Catalyzed Asymmetric *Diels–Alder* Reactions of Benzoquinone. Total Synthesis of (−)-Ibogamine

by **James D. White*** and **Younggi Choi**

Department of Chemistry, Oregon State University, Corvallis, Oregon, USA
(phone: 541-737-2173; fax: 541-737-2660; e-mail: james.white@orst.edu)

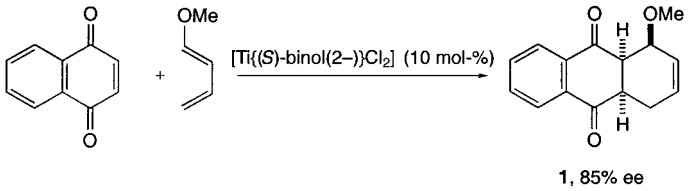
Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday and in recognition of his numerous contributions to asymmetric synthesis.

The *Diels–Alder* reaction of 1,4-benzoquinone with 1,3-dienes catalyzed by *Mikami*'s [Ti{(*S*)-binol(2−)}Cl_2] complex (binol = [1,1′-binaphthalene]-2,2′-diol) gives cycloadducts in good yield and in high enantiomer excess. A model is proposed to explain the observed absolute configuration of cycloadducts, and the reaction is used as the key step in an asymmetric synthesis leading to the alkaloid (−)-ibogamine.

1. Introduction. – The asymmetric *Diels–Alder* reaction has become one of the most widely used constructs for the assembly of enantiomerically enriched chiral carbocycles [1]. In its catalyzed version, the reaction offers an especially powerful synthetic method, which can lead to adducts from achiral materials in good yield and high enantiomer excess (ee) at or below room temperature [2]. Most catalyzed cycloadditions have relied on two-point ligation of an achiral dienophile with the chiral catalyst to form a relatively rigid, highly asymmetric, activated complex [3]. Typical dienophiles in this class are β-dicarbonyl compounds, where chelation with a metal such as titanium bound to a chiral ligand creates a complex in which only one face of the dienophile is exposed for reaction with its diene partner. As a result, asymmetric *Diels–Alder* additions in this mode can be very efficient. The asymmetric *Diels–Alder* reaction with a dienophile such as a simple α,β-unsaturated ketone or a 1,4-quinone raises the question of whether stereocontrol can be exercised effectively by single-point ligation of a chiral catalyst with the lone pair of electrons of only one carbonyl group. This question was first answered in the affirmative by *Mikami* and co-workers who showed that the reaction of 1,4-naphthoquinone with 1-methoxybuta-1,3-diene in the presence of a [Ti^{IV}\{binol(2−)\}] catalyst (binol = [1,1′-naphthalene]-2,2′-diol) led to diketone **1** in high ee (*Scheme 1*) [4]. Subsequently, we found that benzoquinone in the presence of the *Mikami* catalyst underwent *Diels–Alder* cycloaddition with a 1,3-diene derivative in similarly high ee [5]. Other examples from the laboratories of *Corey* [6] and *Nicolaou* [7] illustrate the participation of substituted benzoquinones in asymmetric *Diels–Alder* reactions catalyzed by *Mikami*'s [Ti{binol(2−)}Cl_2] system, although the argument for single-point ligation in these cases is less clear. Recently, it was shown that α,β-unsaturated ketones, for which single-point ligation is obligatory, undergo *Diels–Alder* addition to cyclopentadiene in the presence of a chiral imidazolidinone to give cycloadducts in moderate to high ee; however, the generality

of this process remains to be established [8]. Thus, while precedent exists to suggest that 1,4-benzoquinone may serve as a chiral dienophile in the presence of an asymmetric catalyst, the proposition that this strategy offers a practical and general entry to *Diels–Alder* adducts of consistently high enantiomer purity remained to be demonstrated.

Scheme 1

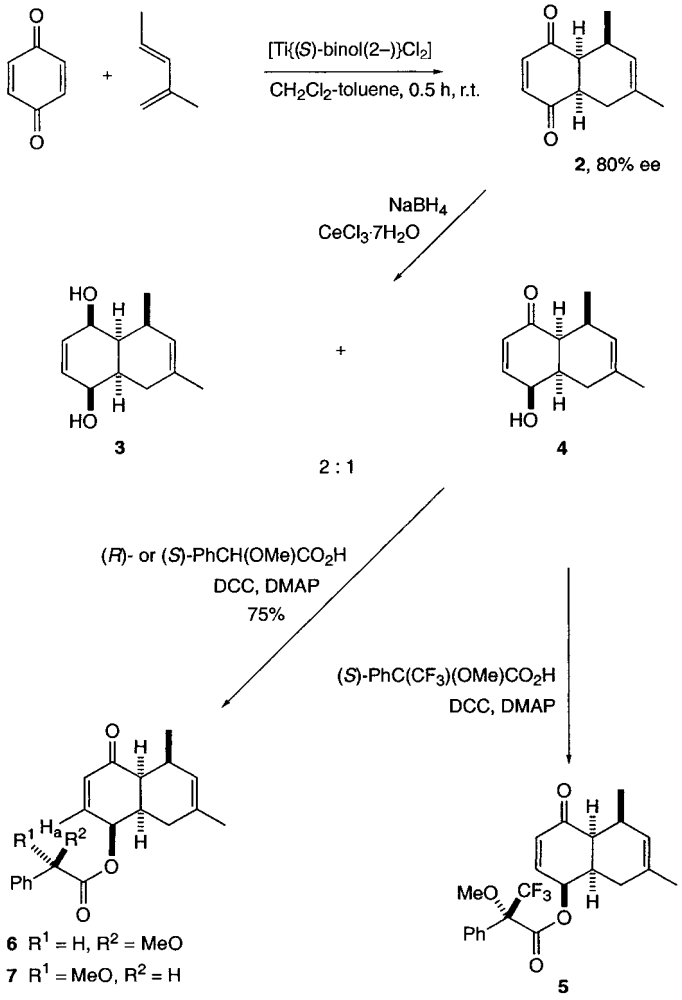


1, 85% ee

2. Results and Discussion. – In principle, any asymmetric catalyst attached to one of the carbonyl groups of 1,4-benzoquinone breaks the D_{2d} symmetry of this dienophile and should, therefore, be capable of producing an asymmetric *Diels–Alder* adduct if *i*) the 1,3-diene component is not symmetrical, and *ii*) the rate of the catalyzed reaction substantially exceeds that of the uncatalyzed process. Our first experiments with 1,4-benzoquinone, various dienes, and the [Ti{taddol(2–)}Cl_2] catalyst [9] (taddol = 2,2-dimethyl-$\alpha,\alpha,\alpha',\alpha'$-tetraphenyl-1,3-dioxolane-1,4-dimethanol) at room temperature were not encouraging, the ee of *Diels–Alder* adducts generally being below 60%; it became clear that this catalyst system was not sufficiently active to accelerate cycloaddition at lower temperatures where improved stereoselectivity might be observed. Therefore, we turned to *Mikami*'s [Ti{binol(2–)}Cl_2] catalyst, an established commodity in the context of asymmetric *Diels–Alder* addition to naphthoquinone [4], and were pleased to find that *Diels–Alder* adducts of 1,4-benzoquinone could be obtained in good yield and high ee with this catalyst. Thus, addition of 2-methylpenta-1,3-diene to benzoquinone in the presence of 10 mol-% of [Ti{(*S*)-binol(2–)}Cl_2] gave **2** in 80% ee (*Scheme 2*). The dione **2** was unstable to chromatography and was immediately subjected to reduction according to *Gemal* and *Luche* [10] with $NaBH_4$ and cerium(III) chloride heptahydrate to afford a mixture of diol **3** and hydroxy ketone **4**. The latter was converted to its (*S*)-*Mosher* ester **5** [11], which permitted the determination of ee by analysis of its ^{19}F-NMR spectrum; **4** was also esterified with (*R*)- and (*S*)-*O*-methylmandelic acids to produce *O*-methylmandelates **6** and **7**. Shielding of H_a by the phenyl ring of (*R*)-*O*-methylmandelate **6** relative to its (*S*)-diastereoisomer **7** and applying the model of *Trost* and co-workers [12] enabled the absolute configuration of these esters and hence **2** to be determined as shown.

We next examined the cycloaddition of (silyloxy)dienes **8** and **9** with 1,4-benzoquinone in the presence of [Ti{(*S*)-binol(2–)}Cl_2] and, again, found that the reaction was greatly accelerated relative to the uncatalyzed process (*Scheme 3*). *Luche* reduction of cycloadducts **10** and **11** to **12** and **13**, respectively, with subsequent ketalization by 2,2-dimethoxypropane and oxidation of the protected allylic alcohols **15** and **16** led to α,β-unsaturated ketones **17** and **18**. These ketones allowed us to determine that the *Diels–Alder* reactions with **8** and **9** had taken place with an ee of 83

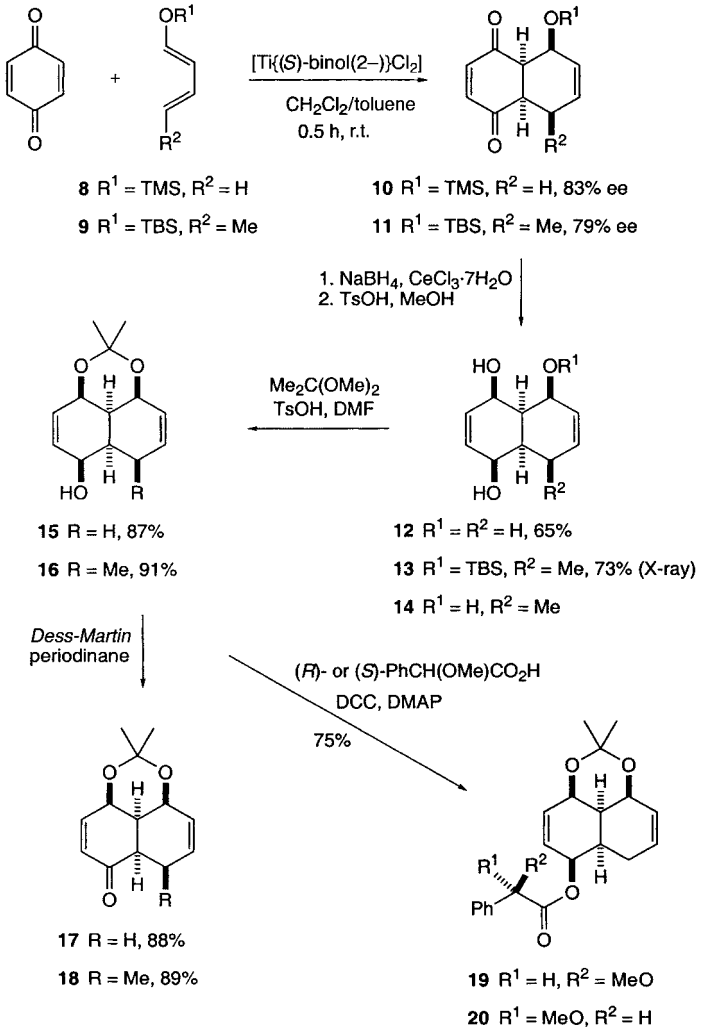
Scheme 2



DCC = dicyclohexylcarbodiimide, DMAP = *N*,*N*-dimethylpyridin-4-amine

and 79%, respectively, as measured by HPLC (chiral *OD* column). Diol **13** was conveniently crystalline, and its absolute configuration was determined by X-ray crystallographic analysis (*Fig. 1*). Although none of the substances in the series originating from diene **8** could be crystallized, the (*R*)- and (*S*)-*O*-methylmandelates **19** and **20**, respectively, prepared from **15** established that **10** possessed the absolute configuration shown [12]. Thus, all three cycloadducts **2**, **10**, and **11** obtained with the [Ti{(*S*)-binol(2−)}Cl_2] complex are found to have the same absolute configuration; furthermore, they are in the same enantiomeric series that *Mikami* and co-workers obtained with 1,4-naphthaquinone using the same catalyst. A transition state that

Scheme 3



TMS = Me_3Si, TBS = $^tBuMe_2Si$, DCC = dicyclohexylcarbodiimide, DMAP = *N*,*N*-dimethylpyridin-4-amine

rationalizes these results is presented in *Fig. 2*, although it must be remembered that the precise structure of the *Mikami* catalyst is unknown.

Unfortunately, an attempt to extend the [Ti{binol(2–)}Cl_2]-catalyzed *Diels–Alder* reaction of quinones to methyl 1,4-benzoquinone-2-carboxylate was less successful (*Scheme 4*). The latter, prepared by oxidation of methyl 2,5-dihydroxybenzoate as reported by *Kraus* and *Taschner* [13] and used *in situ*, was reacted with diene **9** to give cycloadduct **21** in only 36% ee whose absolute configuration was not determined. The racemic version of **21** has provided a convenient platform from which to launch syntheses of polyhydroxylated sesquiterpenoids of the agarofuran family, including

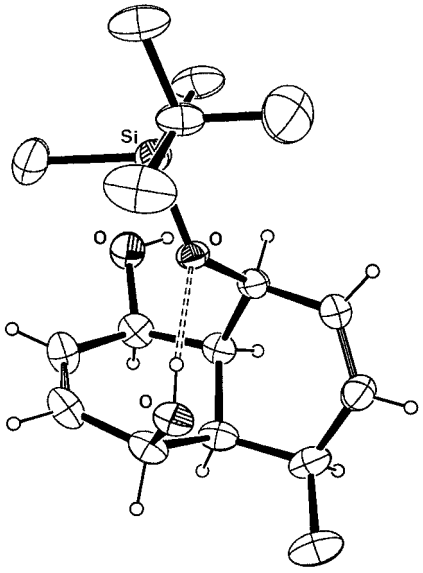


Fig. 1. *ORTEP Plot of* **13** *with displacement ellipsoids at the 30% probability level.* Configuration shown is absolute.

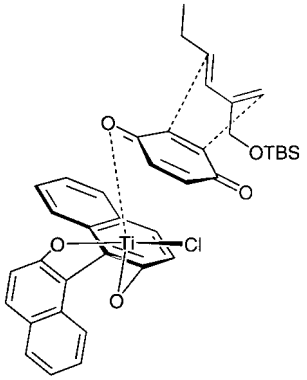
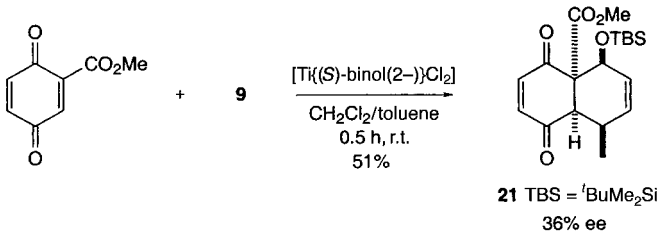


Fig. 2. *Proposed [Ti{(*S*)-binol(2−)}Cl$_2$]−benzoquinone complex in which the top face of the more remote double bond of the quinone is exposed for* endo *cycloaddition with* **24**, *leading to* **27**

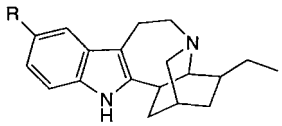
(±)-euonyminol [14], but an efficient asymmetric entry to the highly functionalized decalin core of this group remains elusive at this point. On the other hand, our effort to exploit the catalyzed asymmetric *Diels–Alder* reaction of 1,4-benzoquinone in a synthesis of the indole alkaloid (−)-ibogamine (**22**) was more successful.

(−)-Ibogamine (**22**) and its congener (−)-ibogaine (**23**) are found in the west-African shrub *Tabernanthe iboga* [15]; these alkaloids have attracted attention due to anecdotal evidence that they reduce addiction to heroin and cocaine [16]. The

Scheme 4



structures of **22** and **23** were determined by *Taylor* and co-workers in 1957 who employed both chemical degradation and X-ray crystallographic analysis [17], and the absolute configuration of **22** was established by *Bláha* and co-workers [18]. Following the first synthesis of (±)-ibogamine by the *Büchi* group in 1965 [19], numerous routes to the racemic alkaloid have been published [20], including one by *Sallay* [21], which began with a *Diels–Alder* cycloaddition to 1,4-benzoquinone. Only one asymmetric pathway to ibogamine has been reported, and this concluded at a 80:20 mixture favoring the (+)-enantiomer [22].



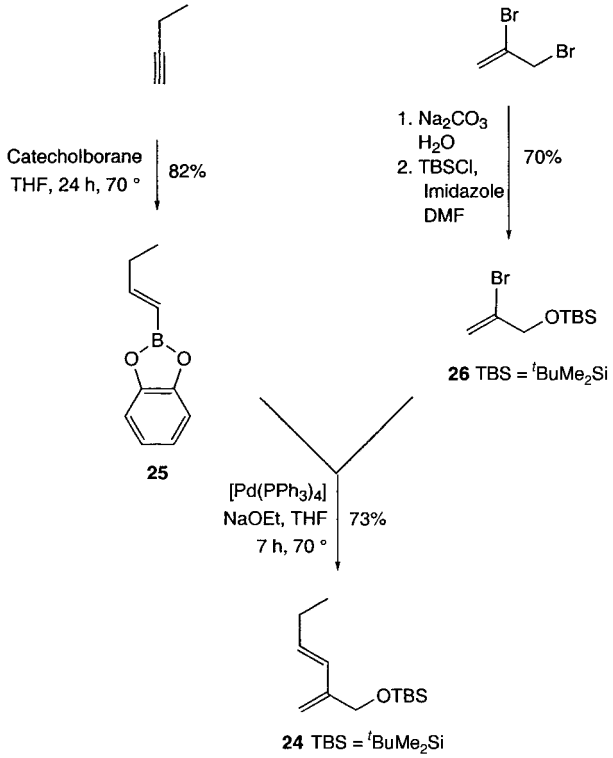
22 R = H, (–)-Ibogamine

23 R = MeO, (–)-Ibogaine

Our plan for the synthesis of (−)-ibogamine (**22**) built upon the earlier work of *Sallay* [21], but foresaw the possibility of turning *Sallay*'s route into one of greater economy by employing a more highly functionalized diene in the initial *Diels–Alder* reaction. Thus, our first focal point became the preparation of a 1,3-disubstituted butadiene, which carried appendages appropriate for constructing the non-indolic portion of **22** without the need to forge additional C–C bonds beyond the *Diels–Alder* step. This led us to the hexa-1,3-diene derivative **24**, which was obtained by a *Suzuki* coupling of (*E*)-boronate **25**, prepared by the reaction of but-1-yne with catecholborane (=1,3,2-benzodioxaborole) [23], with the 2-bromoallyl silyl ether **26** (*Scheme 5*). The latter was acquired from 2-bromoallyl bromide by the method of *Beswick* and *Widdowson* [24].

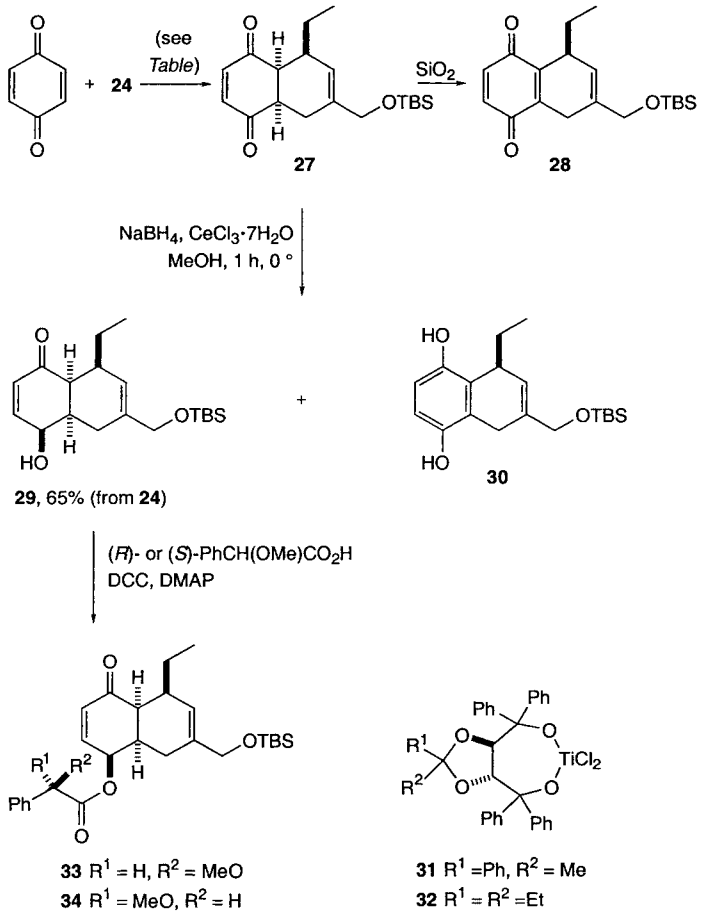
The *Diels–Alder* addition of 1,4-benzoquinone to **24** in the presence of *Mikami*'s [Ti{(*S*)-binol(2−)}Cl_2] complex proceeded to completion in less than 30 min at room temperature and gave a single *endo* adduct assigned structure **27** (*Scheme 6*). The adduct was unstable towards chromatographic purification on silica gel, which resulted in its conversion to the oxidized product **28**, and it was not possible to determine either the enantiomer purity or the absolute configuration of **27**. For this reason, the crude

Scheme 5



Diels–Alder adduct was subjected immediately to *Luche* reduction with $NaBH_4$ and cerium(III) chloride, and the stable *endo* hydroxy ketone **29** resulting from reduction of the less hindered carbonyl group was purified for further assay. A small amount (7%) of the dihydronaphthalenediol **30** was also isolated from this reaction, presumably a consequence of tautomerization of the diketone **27**. HPLC Analysis of **29**, employing a chiral *OD* column and a hexane/^{i}PrOH mixture as eluent, established that the ee of this substance, and hence **27**, was 81%. An increase in the catalyst concentration from 10 to 30 mol-% improved the ee of **27** to 87%, but no further enhancement occurred with increasing quantities of the catalyst (see *Table*). For comparison, the same *Diels–Alder* reaction between 1,4-benzoquinone and **24** was run in the presence of [Ti{tadol(2–)}Cl_2] catalysts **31** and **32**. In these cases, the reaction was much slower than that with the *Mikami* catalyst and gave only a modest yield of adduct in low ee. The ee improved with catalyst **31** as the reaction temperature was decreased from room temperature to 0° and then to –15°, but this was at the expense of chemical yield. It is clear from the results in the *Table* that binol is a much superior chiral ligand to taddol in catalyzing the addition of 1,4-benzoquinone to **24**; however, it is important to note that only the protocol specified by *Mikami* [4] in which the catalyst is prepared *in situ* from binol and diisopropoxytitanium dichloride was effective. An alternative catalyst

Scheme 6



TBS = ^{t}BuMe$_2$Si, DCC = dicyclohexylcarbodiimide DMAP = *N*,*N*-dimethyl-pyridin-4-amine

preparation in which binol, titanium tetraisopropoxide, and silicon tetrachloride were used [25] resulted in both a lower yield and diminished ee of **27**.

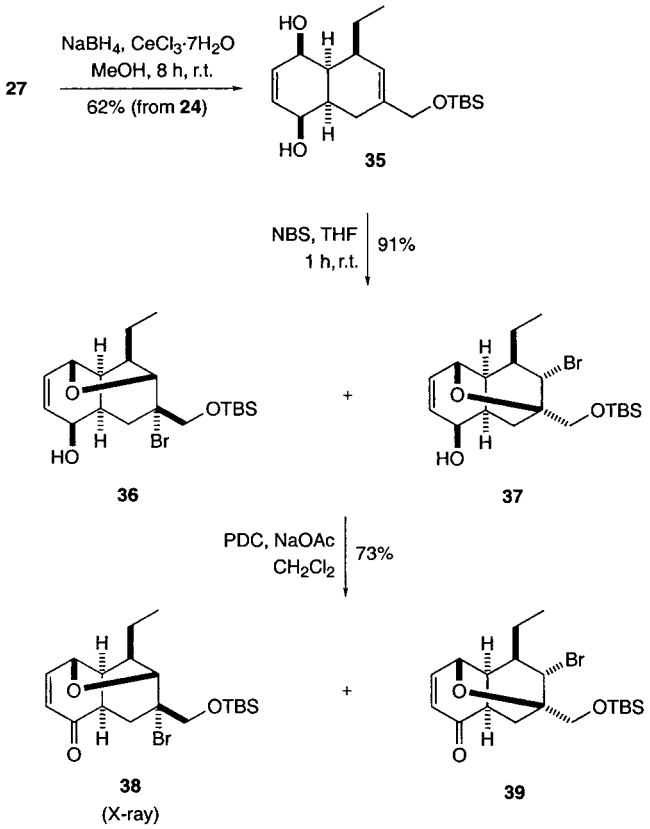
As with **4** and **15**, it was possible to ascertain the absolute configuration of **27** indirectly by employing the (*R*)- and (*S*)-*O*-methylmandelates **33** and **34**, respectively, derived from hydroxy ketone **29**. The upfield shift of H_a (*cf. Formulae* **6** and **7**) in **33** relative to **34** ($\Delta\delta$ 0.2 ppm) conforms to the model of *Trost* and co-workers [12] for this diastereoisomer **33** and gave assurance that we could proceed towards an asymmetric synthesis of (−)-ibogamine from its precursor. Subsequently, we developed a conclusive means for verifying that **27** was in the correct enantiomeric series when exhaustive *Luche* reduction of cycloadduct **27** was found to give *cis*-diol **35** (*Scheme 7*). The latter, when treated with *N*-bromosuccinimide, afforded a mixture of inseparable bromoepoxy alcohols **36** and **37**, which upon oxidation with pyridinium dichromate

Table. *Catalyzed Asymmetric* Diels–Alder *Reaction of 1,4-Benzoquinone with* **24**

Catalyst ([mol-%])	Reaction time [h]	Reaction temp. [°]	Product yield [%]	ee [%]
[Ti{(*S*)-binol}Cl_2] (10)	0.5	r.t.	65	81
[Ti{(*S*)-binol}Cl_2] (20)	0.5	r.t.	62	82
[Ti{(*S*)-binol}Cl_2] (30)	0.5	r.t.	65	87
31 (30)	24	r.t.	41	26
31 (30)	24	0	29	55
31 (30)	24	– 15	25	58
32 (30)	24	r.t.	23	10

yielded bromoepoxy ketones **38** and **39**. These compounds were separated with relative ease by chromatography, and **38**, which was highly crystalline, was subjected to X-ray analysis by the anomalous dispersion technique. *Fig. 3* displays the absolute configuration of **38**, which by extension confirms the absolute configuration of cycloadduct **27**. Importantly, the absolute configuration of **27** is consistent with that of **1**, **2**, **10**, and

Scheme 7



TBS = ^{t}BuMe$_2$Si, NBS = *N*-bromosuccinimide, PDC = pyridinium dichromate

11 obtained with the (*S*)-binol catalyst, lending confidence to future stereochemical predictions that may be made with this system. In contrast to **35**, hydroxy ketone **29** did not produce a bromoepoxy compound upon exposure to *N*-bromosuccinimide but instead gave bromohydrin **40** resulting from external solvolytic attack at the intermediate bromonium ion **41** (*Scheme 8*).

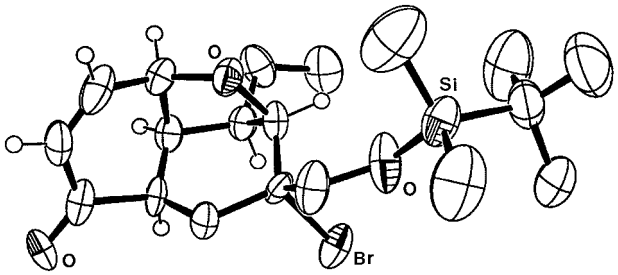
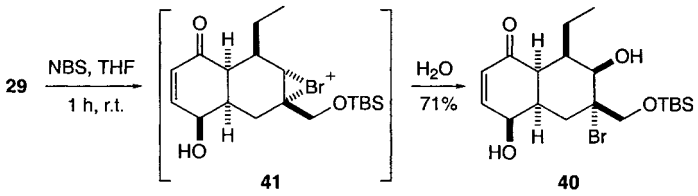


Fig. 3. *ORTEP Plot of* **38** *with displacement ellipsoids at the 30% probability level.* Configuration shown is absolute.

Scheme 8

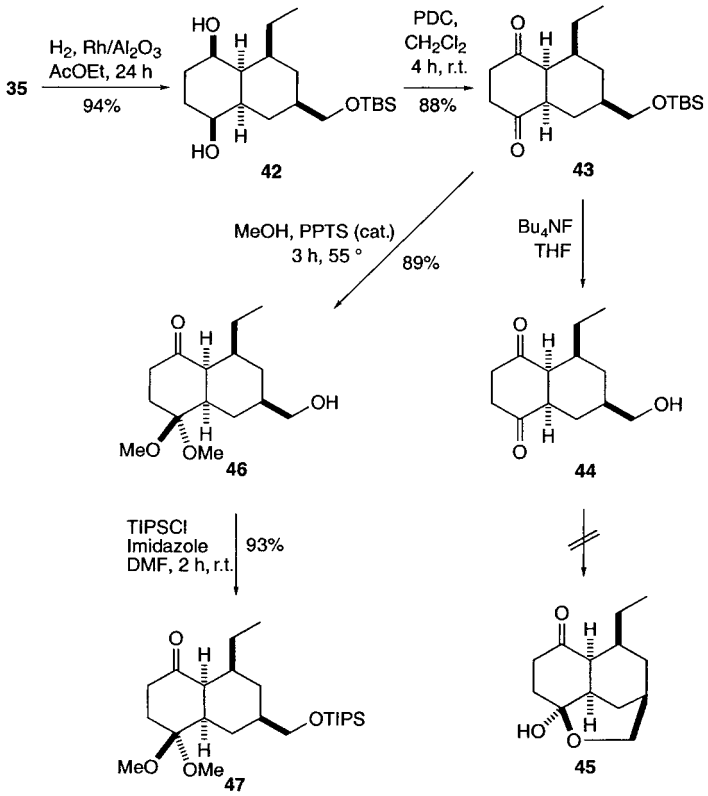


TBS = ^{t}BuMe$_2$Si, NBS = *N*-bromosuccinimide

With diol **35** of known absolute configuration in hand, it was now necessary to modify the left-hand ring of this structure in a way that would lead to the tricyclic framework of the non-indolic portion of **22**. The first requirement toward this end was reduction of both olefinic bonds of **35**, a transformation that was accomplished in a single step by hydrogenation over rhodium on alumina (*Scheme 9*). The selection of this catalyst ensured that no hydrogenolysis of the three allylic O-functions would occur during saturation of **35**, but equally important was delivery of hydrogen to the trisubstituted olefin exclusively from the *exo* face, thereby positioning the alkoxymethyl substituent on the concave interior of the *cis*-decalin structure **42** for a subsequent cyclization that would create the azatricyclic core of **22**.

Oxidation of diol **42** to diketone **43** with pyridinium dichromate was straightforward, but it now became necessary to distinguish between the two keto groups of **43** to proceed with chemistry on the ring that contained them. Our first attempt to discriminate between the keto groups of **43** involved cleavage of the silyl ether to give **44**, which we had hoped could be closed to the six-membered hemiketal **45**. This would have provided a means for blocking one ketone while synthetic operations were conducted on the other. Although the *endo* configuration of the hydroxymethyl substituent in **44** appeared to favor formation of **45**, no means could be found for

Scheme 9



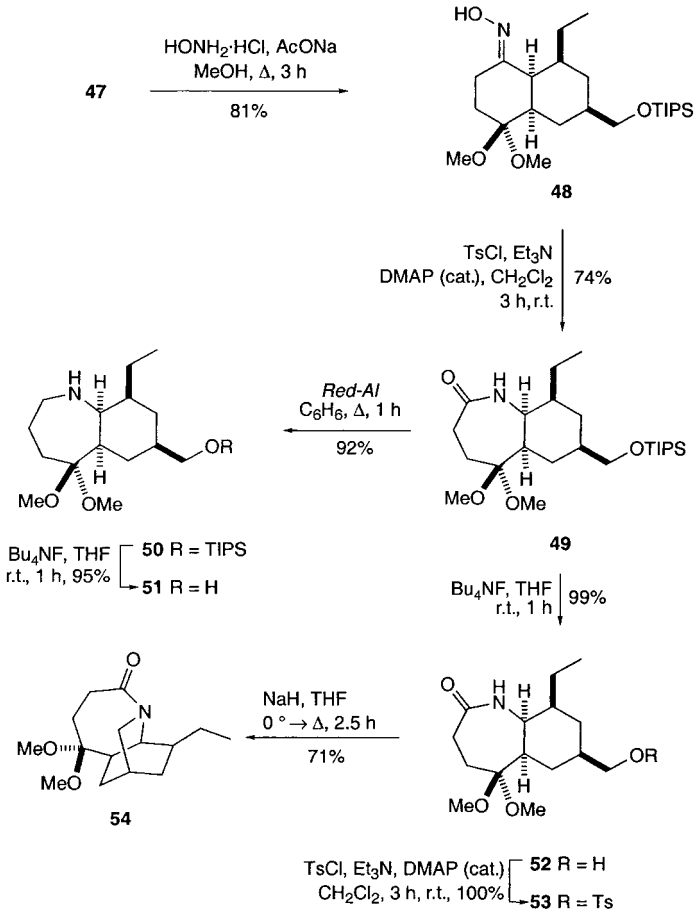
TBS = ^{t}BuMe$_2$Si, TIPS = ^{i}Pr$_3$Si, PDC = pyridinium dichromate, PPTS = pyridinium *p*-toluenesulfonate

effecting this conversion. A possible rationale for this failure is that the *cis*-decalin **44** cannot attain a conformation in which both the hydroxymethyl and ethyl substituents occupy the axial orientation necessary for internal hemiketalization. In any case, this result forced us to consider other means for differentiating the keto groups of **43**, and it was quickly discovered that only the less hindered ketone formed a dimethyl ketal **46**. The process of ketalization led to simultaneous cleavage of the (*tert*-butyl)dimethylsilyl ether of **43**, a result that conveyed the message that more robust protection of the primary alcohol would be needed for the next transformation. Ketal **46** was, therefore, converted to its more durable triisopropylsilyl ether **47**.

The pivotal *Beckmann* rearrangement envisioned for enlargement of the ketone ring of **47** to an ε-lactam required the preparation of (*E*)-oxime **48**, and this was accomplished in high yield with hydroxylamine hydrochloride and AcONa in MeOH at reflux (*Scheme 10*). Although ketoximes are known to undergo *Beckmann* rearrangement under a wide variety of conditions [26][1]), previous experience had taught us that

[1]) For a contemporary view of the *Beckmann* rearrangement, see [26b].

Scheme 10



TIPS = $^{i}Pr_3Si$, DMAP = *N*,*N*-dimethylpyridin-4-amine

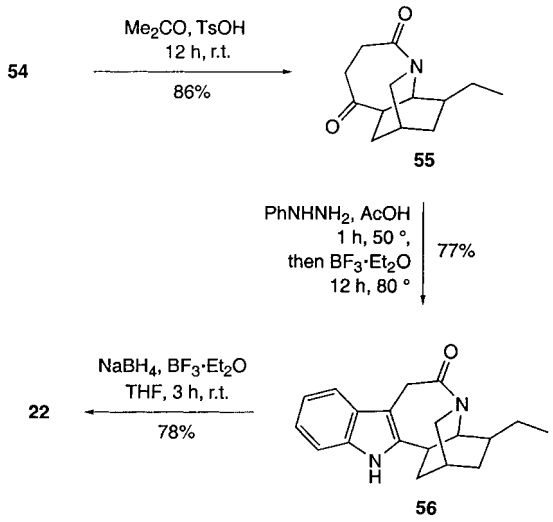
oxime tosylates are particularly good substrates for this transformation [27]. In the event, exposure of **48** to TsCl and Et_3N containing a small quantity of DMAP led to its smooth conversion to lactam **49**. None of the isomeric lactam resulting from migration of the less substituted C-atom was detected in the reaction mixture.

Our attention next turned to conversion of **49** into the azatricyclic core of ibogamine for which connection of the N-atom to the C-atom bearing the $^{i}Pr_3SiO$ group was the key. A displacement across the *endo* face of the bicycle to forge this N–C bond required an active N-nucleophile, and it was initially supposed that the secondary amine derived from reduction of lactam **49** would be best suited to this purpose. Lactam **49** was therefore reduced with sodium bis(2-methoxyethoxy)aluminum hydride (*Red-Al*), and the resulting amine **50** was then treated with Bu_4NF to give amino alcohol **51**. Surprisingly, all attempts to effect transannular cyclization of **51**, for example *via* a *Mitsunobu* reaction [28], were unsuccessful. Subsequent examination of the transition

state for this displacement not only provided an explanation for its failure but also suggested a remedy. Specifically, as the N-atom of **51** is brought towards the CH_2OH group for backside attack, a steric interaction develops between the *endo* H-atom of the CH_2 adjacent to the N-atom and the *endo* MeO substituent in the azepine ring. This steric confrontation is evidently sufficient to block cyclization. On the other hand, **49** with a sp^2 rather than a sp^3 C-atom adjacent to the N-atom would suffer no such steric impediment, and closure of the lactam to the tricyclic core of **22** should, therefore, be more facile. On the basis of this hypothesis, **49** was advanced to alcohol **52** and then to its tosylate **53**. That our conjecture was indeed correct was confirmed by the fact that exposure of **53** to NaH in THF produced the tricyclic lactam **54** cleanly and in good yield. The displacement of tosylate **53** by the lactam N-atom must be energetically quite favorable since the amide resonance of **53** is clearly lost in the course of its conversion to **54**.

The remaining transformation of **54** into (−)-ibogamine (**22**) first required release of the keto function masked as its dimethyl ketal, a process that was most efficiently accomplished by transketalization with acetone in the presence of an acidic catalyst [29] (*Scheme 11*). The resulting keto lactam **55** was next subjected to a *Fischer* indole synthesis [30] with phenylhydrazine in AcOH, the initially formed hydrazone requiring extended treatment with hot $BF_3 \cdot Et_2O$ to complete the reaction. Only one indole can be formed from **55** since the keto group is situated next to a bridgehead C-atom, and **56** was indeed produced in good yield by this process. The final stage, reduction of lactam **56**, proved to be more difficult than expected, conventional reagents such as $LiAlH_4$ being completely ineffective. Fortunately, a protocol due to *Sundberg* and co-workers [31] using diborane generated *in situ* from $NaBH_4$ and $BF_3 \cdot Et_2O$ was successful and furnished crystalline (−)-ibogamine (**22**), identical with a sample of the natural alkaloid kindly provided by Professor *Huffman* of Clemson University.

Scheme 11



3. Conclusions. – The preparation of (−)-ibogamine (**23**) in 14 steps from 1,4-benzoquinone and 10% overall yield is a powerful illustration of the value of the asymmetric *Diels–Alder* reaction as a starting point in a multistep synthesis. Furthermore, the knowledge that catalyzed asymmetric *Diels–Alder* reactions can now be applied with efficiency to 1,4-benzoquinone, at least with *Mikami*'s [Ti{binol(2−)}Cl_2] system, opens the way to more structurally varied chiral products than were attainable previously. It can be expected that much use will be made of this new paradigm of synthesis in the future.

We are grateful to Professor *Alexandre F. T. Yokochi* for the X-ray crystal structures of **13** and **38**. Financial support was provided by the *National Science Foundation* (CHE-0076103) and the *National Institutes of Health* (GM-58889).

Experimental Part

General. CC = Column chromatography. HPLC: t_R in min. IR Spectra: $\tilde{\nu}$ in cm^{-1}. NMR Spectra: δ in ppm rel. to $SiMe_4$, J in Hz. MS: in m/z.

(1S,4R,4aS,5S,8aR)-1,4,4a,5,8,8a-Hexahydro-5,7-dimethylnaphthalene-1,4-diol (**3**) *and (4S,4aR,8S,8aS)-4a,5,8,8a-Tetrahydro-4-hydroxy-6,8-dimethylnaphthalen-1(4H)-one* (**4**). To a soln. of 1M [Ti{(*S*)-binal(2−)}Cl_2] in CH_2Cl_2 (0.1 ml) and 1,4-benzoquinone (108 mg, 1 mmol) in CH_2Cl_2 (5 ml) at r.t. was added a soln. of (3*E*)-2-methylpenta-1,3-diene (121 mg, 1.47 mmol) in toluene (2 ml), and the mixture was stirred for 30 min at r.t. The resultant soln. was diluted with MeOH (5 ml) and cooled to 0°, and $NaBH_4$ (38 mg, 1 mmol) and $CeCl_3 \cdot 7H_2O$ (373 mg, 1 mmol) were added. The mixture was stirred for 1 h at 0° and then diluted with Et_2O (30 ml). The soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue separated by column chromatography (silica gel; AcOEt/hexanes 1:3): 138 mg (71% from benzoquinone) of **3/4** as a colorless oil.

Data of **3**: R_f (AcOEt/hexanes 1:3) 0.05. $[\alpha]_D^{23} = -164.5$ ($c = 1.0$, $CHCl_3$). IR (neat): 3405, 2960, 2875, 1437, 1378, 1061, 998, 774. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.23 (*d*, $J = 7.5$, 3 H); 1.69 (*m*, 3 H); 1.77 (br. *s*, 1 H); 1.82–1.89 (*m*, 1 H); 2.00–2.07 (*m*, 2 H); 2.26–2.40 (*m*, 2 H); 2.51–2.64 (*m*, 1 H); 4.15–4.22 (*m*, 1 H); 4.39–4.47 (*m*, 1 H); 5.43–5.58 (*m*, 1 H); 5.63–5.69 (*m*, 1 H); 5.82 (*ddd*, $J = 2.3$, 4.4, 10.2, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.4; 24.0; 27.7; 34.1; 37.6; 39.0; 64.9; 70.7; 128.9; 129.3; 130.7; 135.4. CI-MS: 193 ($[M+H]^+$), 176, 159, 147, 143, 131, 119, 109, 98, 86. HR-CI-MS: 194.1306 ($C_{12}H_{18}O_2^+$; calc. 194.1307).

Data of **4**: R_f (AcOEt/hexanes 1:3) 0.05. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.35 (*d*, $J = 7.6$, 3 H); 1.58–1.62 (*m*, 3 H); 1.93–2.06 (*m*, 3 H); 2.25–2.62 (*m*, 2 H); 2.67–2.78 (*m*, 1 H); 4.84–4.89 (*m*, 1 H); 5.27–5.31 (*m*, 1 H); 5.77–5.85 (*m*, 1 H); 6.56 (*dt*, $J = 2.1$, 10.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.2; 23.7; 26.9; 34.4; 44.5; 50.3; 70.9; 127.0; 130.1; 131.3; 147.9; 200.8.

(R)-O-*Methylmandelate* **6**: ^{1}H-NMR (400 MHz, $CDCl_3$): 6.24 (H_a).

(*S*)-O-*Methylmandelate* **7**: ^{1}H-NMR (400 MHz, $CDCl_3$): 6.42 (H_a).

(1S,4R,4aR,5S,8aR)-1,4,4a,5,8,8a-Hexahydronaphthalene-1,4,5-triol (**12**). To a soln. of 1M [Ti{(*S*)-binol(2−)}Cl_2] in CH_2Cl_2 (0.2 ml) and 1,4-benzoquinone (216 mg, 2 mmol) in CH_2Cl_2 (5 ml) at r.t. was added a soln. of **8** (426 mg, 3 mmol) in toluene (2 ml), and the mixture was stirred for 30 min at r.t. The soln. was diluted with MeOH (5 ml) and cooled to 0°, and $NaBH_4$ (114 mg, 3 mmol) and $CeCl_3 \cdot 7H_2O$ (1.12 g, 3 mmol) were added. The mixture was stirred for 1 h at 0° and diluted with Et_2O (50 ml). The soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated to give a crude diol. To a stirred soln. of this diol (325 mg, 1.3 mmol) in MeOH (5 ml) at 0° was added TsOH (2 mg), and the mixture was stirred for 1 h at 0°. The mixture was evaporated and the residue chromatographed (silica gel; AcOEt/hexanes 1:3, then MeOH/CH_2Cl_2 1:15): 237 mg (65% from benzoquinone) of **12**. Colorless oil. R_f (AcOEt/hexanes 1:3) 0.05. IR (neat): 3345, 3025, 2886, 1406, 1248, 1088, 1039, 1002. ^{1}H-NMR (300 MHz, $CDCl_3$): 2.13–2.23 (*m*, 2 H); 2.29–2.34 (*m*, 1 H); 2.34–2.41 (*m*, 1 H); 3.93 (*s*, 3 H); 3.96–3.99 (*m*, 1 H); 4.43 (*t*, $J = 4.4$, 1 H); 4.50 (*d*, $J = 7.6$, 1 H); 5.76–5.84 (*m*, 3 H); 5.91 (*dt*, $J = 3.6$, 10, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 28.1; 32.9; 39.3; 63.5; 67.3; 67.9; 127.9; 130.4; 130.8; 133.3. CI-MS: 183 ($[M+H]^+$), 165, 147, 130, 129, 119, 105, 91, 86. HR-CI-MS: 183.1021 ($C_{10}H_{15}O_3^+$; calc. 183.1021).

*(1S,4R,4aR,5S,8R,8aR)-5-{[(*tert-*Butyl)dimethylsilyl]oxy}-1,4,4a,5,8,8a-hexahydro-8-methylnaphthalene-1,4-diol* (**13**). To a soln. of 1M [Ti{(*S*)-binol(2−)}Cl_2] in CH_2Cl_2 (0.1 ml) and 1,4-benzoquinone (107 mg,

1.0 mmol) in CH_2Cl_2 (5 ml) at r.t. was added a soln. of **9** (754 mg, 3.81 mmol) in toluene (2 ml), and the mixture was stirred for 30 min at r.t. The mixture was diluted with MeOH (5 ml) and cooled to 0°, and $NaBH_4$ (68 mg, 1.79 mmol) and $CeCl_3 \cdot 7\,H_2O$ (671 mg, 180 mmol) were added. The mixture was stirred for 1 h at 0° and diluted with Et_2O (50 ml). The soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:5): 203 mg (73%, benzoquinone) of **13**. White solid. R_f (AcOEt/hexanes 1:5) 0.16. M.p. 148–149°. $[\alpha]_D^{23} = +246.4$ ($c = 1.26$, $CHCl_3$). IR (KBr): 3412, 3325, 2957, 2929, 2854, 1469, 1248, 1086, 1025. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.18 (*s*, 3 H); 0.19 (*s*, 3 H); 0.91 (*s*, 9 H); 1.27 (*d*, $J = 7.5$, 3 H); 1.95–2.00 (*m*, 1 H); 2.07–2.17 (*m*, 1 H); 2.38 (*dt*, $J = 4.2$, 7.5, 1 H); 2.46–2.53 (*m*, 1 H); 3.89–3.97 (*m*, 1 H); 3.98–4.06 (*m*, 1 H); 4.44–4.54 (*m*, 2 H); 5.66 (*ddd*, $J = 2.9$, 4.8, 10.1, 1 H); 5.71–5.80 (*m*, 2 H); 5.84 (*ddd*, $J = 2.4$, 4.7, 10.1, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −4.4; −3.1; 16.6; 18.3; 26.2; 34.0; 37.9; 41.6; 63.4; 64.6; 69.4; 125.6; 130.4; 133.1; 138.2. CI-MS: 253 ($[M - {}^t\mathrm{Bu}]^+$), 235, 217, 199, 179, 161, 143, 128, 105, 86. HR-CI-MS: 311.2049 ($C_{17}H_{31}O_3Si^+$; calc. 311.2043).

*(1S,4*R*,4a*R*,5S,8*R*,8a*R*)-1,4,4a,5,8,8a-Hexahydro-8-methylnaphthalene-1,4,5-triol* (**14**). To a stirred soln. of **13** (105 mg, 0.34 mmol) in MeOH (5 ml) at r.t. was added TsOH (1 mg), and the mixture was stirred for 1 h at 50°. The mixture was evaporated and the residue chromatographed (silica gel; AcOEt/hexanes 1:3, then MeOH/CH_2Cl_2 1:15): 56 mg (85%) of **14**. Colorless oil. R_f (AcOEt/hexanes 1:3) 0.05. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.23 (*d*, $J = 7.6$, 3 H); 1.97 (*dt*, $J = 4.2$, 6.4, 1 H); 2.44 (*dt*, $J = 4.6$, 7.9, 1 H); 2.48–2.57 (*m*, 1 H); 3.03 (*d*, $J = 8.7$, 1 H); 3.23 (*d*, $J = 7$, 1 H); 3.69 (*d*, $J = 7.4$, 1 H); 4.18 (*dt*, $J = 4$, 6.6, 1 H); 4.37–4.44 (*m*, 1 H); 4.55 (*t*, $J = 7.6$, 1 H); 5.71–5.76 (*m*, 1 H); 5.80 (*ddd*, $J = 2.7$, 4.4, 10.1, 1 H); 5.84–5.92 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.1; 33.6; 37.7; 40.8; 63.2; 63.4; 68.8; 127.6; 129.9; 134.5; 136.8.

*(3a*R*,6S,6a*R*,9aS,9b*R*)-3a,6,6a,7,9a,9b-Hexahydro-2,2-dimethylnaphtho[1,8-*de*][1,3]dioxin-6-ol* (**15**). To a stirred soln. of **12** (132 mg, 0.73 mmol) in DMF (2 ml) at r.t. was added 2,2-dimethoxypropane (0.2 ml, 1.64 mmol) and TsOH (2 mg), and the mixture was stirred for 16 h. The mixture was diluted with sat. aq. $NaHCO_3$ soln. (1 ml) and extracted with Et_2O (25 ml). The extract was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated and the residue chromatographed (silica gel; AcOEt/hexanes 1:3): 140 mg (87%) of **15**. Colorless oil. R_f (AcOEt/hexanes 1:3) 0.13. $[\alpha]_D^{23} = +17.7$ ($c = 1.39$, $CHCl_3$). IR (neat): 3423, 3024, 2985, 2903, 1378, 1223, 1104, 1062. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.38 (*s*, 3 H); 1.48 (*s*, 3 H); 2.13–2.22 (*m*, 3 H); 2.30–2.39 (*m*, 1 H); 2.52–2.60 (*m*, 1 H); 4.06–4.14 (*m*, 1 H); 4.41–4.48 (*m*, 1 H); 4.48–4.55 (*m*, 1 H); 5.72–5.80 (*m*, 1 H); 5.84 (*ddd*, $J = 0.7$, 3.5, 10.2, 1 H); 5.94 (*ddd*, $J = 1.6$, 3.2, 10.2, 1 H); 6.00–6.08 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.4; 25.7; 29.7; 35.2; 64.3; 65.5; 102.2; 127.5; 129.6; 131.6; 133.0. CI-MS: 223 ($[M + H]^+$), 207, 165, 147, 129, 117, 91. HR-CI-MS: 223.1342 ($C_{13}H_{19}O_3^+$; calc. 223.1334).

*(3a*R*,6S,6a*R*,7R,9aS,9b*R*)-3a,6,6a,7,9a,9b-Hexahydro-2,2,7-trimethylnaphtho[1,8-*de*][1,3]dioxin-6-ol* (**16**). As described for **15**, with **14** (24 mg, 0.12 mmol), DMF (1 ml), 2,2-dimethoxypropane (0.1 ml, 0.82 mmol), and TsOH (1 mg), extraction with Et_2O (15 ml). CC (silica gel; AcOEt/hexanes 1:5) gave 26 mg (91%) of **16**. Colorless oil. R_f (AcOEt/hexanes 1:5) 0.23. $[\alpha]_D^{23} = +150.7$ ($c = 1.9$, $CHCl_3$). IR (neat): 3474, 2984, 2936, 2903, 2878, 1373, 1221, 1068, 1031, 978. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.23 (*d*, $J = 7.5$, 3 H); 1.40 (*s*, 3 H); 1.50 (*s*, 3 H); 1.95 (*ddd*, $J = 3.8$, 6.1, 9.7, 1 H); 2.34–2.46 (*m*, 1 H); 2.69 (*ddd*, $J = 6$, 10.6, 11.9, 1 H); 2.89 (*d*, $J = 12.3$, 1 H); 4.08 (*ddd*, $J = 3.6$, 6, 12.2, 1 H); 4.32–4.39 (*m*, 1 H); 4.72 (*ddt*, $J = 1.2$, 3.5, 10.4, 1 H); 5.62 (*ddd*, $J = 3.1$, 4.1, 10, 1 H); 5.87–5.92 (*m*, 2 H); 6.11 (*ddd*, $J = 1.6$, 6, 10, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.5; 26.3; 29.2; 32.5; 36.6; 38.2; 61.2; 62.9; 68.7; 103.0; 123.2; 132.3; 139.5. CI-MS: 237 ($[M + H]^+$), 221, 179, 161, 144, 143, 123, 117, 106, 91, 86. HR-CI-MS: 237.1491 ($C_{14}H_{21}O_3^+$; calc. 237.1491).

*(3a*R*,6a*R*,9aS,9b*R*)-6a,7,9a,9b-Tetrahydro-2,2-dimethylnaphtho[1,8-*de*][1,3]dioxin-6(3a*H*)-one* (**17**). To a stirred suspension of *Dess–Martin* periodinane (80 mg, 0.19 mmol) in CH_2Cl_2 (5 ml) at r.t. was added a soln. of **15** (28 mg, 0.13 mmol) in CH_2Cl_2 (1 ml), and the mixture was stirred for 30 min at r.t. The reaction was quenched by the simultaneous addition of sat. aq. $NaHCO_3$ soln. (3 ml) and 10% aq. $Na_2S_2O_3$ soln. (3 ml). This mixture was stirred for 30 min. Then the org. layer was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:3): 24 mg (88%) of **17**. White solid. R_f (AcOEt/hexanes 1:3) 0.3. M.p. 80–81°. The ee was measured by HPLC (*Diacel Chiralpak OD*, hexanes/^{i}PrOH 99:1, flow rate 1.05 ml/min): t_{minor} 21.8, t_{major} 24.8. $[\alpha]_D^{23} = +110.2$ ($c = 0.64$, $CHCl_3$). IR (neat) 3033, 2987, 2891, 1681, 1379, 1226, 1084. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.42 (*s*, 3 H); 1.46 (*s*, 3 H); 1.87 (*dddd*, $J = 2.6$, 5.2, 5.2, 16.8, 1 H); 2.70 (*ddd*, $J = 3.4$, 5.1, 6.8, 1 H); 2.85 (*dddt*, $J = 0.9$, 3.3, 6, 16.8, 1 H); 3.16 (*ddd*, $J = 7.6$, 7.6, 7.6, 1 H); 4.36–4.43 (*m*, 1 H); 4.86 (*dt*, $J = 2.7$, 8, 1 H); 5.67 (*m*, 1 H); 5.99–6.05 (*m*, 1 H); 6.06 (*dd*, $J = 2.3$, 10.4, 1 H); 6.94 (*ddd*, $J = 0.8$, 3.1, 10.4, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.1; 25.1; 30.5; 40.3; 42.0; 62.1; 67.3; 102.4; 126.6; 129.8; 130.5; 150.0; 198.8. CI-MS: 221 ($[M + H]^+$), 205, 162, 149, 134, 133, 117, 105, 85. HR-CI-MS: 221.1179 ($C_{13}H_{17}O_3$; calc. 221.1178).

*(3a*R,*6a*R,7R,*9a*S,*9b*R*)-6a,7,9a,9b-Tetrahydro-2,2,7-trimethylnaphtho[1,8-*de*][1,3]dioxin-6(3a*H*)-one* (**18**). To a stirred suspension of *Dess–Martin* periodinane (46 mg, 0.11 mmol) in CH_2Cl_2 (5 ml) at r.t. was added a soln. of **16** (17 mg, 0.07 mmol) in CH_2Cl_2 (1 ml), and the mixture was stirred for 1 h at r.t. The reaction was quenched by the simultaneous addition of sat. aq. $NaHCO_3$ soln. (2 ml) and 10% aq. $Na_2S_2O_3$ soln. (2 ml), and the mixture was stirred for 1 h. The org. layer was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:5): 15 mg (89%) of **18**. White solid. R_f (AcOEt/hexanes 1:5) 0.14. M.p. 73–74°. The ee was measured by HPLC (*Diacel Chiralpak OD*, hexanes/^{i}PrOH 97:3, flow rate 0.9 ml/min): t_{minor} 13.3, t_{major} 14.8. $[\alpha]_D^{23} = +52.6$ ($c = 0.94$, $CHCl_3$). IR (neat): 2988, 2936, 2876, 1686, 1375, 1225, 1087. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.43 (*d*, *J* = 6.8, 3 H); 1.44 (*s*, 3 H); 1.48 (*s*, 3 H); 2.22–2.30 (*m*, 1 H); 2.72 (*ddd*, *J* = 0.8, 4, 6.5, 1 H); 3.11 (*ddd*, *J* = 7.5, 7.5, 7.5, 1 H); 4.43 (*ddd*, *J* = 2.6, 5.3, 7.8, 1 H); 4.88 (*dt*, *J* = 2.7, 8, 1 H); 5.63 (*dt*, *J* = 2.9, 10.1, 1 H); 5.95 (*ddt*, *J* = 0.9, 2.5, 10.1, 1 H); 6.03 (*dd*, *J* = 2.3, 10.3, 1 H); 6.86 (*ddd*, *J* = 0.8, 3.2, 10.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.7; 25.1; 30.4; 32.9; 42.9; 47.5; 62.4; 67.6; 102.3; 125.7; 131.7; 136.7; 148.3; 199.8. CI-MS: 235 ($[M+H]^+$), 219, 177, 159, 148, 131, 121, 105, 94, 91. HR-CI-MS: 235.1333 ($C_{14}H_{19}O_3^+$; calc. 235.1334).

*(*R*)-*O*-Methylmandelate* **19**: ^{1}H-NMR (400 MHz, $CDCl_3$): 1.39 (*s*, 3 H); 1.48 (*s*, 3 H); 1.88 (*dt*, *J* = 5.5, 17.1, 1 H); 2.13 (*dddd*, *J* = 3.1, 4.9, 11.2, 17.1, 1 H); 2.42 (*ddt*, *J* = 1.3, 5, 16.5, 1 H); 2.49–2.56 (*m*, 1 H); 3.47 (*s*, 3 H); 4.22–4.27 (*m*, 1 H); 4.63–4.68 (*m*, 1 H); 4.84 (*s*, 1 H); 5.32–5.36 (*m*, 1 H); 5.51 (*ddd*, *J* = 1.6, 1.9, 10.3, 1 H); 5.82 (*ddd*, *J* = 2.5, 3.4, 10.3, 1 H); 5.84 (*dt*, *J* = 2.9, 10.3, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.7; 25.3; 30.0; 33.7; 34.8; 57.8; 60.9; 68.7; 73.1; 83.0; 101.7; 127.4; 128.7; 128.9; 129.1; 129.2; 129.7; 130.6; 136.5; 170.6.

*(*S*)-*O*-Methylmandelate* **20**: ^{1}H-NMR (400 MHz, $CDCl_3$): 1.24 (*dt*, *J* = 5.2, 17.2, 1 H); 1.38 (*s*, 3 H); 1.46 (*s*, 3 H); 1.83–1.99 (*m*, 1 H); 2.13–2.29 (*m*, 1 H); 2.35–2.45 (*m*, 1 H); 3.46 (*s*, 3 H); 4.17–4.23 (*m*, 1 H); 4.53–4.59 (*m*, 1 H); 4.80 (*s*, 1 H); 5.33–5.37 (*m*, 1 H); 5.63–5.73 (*m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.1; 25.3; 29.9; 33.5; 34.7; 57.7; 60.9; 68.7; 72.9; 82.9; 101.6; 127.7; 128.8; 129.1; 129.3; 129.7; 130.3; 136.6; 170.5.

*Methyl (1*R,*4*S,*4a*S,*8a*R*)-4-{[(*tert*-Butyl)dimethylsilyl]oxy}-4,5,8,8a-tetrahydro-1-methyl-5,8-dioxonaphthalene-4a(1*H*)-carboxylate* (**21**). To a stirred soln. of methyl gentisate (= methyl 3,6-dioxocyclohexa-1,4-diene-1-carboxylate; 168 mg, 1 mmol) at 0° was added silver(I) oxide (464 mg, 2 mmol) in one portion. The mixture was warmed to r.t. and stirred for 4 h. To 0.1M [Ti{(*S*)-binol(2–)}Cl_2] in CH_2Cl_2 (1 ml, 0.1 mmol) in CH_2Cl_2 (5 ml) was added the soln. obtained above, and the mixture was stirred for 5 min at r.t. A soln. of **9** (713 mg, 3.6 mmol) in toluene (1 ml) was added, and the mixture was stirred for 30 min at r.t. The mixture was evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:10): 186 mg (51%) of **21**. Colorless oil. R_f (AcOEt/hexanes 1:10) 0.13. The ee was measured by HPLC (*Diacel Chiralpak OD*, hexanes/^{i}PrOH 98:2, flow rate 1 ml/min): t_{major} 7.4, t_{minor} 19.0. $[\alpha]_D^{23} = -67.7$ ($c = 1.18$, $CHCl_3$). IR (neat): 1749, 1710, 1686, 1253, 1227, 1089, 1058, 1037, 842. ^{1}H-NMR (300 MHz, $CDCl_3$): −0.09 (*s*, 3 H); 0.01 (*s*, 3 H); 0.76 (*s*, 9 H); 1.42 (*d*, *J* = 7.6, 3 H); 2.13–2.22 (*m*, 1 H); 3.66 (*d*, *J* = 4.8, 1 H); 3.80 (*s*, 3 H); 4.77–4.79 (*m*, 1 H); 5.67–5.70 (*m*, 2 H); 6.58 (*d*, *J* = 10.3, 1 H); 6.77 (*d*, *J* = 10.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −4.9; −4.8; 17.5; 18.2; 26.0; 30.1; 50.8; 53.4; 66.6; 67.5; 126.3; 133.1; 133.8; 144.7; 169.5; 196.4. CI-MS: 365 ($[M+H]^+$), 349, 307, 275, 267, 247, 225, 201, 195, 173, 141, 91. HR-CI-MS: 365.1782 ($C_{19}H_{29}O_5Si^+$; calc. 365.1784).

*2-{[(*tert*-Butyl)dimethylsilyl]oxy}methyl}hexa-1,3-diene* (**24**). Into a flame-dried pressure bottle cooled to −78° was condensed but-1-yne (3.25 g, 60.1 mmol) under Ar. Then 1M catecholborane in THF (60 ml, 60 mmol) was injected into the stirred mixture, and the soln. was heated at 70° for 24 h. After the soln. had cooled to r.t., it was distilled under reduced pressure: 8.57 g (82%) of *2-[(1E)-but-1-enyl]-1,3,2-benzodioxoborole* (**25**). Colorless oil. B.p. 77–78°/2.5 Torr. IR (neat): 3199, 2959, 1643, 1246, 742. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.11 (*t*, *J* = 7.4, Me); 2.33 (*ddq*, *J* = 1.7, 7.5, 7.5, 2 H); 5.83 (*dt*, *J* = 1.7, 18.0, 1 H); 7.01–7.28 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.2; 28.8; 106.1; 112.2; 122.5; 148.2; 159.2. CI-MS: 174 (M^+), 159, 146, 134, 120, 115, 101, 93, 69. HR-CI-MS: 174.0852 ($C_{10}H_{11}{}^{11}BO_2^+$; calc. 174.0852).

To a soln. of 1.04 g (3 mol%) of [Pd(PPh_3)$_4$] in THF (80 ml) was added a soln. of **26** (7.53 g, 30.0 mmol) in THF (10 ml), and the mixture was stirred for 1 h at r.t. To this mixture was added a soln. of **25** (5.80 g, 33.3 mmol) in THF (10 ml) followed by 66.6 mmol (2 equiv.) of EtONa, and the resultant mixture was heated under reflux for 7 h. The mixture was allowed to cool to r.t. during 1 h and was treated with 3M aq. NaOH (1 ml) and H_2O_2 (30%, 1 ml) for 1 h at r.t. The mixture was extracted with hexane (3 × 30 ml), the extract washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; Et_2O/pentane 1:30): 4.96 g (73%) of **24**. Colorless oil. R_f (hexanes) 0.4. IR (neat): 2957, 2883, 2359, 2337, 1253, 1110. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.09 (*s*, 6 H); 0.92 (*s*, 9 H); 1.02 (*t*, *J* = 7.4, Me); 2.11 (*m*, 2 H); 4.32 (*m*, 2 H); 4.98 (*s*, 1 H); 5.19 (*m*, 1 H); 5.70 (*dt*, *J* = 6.5, 16.1, 1 H); 6.06 (*d*, *J* = 16.1, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.4 (2 C); 13.5; 18.3; 25.9 (3 C); 26.1; 63.0; 112.1; 128.7; 131.4; 144.8. CI-MS: 227 ($[M+H]^+$), 211, 195, 193, 169, 139, 137, 95, 83, 75. HR-CI-MS: 227.1815 ($C_{13}H_{27}OSi^+$; calc. 227.1831).

*(4aS,5S,8aR)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyl-4a,5,8,8a-tetrahydronaphthalene-1,4-dione* (**27**). To 1M [Ti{(*S*)-binol(2–)}Cl_2] in CH_2Cl_2 (1.7 ml) and 1,4-benzoquinone (603 mg, 5.58 mmol) in CH_2Cl_2 (3 ml) at r.t. was added a soln. of **24** (1.47 g, 6.49 mmol) in toluene (2 ml), and the mixture was stirred for 30 min at r.t. The mixture was evaporated, and the crude **27** was used immediately for the next reaction because of its facile oxidation to **28**.

Data of **28**: IR (neat) 2951, 2926, 2847, 1664, 838. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.04 (*s*, 6 H); 0.80 (*t*, *J* = 7.5, 3 H); 0.93 (*s*, 9 H); 1.51–1.72 (*m*, 2 H); 2.85 (*dd*, *J* = 2.4, 6.3, 23.6, 1 H); 3.13 (*dd*, *J* = 4.7, 23.6, 1 H); 3.47–3.53 (*m*, 1 H); 4.22 (br. *s*, 1 H); 5.77 (*m*, 1 H); 6.71 (*d*, *J* = 1.6, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.4 (2 C); 9.9; 18.4; 25.0; 25.9 (3 C); 28.2; 35.5; 66.1; 121.8; 134.9; 136.1; 136.6; 140.4; 143.2; 186.6; 186.9.

*(4S,4aR,8S,8aS)-6-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-8-ethyl-4a,5,8,8a-tetrahydro-4-hydroxynaphthalen-1(4*H*)-one* (**29**) *and (5S)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyl-5,8-dihydronaphthalene-1,4-diol* (**30**). To a soln. of **27** obtained above in MeOH (5 ml) at 0° was added $NaBH_4$ (211 mg, 5.58 mmol) and $CeCl_3 \cdot 7H_2O$ (2.08 g, 5.58 mmol), and the mixture was stirred for 1 h at 0°. The mixture was diluted with Et_2O (30 ml), the soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:3): **29** (1.23 g, 65% from benzoquinone) and **30** (130 mg, 7%).

Data of **29**: R_f (AcOEt/hexanes 1:3) 0.34. $[\alpha]_D^{23} = -35.3$ (*c* = 1.45, $CHCl_3$). IR (neat): 3370, 2953, 2926, 2853, 1685, 1673, 1254, 1073, 836, 777). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 (*t*, *J* = 7.4, 3 H); 1.80–2.27 (*m*, 5 H); 2.73 (*m*, 2 H); 3.98 (*m*, 2 H); 4.92 (*m*, 1 H); 5.62 (*s*, 1 H); 5.83 (*dd*, *J* = 2, 7, 10.3, 1 H); 6.57 (*ddd*, *J* = 2, 3.5, 10.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.3; –5.2; 12.5; 18.4; 22.2; 25.6; 25.9 (3 C); 41.3; 43.7; 48.2; 67.0; 70.7; 125.7; 129.6; 134.1; 147.4; 199.7. CI-MS: 335 ([*M* – H]$^+$), 321, 279, 261, 205, 187, 159, 75. HR-CI-MS: 335.2047 ($C_{19}H_{31}O_3Si^+$; calc. 335.2043).

Data of **30**. IR (neat): 3363, 2930, 2958, 2858, 1487, 1463, 1256, 1071, 836, 779. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.09 (*s*, 6 H); 0.79 (*t*, *J* = 7.4, 3 H); 0.95 (*s*, 9 H); 1.62–1.75 (*m*, 2 H); 3.04 (*dt*, *J* = 3.1, 21, 1 H); 3.28 (*dd*, *J* = 2.7, 21, 1 H); 3.55–3.64 (*m*, 1 H); 4.21–4.24 (*m*, 2 H); 4.74–4.86 (*m*, 2 H); 5.87–5.92 (*m*, 1 H); 6.50–6.51 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): –4.8; 10.5; 18.9; 25.6; 26.4; 29.0; 36.2; 67.3; 112.8; 113.4; 123.7; 123.8; 127.5; 135.1; 147.0. CI-MS: 334 (*M*$^+$), 319, 305, 277, 259, 247, 231, 189, 173, 145, 131, 115, 86. HR-CI-MS: 334.1968 ($C_{19}H_{30}O_3Si^+$; calc. 334.1964).

*(1S,4aS,5S,8aR)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyl-1,4,4a,5,8,8a-hexahydro-4-oxonaphthalen-1-yl (*R*)-O-Methylmandelate* (**33**). To a soln. of **29** (45 mg, 0.13 mmol), (*R*)-*O*-methylmandelic acid (24 mg, 0.15 mmol), and DCC (30 mg, 0.15 mmol) in CH_2Cl_2 (4 ml) at r.t. was added DMAP (8 mg, 0.07 mmol). After 30 min, the mixture was passed through a plug of cotton, which was rinsed with hexanes. The eluant was diluted with sat. aq. $NaHCO_3$ soln. (1 ml), the org. phase, washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:7): 53 mg (82%) of **33**. Colorless oil. R_f (AcOEt/hexanes 1:7) 0.25. $[\alpha]_D^{23} = -67.1$ (*c* = 1.2, $CHCl_3$). IR (neat): 2950, 2920, 2852, 1751, 1689, 1252, 1168. ^{1}H-NMR (300 MHz, $CDCl_3$) (integrations for the crude product in two regions, labeled a and b): 0.05 (*s*, 6 H); 0.91 (*s*, 9 H); 0.92 (*t*, *J* = 7.4, 3 H); 1.72–2.09 (*m*, 4 H); 2.15 (*m*, 1 H); 2.79 (*t*, *J* = 3.9, 1 H); 2.89 (*m*, 1 H); 3.42 (*s*, 3 H); 3.88–4.01[a] (*m*, 2 H); 4.81 (*s*, 1 H); 5.58 (*m*, 1 H); 5.83 (*dd*, *J* = 2.5, 10.4, 1 H); 5.93 (*dt*, *J* = 2.4, 5.3, 1 H); 6.24[b] (*ddd*, *J* = 2.1, 4.0, 10.4, 1 H); 7.31–7.52 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.3; –5.2; 12.4; 18.4; 22.8; 25.5; 25.9 (3 C); 40.9; 41.0; 47.9; 57.4; 66.9; 73.3; 82.4; 125.5; 127.0 (2 C); 128.9; 131.0; 133.9; 135.8; 142.4; 170.0; 198.7. CI-MS: 483 ([*M* – H]$^+$), 469, 427, 353, 319, 261, 187, 121. CI-MS: 483 ([*M* – H]$^+$), 469, 427, 353, 319, 261, 187, 121. HR-CI-MS: 483.2567 ($C_{28}H_{39}O_5Si^+$; calc. 483.2559).

*(1S,4aS,5S,8aR)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyl-1,4,4a,5,8,8a-hexahydro-4-oxonaphthalen-1-yl (*S*)-O-Methylmandelate* (**34**). As described for **33**, with **29** (14 mg, 0.04 mmol), (*S*)-*O*-methylmandelic acid (11 mg, 0.06 mmol), DCC (13 mg, 0.06 mmol), CH_2Cl_2 (3 ml), and DMAP (3 mg, 0.02 mmol). CC (silica gel; AcOEt/hexanes 1:5) gave 17 mg (82%) of **34**. Colorless oil. R_f (AcOEt/hexanes 1:5) 0.22. $[\alpha]_D^{23} = -29.0$ (*c* = 1.53, $CHCl_3$). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.02 (*s*, 6 H); 0.89 (*s*, 9 H); 0.91 (*t*, *J* = 7.7, 3 H); 1.36 (*m*, 1 H); 1.71–1.97 (*m*, 3 H); 2.09 (*m*, 1 H); 2.64–2.78 (*m*, 2 H); 3.42 (*s*, 3 H); 3.70 (*d*, *J* = 12.9, 1 H); 3.78 (*d*, *J* = 12.9, 1 H); 4.81 (*s*, 1 H); 5.52 (*m*, 1 H); 5.87 (*dd*, *J* = 2.7, 10.3, 1 H); 5.94 (*dt*, *J* = 2.5, 5.1, 1 H); 6.45 (*ddd*, *J* = 1.7, 3.8, 10.3, 1 H); 7.31–7.49 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): –5.3 (2 C); 12.4; 18.3; 22.4; 25.5; 25.9 (3 C); 40.7; 40.9; 47.9; 57.3; 66.4; 73.2; 82.3; 124.5; 127.2 (2 C); 128.8 (2 C); 129.0; 131.1; 133.7; 136.0; 142.5; 169.9; 198.6.

*(1S,4R,4aS,5S,8aR)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyl-1,4,4a,5,8,8a-hexahydronaphthalene-1,4-diol* (**35**). To a soln. of **27**, obtained from **24** as described above, in MeOH (15 ml) at r.t. was added $NaBH_4$ (633 mg, 16.7 mmol) and $CeCl_3 \cdot 7H_2O$ (6.24 g, 16.7 mmol), and the mixture was stirred for 8 h at r.t. Workup as for **29** gave **35** (1.18 g, 62% from benzoquinone). White solid. R_f (AcOEt/hexanes 1:3) 0.33. M.p. 105–106°. $[\alpha]_D^{23} = -129.7$ (*c* = 1.95, $CHCl_3$). IR (neat) 3387, 2956, 2928, 2881, 2858, 1254, 1005, 834, 776.

^{1}H-NMR (300 MHz, $CDCl_3$): 0.02 (*s*, 6 H); 0.91 (*s*, 9 H); 1.04 (*t*, *J* = 7.4, 3 H); 1.69 (*m*, 2 H); 1.89–2.11 (*m*, 4 H); 2.14 (*d*, *J* = 6, 1 H); 2.23–2.35 (*m*, 2 H); 4.01 (*m*, 2 H); 4.15 (*m*, 1 H); 4.44 (*m*, 1 H); 5.65 (*d*, *J* = 10.2, 1 H); 5.76–5.83 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.3 (2 C) 12.4; 18.3; 23.1; 24.2; 25.9 (3 C); 37.0; 37.3; 40.9; 64.4; 66.7; 70.3; 127.2; 128.4; 130.3; 137.5. CI-MS: 337 ([*M* − H]$^+$), 321, 303, 262, 205, 189, 171, 161. HR-CI-MS: 337.2202 ($C_{19}H_{33}O_3Si^+$; calc. 337.2199).

*(1*R*,2*S*,4*R*,8*R*,9*S*,10*R*)-2-Bromo-2-{[[(*tert*-butyl)dimethylsilyl]oxy}methyl}-10-ethyl-11-oxatricyclo[6.2.1.0^{4,9}]-undec-6-en-5-one* (**38**) *and (1*R*,3*R*,7*R*,8*R*,9*R*,10*S*)-10-Bromo-1-{[[(*tert*-butyl)dimethylsilyl]oxy}methyl}-9-ethyl-11-oxatricyclo[5.3.1.0^{3,8}]undec-5-en-4-one* (**39**). To a soln. of **35** (28 mg, 0.08 mmol) in THF (4 ml) was added NBS (16 mg, 0.09 mmol), and the mixture was stirred for 1 h at r.t. The mixture was passed through a short pad of silica gel, with AcOEt/hexanes 1:5, the eluent was evaporated, and the residue was purified by CC (AcOEt/hexanes 1:5): 31 mg (91%) of **36**/**37** as colorless oil. The mixture was dissolved in CH_2Cl_2 (2 ml), and the soln. was added dropwise to a suspension of PDC (68 mg, 0.18 mmol) and AcONa (15 mg, 0.18 mmol) in CH_2Cl_2 (4 ml). The resulting mixture was stirred for 2 h at r.t. and then filtered through *Florisil*, and the filtrate was evaporated. CC (AcOEt/hexanes 1:20 → 1:10) of the residue afforded 22 mg (73%) of **38**/**39**.

Data of **38**: A pure sample of **38** was obtained as a white solid by repeated chromatography. R_f (AcOEt/hexanes 1:5) 0.24. M.p. 106–107°. $[\alpha]_D^{23} = -29.2$ (*c* = 0.36, $CHCl_3$). IR (neat): 1689. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.05 (*s*, 6 H); 0.91 (*s*, 9 H); 1.01 (*t*, *J* = 7.4, 3 H); 1.33–1.62 (*m*, 2 H); 1.99 (*dd*, *J* = 10.3, 16.1, 1 H); 2.25 (*dd*, *J* = 8.1, 16.1, 1 H); 2.50 (*t*, *J* = 3.8, 1 H); 2.72 (*t*, *J* = 7.5, 1 H); 2.85 (*ddd*, *J* = 3.8, 8.1, 11.0, 1 H); 3.64 (*d*, *J* = 10.7, 1 H); 3.75 (*d*, *J* = 10.7, 1 H); 4.23 (*s*, 1 H); 4.47 (*t*, *J* = 4.4, 1 H); 5.96 (*d*, *J* = 9.9, 1 H); 6.84 (*dd*, *J* = 5.0, 9.9, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.4; 11.4; 18.3; 22.6; 25.8; 35.6; 43.1; 44.5; 46.5; 69.9; 70.8; 71.6; 82.9; 128.8; 141.5; 201.6. CI-MS: 415 (*M*$^+$), 359, 335, 277, 259, 203, 175, 161, 105. HR-CI-MS: 413.1142 ($C_{19}H_{30}BrO_3Si^+$, calc. 413.1148).

Data of **39**: determined from the mixture with **38**. R_f (AcOEt/hexanes 1:5) 0.22. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.08 (*t*, *J* = 7.4, 3 H); 1.61 (*m*, 1 H); 1.70 (*m*, 1 H); 1.76 (*m*, 1 H); 2.13–2.21 (*m*, 2 H); 2.37 (*dd*, *J* = 12.1, 14.5, 1 H); 2.68 (*m*, 1 H); 3.59 (*s*, 2 H); 3.93 (*m*, 1 H); 4.38 (*m*, 1 H); 5.96 (*d*, *J* = 9.9, 1 H); 7.01 (*dd*, *J* = 5.7, 9.9, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.3 (2 C); 11.7; 23.7; 25.9 (3 C); 36.1; 42.1; 49.5; 51.4; 63.5; 66.9; 106.0; 127.2; 147.0; 201.6.

*(4*S*,4a*R*,6*S*,7*R*,8*R*,8a*R*)-6-Bromo-6-{[[(*tert*-butyl)dimethylsilyl]oxy}methyl}-8-ethyl-4a,5,6,7,8,8a-hexahydro-4,7-dihydroxynaphthalen-1(4*H*)-one* (**40**). To a soln. of **29** (28 mg, 0.08 mmol) in CH_2Cl_2 (3 ml) at r.t. was added NBS (16 mg, 0.09 mmol), and the mixture was stirred for 1 h. The mixture was passed through a short pad of silica gel with AcOEt/hexanes 1:3, the eluent was evaporated, and the residue was purified by CC (silica gel; AcOEt/hexanes 1:3): 25 mg of **40** (71%). Colorless oil. R_f (AcOEt/hexanes 1:3) 0.16. IR (neat). 3445, 2953, 2853, 1663, 1248. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*t*, *J* = 7.4, 3 H); 1.79–2.13 (*m*, 4 H); 2.31 (*m*, 1 H); 2.64 (*dt*, *J* = 1.0, 4.4, 1 H); 3.00 (*m*, 1 H); 3.48 (*d*, *J* = 3.3, 1 H); 3.97 (*d*, *J* = 10.9, 1 H); 4.01 (*d*, *J* = 10.9, 1 H); 4.07 (br. *s*, 1 H); 4.91 (*m*, 1 H); 5.94 (*dd*, *J* = 2.6, 10.3, 1 H); 6.70 (*ddd*, *J* = 1.8, 3.2, 10.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.4 (2 C); 12.3; 18.3; 23.3; 25.8 (3 C); 26.7; 42.4; 42.8; 46.5; 69.2; 70.7; 74.4; 75.2; 129.7; 149.4; 202.1. HR-CI-MS: 435.1391 ($C_{19}H_{34}BrO_4Si^+$; calc. 435.1389).

*(1*S*,4*R*,4a*S*,5*S*,7*R*,8a*R*)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyldecahydronaphthalene-1,4-diol* (**42**). To a soln. of **35** (913 mg, 2.70 mmol) in AcOEt (10 ml) was added 5% Rh on Al_2O_3 (1.40 g), and the mixture was placed under a balloon filled with H_2. After 24 h, the mixture was filtered through a pad of *Celite* with AcOEt (10 ml), and the filtrate was evaporated. CC (silica gel; AcOEt/hexanes 1:3) of the residue gave **42** (871 mg, 94%). Colorless oil. R_f (AcOEt/hexanes 1:3) 0.22. M.p. 123–124°. $[\alpha]_D^{23} = -3.4$ (*c* = 2.3, $CHCl_3$). IR (neat): 3439, 2952, 2928, 2856, 1500, 1462, 1254, 1104, 1079, 836. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.04 (*s*, 6 H); 0.89 (*s*, 9 H); 0.93 (*t*, *J* = 7.1, 3 H); 1.06 (br. *s*, 1 H); 1.23–1.91 (*m*, 15 H); 3.44 (*dd*, *J* = 6.4, 9.9, 1 H); 3.49 (*dd*, *J* = 4.5, 9.9, 1 H); 3.74 (*ddd*, *J* = 4.5, 9.4, 11.5, 1 H); 4.09 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −5.3 (2 C); 12.3; 18.4; 24.3; 24.7; 26.0 (3 C); 26.5; 32.9; 33.3; 39.9; 41.3; 41.9; 43.1; 66.7; 69.0; 73.2. CI-MS: 343 ([*M* + H]$^+$), 325, 283, 267, 209, 193, 175. HR-CI-MS: 343.2674 ($C_{19}H_{39}O_3Si^+$; calc. 343.2669).

*(4a*S*,5*S*,7*R*,8a*R*)-7-{[[(*tert*-Butyl)dimethylsilyl]oxy}methyl}-5-ethyloctahydronaphthalene-1,4-dione* (**43**). To a soln. of pyridinium dichromate (1.20 g, 3.20 mmol) in CH_2Cl_2 (10 ml) was added a soln. of **42** (730 mg, 2.13 mmol) in CH_2Cl_2 (3 ml), and the mixture was stirred for 4 h at r.t. The mixture was diluted with Et_2O (30 ml), and the soln. was filtered through a *Celite* pad. The filtrate was evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:3): 635 mg (88%) of **43**. Colorless oil. R_f (AcOEt/hexanes 1:5) 0.16. $[\alpha]_D^{23} = +88.5$ (*c* = 1.42, $CHCl_3$). IR (neat): 2959, 2925, 2852, 1713, 1250, 1098, 837. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.02 (*s*, 6 H); 0.86 (*s*, 9 H); 0.87 (overlapping *m*, 1 H); 0.88 (*t*, *J* = 7.4, 3 H); 1.21–1.35 (*m*, 2 H); 1.53–1.76 (*m*, 4 H); 2.00 (*m*, 1 H); 2.35–2.49 (*m*, 1 H); 2.59 (*dt*, *J* = 4.5, 13.6, 1 H); 2.65–2.74 (*m*, 2 H); 2.83 (*m*, 1 H); 3.09 (*m*, 1 H); 3.34 (*dd*, *J* = 6.4, 9.9, 1 H); 3.43 (*dd*, *J* = 5.4, 9.9, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$):

– 5.5 (2 C); 12.3; 18.2; 25.8 (3 C); 26.2; 29.6; 30.6; 37.0 (2 C); 40.4; 40.6; 49.3; 51.8; 67.7; 208.9; 210.9. CI-MS: 339 ($[M+H]^+$), 323, 281, 263, 207, 189, 147, 75. HR-CI-MS: 339.2352 ($C_{19}H_{35}O_3Si^+$; calc. 339.2356).

*(4a*R*,6*R*,8*S*,8a*S*)-8-Ethyl-3,4,4a,5,6,7,8,8a-octahydro-6-(hydroxymethyl)naphthalen-1(2*H*)-one* (**46**). A soln. of **43** (570 mg, 1.68 mmol) and PPTS (43 mg, 0.17 mmol) in MeOH (10 ml) was heated at 55° for 3 h, after which the mixture was allowed to cool to r.t. The soln. was diluted with sat. aq. $NaHCO_3$ soln. (3 ml) and extracted with Et_2O (20 ml). The extract was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:2): 404 mg (89%) of **46**. Colorless oil. R_f (AcOEt/hexanes 1:2) 0.16. $[\alpha]_D^{23} = +15.7$ ($c = 0.21$, $CHCl_3$). IR (neat): 3419, 2923, 2867, 2831, 1712, 1461, 1123, 1097. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.66 (*ddd*, *J* = 12.7, 12.7, 12.7, 1 H); 0.84 (*t*, *J* = 7.5, 3 H); 1.18 (*m*, 1 H); 1.31 (*ddd*, *J* = 12.3, 12.3, 12.3, 1 H); 1.49–1.67 (*m*, 4 H); 1.76 (*m*, 1 H); 1.79 (*dt*, *J* = 5.0, 14.3, 1 H); 1.89 (br. *s*, OH); 2.08 (*ddd*, *J* = 2.1, 5.0, 14.3, 1 H); 2.13 (*ddt*, *J* = 2.5, 9, 14.3, 1 H); 2.22 (*ddt*, *J* = 2.6, 4.6, 13.1, 1 H); 2.41 (*dt*, *J* = 6.8, 14.3, 1 H); 2.91 (*m*, 1 H); 3.19 (*s*, 3 H); 3.29 (*s*, 3 H); 3.44 (*dd*, *J* = 6.0, 10.6, 1 H); 3.46 (*dd*, *J* = 6.4, 10.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.4; 26.3; 28.1; 28.2; 30.1; 38.6; 40.5; 41.7; 45.7; 47.2; 47.9; 48.2; 68.1; 100.5; 211.6. CI-MS: 270 (M^+), 253, 239, 221, 207, 189, 125, 101, 84. HR-CI-MS: 270.1830 ($C_{15}H_{26}O_4^+$; calc. 270.1831).

*(4a*R*,6*R*,8*S*,8a*S*)-8-Ethyl-3,4,4a,5,6,7,8,8a-octahydro-4,4-dimethoxy-6-{[(triisopropylsilyl)oxy]methyl}-naphthalen-1(2*H*)-one* (**47**). To a soln. of ^{i}Pr$_3$SiCl (332 mg, 1.72 mmol) and 1*H*-imidazole (117 mg, 1.72 mmol) in DMF (5 ml) at r.t. was added a soln. of **46** (310 mg, 1.15 mmol) in DMF (1 ml, 1.15 mmol), and the mixture was stirred for 2 h at r.t. The mixture was diluted with pentane (20 ml), the soln. was washed with H_2O (3 × 10 ml) and sat. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:5): 456 mg (93%) of **47**. Colorless oil. R_f (AcOEt/hexanes 1:10) 0.23. $[\alpha]_D^{23} = +6.6$ ($c = 1.16$, $CHCl_3$). IR (neat): 2956, 2942, 2864, 2361, 1719, 1116, 1097, 1055. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.64 (*ddd*, *J* = 13.1, 13.1, 13.1, 1 H); 0.85 (*t*, *J* = 7.5, 3 H); 1.03–1.07 (*m*, 21 H); 1.19 (*m*, 1 H); 1.28 (*ddd*, *J* = 12.0, 12.0, 12.0, 1 H); 1.49–1.69 (*m*, 4 H); 1.73–1.87 (*m*, 2 H); 2.08 (*ddd*, *J* = 2.1, 4.8, 11.3, 1 H); 2.21 (*ddt*, *J* = 2.8, 5.3, 13.1, 1 H); 2.40 (*dt*, *J* = 6.1, 13.5, 1 H); 2.92 (*m*, 1 H); 3.19 (*s*, 3 H); 3.30 (*s*, 3 H); 3.45 (*dd*, *J* = 6.8, 9.5, 1 H); 3.53 (*dd*, *J* = 5.8, 9.5, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9; 12.4; 17.9; 26.3; 28.0; 28.4; 30.3; 38.6; 41.0; 41.8; 45.9; 47.7; 47.8; 48.4; 68.5; 100.6; 211.5. CI-MS: 426 (M^+), 409, 383, 351, 221, 184, 171, 147, 101. HR-CI-MS: 426.3162 ($C_{24}H_{46}O_4Si^+$; calc. 426.3165).

*(4a*R*,6*R*,8*S*,8a*S*)-8-Ethyl-3,4,4a,5,6,7,8,8a-octahydro-4,4-dimethoxy-6-{[(triisopropylsilyloxy]methyl}naphthalen-1(2*H*)-one Oxime* (**48**). A suspension of **47** (312 mg, 0.73 mmol), hydroxylamine hydrochloride (508 mg, 2.31 mmol), and AcONa (600 mg, 7.31 mmol) in MeOH (3 ml) was heated gently under reflux for 3 h. After cooling to r.t., the mixture was evaporated, and the residue was chromatographed (silica gel; MeOH/CH_2Cl_2 1:60): 261 mg (81%) of **48**. Colorless oil. R_f (AcOEt/hexanes 1:5) 0.21. $[\alpha]_D^{23} = +20.1$ ($c = 1.05$, $CHCl_3$). IR (neat): 3404, 2956, 2941, 2864, 1462, 1120, 1099, 1056, 881. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87 (*t*, *J* = 7.5, 3 H); 0.88 (*m*, 1 H); 1.07 (*m*, 21 H); 1.3–1.7 (*m*, 9 H); 1.93 (*m*, 1 H); 2.02 (*m*, 1 H); 2.77 (*t*, *J* = 3.4, 1 H); 3.18 (*s*, 3 H); 3.23 (*s*, 3 H); 3.33 (*m*, 1 H); 3.46–3.57 (*m*, 2 H); 7.06 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9; 12.5; 17.9; 20.1; 26.6; 26.7; 26.8; 30.2; 41.4; 41.7; 43.1; 45.5; 47.3; 47.5; 68.7; 101.2; 158.2.

*(5a*R*,7*R*,9*S*,9a*S*)-9-Ethyldecahydro-5,5-dimethoxy-7-{[(triisopropylsilyl)oxy]methyl}-2*H*-benz[*b*]azepin-2-one* (**49**). To a mixture of TsCl (203 mg, 1.07 mmol), Et_3N (0.15 ml, 1.07 mmol), and a cat. amount of DMAP in CH_2Cl_2 (3 ml) was added a soln. of **48** (186 mg, 0.43 mmol) in CH_2Cl_2 (5 ml), and the mixture was stirred for 3 h at r.t. The mixture was diluted with CH_2Cl_2 (10 ml), the soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; AcOEt/hexanes 1:3, then MeOH/CH_2Cl_2 1:15): 138 mg (74%) of **49**. Colorless oil. R_f (AcOEt/hexanes 1:3) 0.12. $[\alpha]_D^{23} = -8.4$ ($c = 2.38$, $CHCl_3$). IR (neat): 2956, 2941, 2864, 1663, 1461, 1106, 1055, 882. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83 (*ddd*, *J* = 12.8, 12.8, 12.8, 1 H); 0.92 (*t*, *J* = 7.4, 3 H); 0.96–1.13 (*m*, 22 H); 1.31 (*dq*, *J* = 7.4, 7.4, 1 H); 1.49–1.83 (*m*, 6 H); 1.91 (*ddt*, *J* = 1.7, 7.5, 13.6, 1 H); 2.19–2.28 (*m*, 1 H); 2.47 (*dt*, *J* = 1.2, 13.1, 1 H); 3.15 (*s*, 3 H); 3.18 (*s*, 3 H); 3.50 (br. *d*, *J* = 6.0, 2 H); 3.79 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.4; 11.8; 17.9; 23.3; 25.3; 25.8; 29.65; 29.70; 40.6; 42.8; 46.8; 47.2; 47.3; 49.6; 68.2; 102.0; 176.5. CI-MS: 442 ($[M+H]^+$), 410, 398, 378, 366. HR-CI-MS: 442.3353 ($C_{24}H_{48}NO_4Si^+$; calc. 442.3353).

*(5a*R*,7*R*,9*S*,9a*S*)-9-Ethyldecahydro-5,5-dimethoxy-7-{[(triisopropylsilyl)oxy]methyl}-2*H*-benz[*b*]azepine* (**50**). To a soln. of **49** (43 mg, 0.1 mmol) in benzene (3 ml) at r.t. was added 3.4M *Red-Al* in toluene (0.3 ml), and the mixture was refluxed at 80° for 1 h. After the soln. had cooled to r.t., AcOEt (5 ml) was added. The mixture was evaporated, and the residue was chromatographed (silica gel; MeOH/CH_2Cl_2 1:30 → 1:15): 39 mg (92%) of **50**. Colorless oil. R_f (MeOH/CH_2Cl_2 1:15) 0.16. IR (neat): 3441, 2941, 2892, 2863, 2827, 1469, 1462, 1455, 1260, 1108, 1065. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83–0.91 (*m*, 1 H); 0.90 (*t*, *J* = 7.2, 3 H); 1.04–1.10 (*m*, 21 H); 1.23–1.41 (*m*, 4 H); 1.54–1.68 (*m*, 6 H); 1.75–1.82 (*m*, 3 H); 2.81–2.93 (*m*, 2 H); 3.01 (*dt*, *J* = 7.2, 12.8, 1 H); 3.13

(*s*, 3 H); 3.21 (*s*, 3 H); 3.52 (br. *d*, *J* = 5.6, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.8; 11.9; 18.0; 21.9; 24.7; 26.1; 27.5; 30.1; 40.6; 43.7; 46.8; 47.3; 47.7; 47.9; 55.5; 68.7; 104.1. HR-CI-MS: 427.3482 ($C_{24}H_{49}NO_3Si^+$; calc. 427.3482).

*(5a*R*,7*R*,9*S*,9a*S*)-9-Ethyldecahydro-7-(hydroxymethyl)-5,5-dimethoxy-2*H*-benz[*b*]azepin-2-one* (**52**). To a soln. of **49** (125 mg, 0.28 mmol) in THF (3 ml) at r.t. under Ar was added 1M Bu_4NF in THF (0.4 ml, 0.4 mmol), and the mixture was stirred for 1 h at r.t. The mixture was diluted with CH_2Cl_2 (10 ml), the soln. was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; MeOH/CH_2Cl_2 1:15): 79 mg (99%) of **52**. Colorless oil. R_f (MeOH/CH_2Cl_2, 1:15) 0.1. $[\alpha]_D^{23} = -31.7$ (*c* = 1.1, $CHCl_3$). IR (neat): 3385, 2956, 2929, 2872, 1655, 1452, 1104, 1054. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.93 (*ddd*, *J* = 12.3, 12.3, 12.3, 1 H); 0.94 (*t*, *J* = 7.3, 3 H); 1.09 (*ddd*, *J* = 12.4, 12.4, 12.4, 1 H); 1.33 (*dq*, *J* = 7.2, 7.2, 2 H); 1.51–1.87 (*m*, 7 H); 1.93 (*ddt*, *J* = 2.3, 7.6, 15.2, 1 H); 2.26 (*m*, 1 H); 2.48 (*dt*, *J* = 1.4, 13.7, 1 H); 3.16 (*s*, 3 H); 3.18 (*s*, 3 H); 3.49 (*m*, 2 H); 3.79 (*m*, 1 H); 5.25 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.4; 23.2; 25.3; 25.7; 29.4; 29.7; 40.0; 42.8; 46.6; 47.3; 47.4; 49.6; 67.7; 101.9; 176.8. CI-MS: 286 (M^+), 268, 254, 222, 204, 146, 114, 101. HR-CI-MS: 286.2013 ($C_{15}H_{28}NO_4^+$; calc. 286.2019).

*(5a*R*,7*R*,9*S*,9a*S*)-9-Ethyldecahydro-5,5-dimethoxy-7-{[[(4-methylphenyl)sulfonyl]oxy]methyl}-2*H*-benz[*b*]-azepin-2-one* (**53**). To a mixture of TsCl (21 mg, 0.11 mmol), Et_3N (31 µl, 0.23 mmol), and a cat. amount of DMAP in CH_2Cl_2 (3 ml) was added **52** (21 mg, 0.08 mmol), and the mixture was stirred for 3 h at r.t. The mixture was diluted with CH_2Cl_2 (10 ml), the soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; MeOH/CH_2Cl_2 1:15): 33 mg (100%) of **53**. Colorless oil. R_f (MeOH/CH_2Cl_2 1:15) 0.29. $[\alpha]_D^{23} = -27.2$ (*c* = 1.2, $CHCl_3$). IR (neat): 2956, 1660, 1456, 1357, 1188, 1176, 1104, 1052. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.74 (*ddd*, *J* = 12.8, 12.8, 12.8, 1 H); 0.94 (*t*, *J* = 7.3, 3 H); 0.96 (*ddd*, *J* = 12.7, 12.7, 12.7, 1 H); 1.31 (*dq*, *J* = 7.3, 7.3, 2 H); 1.41–1.58 (*m*, 3 H); 1.68 (*dt*, *J* = 3.5, 13.6, 1 H); 1.71–1.95 (*m*, 3 H); 2.15–2.27 (*m*, 1 H); 2.37–2.49 (*m*, 1 H); 2.47 (*s*, 3 H); 3.11 (*s*, 3 H); 3.15 (*s*, 3 H); 3.72–3.80 (*m*, 2 H); 3.82 (*dd*, *J* = 6.6, 9.6, 1 H); 4.97 (br. *s*, 1 H); 7.36 (*d*, *J* = 8.2, 2 H); 7.76 (*d*, *J* = 8.2, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.4; 21.6; 22.9; 25.3; 25.6; 29.0; 29.7; 37.0; 42.5; 46.3; 47.36; 47.44; 49.1; 74.2; 101.7; 127.9; 129.9; 132.7; 144.9; 176.6. CI-MS: 408 ([*M* – MeO]$^+$), 376, 285, 204, 173. HR-CI-MS: 439.2029 ($C_{22}H_{33}NO_6S^+$; calc. 439.2028).

*(5a*R*,7*R*,9*S*,9a*S*)-9-Ethyl-4,5,5a,6,7,8,9,9a-octahydro-5,5-dimethoxy-1,7-methano-1*H*-benz[*b*]azepin-2(3*H*)-one* (**54**). To a soln. of NaH (3 mg, 0.11 mmol) in THF (3 ml) at 0° under Ar was added a soln. of **53** (16 mg, 0.04 mmol) in THF (1 ml), and the mixture was stirred for 30 min at r.t. and then refluxed for 1 h. The mixture was diluted with sat. aq. NH_4Cl soln. (0.5 ml), the soln. extracted with CH_2Cl_2, the extract was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; MeOH/CH_2Cl_2 1:15): 6.6 mg (71%) of **54**. Colorless oil. R_f (MeOH/CH_2Cl_2 1:15) 0.1. $[\alpha]_D^{23} = -21.2$ (*c* = 1.1, $CHCl_3$). IR (neat): 2930, 2358, 1658, 1634, 1454, 1404, 1102, 1064, 1051. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.91 (*t*, *J* = 7.3, 3 H); 1.12 (*ddt*, *J* = 2.4, 9.2, 13.6, 1 H); 1.30–1.81 (*m*, 7 H); 1.92–2.13 (*m*, 3 H); 2.27 (*ddd*, *J* = 1.0, 7.4, 13.2, 1 H); 2.72 (*dt*, *J* = 0.9, 13.3, 1 H); 3.09 (*m*, 1 H); 3.17 (*s*, 3 H); 3.19 (*s*, 3 H); 3.60 (br. *d*, *J* = 2.8, 1 H); 3.75 (*ddd*, *J* = 2.6, 4.3, 11.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.2; 25.8; 27.2; 27.4; 28.3; 30.0; 31.4; 40.5; 42.8; 47.7 (2 C); 50.1; 50.7; 103.1; 179.2. CI-MS: (M^+), 267, 252, 236, 220, 204, 138, 101. HR-CI-MS: 267.1835 ($C_{15}H_{25}NO_3^+$; calc. 267.1834).

*(5a*R*,7*R*,9*S*,9a*S*)-9-Ethyl-3,4,5a,6,7,8,9,9a-octahydro-1,7-methano-1*H*-benz[*b*]azepine-2,5-dione* (**55**). To a soln. of TsOH · H_2O (11 mg, 0.06 mmol) in acetone (3 ml) at 0° under Ar was added a soln. of **54** (15 mg, 0.06 mmol) in acetone (1 ml), and the mixture was stirred for 12 h at r.t. The mixture was diluted with sat. aq. $NaHCO_3$ soln. (0.5 ml) and extracted with $CHCl_3$. The extract was washed with sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated: 11 mg of **55** (86%). Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.97 (*t*, *J* = 7.3, Me); 1.33–1.60 (*m*, 4 H); 1.69–1.87 (*m*, 2 H); 1.89–2.06 (*m*, 2 H); 2.54 (*ddd*, *J* = 4.9, 9.7, 13.8, 1 H); 2.62–2.74 (*m*, 3 H); 3.02 (*ddd*, *J* = 7.4, 10.1, 13.6, 1 H); 3.17 (*d*, *J* = 11.8, 1 H); 3.84–3.97 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.0; 26.0; 27.1; 28.6; 30.2; 31.5; 37.1; 38.4; 49.6; 49.9; 52.1; 175.8; 210.5.

(+)-Ibogamine-7-one (**56**). To a soln. of **55** (7 mg, 0.03 mmol) in AcOH (1 ml) at r.t. was added a soln. of phenylhydrazine (5 mg, 0.05 mmol) in AcOH (1 ml), and the mixture was stirred for 1 h at 50°. The mixture was allowed to cool to r.t. during 1 h, after which $BF_3 \cdot Et_2O$ (9 mg, 0.06 mmol) was added. The resulting yellow soln. was stirred for 12 h at 80°. After the mixture had cooled to r.t., it was diluted with CH_2Cl_2, the soln. was washed with H_2O and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the residue was chromatographed (silica gel; MeOH/CH_2Cl_2 1:30): 7 mg (77%) of **56**. Pale yellow solid. R_f (MeOH/CH_2Cl_2 1:30) 0.23. M.p. 230–232°. $[\alpha]_D^{23} = +27.9$ (*c* = 0.7, $CHCl_3$). IR (neat): 3429, 1631. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.98 (*t*, *J* = 7.4, 3 H); 1.48–2.19 (*m*, 8 H); 3.03 (*m*, 1 H); 3.18 (*d*, *J* = 11.8, 1 H); 3.74 (*d*, *J* = 15.7, 1 H); 3.81 (*m*, 1 H); 3.97 (*dd*, *J* = 1.7, 15.7, 1 H); 4.15 (*s*, 1 H); 7.06–7.18 (*m*, 2 H); 7.25 (*m*, 1 H); 7.50 (*m*, 1 H); 7.89 (br. *s*, 1 H). ^{13}C-NMR (75 MHz,

$CDCl_3$): 12.1; 27.5; 28.6; 30.7; 32.1; 32.8; 35.9; 38.9; 49.3; 51.5; 102.6; 110.3; 118.2; 119.7; 121.7; 127.8; 135.0; 138.8; 175.8. CI-MS ($[M+H]^+$): 295, 279, 135, 122, 91, 73. HR-CI-MS: 294.1731 ($C_{19}H_{22}N_2O^+$; calc. 294.1732).

(−)-Ibogamine (**22**). To a soln. of **56** (4.2 mg, 0.014 mmol) in dry THF (3 ml) was added $NaBH_4$ (28 mg, 0.74 mmol) in one portion. The mixture was cooled to 0°, and $BF_3 \cdot Et_2O$ (160 mg, 1.13 mmol) was syringed into the mixture dropwise. The resulting yellow suspension was stirred at r.t. for 3 h under Ar. The solvent was evaporated, and MeOH (2 ml), H_2O (0.4 ml), and 10% HCl soln. (0.2 ml) were added. This soln. was stirred at r.t. for 4 h, after which the MeOH was evaporated, and the residue was taken up in CH_2Cl_2 (10 ml). The mixture was neutralized with sat. aq. $NaHCO_3$ soln., and the aq. layer was extracted with CH_2Cl_2. The org. extract was dried ($MgSO_4$) and evaporated and the residual yellow solid was chromatographed (silica gel; MeOH/CH_2Cl_2 1:30): 3.1 mg (78%) of **22** (78%). Pale yellow crystalline solid. R_f (MeOH/CH_2Cl_2 1:15) 0.23. M.p. 156–157°. $[\alpha]_D^{23} = -45.8$ ($c = 0.2$, EtOH). IR (neat): 3400. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.91 (*t*, *J* = 7.1, 3 H); 1.24 (*m*, 1 H); 1.43–1.62 (*m*, 3 H); 1.66 (*ddd*, *J* = 3.4, 6.4, 13.2, 3 H); 1.77–1.90 (*m*, 2 H); 2.06 (*m*, 1 H); 2.72 (*m*, 1 H); 2.91 (*s*, 1 H); 2.96 (*ddd*, *J* = 1.6, 3.8, 11.7, 1 H); 3.02–3.11 (*m*, 2 H); 3.17 (*m*, 1 H); 3.33 (*ddd*, *J* = 4.4, 12.3, 16.6, 1 H); 3.42 (*m*, 1 H); 7.06–7.31 (*m*, 3 H); 7.48 (*d*, *J* = 7.1, 1 H); 7.67 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.9; 20.5; 26.3; 27.7; 31.9; 34.0; 41.1; 41.9; 49.9; 54.3; 57.7; 109.1; 110.1; 117.9; 119.2; 121.1; 129.6; 134.7; 141.5. CI-MS: 281 ($[M+H]^+$), 195, 149, 136, 97, 69. HR-CI-MS: 280.1938 ($C_{19}H_{24}N_2^+$; calc. 280.1940).

REFERENCES

[1] W. Carruthers, in 'Cycloaddition Reactions in Organic Synthesis', Pergamon, Oxford, 1990.

[2] H. B. Kagan, O. Riant, *Chem. Rev.* **1992**, *92*, 1007; L. C. Diaz, *J. Braz. Chem. Soc.* **1997**, *8*, 289; D. A. Evans, J. S. Johnson, in 'Comprehensive Asymmetric Catalysis', Eds. E. N. Jacobsen, A. Pfaltz, and H. Yamamoto, Springer, New York, 1999, Vol. 3, p. 1177; E. J. Corey, *Angew. Chem., Int. Ed.* **2002**, *41*, 1650; K. C. Nicolaou, S. A. Snyder, T. Montagnon, G. Vassilikogiannakis, *Angew. Chem., Int. Ed*. **2002**, *41*, 1668.

[3] J. M. Hawkins, S. Loren, *J. Am. Chem. Soc*. **1991**, *113*, 7794.

[4] K. Mikami, M. Terada, Y. Motoyama, T. Nakai, *Tetrahedron: Asymmetry* **1991**, *2*, 643; K. Mikami, Y. Motoyama, M. Terada, *J. Am. Chem. Soc*. **1994**, *116*, 2812.

[5] J. D. White, Y. Choi, *Org. Lett*. **2000**, *2*, 2373.

[6] M. Breuning, E. J. Corey, *Org. Lett*. **2001**, *3*, 1559.

[7] K. C. Nicolaou, G. Vassilikogiannakis, W. Mägerlein, R. Kranich, *Angew. Chem*. **2001**, *113*, 2543; *Angew. Chem., Int. Ed*. **2001**, *40*, 2482; K. C. Nicolaou, G. Vassilikogiannakis, W. Magerlein, R. Kranich, *Chem.–Eur. J.* **2001**, *7*, 5359.

[8] A. B. Northrup, D. W. C. MacMillan, *J. Am. Chem. Soc*. **2002**, *124*, 2458.

[9] K. Narasaka, N. Iwasawa, M. Inoue, T. Yamada, M. Nakashima, J. Sugimori, *J. Am. Chem. Soc.* **1989**, *111*, 5340; T. A. Engler, M. A. Letavic, F. Takusagawa, *Tetrahedron Lett*. **1992**, *33*, 6731; T. A. Engler, M. A. Letavic, K. O. Lynch Jr., F. Takusagawa, *J. Org. Chem*. **1994**, *59*, 1179; D. Seebach, R. Dahinden, R. E. Marti, A. K. Beck, D. A. Plattner, F. N. M. Kühnle, *J. Org. Chem*. **1995**, *60*, 1788; C. Haase, C. R. Sarko, M. Dimare, *J. Org. Chem*. **1995**, *60*, 1777.

[10] A. L. Gemal, J. L. Luche, *J. Am. Chem. Soc*. **1981**, *103*, 5454.

[11] J. A. Dale, H. S. Mosher, *J. Am. Chem. Soc*. **1973**, *95*, 512.

[12] B. M. Trost, J. L. Belletire, S. Godleski, P. G. McDougal, J. M. Balkovec, J. J. Baldwin, M. E. Christy, G. S. Ponticello, S. L. Varga, J. P. Springer, *J. Org. Chem*. **1986**, *51*, 2370.

[13] G. A. Kraus, M. J. Taschner, *J. Org. Chem*. **1980**, *45*, 1175.

[14] J. D. White, N. S. Cutshall, T. S. Kim, H. Shin, *J. Am. Chem. Soc*. **1995**, *117*, 9780; J. D. White, H. Shin, T. S. Kim, N. S. Cutshall, *J. Am. Chem. Soc*. **1997**, *119*, 2404.

[15] T. A. Henry, 'The Plant Alkaloids', J. A. Churchill Ltd., London, 1949.

[16] P. Popik, P. Skolnick, in 'The Alkaloids: Chemistry and Biology', Ed. G. A. Cordell, Academic Press, San Diego, 1998, Vol. 52, p. 197.

[17] W. I. Taylor, *J. Am. Chem. Soc*. **1957**, *79*, 3298; D. F. Dickel, C. L. Holden, R. C. Maxfield, L. E. Paszek, W. I. Taylor, *J. Am. Chem. Soc*. **1958**, *80*, 123; M. F. Bartlett, D. F. Dickel, W. I. Taylor, *J. Am. Chem. Soc*. **1958**, *80*, 126.

[18] K. Bláha, Z. Koblicová, J. Trojanek, *Collect. Czech. Chem. Commun*. **1974**, *39*, 2258.

[19] G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, F. E. Ziegler, *J. Am. Chem. Soc.* **1965**, *87*, 2073; G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, F. E. Ziegler, *J. Am. Chem. Soc.* **1966**, *88*, 3099.

[20] W. Nagata, S. Hirai, T. Okumura, K. Kawata, *J. Am. Chem. Soc*. **1968**, *90*, 1650; M. Ikezaki, T. Wakamatsu, Y. Ban, *J. Chem. Soc., Chem. Commun*. **1969**, 88; P. Rosenmund, W. H. Haase, J. Bauer, R. Frische, *Chem. Ber.* **1975**, *108*, 1871; Atta-ur-Rahman, J. A. Beisler, J. Harley-Mason, *Tetrahedron* **1980**, *36*, 1063; T. Imanishi, N. Yagi, M. Hanaoka, *Chem. Pharm. Bull*. **1985**, *33*, 4202; J. W. Huffman, G. Shanmugasundaram, R. Sawdaye, P. C. Raveendranath, R. C. Desai, *J. Org. Chem*. **1985**, *50*, 1460; M. E. Kuehne, P. J. Reider, *J. Org. Chem*. **1985**, *50*, 1464; C. Herdeis, C. Hartke-Karger, *Liebigs Ann. Chem*. **1991**, 99; K. J. Henry Jr., P. A. Grieco, W. J. Dubay, *Tetrahedron Lett*. **1996**, *37*, 8289.
[21] S. I. Sallay, *J. Am. Chem. Soc*. **1967**, *89*, 6762.
[22] B. M. Trost, S. A. Godleski, J. P. Genêt, *J. Am. Chem. Soc*. **1978**, *100*, 3930.
[23] H. C. Brown, S. K. Gupta, *J. Am. Chem. Soc*. **1972**, *94*, 4370; F. Björkling, T. Norin, C. R. Unelius, *J. Org. Chem*. **1987**, *52*, 292.
[24] P. J. Beswick, D. A. Widdowson, *Synthesis* **1985**, 492.
[25] E. J. Corey, Y. Matsumura, *Tetrahedron Lett*. **1991**, *32*, 6289.
[26] a) R. E. Gawley, *Org. React*. **1998**, *35*, 1; b) M. T. Nguyen, G. Raspoet, L. G. Vanquickenborne, *J. Am. Chem. Soc*. **1997**, *119*, 2552.
[27] J. D. White, P. Hrnciar, F. Stappenbeck, *J. Org. Chem*. **1999**, *64*, 7871.
[28] C. Simon, S. Hosztafi, S. Makleit, *J. Heterocycl. Chem*. **1997**, *34*, 349.
[29] S. Atarashi, J. K. Choi, D. C. Ha, D. J. Hart, D. Kuzmich, C. S. Lee, S. Ramesh, S. C. Wu, *J. Am. Chem. Soc*. **1997**, *119*, 6226.
[30] B. Robinson, 'The Fischer Indole Synthesis', Wiley & Sons, New York, 1982.
[31] R. J. Sundberg, J. Hong, S. Q. Smith, M. Sabat, *Tetrahedron* **1998**, *54*, 6259.

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