.09 (d, $J = 11.5$ Hz, 1H, C*H*HPh), 5.09 (s, 1H, H-*1*), 4.85 (d, $J = 11.5$ Hz, 1H, CH*H*Ph), 4.85 (d, $J = 11.7$ Hz, 1H, C*H*HOCO), 4.41 (d, $J = 11.7$ Hz, 1H, CH*H*OCO), 2.93 (*virt.* t, $J \cong 5.3$ Hz, 1H, H-*4*), 2.41 (dd, $J = 10.1$, 6.5 Hz, 1H, *H*H-*5*), 2.11 (ddd, $J = 9.0$, 7.9, 3.4 Hz, 1H, *H*H-*3*), 2.08–1.95 (m, 3H, H*H*-*3*, H-*2*), 1.89 ppm (d, $J = 10.1$ Hz, 1H, H*H*-*5*); ^{13}C NMR (91 MHz, $CDCl_3$): $\delta = 174.1$ (C-*8*), 166.2 (*C*OPh), 138.0 (*Ph*), 133.2 (*Ph*), 129.6 (*Ph*), 129.4 (*Ph*), 128.5 (*Ph*),

128.3 (*Ph*), 127.6 (*Ph*), 127.4 (*Ph*), 85.2 (C-*7*), 82.6 (C-*1*), 68.2 (*C*H$_2$Ph), 63.2 (*C*H$_2$OCO), 51.5 (C-*6*), 38.1 (C-*4*), 25.0 (C-*5*), 23.2 (C-*2*), 22.7 ppm (C-*3*); IR (ATR): $\tilde{\nu}$ = 3065, 3031, 2964, 2871, 1769, 1717, 1601, 1584, 1453, 1268 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 378 (1) [M^+], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{23}H_{22}O_5$ [M^+] calcd. 378.1462, found 378.1454.

Intramolecular photocycloaddition reaction of butenolide *rac*-21a: The reaction of butenolide *rac*-**21a** (28.0 mg, 64.7 μmol) in CH_2Cl_2 (13 mL) afforded straight product *rac*-**24a** (5.0 mg, 18%) and crossed product *rac*-**25a** (13.4 mg, 48%) after flash chromatography (eluent: pentane/EtOAc = 9:1).

(1*R**,4*R**,6*R**,7*S**,9*R**)-4-Benzyloxy-9-methoxycarbonyl-7-(*tert*-butyldimethylsilyl-oxy)-2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one (*rac*-**24a**): R_f = 0.39 (Pentane/EtOAc = 8:1, CAM); m.p. = 103–105 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5H, CH$_2$*Ph*), 5.33 (d, *J* = 4.7 Hz, 1H, H-*1*), 4.61 (d, *J* = 11.0 Hz, 1H, *CH*HPh), 4.55 (d, *J* = 11.0 Hz, 1H, *CH*H*P*h), 4.49 (*virt.* t, *J* ≅ 6.4 Hz, 1H, H-*7*), 3.72 (s, 3H, CO$_2$*Me*), 3.25 (ddd, *J* = 10.8, 7.2, 3.1 Hz, 1H, H-*6*), 2.66 (dd, *J* = 12.5, 3.1 Hz, 1H, *H*H-*5*), 2.56 (dd, *J* = 12.5, 10.8 Hz, 1H, H*H*-*5*), 2.28 (d, *J* = 15.0 Hz, 1H, *H*H-*8*), 1.96 (ddd, *J* = 15.0, 5.5, 4.7 Hz, 1H, H*H*-*8*), 0.90 (s, 9H, SiMe$_2$C*Me*$_3$), 0.08 (s, 3H, Si*Me*MeCMe$_3$), 0.04 ppm (s, 3H, SiMe*Me*CMe$_3$); ^{13}C NMR (91 MHz, $CDCl_3$): δ = 174.3 (C-*3*), 168.9 (*C*O$_2$Me), 137.1 (*Ph*), 128.3 (*Ph*), 127.8 (*Ph*), 127.6 (*Ph*), 83.6 (C-*1*), 80.1 (C-*4*), 71.7 (C-*7*), 67.9 (*C*H$_2$Ph), 63.5 (C-*9*), 52.7 (CO$_2$*Me*), 44.8 (C-*8*), 39.2 (C-*6*), 26.9 (C-*5*), 25.7 (SiMe$_2$C*Me*$_3$), 18.1(SiMe$_2$*C*Me$_3$), −4.9 (Si*Me*MeCMe$_3$), −5.2 ppm (Si*Me*MeCMe$_3$); IR (ATR): $\tilde{\nu}$ = 2952, 2927, 2856, 1770, 1719, 1498, 1436 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 375 (2.8) [M^+-57], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{19}H_{23}O_6Si$ [M^+-57] calcd. 375.1258, found 375.1256; $C_{19}H_{23}O_6Si$ [M^+] calcd. 432.1963, found 432.1951.

(1*R**,3*S**,4*R**,6*R**,7*R**)-7-Benzyloxy-6-methoxycarbonyl-3-(*tert*-butyldimetheylsilyl-oxy)-9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one (*rac*-**25a**): R_f = 0.21 (Pentane/EtOAc = 8:1, CAM); m.p. = 57–59 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 7.1 Hz, 2H, CH$_2$*Ph*), 7.34 (*virt.* t, *J* ≅ 7.2 Hz, 2H, CH$_2$*Ph*), 7.28 (t, *J* = 7.3 Hz, 1H, CH$_2$*Ph*), 5.21 (s, 1H, H-*1*), 4.82 (d, *J* = 11.6 Hz, 1H, *CH*HPh), 4.75 (d, *J* = 11.6 Hz, 1H, CH*H*Ph), 4.41 (*virt.* t, *J* ≅ 4.5 Hz, 1H, H-*3*), 3.72 (s, 3H, CO$_2$*Me*), 2.89–2.82 (m, 2H, *H*H-*5*, H-*4*), 2.18 (ddd, *J* = 15.3, 6.1, 2.8 Hz, 1H, *H*H-*2*), 2.05 (dd, *J* = 15.3, 1.5 Hz, 1H, H*H*-*2*), 1.66–1.60 (m, 1H, H*H*-*5*), 0.89 (s, 9H, SiMe$_2$C*Me*$_3$), 0.07 (s, 3H, Si*Me*MeC*Me*$_3$), 0.05 ppm (s, 3H, SiMe*Me*C*Me*$_3$); ^{13}C NMR (91 MHz, $CDCl_3$): δ = 171.8 (C-*8*), 169.8 (*C*O$_2$Me), 137.8 (*Ph*), 128.3 (*Ph*), 127.7 (*Ph*), 127.5 (*Ph*), 86.3 (C-*7*), 80.1 (C-*1*), 69.0 (C-*3*), 68.0 (*C*H$_2$Ph), 55.8 (C-*6*), 52.4 (CO$_2$*Me*), 47.6 (C-*4*), 33.4 (C-*2*), 25.5 (SiMe$_2$C*Me*$_3$), 24.4 (C-*5*), 17.9 (SiMe$_2$*C*Me$_3$), −5.0 (Si*Me*MeCMe$_3$), −5.1 ppm (SiMe*Me*CMe$_3$); IR (ATR): $\tilde{\nu}$ = 2960, 2929, 2888, 2854, 1776, 1740, 1453, 1343, 1259 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 375 (45) [M^+-57], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{19}H_{23}O_6Si$ [M^+-57] calcd. 375.1258, found 375.1251.

Intramolecular photocycloaddition reaction of butenolide *rac*-23a: The reaction of *rac*-**23a** (30.0 mg, 59.0 μmol) in CH_3CN/acetone (11:1, 12 mL) afforded straight product *rac*-**26a** (7.2 mg, 24%) and crossed product *rac*-**27a** (12.6 mg, 42%) after flash chromatography (eluent: pentane/EtOAc = 10:1→8:1).

(1*R**,4*R**,6*R**,7*S**,9*R**)-9-Benzoyoxymethyl-4-benzyloxy-7-(*tert*-butyldimethylsilyl-oxy)-2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one (*rac*-**26a**): R_f = 0.40 (Pentane/EtOAc = 10:1, CAM); m.p. = 79–81 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.2 Hz, 2H, CO*Ph*), 7.61 (t, *J* = 7.4 Hz, 1H, CO*Ph*), 7.47 (*virt.* t, *J* ≅ 7.8 Hz, 2H, CO*Ph*), 7.37–7.26 (m, 5H, CH$_2$*Ph*), 4.94 (d, *J* = 4.4 Hz, 1H, H-*1*), 4.94 (d, *J* = 11.4 Hz, 1H, *CH*HPh), 4.73 (d, *J* = 11.4 Hz, 1H, CH*H*Ph), 4.67 (d, *J* = 11.9 Hz, 1H, *H*H-*10*), 4.60 (d, *J* = 11.9 Hz, 1H, H*H*-*10*), 4.55 (*virt.* t, *J* ≅ 5.9 Hz, 1H, H-*7*), 2.86 (ddd, *J* = 10.8, 7.1, 3.2 Hz, 1H, H-*6*), 2.68 (dd, *J* = 12.7, 3.2 Hz, 1H, *H*H-*5*), 2.47 (dd, *J* = 12.7, 10.8 Hz, 1H, H*H*-*5*), 2.30 (d, *J* = 14.9 Hz, 1H, *H*H-*8*), 2.08 (ddd, *J* = 14.9, 5.9, 4.4 Hz, 1H, H*H*-*8*), 0.94 (s, 9H, SiMe$_2$C*Me*$_3$), 0.11 (s, 3H, Si*Me*MeCMe$_3$), 0.06 ppm (s, 3H, SiMe*Me*CMe$_3$); ^{13}C NMR (91 MHz, $CDCl_3$): δ = 175.9 (C-*3*), 166.3 (*CO*Ph), 137.6 (*Ph*), 133.4 (*Ph*), 129.51 (*Ph*), 129.49 (*Ph*), 128.6 (*Ph*), 128.3 (*Ph*), 127.7 (*Ph*), 127.5 (*Ph*), 84.6 (C-*1*), 77.5 (C-*4*), 72.2 (C-*7*), 67.5 (*C*H$_2$Ph), 62.3 (C-*10*), 58.3 (C-*9*), 44.6 (C-*8*), 38.7 (C-*6*), 25.7 (SiMe$_2$C*Me*$_3$), 25.6 (C-*5*), 18.1 (SiMe$_2$*C*Me$_3$), −4.8 (Si*Me*MeCMe$_3$), −5.1 ppm (SiMe*Me*CMe$_3$); IR (ATR): $\tilde{\nu}$ = 2957, 2950, 2926, 2855, 1769, 1718, 1602, 1453, 1273 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 417 (2) [M^+-91], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{22}H_{29}O_6Si$ [M^+-91] calcd. 417.1728, found 415.1745.

(1*R**,3*S**,4*R**,6*R**,7*R**)-6-Benzoyoxymethyl-7-benzyloxy-3-(*tert*-butyldimetheylsilyl-oxy)-9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one (*rac*-**27a**): R_f = 0.2 (Pentane/EtOAc = 10:1, CAM); m.p. = 112–115 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 7.8 Hz, 2H, CO*Ph*), 7.55 (t, *J* = 7.1 Hz, 1H, CO*Ph*), 7.43 (*virt.* t, *J* ≅ 7.6 Hz, 2H, CO*Ph*), 7.40 (d, *J* = 7.8 Hz, 2H, CH$_2$*Ph*), 7.33 (*virt.* t, *J* ≅ 7.5 Hz, 2H, CH$_2$*Ph*), 7.29 (t, *J* = 7.3 Hz, 1H, CH$_2$*Ph*), 5.22 (d, *J* = 11.8 Hz, 1H, C*H*HPh), 5.03 (s, 1H, H-*1*), 4.80 (d, *J* = 11.8 Hz, 1H, CH*H*Ph), 4.52 (d, *J* = 11.8 Hz, 1H, *H*H-*10*), 4.45 (*virt.* t, *J* ≅ 5.6 Hz, 1H, H-*3*), 4.39 (d, *J* = 11.8 Hz, 1H, H*H*-*10*), 3.02 (*virt.* t, *J* ≅ 6.0 Hz, 1H, H-*4*), 2.34 (dd, *J* = 10.5, 6.7 Hz, 1H, *H*H-*5*), 2.21 (ddd, *J* = 15.3, 6.2, 2.8 Hz, 1H, *H*H-*2*), 2.04 (d, *J* = 15.3 Hz, 1H, H*H*-*2*), 1.60 (d, *J* = 10.5 Hz, 1H, H*H*-*5*), 0.92 (s, 9H, SiMe$_2$C*Me*$_3$), 0.09 (s, 3H, Si*Me*MeCMe$_3$), 0.08 ppm (s, 3H, SiMe*Me*CMe$_3$); ^{13}C NMR (91 MHz, $CDCl_3$): δ = 174.0 (C-*3*), 166.3 (*C*OPh), 138.4 (*Ph*), 133.2 (*Ph*), 129.7 (*Ph*), 129.6 (*Ph*), 128.5 (*Ph*), 128.3 (*Ph*), 127.6 (*Ph*), 127.4 (*Ph*), 82.2 (C-*7*), 81.3 (C-*1*), 69.5 (C-*3*), 67.7 (*C*H$_2$Ph), 63.0 (C-*10*), 52.9 (C-*6*), 46.7 (C-*4*), 33.5 (C-*2*), 25.6 (SiMe$_2$C*Me*$_3$), 25.1 (C-5), 17.9 (SiMe$_2$*C*Me$_3$), −4.9 (Si*Me*MeCMe$_3$), −5.0 ppm (SiMe*Me*CMe$_3$); IR (ATR): $\tilde{\nu}$ = 2953, 2929, 2857, 1772, 1720, 1342, 1272 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 451 (1) [M^+-57], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{25}H_{27}O_6Si$ [M^+-57] calcd. 415.1571, found 415.1565.

Intramolecular photocycloaddition reaction of butenolide *rac*-21b: The reaction of *rac*-**21b** (28.0 mg, 64.7 μmol) in CH_2Cl_2 (13 mL) afford straight product *rac*-**24b** (10.0 mg, 36%) and crossed product *rac*-**25b** (11.0 mg, 39%) after flash chromatography (eluent: pentane/EtOAc = 10:1).

(1*R**,4*R**,6*R**,7*R**,9*R**)-4-Benzyloxy-9-methoxycarbonyl-7-(*tert*-butyldimethylsilyl-oxy)-2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one (*rac*-**24b**): R_f = 0.56 (Pentane/EtOAc = 10:1, CAM); ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.40–7.26 (m, 5H, CH$_2$*Ph*), 5.42 (dd, *J* = 5.2, 2.0 Hz, 1H, H-*1*), 4.60 (d, *J* = 10.9 Hz, 1H, C*H*HPh), 4.48 (d, *J* = 10.9 Hz, 1H, CH*H*Ph), 4.29 (ddd, *J* = 6.8, 5.6, 3.3 Hz, 1H, H-*7*), 3.73 (s, 3H, CO$_2$*Me*), 3.01 (*virt.* dt, *J*≅11.0, 3.8 Hz, 1H, H-*6*), 2.83 (dd, *J* = 13.5, 11.0 Hz, 1H, *H*H-*5*), 2.45 (ddd, *J* = 14.6, 5.6, 2.0 Hz, 1H, *H*H-*8*), 2.21 (dd, *J* = 13.5, 4.0 Hz, 1H, H*H*-*5*), 2.08 (ddd, *J* = 14.6, 6.8, 5.2 Hz, H*H*-*8*), 0.85 (s, 9H, SiMe$_2$C*Me*$_3$), 0.04 ppm (s, 6H, Si*Me*$_2$CMe$_3$); ^{13}C NMR (91 MHz, $CDCl_3$): δ = 174.4 (C-*3*), 168.7 (*C*O$_2$Me), 136.8 (*Ph*), 128.4 (*Ph*), 127.9 (*Ph*), 127.5 (*Ph*), 83.3 (C-*1*), 79.6 (C-*4*), 78.3 (C-*7*), 68.2 (*C*H$_2$Ph), 61.6 (C-*9*), 52.7 (C-*11*), 44.6 (C-*8*), 42.0 (C-*6*), 32.9 (C-5), 25.6 (SiMe$_2$C*Me*$_3$), 17.9 (SiMe$_2$*C*Me$_3$), −4.87 (Si*Me*MeCMe$_3$), −4.92 ppm (SiMe*Me*CMe$_3$); IR (ATR): $\tilde{\nu}$ = 2952, 2935, 2926, 2856, 1777, 1730, 1435 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 375 (78) [M^+-57], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{19}H_{23}O_6Si$ [M^+-57] calcd. 375.1258, found 375.1256.

(1*R**,3*R**,4*R**,6*R**,7*R**)-7-Benzyloxy-6-methoxycarbonyl-3-(*tert*-butyldimethylsilyl-oxy)-9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one (*rac*-**25b**): R_f = 0.36 (Pentane/EtOAc = 10:1, CAM); m.p. = 78–80 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 7.2 Hz, 2H, CH$_2$*Ph*), 7.36 (t, *J* = 7.2 Hz, 2H, CH$_2$*Ph*), 7.30 (t, *J* = 7.2 Hz, 1H, CH$_2$*Ph*), 5.19 (*virt.* t, *J* ≅ 2.4 Hz, 1H, H-*1*), 4.76 (d, *J* = 11.0 Hz, 1H, C*H*HPh), 4.56 (d, *J* = 11.0 Hz, 1H, CH*H*Ph), 4.22 (*virt.* t, *J* ≅ 7.0 Hz, 1H, H-*3*), 3.72 (s, 3H, CO$_2$*Me*), 2.87 (dd, *J* = 10.5, 6.4 Hz, 1H, *H*H-*5*), 2.67 (dd, *J* = 6.4, 1.5 Hz, 1H, H-*4*), 2.44 (ddd, *J* = 14.5, 6.7, 2.0 Hz, 1H, *H*H-*2*), 2.07 (d, *J* = 10.5 Hz, 1H, H*H*-*5*), 1.85 (ddd, *J* = 14.5, 7.8, 2.8 Hz, 1H, H*H*-*2*), 0.85 (s, 9H, SiMe$_2$C*Me*$_3$), 0.04 (s, 3H, Si*Me*MeCMe$_3$), 0.03 ppm (s, 3H, SiMe*Me*CMe$_3$); ^{13}C NMR (91 MHz, CDCl3): δ = 171.4 (C-*8*), 169.7 (*C*O$_2$Me), 137.0 (*Ph*), 128.4 (*Ph*), 128.0 (*Ph*), 127.7 (*Ph*), 87.9 (C-*7*), 79.6 (C-*1*), 68.7 (*C*H$_2$Ph), 66.2 (C-*3*), 54.8 (C-*6*), 52.5 (CO$_2$*Me*), 46.9 (C-*4*), 34.3 (C-*2*), 25.7 (SiMe$_2$C*Me*$_3$), 21.7 (C-*5*), 17.9 (SiMe$_2$CMe$_3$), −4.8 (SiMe*Me*CMe$_3$), −4.9 ppm (Si*Me*MeCMe$_3$); IR (ATR): $\tilde{\nu}$ = 2952, 2933, 2857, 1776, 1738, 1471, 1234 cm^{-1}; MS (EI, 70 eV): *m*/*z* (%) = 375 (6) [M^+-57], 91 (100) [$C_7H_7^+$]; HRMS (EI): $C_{19}H_{23}O_6Si$ [M^+-57] calcd. 375.1258, found 375.1252; $C_{23}H_{32}O_6Si$ [M^+] calcd. 432.1963, found 432.1952.

Intramolecular photocycloaddition reaction of butenolide *rac*-22b: The reaction of *rac*-**22b** (24.0 mg, 59.3 μmol) in CH_3CN/acetone (11:1, 12 mL) was irradiated at λ = 300 nm for 2 h. The reaction mixture was concentrated in vacuo to afford a residue, which was purified by flash chroma-

tography (eluent: pentane/EtOAc = 6:1) on silica gel to afford straight product *rac*-**31b** (10.7 mg, 45%) and crossed product *rac*-**32b** (4.0 mg, 17%).

(1*R**,4*R**,6*R**,7*R**,9*R**)-4-Benzyloxy-9-hydroxymethyl-7-(*tert*-butyldimethylsilyloxy)-2-oxatricyclo[4.2.1.0^{4,9}]nonan-3-one (*rac*-**31b**): R_f = 0.40 (Pentane/EtOAc = 4:1, CAM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.28 (m, 5H, CH_2*Ph*), 5.01 (d, *J* = 11.3 Hz, 1H, C*H*HPh), 5.00 (d, *J* = 2.6 Hz, 1H, H-*1*), 4.66 (d, *J* = 11.3 Hz, 1H, CH*H*Ph), 4.29 (*virt.* td, *J* ≅ 5.4, 2.9 Hz, 1H, H-*7*), 3.95 (dd, *J* = 11.9, 6.4 Hz, 1H, *H*H-*10*), 3.81 (dd, *J* = 11.9, 6.4 Hz, 1H, H*H*-*10*), 2.66 (dd, *J* = 13.7, 10.8 Hz, 1H, *H*H-*5*), 2.49 (*virt.* dt, *J* ≅ 10.8, 3.5 Hz, 1H, H-*6*), 2.40 (ddd, *J* = 14.9, 5.4, 2.6 Hz, 1H, *H*H-*8*), 2.34 (t, *J* = 6.4 Hz, 1H, O*H*), 2.17–2.10 (m, 2H, H*H*-*8*, H*H*-*5*), 0.87 (s, 9H, $SiMe_2CMe_3$), 0.054 (s, 3H, Si*Me*MeCMe$_3$), 0.047 ppm (s, 3H, SiMe*Me*CMe$_3$); ^{13}C NMR (91 MHz, $CDCl_3$): δ = 176.3 (C-*3*), 137.4 (*Ph*), 128.5 (*Ph*), 128.0 (*Ph*), 127.7 (*Ph*), 83.8 (C-*1*), 78.5 (C-*7*), 77.1 (C-*4*), 67.7 (*C*H$_2$Ph), 61.2 (C-*10*), 59.5 (C-*9*), 44.1 (C-*8*), 41.4 (C-*6*), 30.3 (C-*5*), 25.7 ($SiMe_2CMe_3$), 18.0 ($SiMe_2CMe_3$), −4.9 ppm (Si*Me*$_2$CMe$_3$); IR (ATR): $\tilde{\nu}$ = 3503, 2928, 2856, 1770, 1471, 1462, 1254 cm^{-1}; MS (ESI): 405 $[M+H]^+$; HRMS (ESI): $C_{22}H_{33}O_5Si$ $[M+H]^+$ calcd. 405.2092, found 405.2092.

(1*R**,3*R**,4*R**,6*R**,7*R**)-7-Benzyloxy-6-hydroxymethyl-3-(*tert*-butyldimetheylsilyl-oxy)-9-oxatricyclo[4.3.0.0^{4,7}]nonan-8-one (*rac*-**32b**): R_f = 0.27 (Pentane/EtOAc = 4:1, CAM); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 7.8 Hz, 2H, CH_2*Ph*), 7.37 (*virt.* t, *J* ≅ 7.4 Hz, 2H, CH_2*Ph*), 7.31 (t, *J* = 7.1 Hz, 1H, CH_2*Ph*), 5.11 (d, *J* = 11.3 Hz, 1H, C*H*HPh), 4.79–4.75 (m, 2H, H-*1*, CH*H*Ph), 4.20 (*virt.* t, *J* ≅ 7.2 Hz, 1H, H-*3*), 3.82 (d, *J* = 11.8 Hz, 1H, *H*H-10), 3.67 (dd, *J* = 11.8, 7.2 Hz, 1H, H*H*-10), 2.84 (d, *J* = 6.1 Hz, 1H, H-*4*), 2.47–2.34 (m, 2H, *H*H-5, *H*H-2), 1.95 (brs, 1H, O*H*), 1.93 (d, *J* = 10.5 Hz, 1H, H*H*-*5*), 1.86 (ddd, *J* = 14.3, 7.8, 2.3 Hz, 1H, H*H*-*2*), 0.86 (s, 9H, $SiMe_2CMe_3$), 0.05 (s, 3H, Si*Me*MeCMe$_3$), 0.04 ppm (s, 3H, SiMe*Me*CMe$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.8 (C-*8*), 137.6 (*Ph*), 128.5 (*Ph*), 128.0 (*Ph*), 127.6 (*Ph*), 85.1 (C-*7*), 80.3 (C-*1*), 68.4 (*C*H$_2$Ph), 67.3 (C-*3*), 61.9 (C-*10*), 54.1 (C-*6*), 45.0 (C-*4*), 34.4 (C-*2*), 25.7 ($SiMe_2CMe_3$), 21.1 (C-*5*), 18.0 ($SiMe_2CMe_3$), −4.7 (Si*Me*MeCMe$_3$), −4.8 ppm (SiMe*Me*CMe$_3$); IR (ATR): $\tilde{\nu}$ = 3465, 2928, 2856, 1771, 1471, 1379, 1252 cm^{-1}; MS (ESI): 405 $[M+H]^+$; HRMS (ESI): $C_{22}H_{33}O_5Si$ $[M+H]^+$ calcd. 405.2092, found 405.2093.

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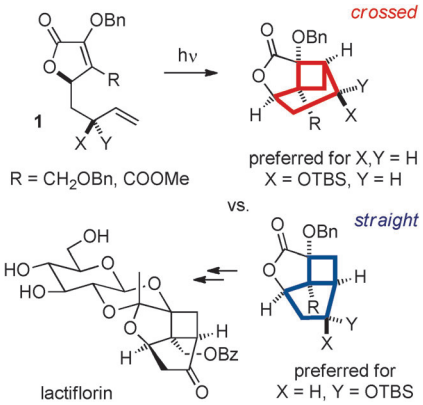
FULL PAPERS

Substitution matters in the [2+2] photocycloaddition of butenolides **1**: For X,Y = H and X = OTBS, Y = H the crossed products were formed as major regioisomers (r.r. = 89:11 to 65:35), whereas the straight products prevailed in the case of X = H, Y = OTBS in particular for R = CH_2OBn (r.r. = 70:30). The latter product (X = H, Y = OTBS, R = CH_2OBn) was successfully converted into the monoterpene glycoside lactiflorin.



Cycloaddition

*Ping Lu, Eberhardt Herdtweck, Thorsten Bach**

Intramolecular [2+2] Photocycloaddition Reactions as an Entry to the 2-Oxatricyclo[4.2.1.$0^{4,9}$]nonan-3-one Skeleton of Lactiflorin