101. Synthesis and Circular Dichroism of Optically Pure (±)-(1*S*,2*S*,5*S*)-5-Methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]oct-2-yl Derivatives. Baker's Yeast Reduction of 4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-one

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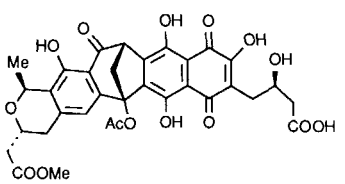
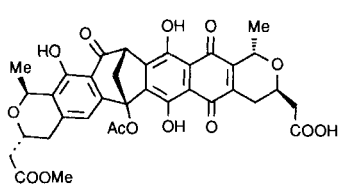
(9.III.90)

Baker's yeast reduction of 4-methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-one (**11**) under fermenting conditions afforded (–)-(1*S*,2*S*,4*R*)-4-methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-ol ((–)-**13**) in 60% yield with an e.e. > 99.5%. Its methanesulfonate (–)-**14** was hydrolyzed and rearranged with high stereoselectivity into (+)-(1*S*,2*S*,5*S*)-5-methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]octan-2-ol ((+)-**15**). The absolute configuration of (–)-**13** was deduced from the CD spectrum of its 4-(dimethylamino)benzoate ((+)-**22**) applying the chiral exciton-coupling method. The CD spectrum of (+)-**15** and of its (*tert*-butyl)dimethylsilyl ether ((+)-**23**) showed exciton-split type of *Cotton* effects attributed to through-space interactions between the s-*gauche*-butadiene and s-*cis*-butadiene chromophores of these systems.

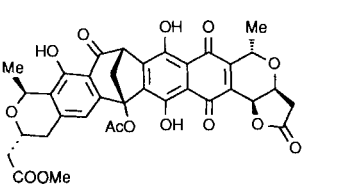
Introduction. – The naphthocyclinones are a subgroup of the family of isochromanequinone antibiotics isolated for the first time by *Zeeck* and coworkers in 1974 [1] from the mycelium of *Streptomyces arenae*. These molecules (see *e.g.* **1–3**) possess two aromatic chromophores grafted onto a bicyclo[3.2.1]octane skeleton [2–4].



1 naphthocyclinone α



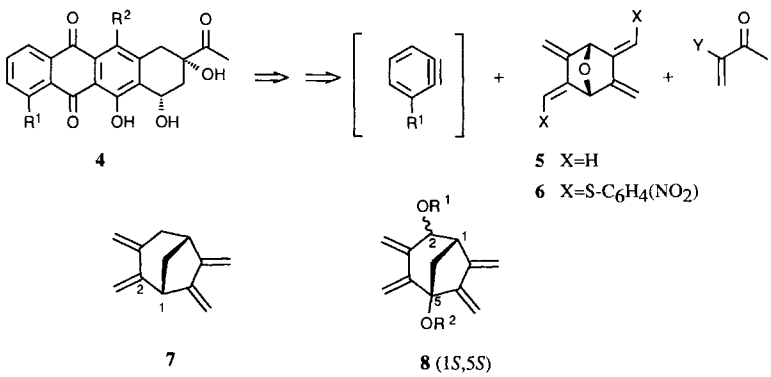
2 naphthocyclinone β



3 naphthocyclinone γ

[1]) Present address: *Ciba-Geigy Ltd.*, CH–1870 Monthey.

Scheme 1



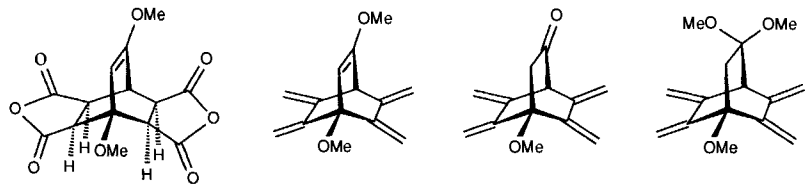
4 **5** X=H; **6** X=S-$C_6H_4(NO_2)$

7 **8** (1*S*,5*S*)

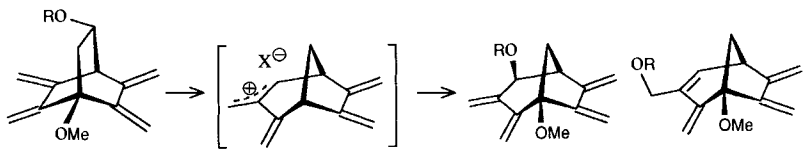
We have proposed (*Scheme 1*) a general, doubly convergent approach to the total synthesis of anthracyclinones **4** based on the tandem-*Diels-Alder* additions of 2,3,5,6-tetramethylidene-7-oxabicyclo[2.2.1]heptane **5** [5] [6] or its disubstituted derivatives **6** [7] [8]. The principle of our strategy rests upon the fact that the rate constant of the *Diels-Alder* addition of **5** and **6** to a first equivalent of a given dienophile is significantly larger than that of the reaction of the second equivalent of dienophile [9]. Preliminary results on the *Diels-Alder* reactivity of (±)-2,3,6,7-tetramethylidenebicyclo[3.2.1]octane (**7**) [10] toward ethylenetetracarbonitrile have shown that the diene moiety at C(2),C(3) is about 300 times more reactive than the diene moiety at C(6),C(7), thus, suggesting that disubstituted derivatives of type **8** might fulfill one of the conditions that could make these tetraenes potential synthetic intermediates in a doubly convergent approach to the synthesis of naphthocyclinones. We wish to report here on the synthesis of optically pure (+)-(1*S*,2*S*,5*S*)-5-methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]octan-2-ol ((+)-**15**) and its derivatives and on our preliminary results on their *Diels-Alder* reactivity.

Results and Discussion. – Our starting material was the bisanhydride **9** [11] which was transformed into 1,3-dimethoxy-5,6,7,8-tetramethylidenebicyclo[3.2.1]oct-2-ene (**10**) in 4 steps and 23.2% overall yield [12]. The methyl enol ether **10** was hydrolyzed ($BF_3 \cdot Et_2O$/CH_2Cl_2, −80°; then H_2O/$NaHCO_3$, 20°) into the corresponding ketone **11** in 77% yield. The reaction was accompanied by formation of the dimethyl acetal **12** which could be isolated in 20% yield. This compound afforded **11** on treatment with CF_3COOH/CH_2Cl_2 (20°), then with H_2O. Reduction of ketone **11** with $NaBH_4$ afforded (±)-**13** (97%) which was mesylated ($MeSO_2Cl$, pyridine, 0°) quantitatively into (±)-**14**. Mesylate (±)-**14** was hydrolyzed and rearranged into tetraenol (±)-**15** (57%) when dissolved in $CF_3CH(OH)CF_3/H_2O$ 2:1 (buffer: 2,6-lutidine). Under these conditions, no trace of alcohol (±)-**16** resulting from allylic rearrangement of (±)-**15** or quenching of the cationic intermediate **17** expected to be generated in the S_N1 solvolysis of (±)-**14** could be seen in the crude reaction mixture (360-MHz ^{1}H-NMR). This was unexpected in the light of related reactions involving 5,6,7,8-tetramethylidenebicyclo[2.2.2]oct-2-yl derivatives [13]. The relatively mediocre yield (57%) observed for (±)-**15** was due to competitive polymerization of this tetraenol.

Attempts to obtain optically active alcohol **13** through reduction of ketone **11** with optically pure hydride reagents were not met with success. With lithium *B*-(isopinocam-



9 **10** **11** **12**



13 R=H **17** **15** R=H **16** R=H

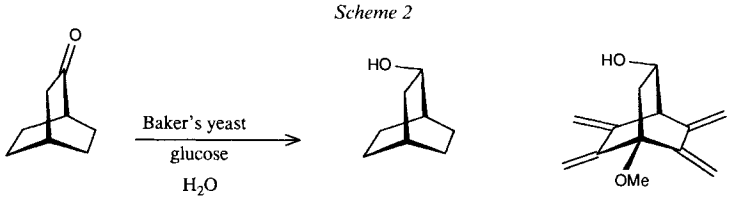
14 R=CH_3SO_2 **23** R=(*t*-Bu)Me_2Si **25** R=Ac

(+)-**22** R=4-$(Me_2N)C_6H_4CO$ **24** R=Ac

pheyl)-9-borabicyclo[3.3.1]nonane hydride (*Alpine-Hydride*) [14] in THF, the reduction of **11** was a slower reaction than the decomposition of the tetraenone. Treatment of **11** with lithium *B*-(*O*-benzylnopol-3-yl)-9-borabicyclo[3.3.1]nonane hydride (*NB-Enantride*) [15] in THF (−100°, 1 h 45 min) gave a 50% conversion and *ca.* 32% yield of alcohol **13** with e.e. ≈ 0! With (*R*)-BINAL-H (resulting from the reaction of $LiAlH_4$ with 1 equiv. of (*R*)-2,2′-dihydroxy-1,1′-binaphthyl and 1 equiv. of EtOH) [16], **11** was reduced (THF, −73°, 40 h) into **13** in 70% isolated yield, again with e.e. ≈ 0, as determined by the 360-MHz ^{1}H-NMR spectrum of the corresponding (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropionates prepared according to *Mosher*'s procedure [17].

Enantioselective reduction of bicyclo[2.2.2]octan-2-one (**18**) with baker's yeast [18] was reported by *Nakazaki* and coworkers [19] to be a relatively slow process under fermenting conditions (*Scheme 2*). After 62% conversion (35°, 48 h), (+)-(1*R*,2*S*,4*S*)-bicyclo[2.2.2]octan-2-ol ((+)-**19**) was isolated in 11% yield, with an optical purity of 78%. Under fermenting conditions (H_2O/KH_2PO_4, baker's yeast, sucrose, 34°, 24 h), tetraenone **11** was converted to (−)-(1*S*,2*S*,4*R*)-4-methoxy-5,6,7,8-bicyclo[2.2.2]octan-2-ol ((−)-**13**). After column chromatography (silica gel), (−)-**13** was isolated in 60% yield. The 360-MHz ^{1}H-NMR spectrum of the corresponding *Mosher*'s ester showed the signals of only one of the two diastereoisomers. No ^{1}H-signal of the other diastereoisomer could be detected, when the ^{13}C satellites were made visible in the ^{1}H-NMR spectrum, this allowing one to establish the e.e. of (−)-**13** to be better than 99.5%. Unpredictably, the baker's yeast reduction of **11** was faster than that of bicyclo[2.2.2]octanone (**18**) and led to

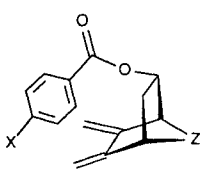
Scheme 2



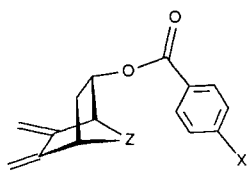
18 (+)-**19** (-)-**13**

better yield and optical purity. Interestingly, the configuration of alcohol (−)-**13** corresponds to that of (+)-**19**. It was established by application of the circular dichroic exciton chirality method [20] [21].

In 1984 [22], we reported on the synthesis of optically pure aryl-substituted 5,6-dimethylidenebicyclo[2.2.1]hept-2-yl [23] and -bicyclo[2.2.2]oct-2-yl benzoates [24]. The esters **20** with the benzoate group '*syn*' to the s-*cis*-butadiene moiety exhibited typical exciton-split *Cotton* effects (CE), whereas the corresponding '*anti*'-stereoisomers **21** did not present such effects. The chiral exciton coupling between the exocyclic diene and remote 4-substituted-benzoate chromophores could be used for unambiguous assignment of the absolute configuration of the bicyclic derivatives **20** [22].



20 Z=CH_2, CH_2CH_2



21 Z=CH_2, CH_2CH_2

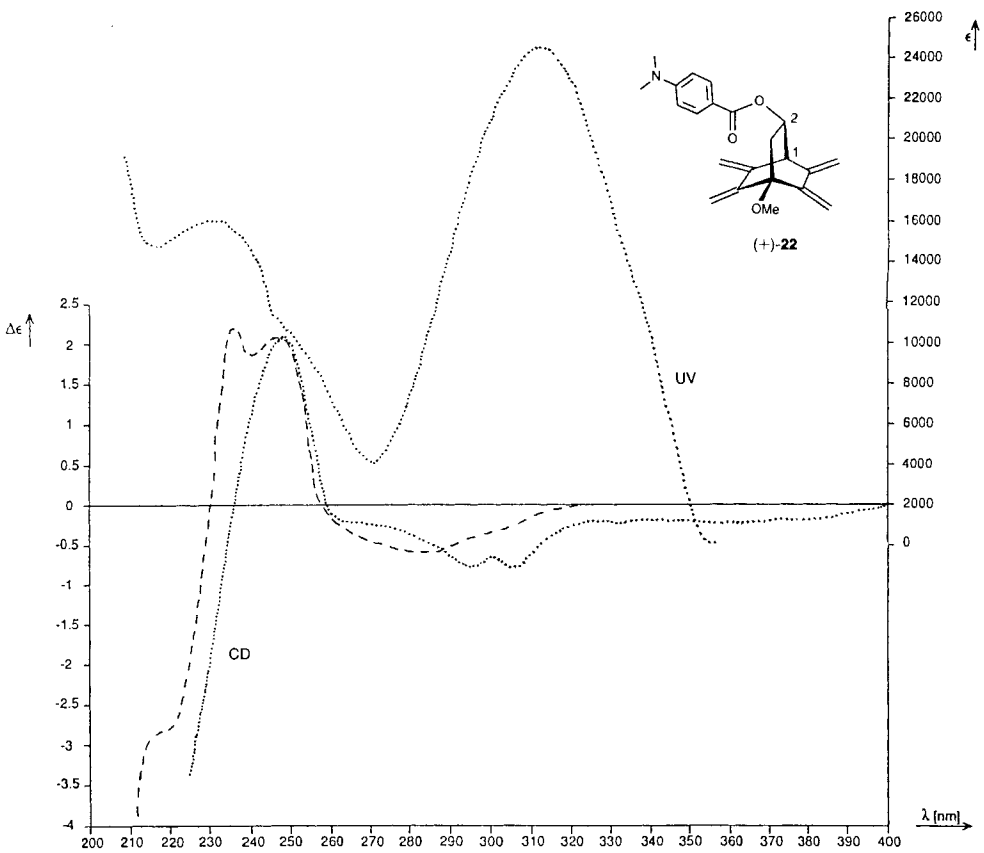


Fig. 1. *UV and CD spectra of (+)-***22** *in isooctane* (---) *and in 95% EtOH* (· · · ·)

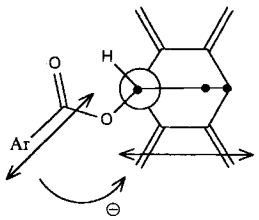


Fig. 2. Newman *projection of (+)-(2S)-***22** *along the C(2)–C(1) bond showing the negative chirality of the electric transition moments of the lowest-energy transitions of the 4-(Me_2N)-C_6H_4COO and* syn*-diene chromophores*

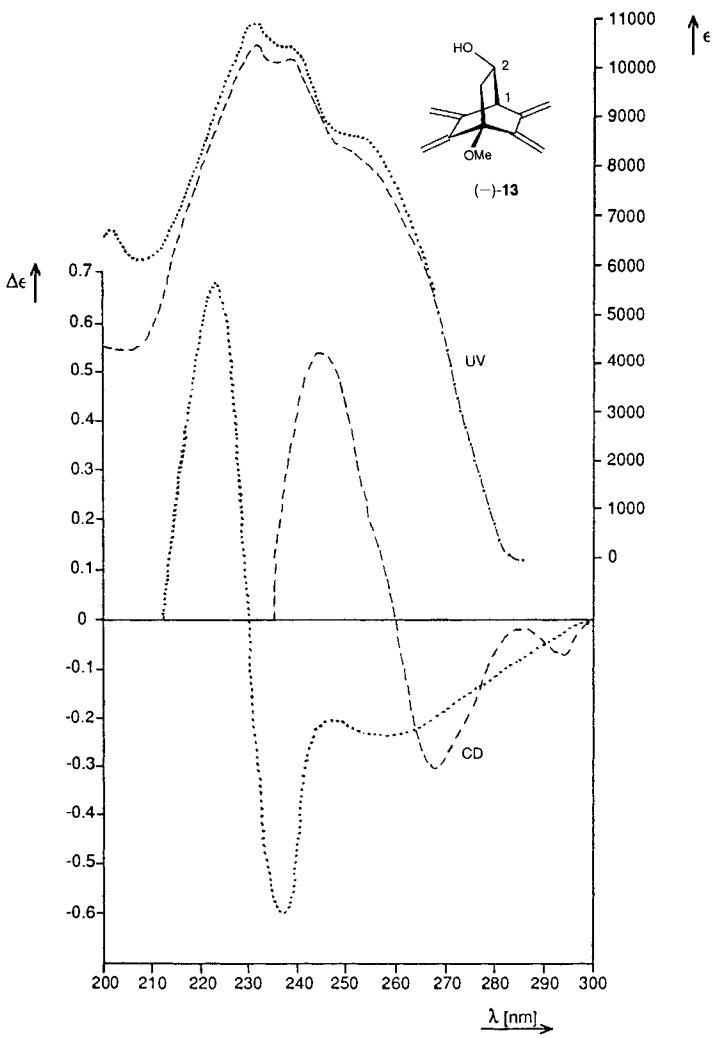


Fig. 3. *UV absorption and CD spectra of (−)-***13** *in isooctane* (---) *and in 95% EtOH* (· · · ·)

Esterification of (−)-**13** with 4-(Me_2N)C_6H_4COCl (pyridine, 50°, 16 h) gave the corresponding benzoate (+)-**22** (63%) whose circular dichroism (CD) spectra are reproduced in *Fig. 1*. Since the maximum of UV absorption of the 4-(dimethylamino)benzoate chromophore at *ca.* 310 nm is well separated from those of the transitions associated with the two homoconjugated s-*cis*-butadiene chromophore, the first *Cotton* effect (CE) observed in the CD spectra of (+)-**22** near 300 nm should not be perturbed by possible exciton-split CE's due to the interaction of the diene moieties between themselves (see below, *Fig. 3*). Thus, the negative sign of this CE determines the chirality of the lowest-energy electric transition moments of the 4-(Me_2N)C_6H_4COO and *syn*-butadiene chromophores, as shown in *Fig. 2*.

The CD spectra of tetraenol (−)-**13** and of the corresponding methanesulfonate (−)-**14** are shown in *Figs. 3* and *4*, respectively. The strong solvent dependence observed

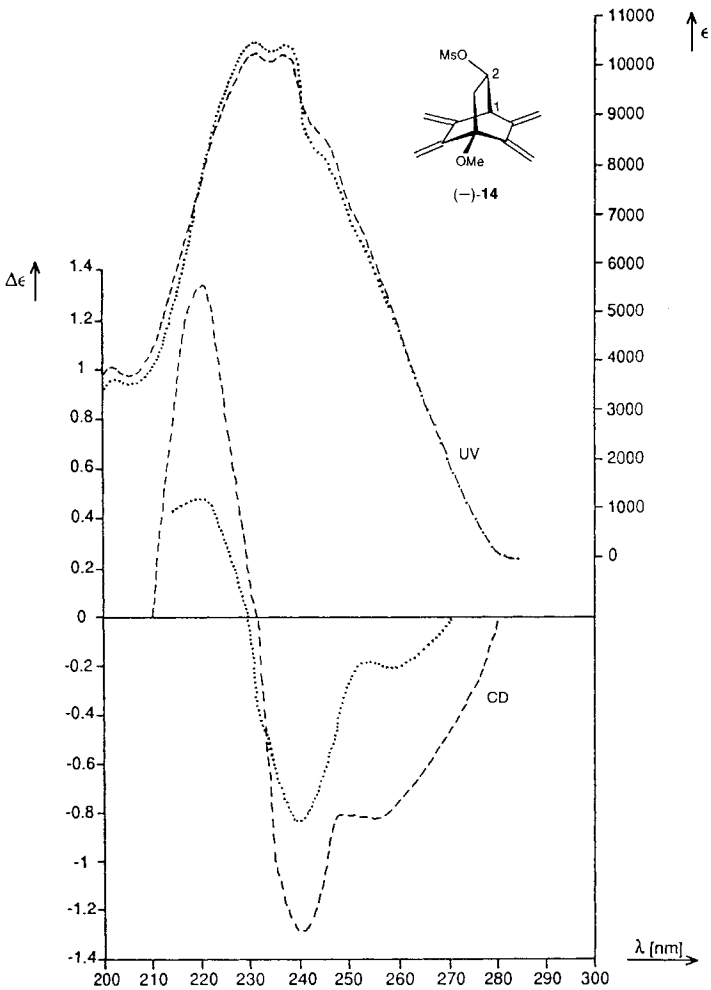


Fig. 4. *UV absorption and CD spectra of (−)-***14** *in isooctane* (---) *and in 95% EtOH* (· · · ·)

for (−)-**13** prohibits any conclusion to be drawn concerning the absolute configuration of this compound based on the shape of the CD spectra that show exciton-split type CE's. The solvent effect suggests possible formation of oligomeric species due to H-bridging between alcoholic functions, a phenomenon known to lead to unpredictable CE's in the

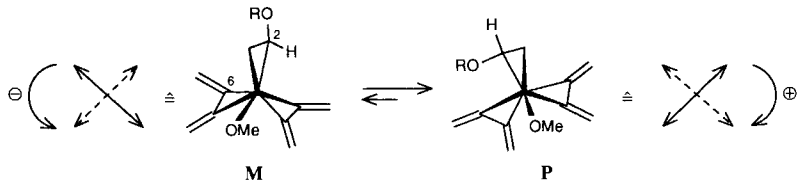


Fig. 5. *Representation of the possible twisting* (conformers **M**, **P**) *in the bicyclic skeletons of (−)-***13** *and (−)-***14**

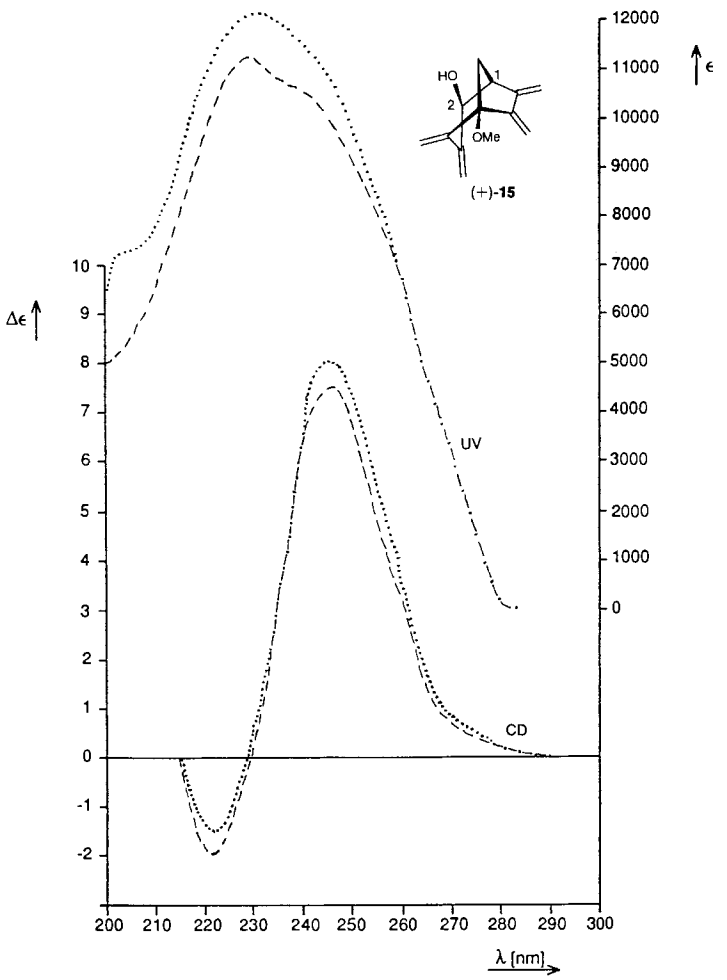


Fig. 6. *UV absorption and CD spectra of (+)-***15** *in isooctane* (---) *and in 95% EtOH* (· · · ·)

CD spectra of dienols [25]. The CD spectra of mesylate (−)-**14** in isooctane and in 95% EtOH are similar; they resemble in fact that of alcohol (−)-**13** in 95% EtOH. One, thus, is tempted to propose that oligomers of (−)-**13** are less abondant in the polar solvent (EtOH) than in the apolar solvent (isooctane). These spectra show relatively weak exciton-split CE's which might be associated with the through-space interaction between the lowest-energy electric transition moments of the two diene chromophores. If this interpretation should be valid, it would imply a twist of the bicyclic skeleton of (−)-**13** and (−)-**14** as shown in *Fig. 5*. In the case of the **M** conformers, it is possible that *gauche* interactions between the substituent at C(2) and C(6) centre are reduced compared with those in the **P** conformers, thus, making **M** more stable than **P** conformers. This leads to a negative chirality for the interaction between the two lowest-energy transition moments of the two diene chromophores, as observed for (−)-**13** (*Fig. 3*) and (−)-**14** (*Fig. 4*). We had shown, however, for (+)-(1*S*,4*R*,7*R*)-2,3,5,6-tetramethylidene(7-^{2}H)bicyclo[2.2.2]octane

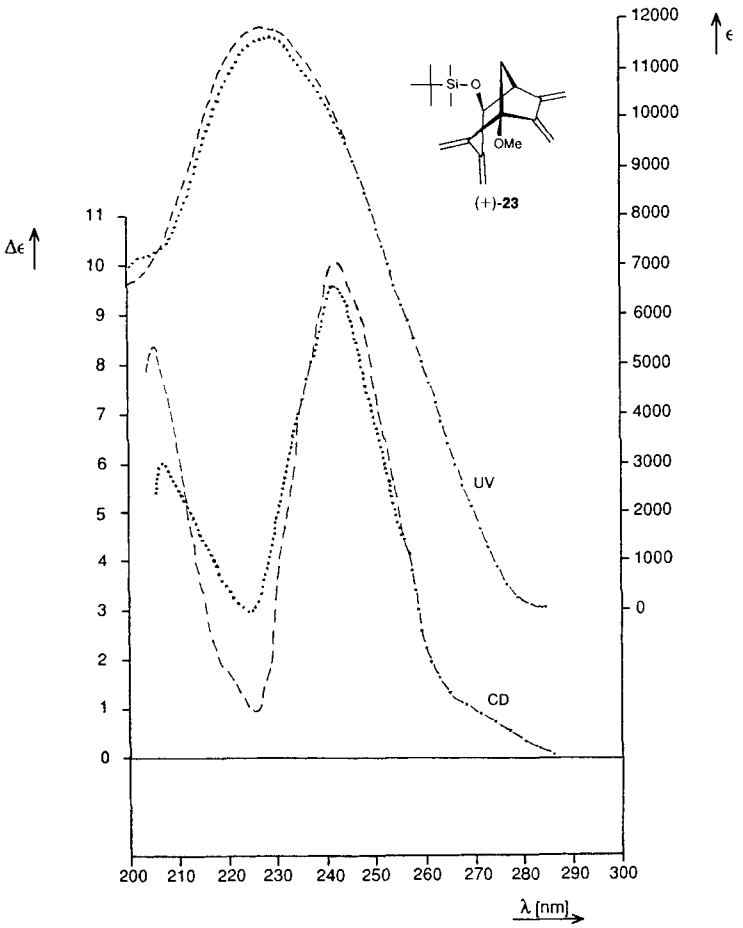


Fig. 7. *UV absorption and CD spectra of (+)-***23** *in isooctane* (---) *and in 95% EtOH* (· · · ·)

and for (+)-(1*R*,4*S*,7*S*)-7-methyl-2,3,5,6-tetramethylidenebicyclo[2.2.2]octane [26] that such a twist was not detected by variable-temperature CD [27]. It is, thus, possible that an other interpretation could apply to explain the observed CD spectra of (−)-**13** and (−)-**14**.

Buffered hydrolysis (see above) of (−)-**14** gave optically pure rearranged tetraenol (+)-**15** whose CD spectra are reproduced in *Fig. 6*. Silylation of (+)-**15** with (*t*-Bu)$Me_2SiOSO_2CF_3$ (CH_2Cl_2, 2,6-lutidine, 20°, 90 min) afforded the corresponding ether (+)-**23** (96%) whose CD spectra are shown in *Fig. 7*. The ^{1}H-NMR spectra of (+)-**15** and (+)-**23** showed a vicinal coupling constant of 4 Hz between H–C(1) and H–C(2) typical of a chair conformation ($^8C_3$) for the C(1)–C(2)–C(3)–C(4)–C(5)–C(8) ring [10], thus, implying loss of conjugation between the two methylidene groups at C(3) and C(4)[2]). Semi-empirical AM1 calculations (with complete geometry optimization) predicted a dihedral angle between CH_2=C(3)–C(4)=CH_2 of 38.7° in the case of (+)-**15** [28]. This implies that the lowest-energy transition of the butadiene chromophore at C(3),C(4) must be of higher energy than that of the s-*cis*-butadiene chromophore at C(6),C(7). Indeed, the maximum of UV absorption in 2,3-dimethylidenecyclohexane and 4,5-dimethylidenecyclohex-1-ene was found at 218 and 220 nm [29], respectively, whereas the maximum of the N → V_1 transition of 7,8-dimethylidenebicyclo[3.2.1]octane was observed at 247 nm [30] [9a]. Thus, in the case of (+)-**15** and (+)-**23**, the lowest-energy transition at *ca.* 245 nm is associated mostly with the N → V_1 transition of the s-*cis*-diene moiety at C(6),C(7) which is perturbed by the s-*gauche*-diene chromophore at C(3),C(4) for which the maximum of absorption is expected near 220 nm [29] [31] (see also UV spectra of **28** and **32**, *Exper. Part*). The interaction of the electric transition moments of these two transitions leads to a positive chirality and is, thus, responsible for the positive CE near 245 nm and the negative CE near 225 nm in the CD spectra of (+)-**15**, and for a positive CE near 245 nm and a trough at 227 nm in the CD spectra of (+)-**23** (see *Fig. 8*).

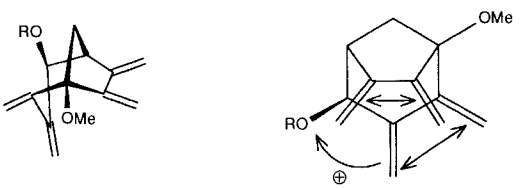


Fig. 8. *Representation of the positive chirality of tetraenes (+)-***15** *and (+)-***23**

Acylation of (±)-**15** with Ac_2O/pyridine afforded a 6:1 mixture of acetates **24** and **25** (93% yield). Treatment of **24** with $CaCO_3$ in acetone/H_2O (100°, 3 h 30 min) [32] led to decomposition of the polyene. Attempts to isomerize **24** into **25** with (dibenzalacetone)(triphenylphosphine)dipalladium (THF, 20°, 2 days) gave traces of rearranged ester **25** together with polymeric material. Esterification of alcohol (+)-**15** with $MeSO_2Cl$/pyridine, followed by workup with 1N HCl/H_2O gave a 3:2 mixture of (+)-**15** and (+)-**16** from which pure (+)-**16** could be isolated in 36% yield by TLC on silica gel.

The CD spectra of (+)-**16** (*Fig. 9*) show relatively strong CE's at 238 nm. The N → V_1 transition of the exocyclic s-*cis*-butadiene chromophore at C(6),C(7) is expected to have

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[2]) For convenience, (+)-**23** is numbered like **15**; for systematic names, see *Exper. Part.*

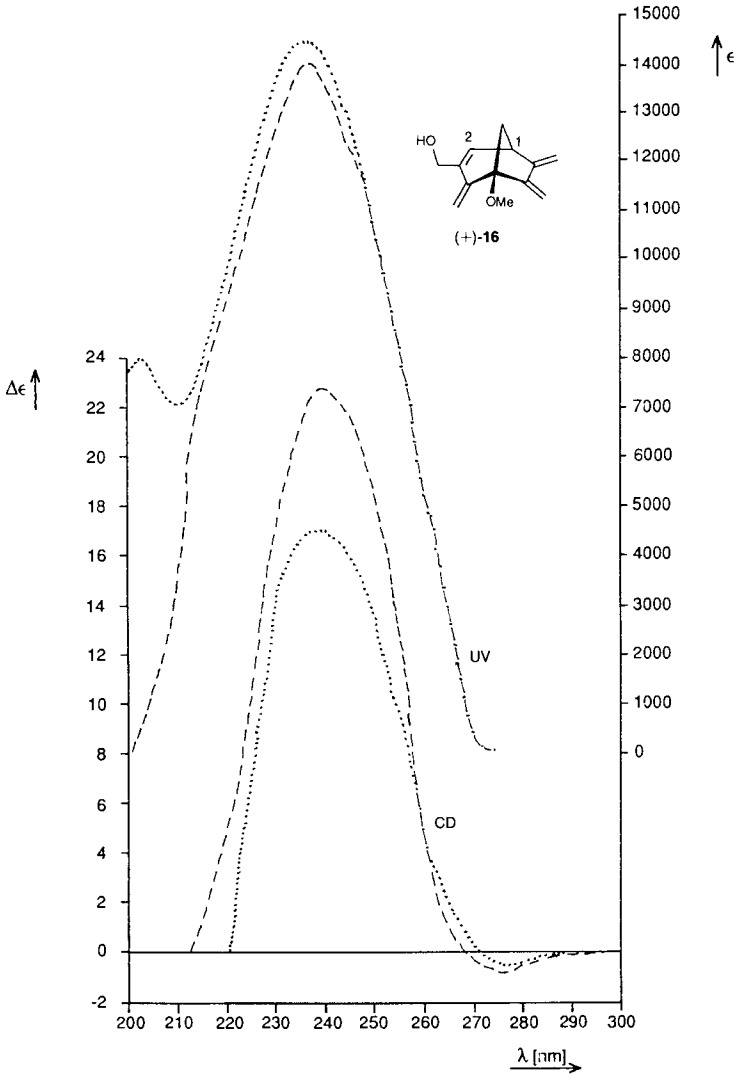
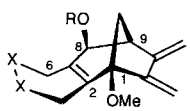


Fig. 9. *UV absorption and CD spectra of (+)-***16** *in isooctane* (---) *and in 95% EtOH* (· · · ·)

its maximum of absorption between 240 and 250 nm, whereas that of the s-*trans*-diene moiety at C(2),C(3),C(4) is expected between 230 and 245 nm [33] (verbenene has a $\lambda_{max} = 245$ nm [34]). These two chromophores should lead to exciton-split type of CE's if the transition electric moments of their $N \rightarrow V_1$ transitions were not coplanar. The single CE observed in the CD spectra of (+)-**16** (*Fig. 9*) is, thus, consistent with coplanar s-*cis*-butadiene and s-*trans*-diene functions, in agreement with molecular models and AM1 calculations [28]. The positive sign of this CE cannot be interpreted at this moment. It might be associated with out-of-plane deformation of the two diene moieties (diene helicity [35]) or with allylic substituent effects [36] [37].

The tetraenol (±)-**15** added to various dienophiles giving mixtures of unstable mono- and bis-adducts. In the case of the *Diels-Alder* addition to ethylenetetracarbonitrile (TCNE), the two mono-adducts **26** and **27** were formed with similar rate constants, together with polymeric material. Less polymerization was observed for the cycloadditions of the silyl-protected tetraenol (±)-**23** which, again, did not show any significant selectivity between the *Diels-Alder* addition of the s-*gauche*-diene moiety at C(3),C(4) and the s-*cis*-butadiene unit at C(6),C(7). The reactions of (±)-**23** with TCNE (→ **28** + **29** + **34**), maleic anhydride (→ **30** + **31**), dimethyl acetylenedicarboxylate (→ **32** + **33** + **35**), and methyl propynoate led to mixtures of bis-adducts and corresponding mono-adducts; the two possible mono-adducts were formed in a ratio of 1:1, 2:1, 2:3, and 1:1, respectively for *ca.* 50% of conversion. Characteristics of mono-adducts **28**–**33** and bis-adducts **34** and **35** are given in the *Exper. Part.* The tricyclo-[7.2.1.$0^{2,7}$]dodec-2(7)-ene derivatives **26**, **28**, **30**, and **32** were distinguished from the corresponding tricyclo[6.3.1.$0^{2,7}$]dodec-2(7)-ene derivatives **27**, **29**, **31**, and **33** by their ^{1}H-NMR spectra. In the former systems, vicinal coupling constants ^3J(H–C(8), H–C(9)) ≈ 0–1 (see also **34** and **35**) and the geminal coupling constants ^2J(H–H) between the methylidene protons were not visible, whereas in the latter systems, ^3J(H–C(8),H–C(9)) = 3.5–4 Hz and ^2J(H,H) of the CH_2=C(10) and CH_2=C(11) groups were found to vary between 1 and 2 Hz.

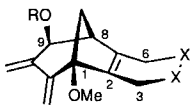


26 X–X = $(NC)_2C$–$C(CN)_2$, R = H

28 X–X = $(NC)_2C$–$C(CN)_2$, R = (*t*-Bu)Me_2Si

30 X–X =  , R = (*t*-Bu)Me_2Si

32 X–X = MeOOC–C=C–COOMe, R = (*t*-Bu)Me_2Si

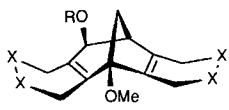


27 X–X = $(NC)_2C$–$C(CN)_2$, R = H

29 X–X = $(NC)_2C$–$C(CN)_2$, R = (*t*-Bu)Me_2Si

31 X–X =  , R = (*t*-Bu)Me_2Si

33 X–X = MeOOC–C=C–COOMe, R = (*t*-Bu)Me_2Si



34 X–X = $(NC)_2C$–$C(CN)_2$, R = (*t*-Bu)Me_2Si

35 X–X = MeOOC–C=C–COOMe, R = (*t*-Bu)Me_2Si

Thus, contrary to the *Diels-Alder* addition of the parent tetraene **7** to TCNE which showed a rate-constant ratio of *ca.* 300 between the reaction of the diene moiety at C(2),C(3) *vs.* that of the diene unit at C(6),C(7), we did not observe any significant reactivity difference between the two butadiene functions of (±)-**15** and (±)-**23**. This suggests that the OH and $OSiMe_2$(*t*-Bu) substituents at C(2) reduce the *Diels-Alder* reactivity of the diene moiety at C(3),C(4) more than that of the diene unit at C(6),C(7). This retarding effect cannot be interpreted in terms of a steric effect only as the selectivity of the TCNE cycloadditions to (±)-**15** and (±)-**23** were the same, and as it did not depend, in the case of (±)-**23**, on the nature of the dienophile. It is, thus, possible that inductive effects of the allylic alcohol and silyl ether at C(2) contribute to the reduced *Diels-Alder* reactivity of the adjacent exocyclic diene function [9]. Another hypothesis could be a reduced flexibility of the C(2),C(3),C(4) bridge in (±)-**15** and (±)-**23** as compared with that in **7**.

These preliminary results on the *Diels-Alder* reactivity of tetraenes (±)-**15** and (±)-**23** are deceiving and limit the potentiality of our optically pure derivatives (+)-**15** and (+)-**23** to become synthetic intermediates in a doubly-convergent approach to the synthesis of naphthocyclinones and analogues. We are exploring various ways to go around that unforeseen difficulty.

Conclusion. – An efficient synthesis of optically pure (+)-(1*S*,2*S*,5*S*)-5-methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]oct-2-yl derivatives ((+)-**15** and (+)-**23**) has been developed based on the baker's yeast reduction of 4-methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-one (**11**) and stereospecific *Wagner-Meerwein* rearrangement of (−)-(1*R*,2*S*,4*R*)-4-methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-ol ((−)-**13**) so-obtained. The configuration of alcohol (−)-**13** corresponds to that of bicyclo[2.2.2]octan-2-ol obtained by baker's yeast reduction of bicyclo[2.2.2]octan-2-one [19]. The absolute configuration of (+)-**15** and (+)-**23** was given by the exciton-split type of CE's observed in their CD spectrum, assuming validity of the *Kuhn-Kirkwood* dipole-coupling mechanism [38] for the interaction between the homoconjugated s-*cis*- and s-*gauche*-butadiene chromophores in these molecules. It was confirmed by the CD spectrum of (+)-(1*R*,2*S*,4*R*)-4-methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]oct-2-yl 4-(dimethylamino)benzoate ((+)-**22**) applying the chiral exciton coupling method to the interacting s-*cis*-butadiene and 4-(dimethylamino)benzoate chromophores in '*syn*'-position.

We thank *F. Hoffmann-La-Roche AG*, Basel, the *Swiss National Science Foundation*, and the *Fonds Herbette*, Lausanne, for financial support. We are grateful also to Prof. *B. Testa*, Ecole de Pharmacie de l'Université de Lausanne, for use of his *Roussel-Jouan Dichrograph Mark III* (*Jobin-Yvon*). We thank also Dr. *D. Stahl*, Institut de chimie physique de l'Ecole polytechnique fédérale de Lausanne (EPFL), for high-resolution mass-spectrometric measurements.

Experimental Part

General. See [37] [39].

4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-one (**11**). $BF_3 \cdot Et_2O$ (100 µl, 0.8 mmol) was added to a soln. of 1,3-dimethoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]oct-2-ene (**10**, 175 mg, 0.81 mmol) [12] in anh. CH_2Cl_2 (2 ml) cooled to −80°. After stirring at −80° for 1 h, a sat. aq. $NaHCO_3$ soln. (10 ml) was added and the mixture allowed to warm up to 20°. CH_2Cl_2 (8 ml) was added and the org. phase separated and washed with H_2O (10 ml, twice). After solvent evaporation, the residue was separated by column chromatography on silica gel (5 g, CH_2Cl_2). The 1st fraction gave 126 mg (77%) of **11**. M.p. 68–69°. UV (isooctane): 322 (250), 310 (450), 300 (450), 290 (370), 249 (11700), 244 (10900), 234 (sh, 8500), 204 (6800). UV (95% EtOH): 300 (380), 250 (11800), 245 (sh, 11100), 204 (7900). IR (KBr): 3120, 3010, 2960, 2940, 2860, 1740, 1610, 1470, 1440, 1400, 1390, 1320, 1210, 1190, 1170, 1120, 1010, 910, 890. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.63, 5.59, 5.38, 5.12 (4*s*, 8 H); 3.86 (*s*, H–C(1)); 3.55 (*s*, MeO); 2.67 (*s*, CH_2(3)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 202.7 (*s*, C(2)); 144.1, 138.1 (2*s*, C(5), C(6), C(7), C(8)); 109.1, 104.9 (2*t*, ^1J(C,H) = 160, 4 CH_2=C); 79.2 (*s*, C(4)); 66.5 (*d*, ^1J(C,H) = 145, C(1)); 52.2 (*q*, ^1J(C,H) = 141, MeO); 44.7 (*t*, ^1J(C,H) = 132, C(3)). MS (70 eV): 202 (39, $M^{+\cdot}$), 160 (100), 145 (17), 129 (21), 115 (73), 91 (36). Anal. calc. for $C_{13}H_{14}O_2$ (202.26): C 77.20, H 6.98; found: C 77.04, H 7.01.

1,3,3-Trimethoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octane (**12**). The 2nd fraction of the chromatography of the reaction mixture **11**/**12** (see above) yielded 40 mg (20%) of **12**. Colourless oil. UV ($CHCl_3$): 251 (sh, 8900), 242 (9700). IR ($CHCl_3$): 3080, 3030, 3000, 2960, 2940, 2830, 1610, 1460, 1430, 1330, 1290, 1260, 1190, 1150, 1120, 1090, 1040, 900. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.51 (br. *s*, 4 H); 5.23 (*s*, 2 H); 5.02 (*s*, 2 H); 3.50 (*s*, MeO); 3.44 (*s*, H–C(4)); 3.26 (*s*, 2 MeO); 2.12 (*s*, CH_2(2)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 144.7, 141.1 (2*s*, C(5), C(6), C(7), C(8)); 107.2, 103.5 (2*t*, ^1J(C,H) = 160, 4 CH_2=C); 101.1 (*s*, C(3)); 79.2 (*s*, C(1)); 54.2 (*d*, ^1J(C,H) = 140, H–C(4)); 51.8 (*q*, ^1J(C,H) = 140 Hz, MeO–C(1)); 48.1 (*q*, ^1J(C,H) = 142, $(MeO)_2$C(3)); 41.6 (*t*, ^1J(C,H) = 132, C(2)). MS

(70 eV): 249 (2), 248 (10, $M^{+\cdot}$), 233 (1), 217 (4), 216 (9), 201 (3), 187 (4), 186 (4), 185 (9), 171 (4), 160 (100), 145 (26), 131 (16), 130 (32), 129 (27), 128 (25), 117 (28), 115 (66), 105 (55), 91 (42).

(±)-4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-ol ((±)-**13**). A mixture of **11** (256 mg, 1.27 mmol), $NaBH_4$ (193 mg, 5.1 mmol), and anh. THF (15 ml) was stirred at 20° for 20 h. After addition of H_2O (30 ml), the mixture was extracted with CH_2Cl_2 (50 ml, 4 times). The org. extract was combined, dried ($MgSO_4$), and evaporated, yielding an oil that solidified at 0°: 250 mg (97%), colourless crystals. M.p. 69–71°. UV (95% EtOH): 250 (sh, 8510), 238 (sh, 10320), 231 (10760), 201 (6650). UV (isooctane): 246 (sh, 8320), 239 (10080), 231 (10340), 201 (4250). IR (KBr): 3320, 3100, 3000, 2960, 2910, 2820, 1790, 1650, 1610, 1440, 1430, 1390, 1330, 1300, 1210, 1120, 1090, 990, 900, 890. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.51 (*s*, H of CH_2=C(5) *cis* to C(6)); 5.42 (*s*, H of CH_2=C(6) *cis* to C(5)); 5.37 (*s*, H of CH_2=C(8) *cis* to C(7)); 5.37 (*s*, H of CH_2C=C(7) *cis* to C(8)); 5.13 (*s*, H of CH_2=C(6) *trans* to C(5)); 5.11 (*s*, H of CH_2=C(7) *trans* to C(8)); 4.95 (*s*, H of CH_2=C(5) *trans* to C(6)); 4.93 (*s*, H of CH_2=C(8) *trans* to C(7)); 4.04 (*dt*, *J* = 9.5, 3.0, H–C(2)); 3.41 (*s*, MeO); 3.10 (*d*, *J* = 3.0, H–C(4)); 2.33 (*dd*, *J* = 13, 9.5, H–C(3) *trans* to OH); 1.68 (*dd*, *J* = 13, 3.0, H–C(3) *cis* to OH); 1.41 (*s*, OH). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 145.6, 145.4, 142.1, 141.0 (4*s*, C(5), C(6), C(7), C(8)); 109.0, 107.2 (2*t*, ^1J(C,H) = 160), 103.8, 103.4 (2*t*, ^1J(C,H) = 158, 4 CH_2=C); 79.9 (*s*, C(4)); 67.6 (*d*, ^1J(C,H) = 155, C(2)); 55.1 (*d*, ^1J(C,H) = 135, C(1)); 51.7 (*q*, ^1J(C,H) = 140, MeO); 40.0 (*t*, ^1J(C,H) = 135, C(3)). MS (70 eV): 205 (2.5), 204 (13, $M^{+\cdot}$), 186 (3), 172 (29), 160 (89), 144 (29), 129 (45), 128 (50), 115 (100), 91 (70). Anal. calc. for $C_{13}H_{16}O_2$ (204.27): C 76.44, H 7.90; found: C 76.37, H 7.92.

(–)-(1S,2S,4R)-4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]octan-2-ol ((–)-**13**). A soln. of KH_2PO_4 (500 mg) in H_2O (60 ml) was heated to 34° in a three-necked flask. Fresh baker's yeast (4 g) and sucrose (7 g) were added portionwise under stirring. When the evolution of CO_2 was regular, **11** (25 mg, 0.124 mmol) in EtOH (1 ml) was added. The mixture was stirred at 34°. Portions of 3.5 g of sucrose were added every 2 h, 5 times. After stirring at 34° for 24 h, the mixture was saturated with NaCl and extracted with AcOEt (180 ml, 4 times). The extracts were combined and solvent evaporated. The residue was purified by filtration on a column of silica gel (5 g, CH_2Cl_2): 15 mg (60%), colourless oil $[\alpha]_D^{26} = -9.8$, $[\alpha]_{578}^{26} = -10.0$, $[\alpha]_{546}^{26} = -11.8$, $[\alpha]_{436}^{26} = -24.9$, $[\alpha]_{365}^{26} = -49.0$ (*c* = 0.88, CH_2Cl_2). CD (*c* = 0.0158, 95% EtOH, 26°): 300 (0), 260 (–0.24), 238 (–0.63), 230 (0), 224 (+0.68); see *Fig. 3*. CD (*c* = 0.0183, isooctane, 26°): 300 (0), 294 (–0.08), 272 (–0.31), 260 (0), 245 (+0.54); see *Fig. 3*.

(±)-4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]oct-2-yl Methanesulfonate ((±)-**14**). CH_3SO_2Cl (318 µl, 2.78 mmol) was added to a soln. of (±)-**13** (212 mg, 1.04 mmol) in anh. pyridine (7 ml) cooled to 0°. After staying at 0° for 23 h, CH_2Cl_2 (40 ml) was added and the soln. washed with aq. 1N HCl (40 ml, 3 times), then with sat. aq. $NaHCO_3$ soln. (40 ml, 5 times). After drying ($MgSO_4$), the solvent was evaporated: 293 mg (100%). Yellowish oil. UV (95%, EtOH): 246 (sh, 8180), 238 (10370), 232 (10390), 202 (3660). UV (isooctane): 246 (sh, 8430), 238 (10160), 231 (10260), 202 (3890). IR ($CHCl_3$): 3070, 3000, 2920, 2820, 1600, 1400, 1360, 1320, 1170, 1110, 950, 920, 890. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.50, 5.46, 5.45, 5.41, 5.16, 5.05, 5.00 (7*s*, 8 H); 4.96 (*m*, H–C(2)); 3.45 (*s*, MeO); 3.43 (*d*, *J* = 4, H–C(1)); 3.03 (*s*, $MeSO_3$); 2.45 (*dd*, *J* = 13.5, 10, H–C(3) *trans* to MsO); 2.03 (*dd*, *J* = 13.5, 3, H–C(3) *cis* to MsO). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 144.8, 144.4, 140.3, 139.6 (4*s*, C(5), C(6), C(7), C(8)); 109.1, 108.9, 104.2, 103.8 (4*t*, ^1J(C,H) = 160, 4 CH_2=C); 78.3 (*s*, C(4)); 76.2 (*d*, ^1J(C,H) = 150, C(2)); 52.4 (*d*, ^1J(C,H) = 142, C(1)); 51.8 (*q*, ^1J(C,H) = 140, MeO); 38.8 (*q*, ^1J(C,H) = 139, $MeSO_3$); 36.8 (*t*, ^1J(C,H) = 132, C(3)). MS (70 eV): 282 (13, $M^{+\cdot}$), 186 (51), 171 (29), 160 (24), 155 (25), 145 (20), 143 (21), 141 (22), 128 (55), 115 (50), 79 (100).

(–)-(1S,2S,4R)-4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]oct-2-yl Methanesulfonate ((–)-**14**). Same procedure as for (±)-**14**, starting with (–)-**13**. $[\alpha]_D^{20} = -7.6$, $[\alpha]_{578}^{20} = -12.1$, $[\alpha]_{546}^{20} = -13.6$, $[\alpha]_{436}^{20} = -21.2$, $[\alpha]_{365}^{20} = -36.4$ (*c* = 0.66, CH_2Cl_2). CD (*c* = 0.0132, 95% EtOH, 20°): 300 (0), 257 (–0.23), 239 (–0.87), 229 (0), 220 (+0.5). CD (*c* = 0.0138, isooctane, 20°): 280 (0), 256 (–0.83), 240 (–1.3), 230 (0), 220 (+1.35); see *Fig. 4*.

(±)-(1RS,2RS,5RS)-5-Methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]octan-2-ol ((±)-**15**). A soln. of (±)-**14** (41 mg, 0.145 mmol) in $CF_3CH(OH)CF_3$ (5 ml), H_2O (2.5 ml), and 2,6-lutidine (75 µl) was stirred at 20° for 2½ h. After addition of H_2O (12 ml), the soln. was extracted with CH_2Cl_2 (25 ml, 4 times). The org. extract was washed with sat. aq. $NaHCO_3$ soln. (100 ml, twice) and evaporated. The residue was purified by column chromatography on silica gel (*Lobar*, column *A*, CH_2Cl_2): 17 mg (57%), Colourless oil. UV (95% EtOH): 321 (12100). UV (isooctane): 238 (sh, 10600), 229 (11200). IR ($CHCl_3$): 3600, 3080, 3000, 2950, 2900, 2840, 1450, 1310, 1170, 1110, 1020, 900. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.42 (*s*, 2 H); 5.36 (*d*, *J* = 1.5, 1 H); 5.17 (*d*, *J* = 1.5, 1 H); 5.15 (*d*, *J* = 1.5, 1 H); 5.02 (*d*, *J* = 1.5, 1 H); 5.02 (*s*, 1 H); 4.96 (*s*, 1 H); 4.19 (*d*, *J* = 4.0, H–C(2)); 3.37 (*s*, MeO); 3.0 (*dd*, *J*(H–C(1),H–C(8*anti*)) = 5, *J*(H–C(1),H–C(2)) = 4, H–C(1)); 2.17 (*d*, ^2J = 11, H–C(8) *syn* to OH); 2.02 (*dd*, ^2J = 11, ^3J = 5, H–C(8) *anti* to OH). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 149.7, 147.9, 146.9, 145.7 (4*s*, C(3), C(4), C(6), C(7)); 116.7 (*t*, ^1J(C,H) = 160), 106.4 (*t*, ^1J(C,H) = 158), 105.4 (*t*, ^1J(C,H) = 160), 104.2 (*t*, ^1J(C,H) = 160, 4 CH_2=C); 76.2 (*s*, C(5)); 75.4 (*d*, ^1J(C,H) = 160, C(2)); 51.3 (*q*, ^1J(C,H) = 140, MeO); 46.2 (*d*, ^1J(C,H) = 135, C(1));

31.7 (*t*, ^1J(C,H) = 135, C(8)). MS (70 eV): 205 (11), 204 (68, $M^{+\cdot}$), 189 (18), 175 (14), 171 (14), 161 (25), 143 (39), 129 (66), 128 (74), 121 (100), 115 (33), 91 (67), 77 (94).

(+)-(1S,2S,5S)-5-Methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]octan-2-ol ((+)-**15**). Same procedure as for (±)-**15**, starting with (−)-**14**. $[\alpha]_D^{20}$ = +279, $[\alpha]_{578}^{20}$ = +291, $[\alpha]_{546}^{20}$ = +336, $[\alpha]_{436}^{20}$ = +620, $[\alpha]_{365}^{20}$ = +1105 (*c* = 1.83, CH_2Cl_2). CD (*c* = 0.0109, 95% EtOH, 20°): 290 (0), 246 (+8.0), 228 (0), 222 (−1.68), 215 (0). CD (*c* = 0.018, isooctane, 20°): 287 (0), 246 (+7.5), 229 (0), 222 (−2.0), 215 (0).

(+)-(1R,5S)-5-Methoxy-4,6,7-trimethylidenebicyclo[3.2.1]oct-2-ene-3-methanol ((+)-**16**). $MeSO_2Cl$ (42 µl, 0.54 mmol) was added under Ar to a stirred soln. of (+)-**15** (28 mg, 0.14 mmol) in anh. pyridine (2 ml) cooled to 0°. After staying at 2° for 22 h, ice (10 g) was added and the mixture extracted with CH_2Cl_2 (10 ml, 4 times). The org. extracts were washed with aq. 1N HCl (50 ml, 4 times) and evaporated, and the residue was purified by TLC (silica gel, CH_2Cl_2/Et_2O 9:1). The less polar product was (+)-**15** (15 mg); the more polar fraction gave (+)-**16**: 10 mg (36%). Colourless oil. $[\alpha]_D^{20}$ = +320, $[\alpha]_{578}^{20}$ = +340, $[\alpha]_{546}^{20}$ = +390, $[\alpha]_{436}^{20}$ = +730, $[\alpha]_{365}^{20}$ = +1340 (*c* = 0.48, CH_2Cl_2). CD (*c* = 0.0121, 95% EtOH, 24°): 297 (0), 277 (−0.8), 270 (0), 238 (+17), 222 (0). CD (*c* = 0.0036, isooctane, 24°): 300 (0), 275 (−1.1), 268 (0), 239 (+22.7), 213 (0); see *Fig. 9*. UV (95% EtOH): 237 (14400), 202 (8000). UV (isooctane): 237 (14000). ^{1}H-NMR (250 MHz, $CDCl_3$): 6.19 (*d*, *J* = 7, H–C(2)); 5.51 (*s*), 5.32 (*d*, *J* = 2), 5.23 (*s*), 5.18 (*s*), 4.98 (*s*), 4.86 (*s*, CH_2=C(3), CH_2=C(6), CH_2=C(7)); 4.26 (*dd*, *J* = 5, 1, CH_2–C(3)); 3.37 (*s*, MeO); 3.29 (*dd*, *J* = 7, 5, H–C(1)); 1.98 (*m*, CH_2(8)). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 149.1, 148.5, 147.4, 146.5 (4*s*, C(3), C(4), C(6), C(7)); 132.1 (*d*, ^1J(C,H) = 165, C(2)); 105.8, 103.7, 102.4 (3*t*, ^1J(C,H) = 160, 3 CH_2=C); 76.8 (*s*, C(5)); 62.8 (*t*, ^1J(C,H) = 142, CH_2–C(3)); 51.5 (*q*, ^1J(C,H) = 140, MeO); 41.9 (*d*, ^1J(C,H) = 135, C(1)); 38.8 (*t*, ^1J(C,H) = 135, C(8)). HR-MS (ref. C_6H_5I (203.9437834)): 204.113056 ($C_{13}H_{16}O_2$, calc. 204.1150).

(+)-(1S,2S,4R)-4-Methoxy-5,6,7,8-tetramethylidenebicyclo[2.2.2]oct-2-yl 4-(Dimethylamino)benzoate ((+)-**22**). A mixture of (−)-**13** (10 mg, 0.049 mmol), anh. pyridine (0.5 ml), and 4-(dimethylamino)benzoyl chloride (24 mg, 0.15 mmol) was stirred at 50° for 16 h. After solvent evaporation, the residue was taken with Et_2O (10 ml) and the precipitate filtered off. The soln. was washed with aq. 1N HCl (10 ml, twice), then with brine (10 ml, once), dried ($MgSO_4$), and evaporated. The residue was purified by column chromatography on silica gel (2 g, CH_2Cl_2): 8 mg (47%). Colourless oil. $[\alpha]_D^{26}$ = +10.9, $[\alpha]_{578}^{26}$ = +11.9, $[\alpha]_{546}^{26}$ = +13.6, $[\alpha]_{436}^{26}$ = +26.8 (*c* = 0.88, CH_2Cl_2). CD (*c* = 0.0127, 95% EtOH, 26°): 400 (0), 364 (−0.2), 305 (−0.8), 294 (−0.8), 259 (0), 248 (+2.1), 235 (0), 224 (−3.4). CD (*c* = 0.0127, isopentane/methylcyclohexane 3:1, 26°): 320 (0), 284 (−0.55), 258 (0), 248 (+2.1), 236 (+2.35), 230 (0), 222 (−2.77), 216 (−2.9), 212 (−3.88). UV (95% EtOH): 313 (24500), 246 (sh, 11300), 231 (16100); see *Fig. 1*. IR ($CHCl_3$): 3080, 3000, 2940, 2860, 2840, 2650, 2540, 2450, 2250, 2110, 1680, 1600, 1520, 1440, 1360, 1310, 940, 900, 830. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.87 (*d*, *J* = 9, 2 H); 6.65 (br. *d*, *J* = 9, 2 arom. H); 5.44, 5.43, 5.40, 5.15, 5.14, 5.02, 4.91 (7*s*, 8 H); 5.14 (*m*, H–C(2)); 3.43 (*s*, MeO); 3.40 (*d*, *J* = 3.5, H–C(1)); 3.02 (*s*, Me_2N); 2.49 (*dd*, ^2J = 13, ^3J = 10, H of CH_2(3) *trans* to C(2)–O); 1.92 (*dd*, ^2J = 13, ^3J = 3, H of CH_2(3) *cis* to C(2)–O). MS (70 eV): 226 (0.3), 206 (0.4), 193 (18), 192 (100), 148 (90).

(+)-(1S,4S,5S)-4-[(tert-Butyl)dimethylsilyloxy]-1-methoxy-2,3,6,7-tetramethylidenebicyclo[3.2.1]octane ((+)-**23**). (*t*-Bu)$Me_2SiOSO_2CF_3$ (153 µl, 231 mg, 0.88 mmol) was added to a stirred soln. of (+)-**15** (119 mg, 0.58 mmol) in anh. CH_2Cl_2 (5 ml) and 2,6-dimethylpyridine (203 µl, 187 mg, 0.174 mmol). After stirring at 20° for 1½ h, CH_2Cl_2 (5 ml) was added and the soln. washed with brine (10 ml). After solvent evaporation, the residue was purified by column chromatography on silica gel (14 g, CH_2Cl_2): 178 mg (96%). Colourless oil. $[\alpha]_D^{20}$ = +215, $[\alpha]_{578}^{20}$ = +225, $[\alpha]_{546}^{20}$ = +260, $[\alpha]_{436}^{20}$ = +480, $[\alpha]_{365}^{20}$ = +850 (*c* = 1.86, CH_2Cl_2). CD (*c* = 0.0093, 95% EtOH, 20°): 287 (0), 241 (+9.5), 225 (+2.9), 207 (+6.0). CD (*c* = 0.093, isooctane, 20°): 287 (0), 242 (+10), 224 (+0.8), 209 (+8.4). UV (95% EtOH): 228 (11700). UV (isooctane): 228 (11900); see *Fig. 7*. IR ($CHCl_3$): 3080, 3000, 2960, 2940, 2900, 2860, 1470, 1250, 1080, 900, 870, 840. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.43 (*s*, 2 H); 5.22 (*d*, *J* = 2, 1 H); 5.10 (*d*, *J* = 2, 1 H); 5.04 (*d*, *J* = 2, 1 H); 4.98 (*s*, 1 H); 4.93 (*s*, 1 H); 4.85 (*d*, *J* = 2); 4.13 (*d*, *J* = 4, H–C(4)); 3.37 (*s*, MeO); 2.86 (*t*, *J* = 5, H–C(5)); 2.26 (*d*, *J* = 10, H–C(8) *syn* to (*t*-Bu)Me_2SiO); 1.96 (*dd*, ^2J = 10, ^3J = 5, H–C(8) *anti* to (*t*-Bu)Me_2SiO); 0.89 (*s*, *t*-BuSi); 0.11, 0.06 (2*s*, Me_2Si). ^{13}C-NMR (90.55 MHz, $CDCl_3$): 154.1, 151.8, 150.4, 149.2 (4*s*, C(2), C(3), C(6), C(7)); 117.8 (*t*, ^1J(C,H) = 160), 107.7 (*t*, ^1J(C,H) = 158), 106.1 (*t*, ^1J(C,H) = 160), 105.2 (*t*, ^1J(C,H) = 160, 4 CH_2=C); 86.6 (*s*, C(1)); 76.7 (*d*, ^1J(C,H) = 160, C(4)); 50.6 (*q*, ^1J(C,H) = 142, MeO); 46.9 (*d*, ^1J(C,H) = 142, C(5)); 30.2 (*t*, ^1J(C,H) = 136, C(8)); 24.0 (3*q*, ^1J(C,H) = 125, $(CH_3)_3$CSi); 16.0 (*s*, $(CH_3)_3C$Si); 0.8, 0.3 (2*q*, ^1J(C,H) = 120, (*t*-Bu)Me_2Si). MS (70 eV): 318 (31, $M^{+\cdot}$), 303 (7), 288 (7), 275 (4), 261 (25), 246 (13), 231 (16), 229 (26), 171 (17), 155 (26), 89 (33), 75 (58), 73 (100). HR-MS (ref. $C_{20}H_{14}O_4$ (318.089201)): 318.199226 ($C_{19}H_{30}O_2Si$, calc. 318.20148).

(1RS,2RS,5RS)-5-Methoxy-3,4,6,7-tetramethylidenebicyclo[3.2.1]oct-2-yl Acetate (**24**). A soln. of (±)-**15** (6 mg, 0.029 mmol) in anh. pyridine (1 ml) and Ac_2O (1 ml) was stirred at 20° for 18 h. After addition of sat. aq. $NaHCO_3$ soln. (8 ml), the mixture was extracted with CH_2Cl_2 (10 ml, 3 times). The org. extract was washed with sat. aq. $NaHCO_3$ soln. (25 ml, 3 times), then with aq. 0.5N HCl (25 ml, 3 times), and finally with H_2O (25 ml, twice)

and evaporated, and the residue purified by TLC on silica gel (CH_2Cl_2). The less polar compound was **24**: 6 mg (83%). Colourless oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 5.50 (*s*, 1 H); 5.46 (*d*, *J* = 2, 2 H); 5.17, 5.15, 5.14, 5.12 (4*d*, *J* = 1.5, 4 H); 4.98 (*s*, 1 H); 5.27 (*d*, *J* = 4, H–C(2)); 3.38 (*s*, MeO); 3.09 (*m*, H–C(1)); 2.33 (br. *s*, CH_2(8)); 2.08 (*s*, Ac).

(1RS,5SR)-(5-Methoxy-4,6,7-trimethylidenebicyclo[3.2.1]oct-2-en-3-yl)methyl Acetate (**25**). The more polar compound in the TLC described above (see **24**) was **25**: 1 mg (14%). Colourless oil. ^{1}H-NMR (250 MHz, $CDCl_3$): 6.19 (*d*, *J* = 6, H–C(2)); 5.52 (*s*); 5.32 (2*d*, *J* = 2); 5.25, 5.19, 4.92, 4.88 (4*s*, 6 H); 4.67 (*dd*, *J* = 12, 9 CH_2–C(3)); 3.36 (*s*, MeO); 3.24 (*m*, H–C(1)); 2.33 (br. *s*, CH_2(8)); 2.08 (*s*, AcO).

*Cycloaddition of Ethylenetetracarbonitrile (TCNE) to (±)-***23**. A mixture of (±)-**23** (20 mg, 0.063 mmol), TCNE (12.6 mg, 0.063 mmol), and degassed benzene (1.5 ml) was stirred at 20° for 14 h. After solvent evaporation, the residue was separated by column chromatography on silica gel (5 g, CH_2Cl_2/petroleum ether 4:1). The first fraction yielded 7 mg (26%) of **28**, the second 6.5 mg (23%) of **29**, and the third 6 mg (16%) of **34**.

*(1RS,8RS,9RS)-8-[(*tert*-Butyl)dimethylsilyloxy]-1-methoxy-10,11-dimethylidenetricyclo[7.2.1.0^{2,7}]dodec-2(7)-ene-4,4,5,5-tetracarbonitrile* (**28**). Colourless oil. UV (95% EtOH): 239 (sh, 7500), 214 (sh, 12000), 207 (sh, 16000), 201 (19000). UV (isooctane): 233 (sh, 9000), 214 (sh, 12000), 200 (16600). ^{1}H-NMR (360 MHz, $CDCl_3$): 5.59, 5.38, 5.16, 4.93 (4*s*, CH_2=C(10), CH_2=C(11)); 3.76 (br. *s*, H–C(8)); 3.33 (*s*, MeO); 3.27–3.12 (*m*); 2.78 (*m*, CH_2(3), CH_2(6)); 2.95 (*m*, H–C(9)); 2.12, 1.93 (2*m*, CH_2(12)); 0.97 (*s*, *t*-Bu); 0.19, 0.17 (2*s*, Me_2Si). MS (70 eV): 431 (1), 403 (4), 389 (26), 371 (3), 315 (1), 302 (1), 288 (5), 172 (9), 89 (9), 75 (100).

*(1RS,8RS,9RS)-9-[(*tert*-Butyl)dimethylsilyloxy]-1-methoxy-10,11-dimethylidenetricyclo[6.3.1.0^{2,7}]dodec-2(7)-ene-4,4,5,5-tetracarbonitrile* (**29**). Colourless crystals. M.p. 195–196°. UV (95% EtOH): 239 (sh, 5400), 214 (sh, 9400), 207 (sh, 13000), 201 (16000). UV (isooctane): 213 (9400), 208 (sh, 8700), 202 (7900). IR (KBr): 3080, 2960, 2940, 2900, 1860, 1470, 1440, 1300, 1250, 1090, 910, 870, 830, 780. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.43, 5.34, 5.14, 5.02 (4*d*, *J* = 1, CH_2=C(10), CH_2=C(11)); 4.19 (*d*, *J* = 3.5, H–C(9)); 3.34 (*s*, MeO); 3.31–2.82 (*m*, CH_2(3), CH_2(6)); 2.79 (*tm*, *J* = 5, H–C(8)); 2.48 (*d*, *J* = 10), 2.27 (*dd*, *J* = 10, 5, CH_2(12)); 0.89 (*s*, *t*-Bu); 0.11, 0.06 (2*s*, Me_2Si). MS (70 eV): 446 (0.4, M^+), 431 (2), 403 (2), 390 (10), 389 (29), 359 (4), 357 (4), 335 (2), 314 (4), 283 (4), 207 (6), 153 (4), 139 (33), 89 (41), 75 (51), 73 (100), 57 (83). Anal. calc. for $C_{25}H_{30}N_4O_2Si$ (446.63): C 67.23, H 6.77; found: C 66.97, H 6.69.

*(1RS,8RS,9RS)-8-[(*tert*-Butyl)dimethylsilyloxy]-1-methoxytetracyclo[7.6.1.0^{2,7}0^{10,15}]hexa-2(7),10(15)-diene-4,4,5,5,12,12,13,13-octacarbonitrile* (**34**). Colourless oil. UV (95% EtOH): 233 (sh, 4200), 214 (sh, 6700), 207 (sh, 8100), 203 (8800). ^{1}H-NMR (360 MHz, $CDCl_3$): 3.77 (br. *s*, H–C(8)); 3.32 (*s*, MeO); 3.45–2.55 (CH_2(3), CH_2(6), H–C(9), CH_2(11), CH_2(4)); 2.50 (*dd*, *J* = 10, 5), 2.27 (*d*, *J* = 10, CH_2(16)); 0.94 (*s*, *t*-Bu); 0.18, 0.17 (2*s*, Me_2Si). MS (70 eV): 573 (0.2), 559 (1.2), 518 (13), 517 (35), 516 (7), 458 (1), 416 (3), 389 (1), 360 (1), 305 (1), 275 (5), 231 (2), 217 (4), 105 (9), 91 (31), 75 (100).

*Cycloaddition of Maleic Anhydride to (±)-***23**. A mixture of (±)-**23** (15 mg, 0.047 mmol), maleic anhydride (4.5 mg, 0.047 mmol), and anh. benzene (1 ml) was allowed to stand at 20° for 18 h. After solvent evaporation, the residue containing a 2:1 mixture **30**/**31** was separated by TLC on silica gel (CH_2Cl_2/petroleum ether 3:2). The less polar (R_f 0.85) product gave 4 mg (20%) of **31**, the more polar (R_f 0.1–0.15) yielded 8 mg (40%) of **30**.

*(1RS,4SR,5RS,8RS)- and (1RS,4RS,5SR,8RS)-8-[(*tert*-Butyl)dimethylsilyloxy]-1-methoxy-10,11-dimethylidenetricyclo[7.2.1.0^{2,7}]dodec-2(7)-ene-4,5-dicarboxylic Anhydride* (**30**). Colourless oil. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.44, 5.37, 5.17, 5.12, 5.05, 4.99, 4.89, 4.83 (8*s*, CH_2=C(10), CH_2=C(11)); 3.67 (*m*, H–C(8)); 3.30, 3.27 (2*s*, MeO); 3.19 (*m*, H–C(9)); 2.84 (*m*, H–C(4), H–C(5)); 2.68–2.0, 1.67 (*m*, CH_2(3), CH_2(6), CH_2(12)); 0.93, 0.91 (2*s*, *t*-Bu); 0.14 (*s*, Me_2Si). MS (70 eV): 401 (0.1), 360 (1), 284 (1), 225 (1), 211 (4), 197 (1), 179 (2), 132 (3), 128 (2), 115 (3), 75 (100).

*(1RS,4RS,5SR,8RS,9RS)- and (1RS,4SR,5RS,8RS,9RS)-9-[(*tert*-Butyl)dimethylsilyloxy]-1-methoxy-10,11-dimethylidenetricyclo[6.3.1.0^{2,7}]dodec-2(7)-ene-4,5-dicarboxylic Anhydride* (**31**). Colourless oil. ^{1}H-NMR (360 MHz, $CDCl_3$): 5.44 (br. *s*), 5.22 (*d*, *J* = 2), 5.10 (*d*, *J* = 2), 5.04 (*d*, *J* = 2), 4.98 (br. *s*), 4.94 (br. *s*), 4.86 (*d*, *J* = 2, CH_2=C(10), CH_2=C(11)); 4.13 (*d*, *J* = 4, H–C(9)); 3.37 (*s*, MeO); 3.30 (*m*, H–C(4), H–C(5)); 2.87 (*dd*, *J* = 5, 4, H–C(8)); 2.27 (*d*, *J* = 10, H–C(12) *cis* to C(9)–O); 1.96 (*dd*, *J* = 10, 5, H–C(12) *trans* to C(9)–O); 1.59 (br. *s*, CH_2(3), CH_2(6)); 0.89 (*s*, *t*-Bu); 0.10, 0.05 (2*s*, Me_2Si). MS (70 eV): 371 (0.1), 334 (1), 333 (4), 332 (13), 318 (23), 303 (6), 288 (6), 275 (5), 261 (17), 247 (5), 246 (8), 243 (7), 215 (6), 201 (10), 187 (14), 185 (13), 171 (13), 169 (9), 155 (16), 141 (9), 121 (13), 115 (14), 91 (18), 89 (27), 75 (52), 73 (100).

*Cycloaddition of Dimethyl Acetylenedicarboxylate to (±)-***23**. A mixture of (±)-**23** (20 mg, 0.063 mmol), dimethyl acetylenedicarboxylate (9 mg, 0.002 mmol), and degassed benzene (1 ml) was stirred at 20° for 24 h. After solvent evaporation, the residue was separated by column chromatography on silica gel (5 g, CH_2Cl_2/petroleum ether 7:3). The 1st fraction contained a mixture (±)-**23**/**32**. The 2nd fraction gave 12 mg (41%) of **33**, and the 3rd fraction 4 mg (10%) of **35**.

Dimethyl (1RS,8RS,9RS)-9-[(tert-Butyl)dimethylsilyloxy]-1-methoxy-10,11-dimethylidenetricyclo-[6.3.1.0^{2,7}]dodec-2(7),4-diene-4,5-dicarboxylate (**33**). Colourless oil. UV (95% EtOH): 220 (sh, 9500), 207 (sh, 13700), 202 (15300). UV (isooctane): 220 (sh, 9100), 203 (16200), 201 (16000). ^{1}H-NMR (360 MHz, $CDCl_3$): 5.24, 5.20, 5.07, 4.88 (4*m*, CH_2=C(10), CH_2=C(11)); 4.12 (*m*, H–C(9)); 3.79, 3.77 (2*s*, COOMe); 3.69, 3.17–2.58, 1.82 (*m*, CH_2(3), CH_2(6), H–C(8)); 3.31 (*s*, MeO); 2.30, 2.18 (2*m*, CH_2(12)); 0.88 (*s*, *t*-Bu); 0.15, 0.09 (2*s*, Me_2Si). MS (70 eV): 460 (20, M^+), 429 (7), 428 (7), 417 (4), 403 (25), 385 (3), 371 (9), 328 (3), 313 (4), 297 (7), 281 (5), 269 (6), 237 (23), 211 (19), 207 (19), 197 (22), 179 (22), 178 (23), 165 (24), 139 (24), 89 (24), 75 (58), 73 (100).

Tetramethyl (1RS,8RS,9RS)-8-[(tert-Butyl)dimethylsilyloxy]-1-methoxytetracyclo[7.6.1.0^{2,7}0^{10,15}]hexa-deca-2(7),4,10(15),12-tetraene-4,5,12,13-tetracarboxylate (**35**). UV (95% EtOH): 202 (19800). ^{1}H-NMR (360 MHz, $CDCl_3$): 3.80, 3.79, 3.78 (3*s*, 4 MeOOC); 3.68 (*m*, H–C(8)); 3.26 (*s*, MeO); 3.39–2.96, 2.65 (*m*, CH_2(3), CH_2(6), CH_2(11), CH_2(14), H–C(9)); 2.20 (*m*, CH_2(16)); 0.92 (*s*, *t*-Bu); 0.12, 0.11 (2*s*, Me_2Si). MS (70 eV): 572 (22), 571 (58), 570 (100), 546 (28), 545 (49), 513 (12), 438 (24), 423 (10), 407 (9), 381 (10), 231 (15), 203 (19), 191 (19), 189 (17), 75 (45), 73 (82).

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