The First Enantiomerically Pure [*n*]Triangulanes and Analogues: σ-[*n*]Helicenes with Remarkable Features**

Armin de Meijere,*[a] Alexander F. Khlebnikov,[c] Sergei I. Kozhushkov,[a] Rafael R. Kostikov,[c] Peter R. Schreiner,[a, b] Alexander Wittkopp,[a, b] Christopher Rinderspacher,[a, b] Henning Menzel,[d] Dmitrii S. Yufit,[e] and Judith A. K. Howard[e]

Dedicated to Professor Lutz F. Tietze on the occasion of his 60th birthday

Abstract: (*M*)-(−)- and (*P*)-(+)-Trispiro-[2.0.0.2.1.1]nonanes [(*M*)- and (*P*)-**3**] as well as (*M*)-(−)- and (*P*)-(+)-tetraspiro-[2.0.0.0.2.1.1.1]undecanes [(*M*)- and (*P*)-**4**]-enantiomerically pure unbranched [4]- and [5]triangulanes – have been prepared starting from racemic bicyclopropylidenecarboxylic [(1*RS*)-**12**] and *exo*-dispiro[2.0.2.1]heptane-1-carboxylic [(1*RS*,3*SR*)-**13**] acids. The optical resolutions of *rac*-**12** and *rac*-**13** furnished enantiomerically pure acids (*S*)-(+)-**12**, (*R*)-(−)-**12**, (1*R*,3*S*)-(−)-**13**, and (1*S*,3*R*)-(+)-**13**. The ethyl ester (*R*)-**25** of the acid (*R*)-(−)-**12** was cyclopropanated to give carboxylates (1*R*,3*R*)-**26** and (1*R*,3*S*)-**26**. The ester (1*R*,3*S*)-**26** and acids (1*R*,3*S*)-**13** and (1*S*,3*R*)-**13** were converted into enantiomerically pure methylene[3]triangulanes (*S*)-(−)- and (*R*)-(+)-**28**. An alternative approach consisted of an enzymatic deracemization of *endo*-[(1*SR*,3*SR*)-dispiro[2.0.2.1]heptyl]methanol (*rac*-**20**) or *anti*-[(1*SR*,3*RS*)-4-methylenespiropentyl]methanol (*rac*-**18**). This afforded (*S*)-(−)- and (*R*)-(+)-**28** (starting from *rac*-**20**), as well as enantiomerically pure (*M*)-(−)- and (*P*)-(+)-1,4-dimethylenespiropentanes [(*M*)- and (*P*)-**23**] starting from *rac*-**18**. The methylenetriangulanes (*S*)-(−)- and (*R*)-(+)-**28** were cyclopropanated furnishing (*M*)- and (*P*)-**3**. The rhodium-catalyzed cycloaddition of ethyl diazoacetate onto (*S*)-(−)- and (*R*)-(+)-**28** yielded four diastereomeric ethyl trispiro[2.0.0.2.1.1]nonane-1-carboxylates in approximately equal proportions. The enantiomerically pure esters (1*R*,3*S*,4*S*)- and (1*S*,3*R*,4*R*)-**30** were isolated by careful distillation and then transformed into [5]triangulanes (*M*)- and (*P*)-**4** using the same sequence of reactions as applied for (*M*)- and (*P*)-**3**. The structures of the key intermediates (*R*)-**12** and *rac*-**31** were confirmed by X-ray analyses. Although [4]- and [5]triangulanes have no chromophore which would lead to any significant absorption above 200 nm, they have remarkably high specific rotations even at 589 nm with $[\alpha]_D^{20} = -192.7$ [(*M*)-**3**, $c = 1.18$, $CHCl_3$)] or +373.0 [(*P*)-**4**, $c = 1.18$, $CHCl_3$)]. This remarkable optical rotatation is in line with their helical arrangement of σ bonds, as confirmed by a full valence space single excitation configuration interaction treatment (SCI) in conjunction with DFT computations at the B3LYP/TZVP//B3LYP/6-31+G(d,p) level of theory which reproduce the ORD very well. Thus, it is appropriate to call the helically shaped unbranched [*n*]triangulanes the "σ-[*n*]helicenes", representing the σ-bond analogues of the aromatic [*n*]helicenes.

Keywords: ab initio calculations · chiral resolution · cycloaddition · small ring systems · triangulanes

[a] Prof. Dr. A. de Meijere, Dr. S. I. Kozhushkov, Prof. Dr. P. R. Schreiner, Dr. A. Wittkopp, Dipl.-Chem. C. Rinderspacher
Institut für Organische Chemie
der Georg-August-Universität Göttingen
Tammannstrasse 2, 37077 Göttingen (Germany)
Fax: (+49) 551-399475
E-mail: Armin.deMeijere@chemie.uni-goettingen.de

[b] Prof. Dr. P. R. Schreiner, Dr. A. Wittkopp, Dipl.-Chem. C. Rinderspacher
Current address: Department of Chemistry
The University of Georgia, Athens, GA 30602-2556 (USA)

[c] Prof. Dr. A. F. Khlebnikov, Prof. Dr. R. R. Kostikov
St.-Petersburg State University, Chemical Department
Universitetskii Prosp. 2, Petrodvorets
198504, St.-Petersburg (Russia)

[d] Dr. H. Menzel
Institut für Makromolekulare Chemie der Universität Hannover
Am Kleinen Felde 30, 30167 Hannover (Germany)

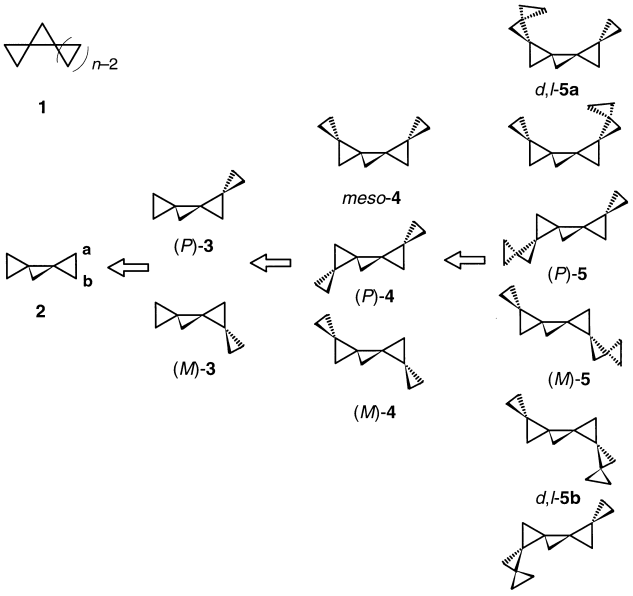
[e] Dr. D. S. Yufit, Prof. Dr. J. A. K. Howard
Department of Chemistry, University of Durham
Durham, South Rd., DH1 3LE (UK)

[**] Preliminary communication: A. de Meijere, A. F. Khlebnikov, R. R. Kostikov, S. I. Kozhushkov, P. R. Schreiner, A. Wittkopp, D. S. Yufit, *Angew. Chem.* **1999**, *111*, 3682 – 3685; *Angew. Chem. Int. Ed.* **1999**, *38*, 3474 – 3477.

0947-6539/02/0804-0828 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

Introduction

Enantiomerically pure chiral compounds, which in the ordinarily accessible UV/Vis spectral range (200–800 nm) do not show any optical activity, may be termed crypto-optically active.[1] As has been demonstrated by Wynberg et al. some 35 years ago,[2] chiral hydrocarbons with four different alkyl substituents at their centers of chirality, even in neat form, do not exhibit any optical rotation and are thus crypto-optically active. This essentially must have to do with the conformational mobility in such acyclic hydrocarbons. In contrast, unbranched [*n*]triangulanes **1** ([*n*]UT),[3] that is, hydrocarbons which consist of spiro-annelated and thereby mutually orthogonal cyclopropane rings only, are completely rigid, and many of the higher [*n*]triangulanes **1** ($n \geq 4$) are chiral.[4]



Achiral dispiro[2.0.2.1]heptane ([3]UT) **2** has two enantiotopic positions: spiroannelation of a fourth cyclopropane ring in either position **a** or **b** of **2** will lead to two enantiomeric [4]UTs (*M*)- and (*P*)-**3**. They should not be crypto-optically active due to their rigidity, although they are saturated hydrocarbons and their spiro-carbon atoms, which are stereogenic centers, formally also contain four different alkyl substituents only. To test this hypothesis, it ought to be interesting to prepare and study enantiomerically pure (*M*)- and (*P*)-[4]triangulanes [(*M*)-**3** and (*P*)-**3**] – the smallest chiral [*n*]triangulanes,[4] and their higher analogues (*M*)- and (*P*)-[5]triangulanes [(*M*)-**4** and (*P*)-**4**] for comparison. Essentially, the C_2-symmetric molecules of (*M*)- and (*P*)-**3**–**5** are sections of a helix, and therefore the stereochemical descriptors for helicenes[5] should best be applied for **3** and certain extended unbranched triangulanes **1**.[6] Racemic [4]triangulane *rac*-**3** was first synthesized 28 years ago, yet in the meantime improved syntheses as well as spectral, structural, and thermochemical properties of *rac*-**3** have been sufficiently well documented.[3a,b] Racemic [5]triangulane *rac*-**4** had previously been prepared only as a mixture with *meso*-**4**.[4] Among the most interesting features of these σ-helicenes, however, are their potential rotatory powers in view of their molecular helicity. We have therefore developed syntheses of enantiomerically pure [4]- and [5]triangulanes as well as their precursors, methylene- and dimethylene[*n*]triangulanes. Their experimentally determined specific rotations are compared with the best currently available computational results.

Results

A feasible synthetic approach to a whole series of enantiomerically pure [*n*]triangulanes appeared to be starting from appropriately *syn*-1,3-disubstituted spiropentane derivatives. However, it is difficult to prepare such compounds stereoselectively on a large scale.[7] Since intramolecular cyclopropanations of a remote double bond in alkenyl diazoacetate catalyzed by a dirhodium tetrakis(carboxamidate) with chiral ligands have been demonstrated to proceed with high diastereoselectivities,[8] we examined this type of reaction for (2-methylenecyclopropyl)methyl diazoacetate (**10**), prepared from (2-methylenecyclopropyl)methanol (**6**) and *N*-Boc-glycine (**7**) (Scheme 1), utilizing the [Rh_2(5*R*-MEPY)$_4$] catalyst.[8] Unfortunately, this approach to the tricyclic lactone **11** turned out to be not more efficient than the previously reported one:[9] the yield in the cyclization step was only 7% of almost racemic **11** (*ee* = 10%), the structure of which was confirmed by X-ray crystallography (Figure 1).[10]

Other appropriate enantiomerically pure starting materials for the preparation of (*M*)- or (*P*)-**3** and **4** were obtained from racemic bicyclopropylidenecarboxylic acid (*rac*-**12**), which is easily available from the multifunctional C_6-building block bicyclopropylidene[11] by deprotonation and carboxylation,[12]

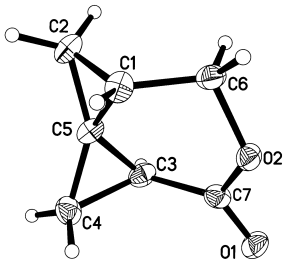
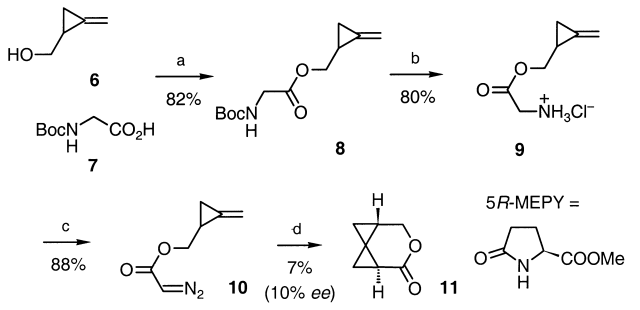


Figure 1. Structure of the tricyclic lactone **11** in the crystal.



Scheme 1. Attempted preparation of the tricyclic lactone **11** in enantiomerically pure form by intramolecular cyclopropanation. a) DCC, DMAP, CH_2Cl_2, 0 → 25 °C, 3 h; b) 4 N HCl in Et_2O, 0 → 25 °C, 15 h; c) $NaNO_2$, 5% H_2SO_4, CH_2Cl_2/H_2O, −5 °C, 0.5 h; d) Rh_2(5*R*-MEPY)$_4$ (0.3 mol%), CH_2Cl_2, 40 °C, 13 h. DCC = dicyclohexylcarbodiimde, DMAP = 4-dimethylaminopyridine, MEPY = methyl 2-pyrrolidone-5(*R*)-carboxylate.

and from racemic *exo*-dispiro[2.0.2.1]heptane-1-carboxylic acid (*rac*-**13**).[13] These two acids were optically resolved by crystallization of suitable mixtures of diastereomeric salts.[14] Among several tested enantiomerically pure bases such as (+)-2-amino-1-phenyl-1,3-propanediol, brucine, cinchonidine, quinine, strychnine, and dehydroabietylamine, only the latter gave readily crystallizing N and P[15] salts **14a**, **b** and **15a**, **b** with the acids *rac*-**12** and *rac*-**13**, respectively. Two crystallizations each from ethanol (for the purification of the P salt **15b** see Experimental Section), subsequent cleavage by treatment with aqueous sodium hydroxide and then acidification with concentrated hydrochloric acid furnished enantiomerically pure bicyclopropylidenecarboxylic acids (*R*)-(−)-**12** ($[\alpha]_D^{20} = -183.7$, $c = 1.0$ in $CHCl_3$, *ee* ≥ 98%), (*S*)-(+)-**12** ($[\alpha]_D^{20} = +183.2$, $c = 1.0$ in $CHCl_3$, *ee* ≥ 98%), (1*R*,3*S*)-(−)-**13** ($[\alpha]_D^{20} = -391.4$, $c = 1.0$ in $CHCl_3$, *ee* ≥ 98%), and (1*S*,3*R*)-(+)-**13** ($[\alpha]_D^{20} = +361.9$, $c = 1.0$ in $CHCl_3$, *ee* ≥ 98%) (Scheme 2).

The absolute configuration of the acid (*R*)-**12** was assigned on the basis of the relative configuration of its (*R*)-α-phenylethylamide (*R*,*R*)-**17a** as determined by an X-ray crystal structure analysis (Scheme 2 and Figure 2). The amides (*R*,*R*)-**17a** and (*R*,*S*)-**17b** were prepared from the racemic acid *rac*-**12** and (*R*)-(1-phenylethyl)amine (**16**) according to a standard procedure,[16] separated by column chromatography and assigned by comparison with authentic samples prepared from the enantiomerically pure acids (*R*)-(−)-**12** and (*S*)-(+)-**12**. This established the absolute configuration of (*R*,*R*)-**17a**.

As an indirect evidence for the relative configuration of the diastereomeric amides **17a**, **b**, their order of elution from silica gel may be used. According to the rule established by Helmchen et al.,[17] the first eluting amide **17b** prepared from the acid (+)-**12** and (*R*)-1-(phenylethyl)amine (**16**) should have (*S*)-configuration and its antipode (−)-**12** should have (*R*)-configuration, in complete agreement with the assignment from the crystal structure analysis. The absolute configurations of the acids (1*R*,3*S*)-**13** and (1*S*,3*R*)-**13** were established by comparing the optical rotations of identical products obtained after further transformations of the two acids **12** and **13** (see below).

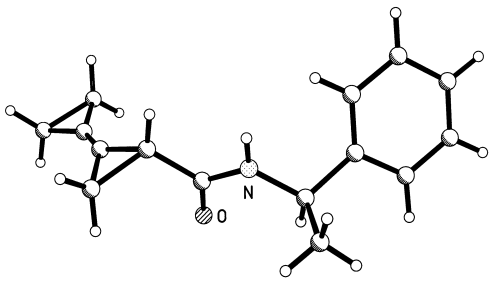
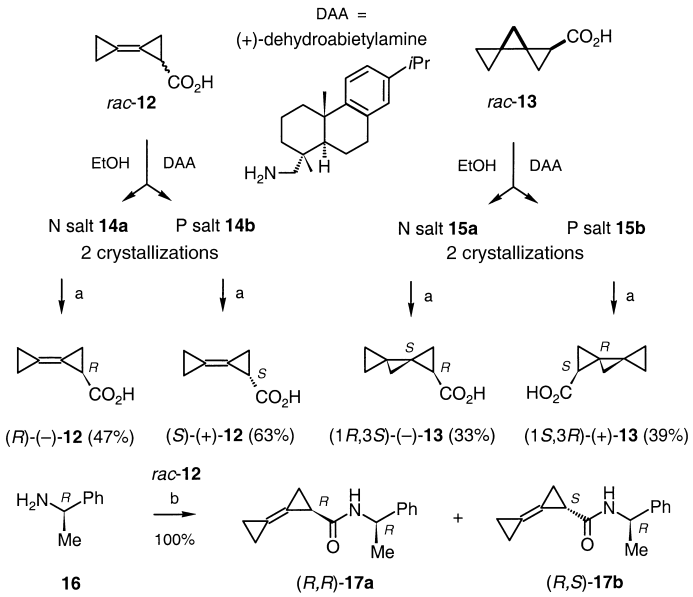


Figure 2. X-ray structure of (*R*)-bicyclopropylidenecarboxylic acid (*R*)-*N*-(1-phenylethyl)amide [(*R*,*R*)-**17a**].

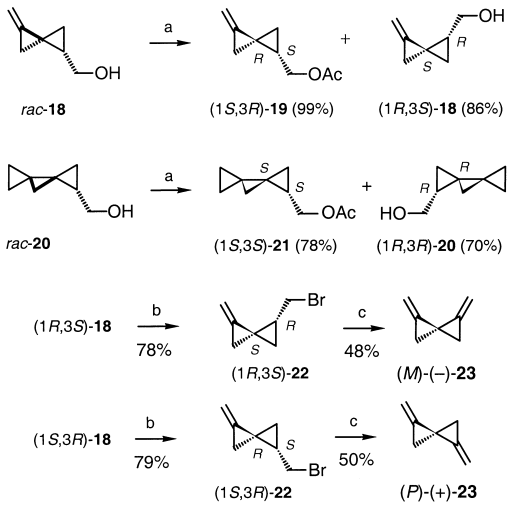
In spite of its being successful for the preparation of (*M*)- and (*P*)-**3**, the methodology starting from *rac*-**12** and *rac*-**13** appeared to be too elaborate for higher analogues in enantiomerically pure form. Therefore, our recently developed access to enantiomerically pure (1*S*,3*R*)- and [(1*R*,3*S*)-4-methylenespiropentyl]methanol [(1*S*,3*R*)-**18** and (1*R*,3*S*)-**18**] as well as racemic *endo*-(1*S*,3*S*)- and [(1*R*,3*R*)-dispiro[2.0.2.1]-heptyl]methanol [(1*S*,3*S*)-**20** and (1*R*,3*R*)-**20**] by means of an enantioselective enzymatic acylation of the racemic alcohols *rac*-**18** and *rac*-**20** catalyzed by Lipase PS (*Pseudomonas sp.*) was considered (Scheme 3).[18] The acetates (1*S*,3*R*)-**19** and (1*S*,3*S*)-**21** can be cleaved in a clean reaction by reduction with $LiAlH_4$ to give the corresponding alcohols (1*S*,3*R*)-**18** and (1*S*,3*S*)-**20** in 95 and 99% yield, respectively,[18] and the enantiomeric excess values of compounds prepared by this route all exceeded 95%. The enantiomerically pure alcohols (1*R*,3*S*)-**18** and (1*S*,3*R*)-**18** could be transformed to the enantiomerically pure (*M*)-(−)- and (*P*)-(+)-1,4-dimethylenespiropentanes (*M*)-**23** and (*P*)-**23** applying a sequence of routine transformations already established in the preparation of racemic triangulanes.[3] First, (1*R*,3*S*)-**18** and (1*S*,3*R*)-**18** were converted to the (bromomethyl)methylenespiropentanes (1*R*,3*S*)-**22** and (1*S*,3*R*)-**22** by treatment with the triphenylphosphane/bromine reagent in 78 and 79% yield, respectively. Dehydrobromination of the latter with potassium *tert*-butoxide gave the enantiomerically pure (*M*)-(−)- and (*P*)-(+)-1,4-dimethylenespiropentanes (*M*)-**23** and (*P*)-**23** in 48 and 50% yield, respectively, after gas chromatographic separation in the last step, corresponding to 32 and 37% overall yield from the racemic alcohol *rac*-**18**, with *ee* values of 96% for both, as determined by gas chromatography on a chiral phase capillary column (see Experimental Section for determinations of *ee* values and preparation of *rac*-**23**) (Scheme 3).

Assuming that a successful diastereoselective cyclopropanation of the central double bond in a suitable derivative of **12** would play a key role in any enantioselective synthesis of the [4]- and [5]triangulanes **3** and **4**, the acid (*R*)-**12** was reduced to the alcohol (*R*)-**24**,[19] since allyl and homoallyl alcohols are known to be cyclopropanated diastereoselectively.[20] Unfortunately, however, the cyclopropanation of (*R*)-**24** with the

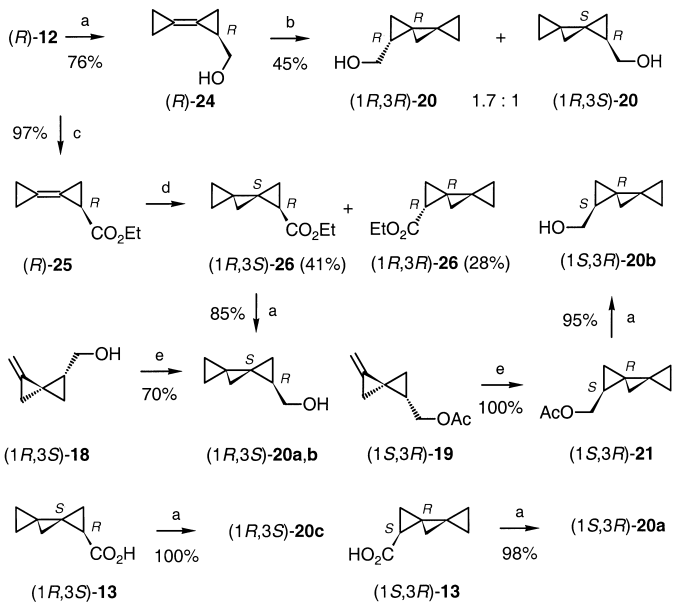


Scheme 2. Optical resolution of racemic bicyclopropylidenecarboxylic (*rac*-**12**) and *exo*-dispiro[2.0.2.1]heptane-1-carboxylic (*rac*-**13**) acids and preparation of diastereomeric (*R*)-α-phenylethylamides (**17a**,**b**) of the former. a) 1) aq. NaOH; 2) conc. HCl; 3) crystallization; b) $Ph_2P(O)Cl$, Et_3N, EtOAc, −10°C, 1 h.

0947-6539/02/0804-0830 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4



Scheme 3. Enzymatic deracemization (kinetic resolution) of *anti*-[(1*SR*,3*RS*)-4-methylenespiropentyl]methanol (*rac*-**18**) and *endo*-[(1*SR*,3*SR*)-dispiro[2.0.2.1]heptyl]methanol (*rac*-**20**) and preparation of enantiomerically pure (*M*)-(−)- and (*P*)-(+)-1,4-dimethylenespiropentanes (*M*)-**23** and (*P*)-**23**. a) Vinyl acetate, Lipase PS, Et_2O, 20 °C, 12 h; b) $Ph_3P \cdot Br_2$, Py, CH_2Cl_2, −10 °C, 1.5 h, then 20 °C, 7 h; c) *t*BuOK, DMSO, 20 °C, 0.75 h, inverse addition of a solution of *t*BuOK in DMSO.



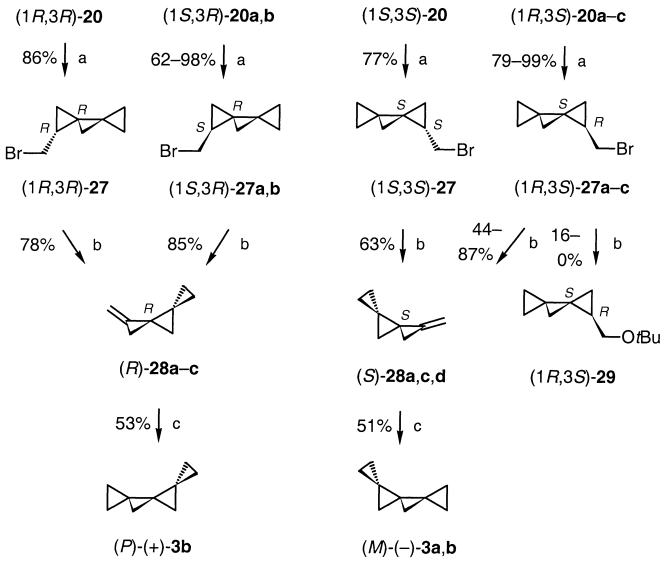
Scheme 4. Preparation of enantiomerically pure (1-dispiro[2.0.2.1]heptyl)methanols **20** along different routes. a) $LiAlH_4$, Et_2O, 34 °C, 2 h; b) CH_2I_2, Me_3Al, CH_2Cl_2, 20 °C, 19 h; c) $BF_3 \cdot Et_2O$, EtOH, 78 °C, 2 h; d) CH_2I_2, Zn, 1,2-dimethoxyethane, ultrasonication, 80 °C, 2 h; e) CH_2N_2, $Pd(OAc)_2$, Et_2O, −5 °C.

CH_2I_2/Me_3Al reagent[21] (Scheme 4) proceeded in low yield (45 %) and with poor stereoselectivity to give the alcohols (1*R*,3*R*)-**20** and (1*R*,3*S*)-**20** in a ratio of 1.7:1, and even worse, they could not be separated by chromatography. In a second approach, the acid (*R*)-**12** was first transformed into its ethyl ester (*R*)-**25**,[12, 19a] following a standard procedure,[22] and then (*R*)-**25** was cyclopropanated with the Simmons–Smith reagent (CH_2I_2/Zn).[20] The reaction was accelerated by ultrasonication[23] to give a mixture of ethyl *endo*-(1*R*,3*R*)- and *exo*-(1*R*,3*S*)-[3]triangulane-1-carboxylates (1*R*,3*R*)-**26** and (1*R*,3*S*)-**26**. These diastereomers were easily separated by column chromatography and isolated in 28 and 41 % yield, respectively (Scheme 4). Thus, enantiomerically pure (1*R*,3*S*)-**26** was obtained in 19 % yield from the racemic acid *rac*-**12**. The enantiomerically pure ester (1*R*,3*S*)-**26** was reduced to the alcohol (1*R*,3*S*)-**20a** which was also prepared in 70 % yield by cyclopropanation of the alcohol (1*R*,3*S*)-**18** with diazomethane under $Pd(OAc)_2$ catalysis[24] (**20b**, the letters **a**, **b**, **c** are used to distinguish identical compounds prepared from different sources of enantiomerically pure materials). Reduction of the enantiomerically pure acids (1*R*,3*S*)- and (1*S*,3*R*)-**13** furnished (1*R*,3*S*)-**20c** and (1*S*,3*R*)-**20a** quantitatively. The enantiomer (1*S*,3*R*)-**20b** was also synthesized in two steps from the acetate (1*S*,3*R*)-**19** in 95 % overall yield (Scheme 4).

The enantiomerically pure alcohols **20** were transformed to the enantiomerically pure (*S*)- or (*R*)-methylenedispiro-[2.0.2.1]heptanes [(*S*)-(−)-**28** or (*R*)-(+)-**28**] in two steps. First, treatment with the triphenylphosphane/bromine reagent furnished 1-(bromomethyl)-[3]triangulanes (1*R*,3*S*)-, (1*R*,3*R*)-, (1*S*,3*S*)-, and (1*S*,3*R*)-**27** in 77–99 % yield (Scheme 5). Dehydrobromination of the latter with potassium *tert*-butoxide gave (*S*)-(−)-**28** or (*R*)-(+)-**28** in 44–87 % yield. The dehydrobromination was complicated by a direct nucleophilic substitution of bromine with *tert*-butoxide anion in different proportions; in one preparation the corresponding (1*R*,3*S*)-(−)-1-(*tert*-butoxymethyl)dispiro[2.0.2.1]heptane [(1*R*,3*S*)-**29**] was isolated and characterized (see Experimental Section). Although the methylene[3]triangulane **28** and the *tert*-butyl ether **29** can easily be separated by an appropriate choice of conditions for the "bulb-to-bulb" distillation, probably, a sterically more demanding base should be applied in this reaction to increase the yield of **28**. Better *ee* values were obtained in preparations of the methylene[3]triangulanes **28** starting from the acid (*R*)-**12**, while the *ee* values of alkenes prepared from the acid *rac*-**13** or alcohol *rac*-**20** were similar in most cases.

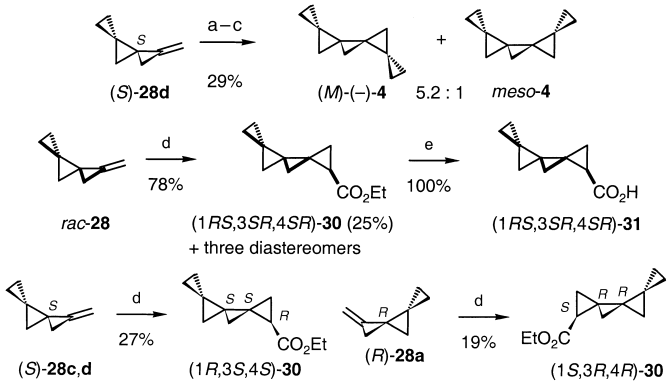
Cyclopropanation of (*S*)-(−)-**28a** or (*R*)-(+)-**28b** under the conditions mentioned above furnished the enantiomerically pure (*M*)-(−)- and (*P*)-(+)-[4]triangulane (*M*)-(−)-**3a** and (*P*)-(+)-**3b** in 51 and 53 % yield, respectively, after gas chromatographic separation in the last step (Scheme 5), corresponding to 7 and 19 % overall yield from the racemic acid *rac*-**12** or the alcohol *rac*-**20**, respectively, with an *ee* of ≥99 % and ≥96 %, respectively, as determined by gas chromatography on a chiral phase capillary column.[25] Attempted twofold cyclopropanation of the dimethylenespiropentane (*M*)-(−)-**23** furnished (*M*)-(−)-[4]triangulane (*M*)-(−)-**3b** in only 14 % yield, most probably because (*M*)-(−)-**23** is unstable towards the palladium acetate catalyst.

It should, in principle, be possible to prepare enantiomerically enriched or pure [5]- and [6]triangulanes [(*M*)-**4** or (*P*)-**4** and (*M*)-**5** or (*P*)-**5**] from the same synthetic precursor as the one used for (*M*)-**3** and (*P*)-**3**, that is, methylene[3]triangulane (*S*)-**28** and (*R*)-**28**, since the position of the methylene group predetermines any further extension of the helix. As the *meso*-[5]triangulane (*meso*-**4**) is not optically active, the alkene (*S*)-**28d** was transformed into a mixture of *meso*-**4** and (*M*)-**4** (ratio 1:5.2 according to the ^1H NMR spectrum)



Scheme 5. Preparation of enantiomerically pure (*S*)- and (*R*)-methylenedispiro[2.0.2.1]heptanes [(*S*)-(−)-**28** and (*R*)-(+)-**28**] as well as (*M*)- and (*P*)-[4]triangulanes [(*M*)-(−)-**3** and (*P*)-(+)-**3**]. a) $Ph_3P \cdot Br_2$, Py, CH_2Cl_2, −10 °C, 1.5 h, then 20 °C, 7 h; b) *t*BuOK, DMSO, 50 °C, 2 h; c) CH_2N_2, $Pd(OAc)_2$, Et_2O, −5 °C.

using the established three-step procedure[4] in 29% overall yield after gas chromatographic separation (Scheme 6). While all attempts to isolate pure (*M*)-**4** from this mixture were unsuccessful, the mixture had a specific rotation of $[\alpha]_D^{20} = -334.2$ ($c = 1.5$ in $CHCl_3$), from which by correction for the concentration of (*M*)-**4** in the mixture, the value of $[\alpha]_D^{20} = -381.2$ ($c = 1.3$ in $CHCl_3$) for enantiomerically pure (*M*)-**4** can be derived.



Scheme 6. Elaboration of synthetic approaches to enantiomerically pure (*P*)- and (*M*)-[5]triangulanes **4**. a) CH_3CHCl_2, *n*BuLi, Et_2O, −35 °C, 1 h; b) *t*BuOK, DMSO, 50 °C, 2 h; c) CH_2N_2, $Pd(OAc)_2$, Et_2O, −5 °C; d) N_2CHCO_2Et, $[Rh(C_7H_{15}COO)_2]_2$ (0.6–0.8 mol%), CH_2Cl_2, 0 °C, 24 h; e) KOH, $EtOH/H_2O$, 78 °C, 4 h.

The addition of ethoxycarbonylcarbene, generated by decomposition of ethyl diazoacetate in the presence of dirhodium tetraoctanoate, to *rac*-**28** was tested and found to afford a mixture of four diastereomeric esters **30** (78% overall yield) in a ratio of 26:15:26:33. The major diastereomer was isolated in 25% yield by simply distilling off the other three through a concentric tube column, and it turned out to possess the appropriate (1*RS*,3*SR*,4*SR*) relative configuration, as confirmed by X-ray crystal structure analysis of the corresponding acid (1*RS*,3*SR*,4*SR*)-**31** (Scheme 6 and Figure 3).

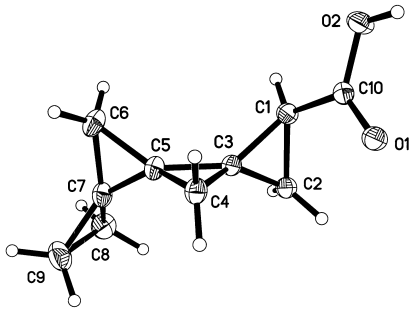
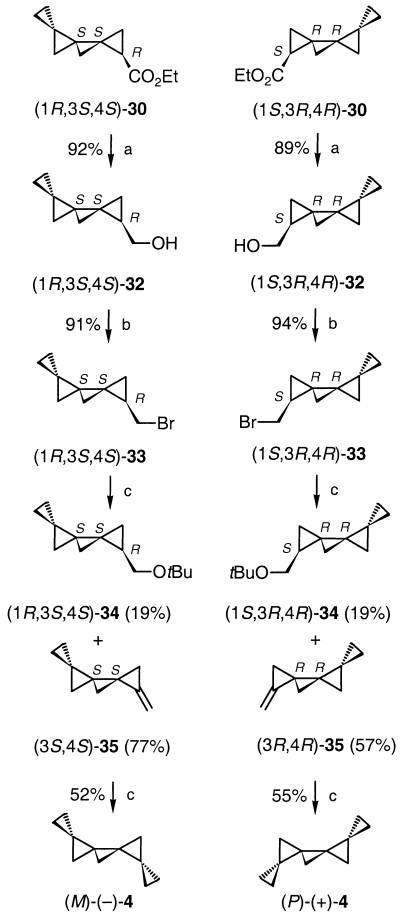


Figure 3. Structure of the racemic (1*RS*,3*SR*,4*SR*)-trispiro[2.0.0.2.1.1]nonane-1-carboxylic acid [(1*RS*,3*SR*,4*SR*)-**31**] in the crystal.

With these results in hand, the synthesis of enantiomerically pure esters (1*R*,3*S*,4*S*)-(−)-**30** and (1*S*,3*R*,4*R*)-(+)-**30** could be performed analogously starting from the enantiomerically pure methylene[3]triangulanes (*S*)-(−)-**28** and (*R*)-(+)-**28** in 27 and 19% isolated yield, respectively (Scheme 6). From these esters the enantiomerically pure triangulanes (*M*)-**4** and (*P*)-**4** could be prepared by a set of routine synthetic transformations (Scheme 7) which were previously applied for the [4]triangulanes (*M*)-**3** and (*P*)-**3**. As in the analogous sequence (Scheme 5), nucleophilic substitution of bromine with *tert*-butoxide anion in the bromides (1*R*,3*S*,4*S*)- and (1*S*,3*R*,4*R*)-**33** essentially decreased the yield in the dehydrobromination step, leading to the formation of the *tert*-butyl ethers (1*R*,3*S*,4*S*)- and (1*S*,3*R*,4*R*)-**34** (19% yield in both cases) (Scheme 7). Along this route, the enantiomerically pure (*M*)-(−)- and (*P*)-(+)-[5]triangulane (*M*)-(−)-**4** and (*P*)-(+)-**4** were prepared in 52 and 55% yield, respectively, after gas chromatographic separation after the last step (Scheme 7), corresponding to a 34 and 26% overall yield from the esters **30**, or 9 and 5% from (*S*)-**28** and (*R*)-**28**, respectively. The enantiomeric excess was $\geq 94\%$ for both, as determined by gas chromatography on a chiral phase capillary column.[25] The racemic (*PM*)-**4** for these determinations was prepared similarly from the acid (1*RS*,3*SR*,4*SR*)-**31** in 39% overall yield (see Experimental Section).

The structures of (*P*)-(+)-[5]triangulane (*P*)-(+)-**4** and *rac*-**4** were both examined by X-ray crystal structure analysis (Figure 4). Naturally, the geometrical parameters of the molecules (*P*)-**4** and *rac*-**4** are identical. The bond lengths and angles in (*P*)-(+)-**4** and *rac*-**4** are very close to those in [3]- and [4]triangulanes[26] and correspond relatively well to the general bond increment scheme which was previously developed for [*n*]triangulanes.[26] As it would be expected, there are no strong intermolecular interactions in the crystals of (*P*)-**4** and *rac*-**4**, and thus the terms "columns" and "layers" are used for convenience only. The packing of the molecules in the two crystals is almost identical in two directions (Figure 4). The columns of the head-to-tail arranged molecules form layers marked AA in Figure 4. However, whereas all the layers are equivalent in the crystal of (*P*)-**4**, the "left" and "right" layers alternate in the crystal of *rac*-**4**. The shortest intermolecular

0947-6539/02/0804-0832 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4



Scheme 7. Preparation of enantiomerically pure (*M*)- and (*P*)-[5]triangulanes (*M*)-(−)-**4** and (*P*)-(+)-**4**. a) $LiAlH_4$, Et_2O, 34 °C, 2 h; b) $Ph_3P \cdot Br_2$, Py, CH_2Cl_2, −10 °C, 1.5 h, then 20 °C, 7 h; c) *t*BuOK, DMSO, 50 °C, 2 h; d) CH_2N_2, $Pd(OAc)_2$, Et_2O, −5 °C.

contacts in the crystals of (*P*)-**4** and *rac*-**4** are very similar. The shortest H···C contacts are H1···C6′ contacts between molecules in the columns [2.92 and 2.98 Å for (*P*)-**4** and *rac*-**4**, respectively] and the shortest H···H contacts of 2.40 and 2.42 Å are between molecules in the "A" layers.

The difference in the crystal packing of the molecules (*P*)-(+)-**4** and *rac*-**4** is reflected in an unusual behavior of the two in the differential scanning calorimetry (DSC). Thus, upon cooling from room temperature to −100 °C *rac*-[5]triangulane (*rac*-**4**) does not show any transition, namely no crystallization peak. However, upon subsequent heating from −100 to 30 °C *rac*-**4** displayed a broad crystallization peak around −32 °C with $\Delta G = -1.82$ kcal mol^{-1} and then melted at −14 °C ($\Delta G = 1.84$ kcal mol^{-1}). Even more interesting is the behavior of the enantiomerically pure [5]triangulane (*P*)-(+)-**4**: Upon cooling from room temperature to −100 °C this sample showed a sharp crystallization peak with $\Delta G = -3.01$ kcal mol^{-1}. The exact crystallization temperature varied from sample to sample from −39 to −53 °C. Upon heating the melting point was represented by a peak at 7.2 °C with the same ΔG. This behavior with more than 45 degrees difference of crystallization and melting temperature has been reproduced in several cooling-heating cycles. However, after having been heated to higher temperatures (100 °C), (*P*)-(+)-**4** changed its behavior although beside the melting peak around 7 °C no more peaks were observed in the heating curve. After having been heated to 100 °C, the sample did not show any crystallization peak upon cooling, but upon subsequent heating from −100 to 30 °C it displayed the first negative peak at −59.6 °C ($\Delta G = 2.73$ kcal mol^{-1}) and then melted at 8.8 °C with the same ΔG. So after having been heated to 100 °C, (*P*)-(+)-**4** does not show a crystallisation upon cooling but only in the subsequent heating sequence. In this respect the thermal behavior of (*P*)-(+)-**4** after having been heated to 100 °C is similiar to that of the racemate. In spite of this, neither the NMR spectra nor the enantiomeric purity of the sample (as determined by gas chromatography on a chiral phase column) showed any change after having been heated to 100 °C.

The enantiomeric purities of all methylenetriangulanes and triangulanes prepared were determined by gas chromatog-

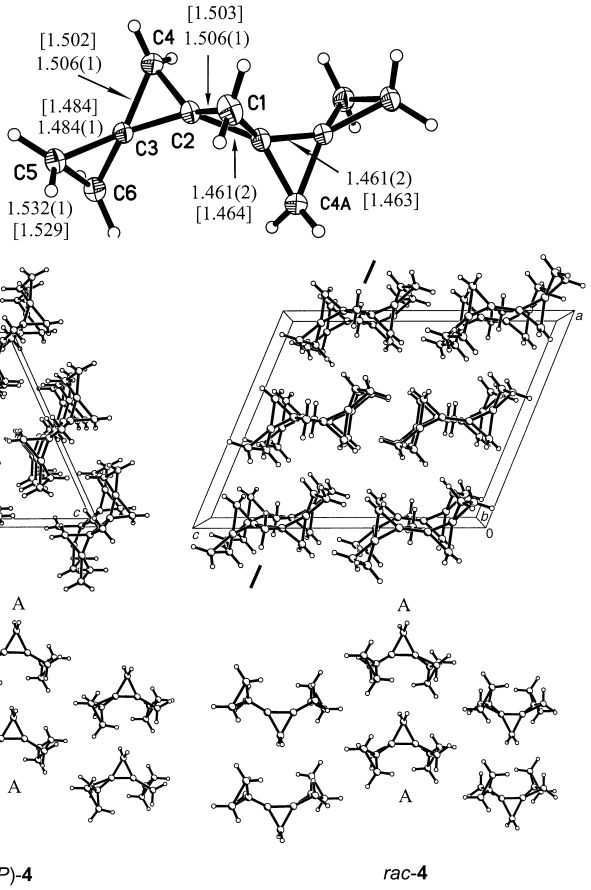


Figure 4. Structure of (*P*)-(+)-[5]triangulane (*P*)-(+)-**4** in the crystal (bond lengths in Å, computed values at B3LYP/6-31+G** in parentheses), as well as packing of the molecules (*P*)-(+)-**4** and *rac*-**4** in the crystals (view along *b* axis), and arrangement of the layers in the crystals of (*P*)-**4** (left) and *rac*-**4** (right).

raphy using a chiral phase capillary column, and found to be between 91% in one case and 94–99% in most cases (Table 1). As different sources of enantiomerically pure starting materials were used in the preparations, only the results for the purest samples are summarized. The specific rotations were determined in $CHCl_3$ for all compounds.

Table 1. Purities, enantiomeric excess values (*ee*) and specific rotations of all methylenetriangulanes and triangulanes prepared.

Entry	Compound	Purity (GC) [%]	*ee* (GC)[a] [%]	$[\alpha]_D^{20}$/ *c* in $CHCl_3$
1	(*P*)-(+)-**23**	≥95	≥96	+125.6/1.1
2	(*M*)-(−)-**23**	≥99	≥96	−123.6/1.2
3	(*S*)-(−)-**28**	≥99	≥94	−219.2/1.1
4	(*R*)-(+)-**28**	≥99	≥91	+213.2/1.1
5	(3*S*,4*S*)-(−)-**35**	≥90	≥94	−385.8/1.1
6	(*P*)-(+)-**3**	≥95	≥96	+187.5/1.0
7	(*M*)-(−)-**3**	≥95	≥99	−192.7/1.2
8	(*P*)-(+)-**4**	≥99	≥94	+373.0/1.0
9	(*M*)-(−)-**4**	≥95	≥94	−334.2/1.2
10	(*M*)-(−)-**4**	84[b]	≥95	−381.2/1.3[c]

[a] Chiral column with octakis(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin (50% in OV 1701 *w*/*w*) phase (Prof. W. A. König, Universität Hamburg). [b] Containing 16% *meso*-**4**. [c] Extrapolated by correcting for the content of achiral *meso*-**4**.

Discussion

Although [4]- (**3**) and [5]triangulane (**4**) do not have a chromophore which would lead to any significant absorption above 200 nm, they have remarkably high specific rotations even at 589 nm with $[\alpha]_D^{20} = +187.5$ ($c = 1.0$ in $CHCl_3$) [(*P*)-(+)-**3**], −192.7 ($c = 1.2$ in $CHCl_3$) [(*M*)-(−)-**3**], +373.0 ($c = 1.0$ in $CHCl_3$) [(*P*)-(+)-**4**], and −334.2 ($c = 1.2$ in $CHCl_3$) [(*M*)-(−)-**4**]. Moreover, these specific rotations increase drastically on going to shorter wavelengths; this indicates that these compounds must have Cotton effects with large amplitudes in the ORD below 200 nm. The same holds true for (*P*)-(+)-dimethylenespiropentane [(*P*)-(+)-**23**] and (*S*)-(−)-1-methylenedispiro[2.0.2.1]heptane [(*S*)-(−)-**28c**] (Table 2). The unusually large difference between the experimentally determined specific rotations for the [5]triangulanes (*P*)-(+)-**4** and (*M*)-(−)-**4** must be due to the lower purity of the latter (99 and 95%, respectively, see Table 1). The larger specific rotation of (*P*)-(+)-**4** appears to be the more reliable value, since the specific rotation for (*M*)-(−)-**4** of $[\alpha]_D^{20} = -381.2$, which was extrapolated from the value for the mixture of (*M*)-(−)-**4** and *meso*-**4**, matches that of (*P*)-(+)-**4** more closely.

For a better understanding of these remarkably high rotatory strengths, density functional theory (DFT) computations were carried out at a reasonably high level of theory [B3LYP/6-31+G(d,p)][27–31] applying a full valence space single excitation configuration interaction treatment[32] (DFT-SCI at B3LYP/TZVP). Indeed, the computed specific rotations over the whole range of wavelengths are in very good agreement with the experimental values and thus confirm the strong Cotton effects in the ORD going along with large ellipticities in the circular dichroism below 200 nm (Table 2).

Table 2. A comparison of the measured (in $CHCl_3$) and DFT/SCI-computed specific rotations of enantiomerically pure methylenetriangulanes and triangulanes.

Compound	λ [nm]	$[\alpha]_D^{20}$ measured	$[\alpha]_D^{20}$ computed[a]
(*P*)-(+)-**23**	589	+125.6	+120.9
	546	+154.2	+181.5
	436	+289.3	+303.8
	365	+525.7	+419.5
(*M*)-(−)-**3**	589	−192.7	−217.9
	546	−229.7	−264.0
	436	−400.2	−407.8
	365	−648.2	−576.7
(*S*)-(−)-**28**	589	−219.2	−261.6
	546	−266.3	−313.7
	436	−487.0	−500.8
	365	−840.1	−749.0
(3*S*,4*S*)-(−)-**35**	589	−385.8	−318.6
	546	−451.6	−461.8
	436	−824.9	−934.3
	365	−1428.9	−1364.6
(*P*)-(+)-**4**	589	+373.0	+394.9
	546	+445.2	+508.1
	436	+777.4	+791.9
	365	+1264.0	+1080.3
(*M*)-(−)-**4**	589	−334.2	−394.9
	546	−398.7	−508.1
	436	−696.3	−791.9
	365	−1033.1	−1080.3

[a] All computed values were shifted by a constant value to account for effects of solvent/solute interactions, which currently cannot be taken into account computationally (see Computational studies).

This good agreement between experiment and theory for the [4]- (**3**) and [5]triangulanes (**4**) as well as dimethylenespiropentane (**23**) and 1-methylenedispiro[2.0.2.1]-heptane (**28**) not only provides confidence in the general applicability of this computational approach to the simulation of ORD and CD spectra,[33] but also confirms that the rotatory powers of **3** and **4** are an outflow of their helical arrangements of σ bonds. Thus [4]- and [5]triangulanes are true "σ-[*n*]helicenes", the first σ-bond analogues of the aromatic [*n*]helicenes which have a helical arrangement of π skeletons and should therefore better be termed π-[*n*]helicenes to distinguish them from these newly established σ-[*n*]helicenes. One important difference has to be noted, though: While the π-[*n*]helicenes have fully conjugated electronic systems, adjacent three-membered rings in [*n*]triangulanes are orthogonal with respect to each other. There is conjugative electronic interaction only between every other spirocyclopropane ring.[34] On the other hand, the inherent helicity of the [*n*]triangulanes is probably an essential contributor to the overall rotatory power of the methylene[*n*-1]triangulanes, which are the synthetic precursors of the [*n*]triangulanes. Thus, when comparing the specific rotations of dimethylenespiropentane (**23**), methylene[3]triangulane (**28**), [4]triangulane (**3**), methylene[4]triangulane (**35**), and [5]triangulane (**4**) (125.6, 219.2, 192.7, 385.8, and 373.0°, respectively), it is noted that the big increases occur on going from dimethylenespiropentane **23** to methylene[3]triangulane **28** and [4]triangulane **3** as well as from **3** to methylene[4]triangulane (**35**) and [5]triangulane (**4**),

0947-6539/02/0804-0834 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

while the specific rotations of methylene[*n*-1]triangulanes and [*n*]triangulanes are all very close to each other.

As predicted by these computations,[35] the rotatory strengths of the [5]triangulanes (*M*)-**4** and (*P*)-**4** turned out to be about twice as large as those of the [4]triangulanes (*M*)-**3** and (*P*)-**3**. It remains to be checked experimentally whether this good agreement will also hold for the next higher analogues, the [6]triangulanes (*M*)-**5** and (*P*)-**5** for which the computed specific rotations at 589 nm ($[\alpha]_D^{20} = 509.7$) are only 29% larger than those of (*M*)-**4** and (*P*)-**4**. Whether this is due to the fact that the sum of all interplanar angles ($\Sigma\vartheta$) between adjacent pairs of spiro-fused cyclopropane rings reaches 360° in the [5]triangulanes (*M*)-**4** and (*P*)-**4**, while it is 450° in [6]triangulanes (*M*)-**5** and (*P*)-**5**, may only be speculated about. The continuous change of interplanar angles can be visualized by a ribbon connecting one methylene group each of the two terminal cyclopropane rings in any [*n*]triangulane with each of the methylene groups in the rings between them (Figure 5). In (*M*)-**4** and (*P*)-**4**, such a ribbon would complete exactly one turn of a helix, while in the [6]triangulanes (*M*)-**5** and (*P*)-**5** it would simply go 90° beyond a full turn. The original computational prediction that the rotatory power of [5]triangulanes (*M*)-**4** and (*P*)-**4** should be about twice as large as that of [4]triangulanes (*M*)-**3** and (*P*)-**3**, has now actually been proved (see Table 2). Apparently, it will be well worth to prepare at least the next higher member in this series of σ-[*n*]helicenes, the [6]triangulanes (*M*)- and (*P*)-**5** in enantiomerically pure form. It will also be quite interesting to investigate the Raman optical activities (ROA) of the whole series of enantiomerically pure methylene[*n*-1]triangulanes and [*n*]triangulanes, since the ROA of (*M*)-(−)-[4]triangulane (*M*)-(−)-**3** has been shown to disclose spectacular effects with Δ values close to 0.5% in the 900 cm^{-1} region.[36]

Experimental Section

General aspects: Racemic bicyclopropylidenecarboxylic acid *rac*-**12**,[12] racemic *exo*-dispiro[2.0.2.1]heptane-1-carboxylic acid *rac*-**13**,[13] racemic *anti-rac*-1-(tetrahydropyranyloxymethyl)-4-methylenespiropentane,[37] racemic 1-methylenedispiro[2.0.2.1]heptane (*rac*-**28**),[38] racemic [4]triangulane (*rac*-trispiro[2.0.0.2.1.1]nonane *rac*-**3**),[38] enantiomerically pure *anti*-(4-methylenespiropentyl)methanols (1*R*,3*S*)- and (1*S*,3*R*)-**18**,[18] enantiomerically pure *endo*-(dispiro[2.0.2.1]heptyl)methanols (1*R*,3*R*)- and (1*S*,3*S*)-**20**,[18] (2-methylenecyclopropyl)methanol (**6**),[39] and (*N-tert*-butoxycarbonyl)glycine (**7**)[40] were prepared according to the previously published procedures. The acid *rac*-**12** was purified by column chromatography on silica gel (eluent hexane/Et_2O 3:2) followed by recrystallization from hexane (*rac*-**12**: m.p. 109–110 °C). All operations in anhydrous solvents were performed under argon in flame-dried glassware. Diethyl ether and 1,2-dimethoxyethane were dried by distillation from sodium/benzophenone, pyridine and DMSO from calcium hydride, CH_2Cl_2 from P_2O_5, MeOH from magnesium dimethoxide. All other chemicals were used as commercially available; Lipase PS (*Pseudomonas sp.*) was purchased from Amano Pharmaceutical Co., Ltd. Organic extracts were dried over $MgSO_4$. NMR spectra were recorded on a Bruker AM 250 instrument (250 MHz for ^1H and 62.9 MHz for ^{13}C NMR). Multiplicities were determined by DEPT (distortionless enhancement by polarization transfer) measurements. Chemical shifts refer to $\delta_{TMS} = 0.00$ according to the chemical shifts of residual $CHCl_3$ signals. IR spectra were recorded on a Bruker IFS 66 FT-IR as KBr pellets or oils between NaCl plates. Mass spectra were measured with Finnigan MAT 95 (EI and HR-EI, at 70 eV, preselected ion peak matching at $R \gg 10000$ to be within ±2 ppm of the exact masses) and Varian CH 5 (CI, at 70 eV) spectrometers. GC analyses were performed on Siemens Sichromat 1-4. Preparative GC separations were performed on Intersmat 130 and Varian Aerograph 920 instruments (20% SE 30 on Chromosorb W-AW-DMCS, 1200 mm × 8.2 mm column). Enantiomeric excess values were determined using a 25 m capillary column with octakis(6-*O*-methyl-2,3-di-*O*-pentyl)-γ-cyclodextrin (50% in OV 1701 *w*/*w*) phase (Prof. W. A. König, Universität Hamburg). Optical rotations were measured on a Perkin–Elmer 241 digital polarimeter in a 1 dm cell. Melting points were determined on a Büchi 510 capillary melting point apparatus, values are uncorrected. TLC analyses were performed on precoated sheets, 0.25 mm Sil G/UV_{254} (Macherey–Nagel). Silica gel grade 60 (230–400 mesh) (Merck) was used for column chromatography.

DSC measurements: Differential scanning calorimetry of (*P*)-(+)-**4** and rac-**4** was performed on a Netzsch DSC 204/1/F instrument. The samples were cooled down from room temperature to −100 °C and then heated up to 30 or 100 °C, respectively, with a rate of 10 degrees per min. The transition temperatures were determined as the peak maxima and the transition enthalpy from the peak areas.

Crystal structure determinations: Suitable crystals of the compounds (3*SR*,7*SR*)-**11**, (*R*,*R*)-**17a**, and (1*RS*,3*SR*,4*SR*)-**31** were grown by slowly concentrating their diluted solutions in hexane/Et_2O mixtures. Crystals of (*P*)-**4** and *rac*-**4** were grown in situ on the diffractometer in the capillary of 0.2 mm diameter. During cooling down the crystals of (*R*,*R*)-**17a**, peak-

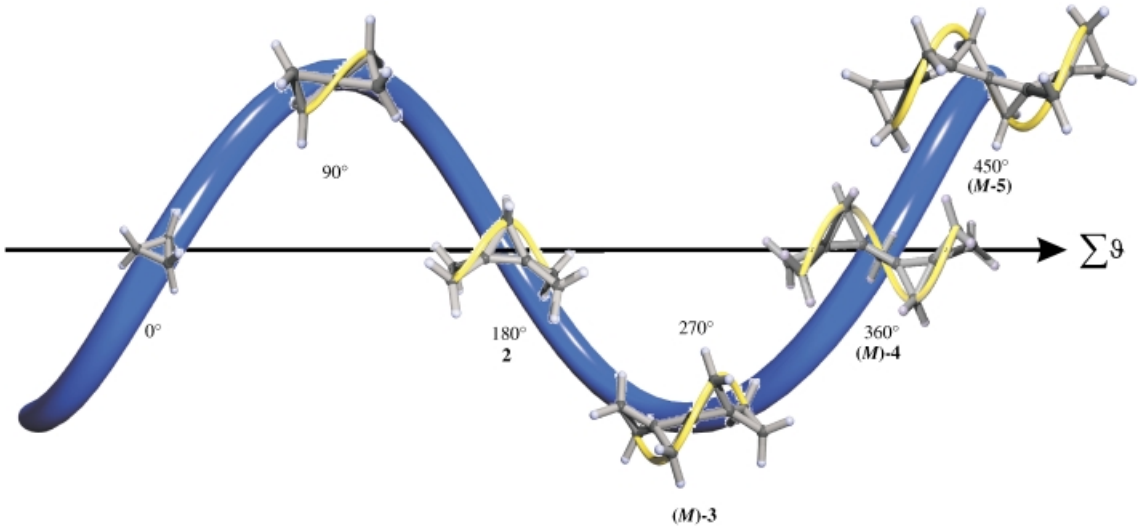


Figure 5. The helicities of (*M*)-[4]triangulane (*M*)-**3** and its higher analogues (*M*)-[5]- **4** and (*M*)-[6]triangulane **5**.

shape broadening occurred. The process was reversible and began at about 250 K. Therefore the X-ray experiment for (*R*,*R*)-**17a** was performed at room temperature. The data were collected on an automated 4-circle diffractometer Nonius CAD-4 [(*R*,*R*)-**17a**] and a Bruker SMART CCD 1 K (other compounds) diffractometer (graphite monochromator, $Mo_{K\alpha}$ radiation, $\omega/2\theta$ scan for **17a**, ω scan for others). The structures were solved by direct methods and refined by full-matrix least squares on F^2. All non-hydrogen atoms were refined anisotropically, all H atoms were located on the difference Fourier maps and refined isotropically. H atoms of (*R*,*R*)-**17a** were placed in calculated positions and refined as "riding" atoms; the absolute configuration was assigned on the basis of the known (*R*)-configuration of **16**, the Flack parameter for the reported configuration is 0(5) and for the inverted model 1(5). In all other structures H atoms were located in the difference Fourier maps and refined isotropically. The parameters of crystal data collections and structure refinements are presented in Table 3.[10] Absolute configurations of all molecules could not be determined reliably and were assigned on the basis of additional chemical information. The lactone **11** forms so-called intergrowth crystals which are highly unusual for molecular compounds. A detailed discussion of the structural study of **11** will be published elsewhere.[41] Molecules in the crystal of (*R*,*R*)-**17a** are connected by hydrogen bonds N-H ··· O(1) [N ··· O 2.807(8) Å] in the chains along the crystallographic *b* axis. Molecules of **31** in the crystal form centrosymmetrical dimers which is common for carboxylic acids; molecules (*P*)-**4** and *rac*-**4** occupy special positions on the twofold axis passing through the C1 atom and the center of the C2–C2a bond.

(2-Methylenecyclopropyl)methyl (*N*-*tert*-butoxycarbonyl)glycinate (8): A solution of (*N*-*tert*-butoxycarbonyl)glycine (**7**) (27.142 g, 155 mmol) in CH_2Cl_2 (50 mL) was added at 0 °C over a period of 20 min to a solution of (2-methylenecyclopropyl)methanol (**6**) (13.795 g, 164 mmol), DMAP (1.894 g, 15.5 mmol) and DCC (35.18 g, 170.5 mmol) in anhydrous CH_2Cl_2 (250 mL). After the reaction mixture was stirred for an additional 3 h at ambient temperature, the precipitate was filtered off. The organic phase was washed with aq. sat. $NaHCO_3$ and brine (100 mL each), dried and concentrated under reduced pressure. The residue was purified by column chromatography (300 g silica gel, 6 × 20 cm column, hexane/Et_2O 1:1) to give the carbamate **8** (30.693 g, 82 %) as a colorless solid. $R_f = 0.42$; m.p. 42–44 °C (hexane); ^{1}H NMR: $\delta = 5.37$ (br s, 1H; =CH_2), 5.32 (br s, 1H; =CH_2), 5.14 (t, $J = 5.3$ Hz, 1H; NH), 4.01 (dd, $J = 6.5$, 11.2 Hz, 1H; CH_2O), 3.93 (dd, $J = 8.3$, 11.2 Hz, 1H; CH_2O), 3.88 (d, $J = 5.3$ Hz, 2H; CH_2N), 1.85–1.70 (m, 1H; CH), 1.37 (s, 9H; $3CH_3$), 1.35–1.15 (m, 1H; CH_2), 1.00–0.96 (m, 1H; CH_2); ^{13}C NMR (D_2O): $\delta = 28.3$ ($3CH_3$); 105.0, 67.7, 42.3, 8.7 (CH_2); 14.0 (CH); 170.3, 155.6, 131.6, 79.7 (C); elemental analysis calcd (%) for $C_{12}H_{19}NO_4$ (241.3): C 59.73, H 7.94, N 5.81; found C 59.68, H 7.77, N 5.74.

(2-Methylenecyclopropyl)methyl glycinate hydrochloride (9): The carbamate **8** (30.05 g, 124.5 mmol) was stirred with 4.5 N HCl/Et_2O solution (100 mL) at 0 °C for 3 h. After additional stirring at ambient temperature for 12 h, the precipitate was filtered off and dried in vacuo to give **9** (17.71 g, 80 %) as a colorless powder. An analytical sample was recrystallized from MeOH/Et_2O 1:10. M.p. 90–92 °C; ^{1}H NMR (D_2O): $\delta = 5.44$ (d, $J = 1.8$ Hz, 1H; =CH_2), 5.40 (d, $J = 1.8$ Hz, 1H; =CH_2), 4.09 (dd, $J = 7.3$, 11.0 Hz, 1H; CH_2O), 3.94 (dd, $J = 8.3$, 11.0 Hz, 1H; CH_2O), 3.71 (s, 2H; CH_2N), 1.80–1.70 (m, 1H; CH), 1.27 (t, $J = 8.8$ Hz, 1H; CH_2), 1.03–0.84 (m, 1H; CH_2); ^{13}C NMR (D_2O): $\delta = 107.2$, 71.9, 42.5, 10.6 (CH_2); 15.8 (CH); 170.6, 134.7 (C); elemental analysis calcd (%) for $C_7H_{12}ClNO_2$ (177.6): C 47.33, H 6.82, N 7.89; found C 47.11, H 6.76, N 7.95.

(3*SR*,7*SR*)-5-Oxatricyclo[5.1.0.0^{1,3}]octan-4-one [(3*SR*,7*SR*)-11]: CH_2Cl_2 (6.5 mL) was added to a solution of hydrochloride **9** (1.57 g, 8.85 mmol) in H_2O (2.2 mL). Under vigorous stirring, a solution of $NaNO_2$ (0.74 g) in H_2O (2.2 mL) at −5 °C and then a solution of H_2SO_4 (43 mg) in H_2O (0.8 mL) at −8 °C were added dropwise. The organic phase was thoroughly washed with $NaHCO_3$ sat. solution (3 × 5 mL), dried, and concentrated under reduced pressure at 0 °C to give crude (2-methylenecyclopropyl)-methyl diazoacetate (**10**) (1.18 g, 88 %). ^{1}H NMR: $\delta = 5.43$ (d, $J = 1.8$ Hz, 1H; =CH_2), 5.40 (d, $J = 1.8$ Hz, 1H; =CH_2), 4.75 (br s, 1H; CH), 4.09 (dd, $J = 6.5$, 11.4 Hz, 1H; CH_2O), 3.94 (dd, $J = 8.0$, 11.4 Hz, 1H; CH_2O), 1.85–1.70 (m, 1H; CH), 1.32 (tt, $J = 2.1$, 9.0 Hz, 1H; CH_2), 1.00–0.96 (m, 1H; CH_2); ^{13}C NMR: $\delta = 105.0$, 67.9, 8.6 (CH_2); 46.0, 14.3 (CH); 166.7, 131.8 (C). This compound was dissolved in CH_2Cl_2 (25 mL), and the resulting solution was added to a solution of $Rh_2(5R\text{-MEPY})_4$ (20 mg, 0.3 mol %) in CH_2Cl_2 (25 mL) at 40 °C during 8 h. After additional stirring at the same temperature for 5 h, the mixture was concentrated at ambient pressure, and the residue was distilled "bulb-to-bulb" in vacuo (0.1 Torr) into a cold trap (−78 °C). The content of the trap was purified by column chromatography (20 g silica gel, 1 × 20 cm column, pentane/Et_2O 1:3) to give (3*SR*,7*SR*)-**11** (75 mg, 7 %) as colorless crystals. $R_f = 0.30$; m.p. 42–43 °C; $[\alpha]_D^{20} = -11.0$ ($c = 3.22$ in $CHCl_3$); *ee* = 10 %; ^{1}H NMR: $\delta = 4.68$ (dd, $J = 6.5$, 12.0 Hz, 1H; CH_2O), 3.77 (dd, $J = 9.0$, 12.0 Hz, 1H; CH_2O), 1.83 (dd, $J = 2.8$, 8.5 Hz, 1H; CH_2), 1.75 (dd, $J = 4.0$, 8.5 Hz, 1H; CH_2), 1.67 (t, $J = 5.9$ Hz, 1H; CH_2), 1.56–1.47 (m, 2H; CH, CH_2), 1.33 (tt, $J = 1.0$, 4.8 Hz, 1H; CH); ^{13}C NMR: $\delta = 65.8$, 16.6, 15.3 (CH_2); 12.7, 11.6 (CH); 171.9, 18.1 (C).

Optical resolution of the acids *rac*-12 and *rac*-*exo*-13 with dehydroabietylamine (General procedure GP 1): a) The pure racemic acid (20 mmol) was

Table 3. Crystal and data collection parameters for compounds (3*SR*,7*SR*)-**11**, (*R*,*R*)-**17a**, (1*RS*,3*SR*,4*SR*)-**31**, (*P*)-**4**, and *rac*-**4**.

	(3*SR*,7*SR*)-**11**	(*R*,*R*)-**17a**	(1*RS*,3*SR*,4*SR*)-**31**	(*P*)-**4**	*rac*-**4**
formula	$C_7H_8O_2$	$C_{15}H_{17}NO$	$C_{10}H_{12}O_2$	$C_{11}H_{14}$	$C_{11}H_{14}$
M_w	124.13	227.30	164.20	146.22	146.22
crystals	orthorhombic	monoclinic	monoclinic	monoclinic	monoclinic
space group	$P2_12_12_1$	$P2_1$	$P2_1/c$	$C2$	$C2/c$
a [Å]	7.4346(8)	10.623(2)	6.7097(4)	12.024(2)	12.0052(8)
b [Å]	8.1758(9)	4.803(1)	9.5859(5)	5.3056(8)	5.3146(3)
c [Å]	9.963(1)	13.283(3)	14.0695(8)	7.609(1)	14.9813(9)
β [°]	–	96.00(3)	95.51(1)	114.08(1)	112.68(2)
V [Å^3]	605.6(1)	674.0(2)	900.75(9)	443.2(1)	882.0(3)
Z	4	2	4	2	4
$F(000)$	264	244	352	160	320
ρ [g cm^{-3}]	1.361	1.120	1.211	1.096	1.101
μ [mm^{-1}]	0.099	0.070	0.083	0.061	0.061
T [K]	110.0(2)	298	100.0(2)	110.0(2)	110.0(2)
Θ_{max} [°]	50	25	60.5	59.4	29.9
refl. collected	4101	1904	10554	2557	4811
refl. independent	1066	1631	2501	1139	1200
R_{int}	0.121	0.073	0.055	0.022	0.020
w$R_2(F^2)$	0.0852	0.141	0.1003	0.1775	0.1167
$R(F)$	0.0486	0.0524	0.0375	0.0695	0.0392
no. parameters refined	115	153	157	79	79
GOF	0.961	1.033	1.061	1.076	1.082

0947-6539/02/0804-0836 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

added with heating and stirring to a solution of pure dehydroabietylamine (DAA, 1 equiv) in ethanol (20 mL). The solution was cooled to room temperature and, after 24 h of resting, the crystalline N salt was separated by filtration, washed with a minimal amount of ethanol and recrystallized twice from EtOH (for **14a**) or 75% aq. EtOH (for **15a**, dissolved in hot EtOH (6 mL), then water (2 mL) was added). The P salt was isolated as indicated below.

b) A suspension of the N or P salt (6 mmol) in a water/Et_2O mixture (30 mL of each) was cooled in an ice bath, and a solution of NaOH (0.3 g, 7.5 mmol) in water (10 mL) was added dropwise with stirring. The mixture was stirred until the salt had completely dissolved. The inorganic layer was washed with diethyl ether (3×30 mL) and acidified by addition of conc. HCl solution (ca. 1 mL) to ca. pH 3 to give a colorless precipitate. The mixture was extracted with diethyl ether (4×30 mL), the combined ethereal solutions were dried, concentrated under reduced pressure, and the residue recrystallized from hexane (for **12**) or from pentane at $-26\,^{\circ}C$ (for **13**) yielding the enantiomerically pure free acid.

N Salt 14a and P salt 14b: From the racemic acid *rac*-**12** (2.49 g, 20 mmol) and DAA (5.72 g, 20 mmol) the N salt **14a** (2.47 g, 60%) was obtained according to GP 1a. The filtrate was concentrated under reduced pressure, the solid residue was washed with a minimal amount of Et_2O and dissolved in EtOH (20 mL). This solution was diluted with water to a volume of ca. 100 mL under stirring and heating, and then carefully concentrated by evaporation under reflux. The transparent solution was cooled to RT, and after 24 h the crystalline P salt **14b** was separated by filtration and recrystallized from EtOH (**14b**: 3.09 g, 75%). **14a**: m.p. 156–157 °C; $[\alpha]_D^{20} = -10.5$ ($c = 1.0$ in $CHCl_3$). **14b**: m.p. 158–160 °C; $[\alpha]_D^{20} = +69.5$ ($c = 1.0$ in $CHCl_3$).

N Salt 15a and P salt 15b: From the racemic *exo*-acid *rac*-**13** (11.08 g, 80.2 mmol) and DAA (38.17 g of 60% purity, 80.2 mmol), the N salt **15a** (8.04 g, 47%) was obtained according to GP 1a; m.p. 158–159 °C; $[\alpha]_D^{20} = -75.6$ ($c = 0.8$ in $CHCl_3$). The combined mother liquors were concentrated, and the residue was distributed between Et_2O (200 mL) and aq. NaOH (6 g NaOH in 200 mL of H_2O). The water layer was extracted with diethyl ether (3×100 mL), acidified with conc. HCl (ca. 4 mL) to pH 3, and then extracted with Et_2O (4×100 mL) and pentane (100 mL). The combined organic solutions were dried, filtered and concentrated under reduced pressure to give the crude acid (1*S*,3*R*)-**13** (9.0 g, ca. 65.1 mmol), which was treated with DAA (18.6 g, 65.1 mmol, pure) in hot ethanol (40 mL). Et_2O (20 mL) was added to the resulting solution, and the mixture was kept at $+2\,^{\circ}C$ for 12 h. The precipitate was separated, washed with Et_2O and dried in vacuo to give the P salt (9.73 g, 23 mmol) with m.p. 138–141 °C. This salt was dissolved in boiling CH_2Cl_2 (60 mL), and then methylene chloride was replaced with Et_2O (ca. 120 mL). After cooling, the precipitate was filtered off and dried in vacuo affording the pure P salt **15b** (8.00 g, 47%) with m.p. 145–147 °C; $[\alpha]_D^{20} = +139.6$ ($c = 1.0$ in $CHCl_3$).

(*R*)-(−)-Bicylopropylidenecarboxylic acid [(*R*)-12]: From the salt **14a** (2.47 g, 6.04 mmol), the acid (*R*)-(−)-**12** (0.584 g, 78%) was obtained according to GP 1b; m.p. 110 °C; $[\alpha]_D^{20} = -183.7$ ($c = 1.0$ in $CHCl_3$); *ee* ≥ 98%; IR (KBr): $\tilde{\nu} = 1724\ cm^{-1}$; MS (EI): *m*/*z* (%): 124 (2) $[M]^+$, 123 (22) $[M-H]^+$, 96 (16) $[M-C_2H_4]^+$, 95 (44) $[M-H-C_2H_4]^+$, 84 (32), 79 (100) $[M-CO_2H]^+$, 77 (65), 67 (25), 51 (43); MS (HR-EI): calcd for $C_7H_8O_2$: 124.0524; found 124.0524).

(*S*)-(+)-Bicylopropylidenecarboxylic acid [(*S*)-12]: From the salt **14b** (3.09 g, 7.55 mmol), the acid (*S*)-(+)-**12** (0.79 g, 84%) was obtained according to GP 1b; m.p. 110 °C; $[\alpha]_D^{20} = +183.2$ ($c = 1.0$ in $CHCl_3$); *ee* ≥ 98%. The ^1H and ^{13}C NMR spectra of (*R*)- and (*S*)-**12** were identical to those reported for *rac*-**12**.[12]

(1*R*,3*S*)-(−)- and (1*S*,3*R*)-(+)-Dispiro[2.0.2.1]heptane-1-carboxylic acids [(1*R*,3*S*)- and (1*S*,3*R*)-13]: **(1*R*,3*S*)-13**: From the N salt **15a** (41.0 g, 96.8 mmol), the acid (1*R*,3*S*-)**13** (9.50 g, 71%) was obtained according to GP 1b after two recrystallizations; m.p. 57 °C; $[\alpha]_D^{20} = -391.4$ ($c = 1.0$ in $CHCl_3$); ^1H NMR: $\delta = 11.2$ (br s, 1H; OH), 1.79 (dd, $J = 4.3$, 7.6 Hz, 1H; CH), 1.63 (t, $J = 4.2$ Hz, 1H; CH_2), 1.38 (d, $J = 4.6$ Hz, 1H; CH_2), 1.34 (d, $J = 4.6$ Hz, 1H; CH_2), 1.29 (dd, $J = 4.1$, 7.6 Hz, 1H; CH_2), 0.92–0.84 (m, 2H; CH_2), 0.70–0.64 (m, 2H; CH_2); ^{13}C NMR: $\delta = 15.3$, 12.2, 5.8, 5.7 (CH_2); 19.9 (CH); 180.9, 25.3, 15.0 (C).

(1*S*,3*R*)-13: From the P salt **15b** (8.00 g, 18.9 mmol), the acid (1*S*,3*R*-)**13** (2.20 g, 84%) was obtained according to GP 1b after two recrystallizations. M.p. 54–55 °C; $[\alpha]_D^{20} = +361.9$ ($c = 1.0$ in $CHCl_3$). Its ^1H and ^{13}C NMR spectra were identical to those of (1*R*,3*S*)-**13**.

***N*-[(*R*)-1-Phenylethyl]-(*R*)-bicyclopropylidenecarboxamide (17a) and *N*-[(*R*)-1-phenylethyl]-(*S*)-bicyclopropylidenecarboxamide (17b)**: A solution of Et_3N (0.303 g, 0.42 mL, 3.0 mmol) was added dropwise to a stirred solution of the acid (1*RS*)-**12** (0.373 g, 3.01 mmol) and diphenylphosphinic chloride (0.712 g, 3.01 mmol) in anhydrous ethyl acetate (5 mL) at $-10\,^{\circ}C$. After stirring for an additional 1 h at $-10\,^{\circ}C$, a solution of (*R*)-1-phenylethylamine (**16**) (0.364 g, 3.01 mmol) in EtOAc (0.5 mL) was added dropwise. The mixture was stirred at room temperature for 14 h and then filtered. The filtrate was washed with 1N HCl (3 mL), 10% K_2CO_3 solution (7 mL), and H_2O (5 mL). The organic layer was dried and concentrated under reduced pressure to give a mixture of **17a** and **17b** (0.682 g, ca. 100%). Their chromatographic separation (80 g silica gel, 20×2 cm column, hexane/Et_2O 7:3) afforded **17b** (1st eluted, 0.226 g, 66%) and **17a** (2nd eluted, 0.226 g, 66%).

Compound **17a**: M.p. 126–127 °C (from hexane/Et_2O); $[\alpha]_D^{20} = +6.5$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3268$, 1639 cm^{-1}; ^1H NMR: $\delta = 7.36-7.22$ (m, 5H; Ph), 5.84 (br d, $J = 6.9$ Hz, 1H; NH), 5.20–5.08 (m, 1H; CHN), 2.26–2.21 (m, 1H; CH), 1.84–1.79 (m, 1H; CH_2), 1.76–1.64 (m, 1H; CH_2), 1.48 (d, $J = 6.8$ Hz, 3H; CH_3), 1.28–1.15 (m, 4H; CH_2); ^{13}C NMR: $\delta = 20.3$ (CH_3); 10.9, 3.5, 3.2 (CH_2); 128.5, 126.0 (2CH); 127.1, 48.6, 21.8 (CH); 170.4, 143.4, 112.8, 111.2 (C); MS (EI): *m*/*z* (%): 227 (4) $[M]^+$, 226 (2) $[M-H]^+$, 212 (1) $[M-CH_3]^+$, 184 (1), 123 (22), 105 (100) $[C_8H_9]^+$, 77 (19) $[C_6H_5]^+$; MS (HR-EI): calcd for $C_{15}H_{17}NO$: 227.1310; found 227.1310).

Compound **17b**: M.p. 155–156 °C (from hexane/Et_2O); $[\alpha]_D^{20} = +128.5$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3268$, 1636 cm^{-1}; ^1H NMR: $\delta = 7.38-7.23$ (m, 5H; Ph), 5.83 (br d, $J = 6.9$ Hz, 1H; NH), 5.19–5.07 (m, 1H; CHN), 2.25–2.18 (m, 1H; CH), 1.84–1.70 (m, 1H; CH_2), 1.70–1.64 (m, 1H; CH_2), 1.46 (d, $J = 6.9$ Hz, 3H; CH_3), 1.43–1.16 (m, 4H; CH_2); ^{13}C NMR: $\delta = 20.4$ (CH_3); 11.5, 3.5, 3.3 (CH_2); 128.6, 126.1 (2CH); 127.2, 48.6, 21.7 (CH); 170.5, 143.3, 112.8, 111.1 (C); MS (EI): *m*/*z* (%): 227 (1) $[M]^+$, 226 (1) $[M-H]^+$, 212 (1) $[M-CH_3]^+$, 198 (1), 184 (2), 123 (19), 105 (100) $[C_8H_9]^+$, 77 (15) $[C_6H_5]^+$; MS (HR-EI): calcd for $C_{15}H_{17}NO$: 227.1310; found 227.1310).

Ethyl (*R*)-bicyclopropylidenecarboxylate [(*R*)-25]: The acid (*R*)-**12** (4.00 g, 32.2 mmol) was treated with $BF_3 \cdot Et_2O$ (3.2 mL) in anhydrous EtOH (40 mL) (78 °C, 2 h) to give ester (*R*)-**25** (4.73 g, 97%) according to the protocol of Kadaba;[22] b.p. 52–54 °C (3 Torr); $[\alpha]_D^{20} = -142.5$ ($c = 1.9$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of (*R*)-**25** were identical with those reported for *rac*-**25**.[19a]

Ethyl *exo*-(1*R*,3*R*)- and *endo*-(1*R*,3*S*)-dispiro[2.0.2.1]heptane-1-carboxylate [(1*R*,3*R*)-26 and (1*R*,3*S*)-26]: A mixture of ester (*R*)-**25** (4.56 g, 30 mmol), Zn (mossy) (17.6 g, 269 mmol), and anhydrous 1,2-dimethoxyethane (40 mL) in a round-bottomed flask was immersed in an ultrasonic cleaning bath, and the mixture was irradiated with ultrasound while being heated to 60 °C, and diiodomethane (64.3 g, 19.4 mL, 240 mmol) was added dropwise. After having been irradiated at 80 °C for another 2 h, the mixture was cooled to RT, diluted with pentane (100 mL), poured into sat. aqueous NH_4Cl solution, and extracted with pentane (4×50 mL). The combined organic layers were washed with water, dried, and concentrated under reduced pressure. The residual oil was distilled under reduced pressure to give a 2:3 mixture (3.70 g, 74%) of (1*R*,3*R*)- and (1*R*,3*S*)-**26**. B.p. 64–67 °C (3 Torr). The pure isomers were obtained by column chromatography [300 g silica gel, 5×30 cm column, hexane/Et_2O 100:1, the (1*R*,3*R*)-isomer was eluted first] and then distilled "bulb-to-bulb" in vacuo.

(1*R*,3*R*)-**26**: Yield: 1.38 g (28%); $[\alpha]_D^{20} = -63.8$ ($c = 1.3$ in $CHCl_3$).

(1*R*,3*S*)-**26**: Yield: 2.03 g (41%); $[\alpha]_D^{20} = -266.0$ ($c = 1.15$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of (1*R*,3*R*)- and (1*R*,3*S*)-**26** were identical to those reported for *rac*-*endo*- and *rac*-*exo*-**26**.[13a,b]

Preparation of triangulanylmethanols

General procedure GP 2: A solution of the respective ester or acid (40 mmol) in anhydrous diethyl ether (30 mL) was added dropwise to a suspension of the specified amount of $LiAlH_4$ in Et_2O (100 mL) at a rate maintaining a gentle reflux. After 2 h of heating under reflux, quenching the reaction with Na_2SO_4 sat. solution and filtration, the precipitate was additionally extracted overnight with Et_2O in a Soxhlet apparatus. The combined organic solutions were dried and concentrated under reduced pressure. The residue was pure enough to be used without further purification.

(*R*)-(−)-Bicyclopropylidenylmethanol [(*R*)-24]: From $LiAlH_4$ (0.95 g, 25 mmol) and acid (*R*)-**12** (2.72 g, 21.9 mmol), alcohol (*R*)-**24** (1.84 g, 76%) was obtained according to GP 2; $[\alpha]_D^{20} = -13.3$ ($c = 0.95$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the alcohol (*R*)-**24** were identical to those reported for the racemic compound.[19a]

(1*R*,3*S*)-(−)-(Dispiro[2.0.2.1]hept-1-yl)methanol [(1*R*,3*S*)-20]: a) From $LiAlH_4$ (0.5 g, 13.2 mmol) and ester (1*R*,3*S*)-**26** (1.95 g, 11.7 mmol), alcohol (1*R*,3*S*)-**20a** (1.24 g, 85%) was obtained according to GP 2 as an oil. $[\alpha]_D^{20} = -104.3$ ($c = 1.2$ in $CHCl_3$); ^1H NMR: $\delta = 3.61$ (dd, $J = 6.4$, 11.1 Hz, 1H; CH_2O), 3.47 (dd, $J = 7.3$, 11.1 Hz, 1H; CH_2O), 2.73 (s, 1H; OH), 1.26–1.18 (m, 1H; CH), 1.15 (d, $J = 4.1$ Hz, 1H; CH_2), 1.05 (d, $J = 4.1$ Hz, 1H; CH_2), 0.80–0.75 (m, 3H; CH_2), 0.66 (t, $J = 4.4$ Hz, 1H; CH_2), 0.58–0.49 (m, 2H; CH_2); ^{13}C NMR: $\delta = 65.94$, 10.41, 9.99, 5.34, 5.24 (CH_2); 18.77 (CH); 13.59 (2C); MS (EI): *m*/*z* (%): 124 (0.8) $[M]^+$, 123 (2) $[M-H]^+$, 109 (12), 105 (18), 95 (38), 91 (100), 79 (86), 77 (47), 67 (50), 53 (42).

b) From $LiAlH_4$ (13.70 g, 361 mmol) and the acid (1*R*,3*S*)-**13** [18.40 g, 133.2 mmol; with $[\alpha]_D^{20} = -380.1$ ($c = 1.0$ in $CHCl_3$) and m.p. 56 °C], alcohol (1*R*,3*S*)-**20c** (16.50 g, 100%) was obtained according to GP 2. $[\alpha]_D^{20} = -112.5$ ($c = 1.2$ in $CHCl_3$).

(1*S*,3*R*)-(+)-(Dispiro[2.0.2.1]hept-1-yl)methanol [(1*S*,3*R*)-20]: a) From $LiAlH_4$ (16.0 g, 421.6 mmol) and acid (1*S*,3*R*)-**13** [21.60 g, 156.3 mmol; with $[\alpha]_D^{20} = +357.0$ ($c = 1.3$ in $CHCl_3$) and m.p. 54–56 °C], alcohol (1*S*,3*R*)-**20a** (19.1 g, 98%) was obtained according to GP 2 as an oil. $[\alpha]_D^{20} = +106.5$ ($c = 1.3$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of the (1*R*,3*S*)-**20**.

b) From $LiAlH_4$ (0.83 g, 21.9 mmol) and the acetate (1*S*,3*R*)-**21** (2.94 g, 17.7 mmol), alcohol (1*S*,3*R*)-**20b** (2.09 g, 95%) was obtained according to GP 1. $[\alpha]_D^{20} = +108.3$ ($c = 1.2$ in $CHCl_3$); MS (CI): *m*/*z* (%): 159 (20) $[M+NH_3+NH_4]^+$, 142 (71) $[M+NH_4]^+$, 124 (39) $[M-H_2O+NH_4]^+$, 107 (100) $[M-OH]^+$.

(1*RS*,3*SR*,4*SR*)-(Trispiro[2.0.0.2.1.1]non-1-yl)methanol (*rac*-32): From $LiAlH_4$ (504 mg, 13.28 mmol) and the acid *rac*-**31** (1.45 g, 8.83 mmol), alcohol *rac*-**32** (1.32 g, ≈100%) was obtained according to GP 2 as an oil. ^1H NMR: $\delta = 3.68$ (dd, $J = 6.4$, 11.0 Hz, 1H; CH_2O), 3.56 (dd, $J = 7.2$, 11.0 Hz, 1H; CH_2O), 2.06 (s, 1H; OH), 1.35–1.25 (m, 1H; CH), 1.21 (d, $J = 3.4$ Hz, 2H; CH_2), 0.97 (d, $J = 3.7$ Hz, 1H; CH_2), 0.95–0.89 (m, 2H; CH_2), 0.84–0.78 (m, 1H; CH_2), 0.71–0.64 (m, 3H; CH_2), 0.58 (t, $J = 4.4$ Hz, 1H; CH_2); ^{13}C NMR: $\delta = 66.2$, 12.2, 9.6, 8.8, 4.7, 4.0 (CH_2); 18.4 (CH); 18.8, 18.0, 14.1 (C); MS (CI): *m*/*z* (%): 185 (29) $[M+NH_3+NH_4]^+$, 168 (100) $[M+NH_4]^+$, 150 (18) $[M]^+$, 133 (69) $[M-OH]^+$, 125 (35), 108 (30), 105 (25).

(1*S*,3*R*,4*R*)-(+)-(Trispiro[2.0.0.2.1.1]non-1-yl)methanol [(1*S*,3*R*,4*R*)-32]: From $LiAlH_4$ (2.0 g, 52.7 mmol) and ester (1*S*,3*R*,4*R*)-**30** (4.40 g, 22.9 mmol), alcohol (1*S*,3*R*,4*R*)-**32** (3.07 g, 89%) was obtained according to GP 2. $[\alpha]_D^{20} = +226.6$ ($c = 1.0$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**32**.

(1*R*,3*S*,4*S*)-(−)-(Trispiro[2.0.0.2.1.1]non-1-yl)methanol [(1*R*,3*S*,4*S*)-32]: From $LiAlH_4$ (2.0 g, 52.7 mmol) and ester (1*R*,3*S*,4*S*)-**30** (4.40 g, 22.9 mmol), the alcohol (1*R*,3*S*,4*S*)-**32** (3.16 g, 92%) was obtained according to GP 2. $[\alpha]_D^{20} = -211.16$ ($c = 1.1$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**32**.

***rac*-1-(Bromomethyl)-4-methylenespiropentane (*rac*-22)**: Bromine (7.497 g, 2.42 mL, 46.91 mmol) was added at −30 to −15 °C over a period of 10 min to a solution of triphenylphosphane (12.304 g, 46.91 mmol) in anhydrous dichloromethane (100 mL). After an additional 15 min of stirring, a solution of racemic *anti*-(1*RS*,3*SR*)-1-(tetrahydropyranyloxymethyl)-4-methylenespiropentane[37] (9.21 g, 47.4 mmol) in CH_2Cl_2 (25 mL) was added dropwise at 0 °C over a period of 0.5 h. The mixture was stirred for an additional 2 h at ambient temperature, washed with brine (4 × 100 mL), dried, and concentrated under reduced pressure at 0 °C. Pentane (100 mL) was added, the mixture was stirred for an additional 2 h, and then filtered. The precipitate was thoroughly washed with pentane (3 × 50 mL), and the combined pentane extracts were concentrated under reduced pressure (ca. 200 Torr). The residue was purified by column chromatography (50 g silica gel, 3 × 20 cm column, pentane) to give *rac*-**22** (7.42 g, 91%) as a slightly yellow oil. $R_f = 0.58$; ^1H NMR: $\delta = 5.30$ (br s, 1H; $=CH_2$), 5.18 (t, $J = 2.1$ Hz, 1H; $=CH_2$), 3.50 (dd, $J = 7.1$, 10 Hz, 1H; CH_2Br), 3.44 (dd, $J = 7.8$, 10 Hz, 1H; CH_2Br), 1.92–1.79 (m, 1H; CH), 1.54 (dd, $J = 0.5$, 7.0 Hz, 1H; CH_2), 1.41 (dd, $J = 4.8$, 7.8 Hz, 1H; CH_2), 1.34 (dd, $J = 2.1$, 7.0 Hz, 1H; CH_2), 1.10 (t, $J = 4.8$ Hz, 1H; CH_2); ^{13}C NMR: $\delta = 99.5$, 36.9, 18.1, 7.3 (CH_2); 23.3 (CH); 134.4, 19.1 (C); MS (CI): *m*/*z* (%): 209/207 (40/41) $[M+NH_3+NH_4]^+$, 192/190 (100/98) $[M+NH_4]^+$, 175/173 (26/24) $[M+H]^+$, 127 (31), 125 (75), 110 (79) $[M-HBr+NH_4]^+$, 108 (100).

Preparation of the bromides

General procedure GP 3: Bromine (1.05 equiv) was added at −30 to −15 °C over a period of 10 min to a solution of triphenylphosphane (1.05 equiv) in anhydrous dichloromethane (50 mL). After an additional 15 min of stirring, a mixture of the respective alcohol (35 mmol) and anhydrous pyridine (1 equiv) in CH_2Cl_2 (15 mL) was added dropwise at −30 °C. The mixture was stirred for 1.5 h at −10 °C, and then at ambient temperature for an additional 7 h. After evaporation of the solvent, pentane (100 mL) was added, the mixture was stirred for 7 h, and then filtered. The precipitate was thoroughly washed with pentane (3 × 50 mL), and the combined pentane extracts were filtered through silica gel (0.5 cm layer). The filtrate was concentrated under reduced pressure (ca. 200 Torr), and the residue was distilled "bulb-to-bulb" in vacuo (0.1 Torr) into a cold trap (−78 °C).

(1*R*,3*S*)-(−)-1-(Bromomethyl)-4-methylenespiropentane [(1*R*,3*S*)-22]: From the alcohol (1*R*,3*S*)-**18** (2.40 g, 21.8 mmol), Ph_3P (5.99 g, 22.8 mmol), Br_2 (3.65 g, 1.18 mL, 22.8 mmol), and pyridine (1.72 g, 1.76 mL, 21.7 mmol), bromide (1*R*,3*S*)-**22** (2.93 g, 78%) was obtained according to GP 3 after additional purification by column chromatography (20 g silica gel, 2.2 × 15 cm column, pentane) followed by distillation under reduced pressure. $R_f = 0.58$; b.p. 58–61 °C (23 mbar); $[\alpha]_D^{20} = -305.6$ ($c = 1.0$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**22**.

(1*S*,3*R*)-(+)-1-(Bromomethyl)-4-methylenespiropentane [(1*S*,3*R*)-22]: From the alcohol (1*S*,3*R*)-**18** (1.42 g, 12.89 mmol), Ph_3P (3.55 g, 13.53 mmol), Br_2 (2.16 g, 0.70 mL, 13.53 mmol), and pyridine (1.02 g, 1.04 mL, 12.89 mmol), bromide (1*S*,3*R*)-**22** (1.77 g, 79%) was obtained according to GP 3. $[\alpha]_D^{20} = +305.2$ ($c = 1.6$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**22**.

(1*S*,3*S*)-(+)-1-(Bromomethyl)dispiro[2.0.2.1]heptane [(1*S*,3*S*-27]: From the alcohol (1*S*,3*S*)-**20** (8.68 g, 69.91 mmol), Ph_3P (19.25 g, 73.4 mmol), Br_2 (11.73 g, 3.78 mL, 73.4 mmol), and pyridine (5.53 g, 5.65 mL, 69.91 mmol), bromide (1*S*,3*S*)-**27** (10.05 g, 77%) was obtained according to GP 3 as an oil. $[\alpha]_D^{20} = +20.0$ ($c = 1.0$ in $CHCl_3$); ^1H NMR: $\delta = 3.39$ (dd, $J = 6.8$, 10 Hz, 1H; CH_2Br), 3.16 (dd, $J = 8.3$, 10 Hz, 1H; CH_2Br), 1.82 (dddd, $J = 4.5$, 6.8, 7.8, 8.3 Hz, 1H; CH), 1.27–1.19 (m, 2H; CH_2), 1.13 (d, $J = 3.8$ Hz, 1H; CH_2), 0.96–0.79 (m, 3H; CH_2), 0.67–0.57 (m, 2H; CH_2); ^{13}C NMR: $\delta = 37.4$, 13.8, 13.4, 5.3, 5.1 (CH_2); 22.1 (CH); 13.8, 12.8 (C); MS (EI): *m*/*z* (%): 188/186 (1/1) $[M]^+$, 187/185 (10/10) $[M-H]^+$, 105 (39) $[M-Br-2H]^+$, 91 (100), 79 (100), 77 (42), 67 (20), 65 (22), 53 (20); MS (HR-EI): calcd for $C_8H_{11}Br$: 188.0024; found: 188.00309.

(1*R*,3*R*)-(−)-1-(Bromomethyl)dispiro[2.0.2.1]heptane [(1*R*,3*R*)-27]: From the alcohol (1*R*,3*R*)-**20** (11.89 g, 95.76 mmol), Ph_3P (26.37 g, 100.55 mmol), Br_2 (16.07 g, 5.18 mL, 100.55 mmol), and pyridine (7.58 g, 7.75 mL, 95.76 mmol), bromide (1*R*,3*R*)-**27** (15.44 g, 86%) was obtained according to GP 3. $[\alpha]_D^{20} = -18.0$ ($c = 1.0$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of (1*S*,3*S*)-**27**.

(1*R*,3*S*)-(−)-1-(Bromomethyl)dispiro[2.0.2.1]heptane [(1*R*,3*S*)-27]: a) From the alcohol (1*R*,3*S*)-**20a** (1.14 g, 9.18 mmol, prepared from ester (1*R*,3*S*)-**26**), Ph_3P (2.53 g, 9.65 mmol), Br_2 (1.56 g, 0.5 mL, 9.76 mmol), and pyridine (0.78 mL), bromide (1*R*,3*S*)-**27a** (1.35 g, 79%) was obtained according to GP 3. $[\alpha]_D^{20} = -110.6$ ($c = 1.5$ in $CHCl_3$); ^1H NMR: $\delta = 3.47$ (d, $J = 7.6$ Hz, 2H; CH_2Br), 1.46 (dq, $J = 4.4$, 7.5 Hz, 1H; CH), 1.33 (d, $J = 3.8$ Hz, 1H; CH_2), 1.12 (d, $J = 3.8$ Hz, 1H; CH_2), 1.03 (dd, $J = 4.7$, 7.6 Hz, 1H; CH_2), 0.89–0.76 (m, 3H; CH_2), 0.68–0.62 (m, 2H; CH_2); ^{13}C NMR: $\delta = 5.4$ (2CH_2); 38.4, 14.2, 10.1 (CH_2); 19.5 (CH); 23.3, 14.4 (C).

b) From alcohol (1*R*,3*S*)-**20b** (1.08 g, 8.7 mmol), Ph_3P (2.40 g, 9.16 mmol), Br_2 (1.46 g, 0.27 mL, 9.14 mmol), and pyridine (712 mg, 0.73 mL, 9.0 mmol), bromide (1*R*,3*S*)-**27b** (1.32 g, 81%) was obtained according to GP 3. $[\alpha]_D^{20} = -105.1$ ($c = 1.2$ in $CHCl_3$).

c) From alcohol (1*R*,3*S*)-**20c** (16.30 g, 131.3 mmol), Ph_3P (34.40 g, 131.1 mmol), Br_2 (21.25 g, 6.85 mL, 133 mmol), and pyridine (10.39 g, 10.62 mL, 131.3 mmol), bromide (1*R*,3*S*)-**27c** (24.30 g, 99%) was obtained according to GP 3. $[\alpha]_D^{20} = -106.8$ ($c = 1.1$ in $CHCl_3$).

(1*S*,3*R*)-(+)-1-(Bromomethyl)dispiro[2.0.2.1]heptane [(1*S*,3*R*)-27]: a) From alcohol (1*S*,3*R*)-**20a** (19.0 g, 153 mmol), Ph_3P (40.20 g, 153.3 mmol), Br_2 (24.82 g, 8.0 mL, 155.3 mmol), and pyridine (12.1 g,

0947-6539/02/0804-0838 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

12.4 mL, 153 mmol), bromide (1*S*,3*R*)-**27a** (28.0 g, 98%) was obtained according to GP 3. $[\alpha]_D^{20} = +108.5$ ($c = 1.2$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of (1*R*,3*S*)-**27**.

b) From alcohol (1*S*,3*R*)-**20b** (2.761 g, 22.23 mmol), Ph_3P (6.12 g, 23.34 mmol), Br_2 (3.73 g, 1.20 mL, 23.34 mmol), and pyridine (1.76 g, 1.8 mL, 22.23 mmol), bromide (1*S*,3*R*)-**27b** (2.58 g, 62%) was obtained according to GP 3. $[\alpha]_D^{20} = +106.4$ ($c = 1.8$ in $CHCl_3$).

(1*RS*,3*SR*,4*SR*)-1-(Bromomethyl)trispiro[2.0.0.2.1.1]nonane (*rac*-33): From alcohol *rac*-**32** (1.33 g, 8.85 mmol), Ph_3P (2.44 g, 9.30 mmol), Br_2 (1.49 g, 0.48 mL, 9.34 mmol), and pyridine (699 mg, 0.72 mL, 8.84 mmol), bromide *rac*-**33** (1.64 g, 87%) was obtained according to GP 3. ^1H NMR: $\delta = 3.47$ (d, $J = 7.5$ Hz, 2H; CH_2Br), 1.51 (tdd, $J = 4.3$, 7.5, 7.8 Hz, 1H; CH), 1.37 (d, $J = 4.0$ Hz, 1H; CH_2), 1.26 (d, $J = 4.0$ Hz, 1H; CH_2), 1.12 (dd, $J = 4.5$, 7.6 Hz, 1H; CH_2), 1.04 (d, $J = 4.0$ Hz, 1H; CH_2), 0.97 (d, $J = 4.0$ Hz, 1H; CH_2), 0.87–0.80 (m, 1H; CH_2), 0.73 (dd, $J = 2.9$, 5.4 Hz, 1H; CH_2), 0.70–0.62 (m, 3H; CH_2); ^{13}C NMR: $\delta = 38.3$, 13.1, 12.2, 9.1, 4.8, 4.2 (CH_2); 19.1 (CH); 23.1, 18.8, 14.2 (C); MS (CI): *m*/*z* (%): 232/230 (8/10) $[M+NH_4]^+$, 215/213 (14/16) $[M+H]^+$, 150 (18) $[M - HBr+NH_4]^+$, 135 (38), 133 (100) $[M - Br]^+$.

(1*R*,3*S*,4*S*)-(−)-1-(Bromomethyl)trispiro[2.0.0.2.1.1]nonane [(1*R*,3*S*,4*S*)-33]: From alcohol (1*R*,3*S*,4*S*)-**32** (3.05 g, 20.3 mmol), Ph_3P (5.34 g, 20.4 mmol), Br_2 (3.29 g, 1.06 mL, 20.6 mmol), and pyridine (1.61 g, 1.64 mL, 20.3 mmol), bromide (1*R*,3*S*,4*S*)-**33** (3.93 g, 91%) was obtained according to GP 3. $[\alpha]_D^{20} = -193.2$ ($c = 1.1$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**33**.

(1*S*,3*R*,4*R*)-(+)-1-(Bromomethyl)trispiro[2.0.0.2.1.1]nonane [(1*S*,3*R*,4*R*)-33]: From alcohol (1*S*,3*R*,4*R*)-**32** (2.90 g, 19.3 mmol), Ph_3P (5.08 g, 19.4 mmol), Br_2 (3.13 g, 1.01 mL, 19.6 mmol), and pyridine (1.53 g, 1.56 mL, 19.3 mmol), bromide (1*S*,3*R*,4*R*)-**33** (3.88 g, 94%) was obtained according to GP 3. $[\alpha]_D^{20} = +208.2$ ($c = 1.5$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**33**.

Preparation of the methylenetriangulanes

General procedure GP 4: A solution of potassium *tert*-butoxide (*t*BuOK) (1.12 g, 10 mmol) in anhydrous DMSO (25 mL) was added over a period of 30 min to a solution of the respective bromide (9 mmol) in anhydrous DMSO (10 mL) kept at 20 °C, and the reaction mixture was stirred at 20 °C for 15 min (GP 4a) or a solution of the bromide (7 mmol) in anhydrous DMSO (10 mL) was added over a period of 1 h dropwise to a solution of *t*BuOK (1.12 g, 10 mmol) in anhydrous DMSO (15 mL) kept at 50 °C, and the reaction mixture was stirred at 50 °C for 1 h (GP 4b). The volatile materials were distilled "bulb-to-bulb" under reduced pressure (0.01 Torr) into a cold (−78 °C) trap at a temperature of 35 to 40 °C inside the distillation flask, then the product was washed thoroughly with ice-cold water and dried (workup 1) or the mixture was poured into ice-cold water and extracted with pentane (3 × 5 mL) (workup 2). The combined pentane solutions were dried and carefully concentrated under ambient pressure. The residue was distilled "bulb-to-bulb" under reduced pressure (0.2 Torr) at the bath temperatures indicated below into a cold (−78 °C) trap.

***rac*-1,4-Dimethylenespiropentane [(*MP*)-23]**: From bromide *rac*-**22** (3.47 g, 20 mmol) and *t*BuOK (2.50 g, 22.3 mmol), diene (*MP*)-**23** (940 mg, 51%) was obtained according to GP 4a after workup 2 (bath temperature 30 °C) and purification by preparative GC. The ^1H and ^{13}C NMR spectra of the product were identical to the reported ones.[37]

(*M*)-(−)-1,4-Dimethylenespiropentane [(*M*)-23]: From bromide (1*R*,3*S*)-**22** (2.85 g, 16.47 mmol) and *t*BuOK (2.05 g, 18.27 mmol), diene (*M*)-**23** (726 mg, 48%) was obtained according to GP 4a after workup 2 (bath temperature 30 °C) and purification by preparative GC. $[\alpha]_D^{20} = -123.6$ ($c = 1.2$ in $CHCl_3$); *ee* ≥ 96%. The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**23**.

(*P*)-(+)-1,4-Dimethylenespiropentane [(*P*)-23]: From bromide (1*S*,3*R*)-**22** (1.73 g, 10.0 mmol) and *t*BuOK (1.36 g, 12.12 mmol), diene (*P*)-**23** (462 mg, 50%) was obtained according to GP 4a after workup 2 (bath temperature 30 °C) and purification by preparative GC. $[\alpha]_D^{20} = +117.3$ ($c = 1.0$ in $CHCl_3$); *ee* ≥ 96%. The ^1H and ^{13}C NMR spectra of the product were identical to those of *rac*-**23**.

(3*S*)-(−)-1-Methylenedispiro[2.0.2.1]heptane [(*S*)-28]: a) From bromide (1*R*,3*S*)-**27a** (1.25 g, 6.7 mmol) and *t*BuOK (1.12 g, 10 mmol), methylenetriangulane (*S*)-**28a** (618 mg, 87%) was obtained according to GP 4b after workup 1; $[\alpha]_D^{20} = -191.2$ ($c = 1.0$ in $CHCl_3$). This alkene contained ca. 10% impurities (according to the ^1H NMR spectrum), but was used in the next step without further purification.

b) Bromide (1*R*,3*S*)-**27c** (24.30 g, 129.9 mmol) was treated with *t*BuOK (18.50 g, 164.9 mmol) according to GP 4a. After workup 2, "bulb-to-bulb" distillation furnished the alkene (*S*)-**28c** (a solution in pentane, ca. 6.0 g according to the ^1H NMR spectrum, 44%) (bath temperature 20–40 °C) and (1*R*,3*S*)-(−)-1-(*tert*-butoxymethyl)dispiro[2.0.2.1]heptane [(1*R*,3*S*)-**29**] (3.70 g, 16%) (bath temperature 50–80 °C). Analytical samples were purified by preparative GC. (*S*)-**28c**: $[\alpha]_D^{20} = -219.2$ ($c = 1.1$ in $CHCl_3$); *ee* ≥ 94%; ^1H NMR: $\delta = 5.28$ (br s, 1H; =CH_2), 5.20 (t, $J = 2.4$ Hz, 1H; =CH_2), 1.59 (d, $J = 3.5$ Hz, 1H; CH_2), 1.47 (d, $J = 3.5$ Hz, 1H; CH_2), 1.42 (t, $J = 1.7$ Hz, 1H; CH_2), 1.24 (d, $J = 7.7$ Hz, 1H; CH_2), 0.93–0.68 (m, 4H; CH_2); the ^{13}C NMR spectrum of the product was identical to that reported for the racemic compound.[34] (1*R*,3*S*)-**29**: $[\alpha]_D^{20} = -124.3$ ($c = 1.3$ in $CHCl_3$); ^1H NMR: $\delta = 3.47$ (dd, $J = 5.7$, 9.4 Hz, 1H; CH_2O), 3.13 (dd, $J = 8.0$, 9.4 Hz, 1H; CH_2O), 1.21–1.18 (m, 1H; CH), 1.16 (s, 9H; $3CH_3$), 1.13 (d, $J = 4.9$ Hz, 1H; CH_2), 1.03 (d, $J = 3.4$ Hz, 1H; CH_2), 0.84 (d, $J = 4.4$ Hz, 1H; CH_2), 0.83–0.76 (m, 2H; CH_2), 0.64 (t, $J = 4.4$ Hz, 1H; CH_2), 0.59 (dd, $J = 4.6$, 6.1 Hz, 2H; CH_2); ^{13}C NMR: $\delta = 27.6$ ($3CH_3$); 65.3, 10.9, 10.4, 5.4, 5.3 (CH_2); 16.9 (CH); 72.3, 18.7, 13.7 (C); elemental analysis calcd (%) for $C_{12}H_{20}O$ (180.28): C 79.94, H 11.18; found C 80.01, H 11.30.

c) From bromide (1*S*,3*S*)-**27** (9.92 g, 53 mmol) and *t*BuOK (8.88 g, 79.1 mmol), the alkene (*S*)-**28d** (3.55 g, 63%) was obtained according to GP 4b after workup 2 (bath temperature 40 °C). An analytical sample was purified by preparative GC; $[\alpha]_D^{20} = -218.5$ ($c = 1.2$ in $CHCl_3$); *ee* ≥ 94%.

(3*R*)-(+)-1-Methylenedispiro[2.0.2.1]heptane [(*R*)-28]: a) From bromide (1*S*,3*R*)-**27a** (28.0 g, 150 mmol) and *t*BuOK (25.0 g, 223 mmol), the methylenetriangulane (*R*)-**28a** (13.60 g, 85%) was obtained according to GP 4b after workup 1. An analytical sample was purified by preparative GC. $[\alpha]_D^{20} = +213.2$ ($c = 1.1$ in $CHCl_3$); *ee* ≥ 91%. ^1H and ^{13}C NMR spectra of the product were identical to those of (*S*)-**28**.

b) From bromide (1*S*,3*R*)-**27b** (700 mg, 3.74 mmol) and *t*BuOK (600 mg, 5.35 mmol), the methylenetriangulane (*R*)-**28b** (a solution in pentane, ca. 320 mg according to the ^1H NMR spectrum, 81%) was obtained according to GP 4b.

c) From bromide (1*R*,3*R*)-**27** (15.44 g, 82.5 mmol) and *t*BuOK (13.82 g, 123.1 mmol), the methylenetriangulane (*R*)-**28c** (a solution in pentane, ca. 6.82 g according to the ^1H NMR spectrum, 78%) was obtained according to GP 4b after workup 2 (bath temperature 40 °C). An analytical sample was purified by preparative GC. $[\alpha]_D^{20} = +166.3$ ($c = 1.0$ in $CHCl_3$); *ee* ≥ 79%.

(3*RS*,4*RS*)-1-Methylenetrispiro[2.0.0.2.1.1]nonane [(3*RS*,4*RS*)-35]: Bromide (1*RS*,3*SR*,4*SR*)-**33** (1.64 g, 7.70 mmol) was treated with *t*BuOK (1.13 g, 10 mmol) according to GP 4b. After workup 2, "bulb-to-bulb" distillation furnished the alkene (3*RS*,4*RS*)-**35** (a solution in pentane, ca. 670 mg according to the ^1H NMR spectrum, 67%) (bath temperature 20–60 °C) and (1*RS*,3*SR*,4*SR*)-1-(*tert*-butoxymethyl)trispiro[2.0.0.2.1.1]nonane [(1*RS*,3*SR*,4*SR*)-**34**] (318 mg, 20%) (bath temperature 60–100 °C). The analytical samples were purified by preparative GC [(3*SR*,4*SR*)-**35**] or column chromatography [(1*RS*,3*SR*,4*SR*)-**34**, 20 g silica gel, 20 × 2 cm column, hexane/Et_2O 10:1].

(3*SR*,4*SR*)-**35**: ^1H NMR: $\delta = 5.30$ (br s, 1H; =CH_2), 5.23 (m, 1H; =CH_2), 1.50 (d, $J = 3.7$ Hz, 1H; CH_2), 1.43 (d, $J = 3.7$ Hz, 1H; CH_2), 1.33–1.32 (m, 2H; CH_2), 1.26 (d, $J = 3.9$ Hz, 1H; CH_2), 1.10 (d, $J = 3.9$ Hz, 1H; CH_2), 0.88–0.69 (m, 4H; $2CH_2$); ^{13}C NMR: $\delta = 99.0$, 15.9, 12.5, 8.3, 4.7, 4.0 (CH_2); 135.8, 22.5, 16.5, 14.3 (C).

[(1*RS*,3*SR*,4*SR*)-**34**: $R_f = 0.45$; ^1H NMR: $\delta = 3.49$ (dd, $J = 5.8$, 9.5 Hz, 1H; CH_2O), 3.15 (t, $J = 9.5$ Hz, 1H; CH_2O), 1.21–1.15 (m, 3H; CH+CH_2), 1.18 (s, 9H; $3CH_3$), 1.01 (d, $J = 3.7$ Hz, 1H; CH_2), 0.93 (dd, $J = 4.4$, 7.7 Hz, 1H; CH_2), 0.88 (d, $J = 3.7$ Hz, 1H; CH_2), 0.81–0.76 (m, 1H; CH_2), 0.68 (t, $J = 6.2$ Hz, 2H; CH_2), 0.62 (dd, $J = 7.7$, 10 Hz, 1H; CH_2), 0.53 (t, $J = 4.4$ Hz, 1H; CH_2); ^{13}C NMR: $\delta = 27.6$ ($3CH_3$); 65.4, 12.3, 9.7, 9.5, 4.7, 4.1 (CH_2); 16.5 (CH); 72.4, 18.7, 18.1, 14.1 (C); elemental analysis calcd (%) for $C_{14}H_{22}O$ (206.32): C 81.49, H 10.75; found C 81.41, H 10.90.

(3*R*,4*R*)-(+)-1-Methylenetrispiro[2.0.0.2.1.1]nonane [(3*R*,4*R*)-35]: From bromide (1*S*,3*R*,4*R*)-**33** (3.80 g, 17.8 mmol) and *t*BuOK (3.50 g, 31.2 mmol), alkene (3*R*,4*R*)-**35** (a solution in pentane, ca. 1.35 g according to the ^1H NMR spectrum, 57%) and (1*S*,3*R*,4*R*)-(+)-1-(*tert*-butoxymethyl)trispiro[2.0.0.2.1.1]nonane [(1*S*,3*R*,4*R*)-**34**] (680 mg, 19%) were obtained according to GP 4b. (3*R*,4*R*)-**35**: $[\alpha]_D^{20} = +506.2$ ($c = 1.0$ in $CHCl_3$).

(1*S*,3*R*,4*R*)-**34**: $[\alpha]_D^{20} = +214.3$ ($c = 1.2$ in $CHCl_3$). Their ^1H and ^{13}C NMR spectra were identical to those of the racemic compounds.

(3*S*,4*S*)-(−)-1-Methylenetrispiro[2.0.0.2.1.1]nonane [(3*S*,4*S*)-35]: From bromide (1*R*,3*S*,4*S*)-**33** (3.80 g, 17.8 mmol) and *t*BuOK (3.50 g, 31.2 mmol), alkene (3*S*,4*S*)-**35** (a solution in pentane, ca. 1.81 g according to the ^1H NMR spectrum, 77%) and (1*R*,3*S*,4*S*)-(−)-1-(*tert*-butoxymethyl)trispiro[2.0.0.2.1.1]nonane [(1*R*,3*S*,4*S*)-**34**] (680 mg, 19%) were obtained according to GP 4b. (3*S*,4*S*)-**35**: $[\alpha]_D^{20} = -385.8$ ($c = 1.1$ in $CHCl_3$). (1*S*,3*S*,4*R*)-**34**: $[\alpha]_D^{20} = -205.0$ ($c = 1.1$ in $CHCl_3$). Their ^1H and ^{13}C NMR spectra were identical to those of the racemic compounds.

Preparation of diastereomers and enantiomers of ethyl trispiro[2.0.0.2.1.1]-nonane-1-carboxylates 30

General procedure GP 5: Ethyl diazoacetate (125 mmol) was added dropwise to a stirred solution of the corresponding methylenedispiroheptane (85 mmol) and dirhodium tetraoctanoate (0.6–0.8 mol%) in anhydrous methylene chloride (120 mL) at 0 °C. The first half was added at a rate of 1 mL per h, the second half at 0.5 mL per h. After 30 min of additional stirring at ambient temperature, the mixture was filtered through a short pad of silica gel, and the solvent was removed. The residue was "bulb-to-bulb" distilled in vacuo (0.01 Torr, bath temperature < 110 °C) into a cooled trap (−78 °C). The content of the trap, consisting of a mixture of four cycloadducts (ratio ca. 26:15:26:33) and diethyl butenedioates, was very carefully distilled using a concentric tube (Fischer Spaltrohr HMS 500) column at 1 Torr during one week, slowly increasing the bath temperature from 71 to 101 °C and the mantle temperature from 20 to 45 °C. The collected fractions had boiling points ranging from 41.1 to 65.1 °C; their compositions were monitored by ^1H NMR spectroscopy. The residue consisted of the practically pure (1*RS*,3*SR*,4*SR*)-diastereomer which was additionally purified by "bulb-to-bulb" distillation.

Ethyl (1*RS*,3*SR*,4*SR*)-trispiro[2.0.0.2.1.1]nonane-1-carboxylate [(1*RS*,3*SR*,4*SR*)-30]: From alkene (3*RS*)-**28** (11.10 g, 104.6 mmol), ethyl diazoacetate (18.0 g, 16.6 mL, 157.8 mmol), and dirhodium tetraoctanoate (0.5 g, 0.6 mol%), ester (1*RS*,3*SR*,4*SR*)-**30** (5.11 g, 25%) was obtained according to GP 5. ^1H NMR: $\delta = 4.12$ (m, 2H; CH_2O), 1.81 (dd, $J = 4.4$, 7.6 Hz, 1H; CH), 1.44 (d, $J = 4.1$ Hz, 1H; CH_2), 1.29–1.18 (m, 4H; CH_2), 1.24 (t, $J = 1.1$ Hz, 3H; CH_3), 1.05 (d, $J = 4.0$ Hz, 1H; CH_2), 0.85–0.80 (m, 1H, CH_2), 0.75–0.62 (m, 3H, CH_2); ^{13}C NMR: $\delta = 14.3$ (CH_3), 60.2, 13.3, 12.5, 11.1, 4.9, 4.3 (CH_2), 19.3 (CH), 173.6, 23.9, 19.3, 14.4 (C).

Ethyl (1*R*,3*S*,4*S*)-(−)-trispiro[2.0.0.2.1.1]nonane-1-carboxylate [(1*R*,3*S*,4*S*)-30]: From alkene (3*S*)-**28** [9.00 g, a mixture of (3*S*)-**28c** (6.00 g) and (3*S*)-**28d** (3.00 g), 84.79 mmol], ethyl diazoacetate (14.11 g, 13.0 mL, 123.6 mmol), and dirhodium tetraoctanoate (0.50 g, 0.80 mol%), ester (1*R*,3*S*,4*S*)-**30** (4.40 g, 27%) was obtained according to GP 5. $[\alpha]_D^{20} = -288.4$ ($c = 1.2$ in $CHCl_3$). The ^1H and ^{13}C NMR spectra of the product were identical to those of (1*RS*,3*SR*,4*SR*)-**30**.

Ethyl (1*S*,3*R*,4*R*)-(+)-trispiro[2.0.0.2.1.1]nonane-1-carboxylate [(1*S*,3*R*,4*R*)-30]: From the alkene (3*R*)-**28a** (13.20 g, 124.3 mmol), ethyl diazoacetate (21.70 g, 20.0 mL, 190 mmol), and dirhodium tetraoctanoate (0.60 g, 0.60 mol%), ester (1*S*,3*R*,4*R*)-**30** (4.53 g, 19%) was obtained according to GP 5; $[\alpha]_D^{20} = +226.6$ ($c = 1.0$ in $CHCl_3$).

(1*RS*,3*SR*,4*SR*)-Trispiro[2.0.0.2.1.1]nonane-1-carboxylic acid [(1*RS*,3*SR*,4*SR*)-31]: A mixture of ester (1*RS*,3*SR*,4*SR*)-**30** (2.80 g, 14.6 mmol) and a solution of KOH (1.32 g, 23.5 mmol) in water (2 mL) and ethanol (20 mL) was heated under reflux for 4 h and then concentrated on a rotatory evaporator. The residue was diluted with water (20 mL), extracted with Et_2O (2 × 25 mL), acidified with 10% HCl to pH 3 under ice-cooling, then extracted with Et_2O (3 × 40 mL) and pentane (2 × 40 mL). The combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give the acid (1*RS*,3*SR*,4*SR*)-**31** (2.39 g, 100%). M.p. 89–91 °C (aq. EtOH); ^1H NMR: $\delta = 10.05$ (s, 1H; OH), 1.85 (dd, $J = 4.1$, 7.4 Hz, 1H; CH), 1.54 (t, $J = 4.1$ Hz, 1H; CH_2), 1.39 (d, $J = 4.7$ Hz, 1H; CH_2), 1.37 (dd, $J = 4.1$, 7.4 Hz, 1H; CH_2), 1.31 (d, $J = 4.1$ Hz, 1H; CH_2), 1.23 (d, $J = 4.7$ Hz, 1H; CH_2), 1.08 (d, $J = 4.1$ Hz, 1H; CH_2), 0.89–0.83 (m, 1H; CH_2), 0.78–0.75 (m, 1H; CH_2), 0.73–0.68 (m, 2H, CH_2); ^{13}C NMR: $\delta = 14.3$, 12.5, 11.3, 4.9, 4.4 (CH_2); 19.4 (CH); 180.5, 25.0, 19.5, 14.5 (C). Attempted optical resolution of this acid with DAA was unsuccessful.

Preparation of triangulanes and substituted triangulanes

General procedure GP 6: A solution of diazomethane [prepared from 6.00 g (58 mmol) of *N*-methyl-*N*-nitrosourea] in Et_2O (60 mL) was added dropwise at −5 to +3 °C to a solution of the respective methylenetriangulane (4.71 mmol) and $Pd(OAc)_2$ (60 mg) in diethyl ether (15 mL). The reaction mixture was filtered through a 3 cm pad of Celite and carefully concentrated at ambient pressure. The residue was distilled "bulb-to-bulb" under reduced pressure (0.01 Torr) into a cold (−78 °C) trap, if not otherwise specified. The content of the trap was purified by preparative GC.

(1*R*,3*S*)-(−)-(Dispiro[2.0.2.1]hept-1-yl)methanol [(1*R*,3*S*)-20a]: From the (methylenespiropentyl)methanol (1*R*,3*S*)-**18** (1.37 g, 12.43 mmol), alcohol (1*R*,3*S*)-**20b** (1.08 g, 70%) was obtained according to GP 6 after purification of the crude product by column chromatography (25 g silica gel, 1.5 × 20 cm column, hexane/Et_2O 1:1); $R_f = 0.42$; $[\alpha]_D^{20} = -110.4$ ($c = 1.2$ in $CHCl_3$).

(1*S*,3*R*)-(Dispiro[2.0.2.1]hept-1-yl)methyl acetate [(1*S*,3*R*)-21]: From acetate (1*S*,3*R*)-**19** (2.69 g, 17.7 mmol), crude acetate (1*S*,3*R*)-**21** (2.94 g) was obtained in quantitative yield according to GP 6 after "bulb-to-bulb" distillation. ^1H NMR: $\delta = 4.09$ (dd, $J = 6.4$, 11.1 Hz, 1H; CH_2O), 3.95 (dd, $J = 7.3$, 11.1 Hz, 1H; CH_2O), 2.05 (s, 3H; CH_3), 1.31–1.18 (m, 1H; CH), 1.15 (d, $J = 4.1$ Hz, 1H; CH_2), 1.05 (d, $J = 4.1$ Hz, 1H; CH_2), 0.80–0.75 (m, 3H; CH_2), 0.66 (t, $J = 4.4$ Hz, 1H; CH_2), 0.58–0.49 (m, 2H; CH_2); ^{13}C NMR: $\delta = 15.2$ (CH_3); 68.2, 10.6, 10.5, 5.4, 5.3 (CH_2); 21.0 (CH); 171.2, 19.0, 13.7 (C).

(*M*)-(−)-Trispiro[2.0.0.2.1.1]nonane [(*M*)-3]: a) From alkene (*S*)-**28a** (0.50 g, 4.71 mmol), [4]triangulane (*M*)-**3a** (0.287 g, 51%) was obtained according to GP 6. $[\alpha]_D^{20} = -192.7$ ($c = 1.2$ in $CHCl_3$); *ee* ≥ 99%. The ^1H and ^{13}C NMR spectra of (*M*)-**3a** were identical to those reported for the racemic compound.[38]

b) From the diene (*M*)-**23** (200 mg, 2.17 mmol), the [4]triangulane (*M*)-**3b** (38 mg, 14%) was obtained after purification by preparative GC; $[\alpha]_D^{20} = -190.1$ ($c = 1.3$ in $CHCl_3$).

(*P*)-(+)-Trispiro[2.0.0.2.1.1]nonane [(*P*)-3]: a) From the alkene (*R*)-**28b** (280 mg, 2.64 mmol), [4]triangulane (*P*)-**3b** (167 mg, 53%) was obtained according to GP 6. $[\alpha]_D^{20} = +187.5$ ($c = 1.0$ in $CHCl_3$); *ee* ≥ 96%. The ^1H and ^{13}C NMR spectra of (*P*)-**3** were identical to those reported for the racemic compound.[38]

b) From the alkene (*R*)-**28c** (590 mg, 5.56 mmol), [4]triangulane (*P*)-**3c** (351 mg, 53%) was obtained according to GP 6. $[\alpha]_D^{20} = +148.5$ ($c = 1.7$ in $CHCl_3$); *ee* ≥ 79%.

***rac*-Tetraspiro[2.0.0.0.2.1.1.1]undecane (*rac*-4)**: From the racemic alkene *rac*-**35** (335 mg, 2.54 mmol), racemic [5]triangulane *rac*-**4** (249 mg, 67%) was obtained according to GP 6. ^1H NMR: $\delta = 1.12$ [d, $J = 3.7$ Hz, 2H; 9(11)-CH_2], 1.09 [d, $J = 3.7$ Hz, 2H; 9(11)-CH_2], 1.06 (s, 2H; 10-CH_2), 0.88–0.65 (m, 8H; 4CH_2); ^{13}C NMR: $\delta = 10.9$, 4.7, 4.3 (2CH_2); 11.2 (CH_2); 18.6, 13.6 (2C).[4]

(*P*)-(+)-Tetraspiro[2.0.0.0.2.1.1.1]undecane [(*P*)-4]: From the alkene (3*R*,4*R*)-**35** (900 mg, 6.8 mmol), [5]triangulane (*P*)-**4** (543 mg, 55%) was obtained according to GP 6. $[\alpha]_D^{20} = +373.0$ ($c = 1.0$ in $CHCl_3$), *ee* ≥ 94%. The ^1H and ^{13}C NMR spectra of (*P*)-**4** were identical to those of the racemic compound.

(*M*)-(−)-Tetraspiro[2.0.0.0.2.1.1.1]undecane [(*M*)-4]: a) From alkene (3*S*,4*S*)-**35** (480 mg, 3.63 mmol), [5]triangulane (*M*)-**4** (274 mg, 52%) was obtained according to GP 6. $[\alpha]_D^{20} = -334.2$ ($c = 1.2$ in $CHCl_3$); *ee* ≥ 94%. The ^1H and ^{13}C NMR spectra of (*M*)-**4** were identical to those of the racemic compound.

b) *n*BuLi (10 mmol, 3.92 mL of a 2.55 M solution in hexane) was added at −35 °C over 1 h to a stirred solution of the alkene (*S*)-**28d** (261 mg, 2.46 mmol) and 1,1-dichloroethane (987 mg, 0.83 mL, 10 mmol) in anhydrous Et_2O. The reaction mixture was allowed to warm to ambient temperature and then poured onto ice. The organic phase was separated, dried, filtered through a 3 cm pad of silica gel and concentrated under reduced pressure. The residue (657 mg) was treated with *t*BuOK (873 mg, 7.78 mmol) according to GP 4a, workup 2 (40 °C bath temperature). The obtained pentane solution, after careful concentration, was subjected to cyclopropanation according to GP 6 with a diazomethane solution prepared from 6.0 g *N*-methyl-*N*-nitroso urea. Purification by preparative GC furnished a non-separable mixture (103 mg, 29% over three steps) of (*M*)-**4** and *meso*-**4** and in a ratio of 5.2:1 (according to the ^1H NMR spectrum[4]) with an optical rotation of $[\alpha]_D^{20} = -319.8$ ($c = 1.5$ in $CHCl_3$). Correction for the content of achiral *meso*-**4** led to the derived value of $[\alpha]_D^{20} = -381.2$ ($c = 1.3$ in $CHCl_3$); *ee* ≥ 95%.

0947-6539/02/0804-0840 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

Computational studies: Geometries were optimized utilizing the GAUSSIAN 98[27] program package within the framework of density functional theory (DFT) employing the non-local gradient-corrected exchange-correlation functional of Becke, Lee, Yang, and Parr (B3LYP)[28–30] in conjunction with the 6-31+G(d,p) basis set.[31] The singlet–singlet excitation energies and rotatory strengths of the lowest lying states were obtained from a full valence space single excitation configuration interaction treatment (SCI).[32] The CI calculations were carried out with the TURBOMOLE[42] program system at the B3LYP level utilizing a TZVP basis set.[43, 44] The resulting circular dichroism after a Kronig–Kramers transformation[45] gave the specific rotations in the ORD at the recorded wavelengths (Table 2). As the calculated data are for the gas phase, whereas the experimental ones are obtained for solutions, significant deviations are to be expected. Any correction for this, of course, requires that the solvent does not interact specifically, e.g., through hydrogen bonding, with the solute, and that the latter only experiences an averaged solvent field effect which currently cannot be accounted for in the computations. As the computed compounds are pure hydrocarbons, the optical rotations of which were measured in chloroform, a correction by shifting the calculated plane dispersion curve by a constant value of 100 nm appears to be justified. Regardless, curvatures of the computed and experimental ORD traces agree remarkably well which emphasizes the quality of the theoretical approach used here.[32]

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and EPSRC (UK). R.R.K. and A.W. are indebted to the German Academic Exchange Service (DAAD) for Research Fellowships. A.W. also thanks the Niedersächsische Graduiertenförderung for a scholarship and Dr. M. Prall for his assistance. We are grateful to the companies BASF AG, Bayer AG, Chemetall GmbH, Degussa AG, and Hüls AG for generous gifts of chemicals. We thank Dr. K. Miyazawa, Chisso Petrochemical Corporation, and Prof. M. P. Doyle, University of Arizona, for the donation of Lipase PS and $Rh_2(5R\text{-MEPY})_4$, respectively. We are grateful to Prof. H. Butenschön, TU Hannover, for his kind help in providing the DSC measurements, and Mrs. E. Pfeil, Universität Göttingen, for measurements of optical rotations. We are particularly indebted to Dr. B. Knieriem, Universität Göttingen, for his careful proofreading of the final manuscript.

[1] a) Originally, the term "cryptochiral" had been suggested for such compounds. See: K. Mislow, P. Bickart, *Isr. J. Chem*. **1976/1977**, *15*, 1. In considering what "cryptochiral" is to describe, one has to point out a serious deficiency, as any racemate might also be called cryptochiral. "Crypto-optically active" appears to be a more appropriate term.

[2] H. Wynberg, G. L. Hekkert, J. P. M. Houbiers, H. W. Bosch, *J. Am. Chem. Soc*. **1965**, *87*, 2635–2639.

[3] Reviews: a) A. de Meijere, S. I. Kozhushkov, *Chem. Rev*. **2000**, *100*, 93–142; b) A. de Meijere, S. I. Kozhushkov in *Advances in Strain in Organic Chemistry*, *Vol. 4* (Ed.: B. Halton), JAI Press, London, **1995**, pp. 225–282; c) N. S. Zefirov, T. S. Kuznetsova, A. N. Zefirov, *Izv. Akad. Nauk* **1995**, 1613–1621; N. S. Zefirov, T. S. Kuznetsova, A. N. Zefirov, *Russian Chem. Bull. (Engl. Transl.)* **1995**, 1613–1621.

[4] The stereochemical features of unbranched triangulanes **1** have been thoroughly analyzed. See: N. S. Zefirov, S. I. Kozhushkov, T. S. Kuznetsova, O. V. Kokoreva, K. A. Lukin, B. I. Ugrak, S. S. Tratch, *J. Am. Chem. Soc*. **1990**, *112*, 7702–7707.

[5] K. P. Meurer, F. Vögtle, *Top. Curr. Chem*. **1985**, *127*, 1–76. Despite the fact that this suggested nomenclature may lead to an association with the σ-aromatic character of the cyclopropane ring (see: D. Cremer, *Tetrahedron* **1988**, *44*, 7427–7454), σ aromaticity is not a precondition for the rotatory strengths of compounds of type **3**–**5**, as the spiro-annelated cyclopropane subunits are perpendicular with respect to each other.

[6] Adopting the [4]triangulanes to possess an axis of chirality which bisects the two central cyclopropane rings and considering the two other spiroannelated cyclopropane rings as substituents, (*M*)-**3** according to the IUPAC rules may also be termed (*R*)-**3**, and (*P*)-**3** would be (*S*)-**3**. See: *IUPAC Tentative Rules for the Nomenclature in Organic Chemistry. Section E. Fundamental Stereochemistry* in *J. Org. Chem*. **1970**, *35*, 2849–2867.

[7] H.-P. Guan, M. B. Ksebati, Y.-C. Cheng, J. C. Drach, E. R. Kern, J. Zemlicka, *J. Org. Chem*. **2000**, *65*, 1280–1290.

[8] a) M. P. Doyle, W. W. Winchester, J. A. A. Hoorn, V. Lynch, S. H. Simonsen, R. Ghosh, *J. Am. Chem. Soc*. **1993**, *115*, 9968–9978; b) M. P. Doyle, C. S. Peterson, M. N. Protopopova, A. B. Marnett, D. L. Parker, Jr., D. G. Ene, V. Lynch, *J. Am. Chem. Soc*. **1997**, *119*, 8826–8837; c) M. P. Doyle, S. B. Davies, W. Hu, *Org. Lett*. **2000**, *2*, 1145–1147.

[9] K. B. Wiberg, J. R. Snoonian, *J. Org. Chem*. **1998**, *63*, 1390–1401.

[10] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-163580 (**11**), CCDC-112810 [(*R*,*R*)-**17a**], CCDC-163581 [(1*RS*,3*SR*,4*SR*)-**31**], CCDC-163582 [(*P*)-**4**], and CCDC-163583 (*rac*-**4**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[11] a) A. de Meijere, S. I. Kozhushkov, T. Spaeth, N. S. Zefirov, *J. Org. Chem*. **1993**, *58*, 502–505; b) A. de Meijere, S. I. Kozhushkov, T. Späth, *Org. Synth*. **2000**, *78*, 142–151. Reviews: c) A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Zh. Org. Khim*. **1996**, *32*, 1607–1626; A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Russ. J. Org. Chem. (Engl. Transl.)* **1996**, *32*, 1555–1575; d) A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Top. Curr. Chem*. **2000**, *207*, 89–147; e) A. de Meijere, S. I. Kozhushkov, *Eur. J. Org. Chem*. **2000**, 3809–3822; f) A. de Meijere, S. I. Kozhushkov, T. Späth, M. von Seebach, S. Löhr, H. Nüske, T. Pohlmann, M. Es-Sayed, S. Bräse, *Pure Appl. Chem*. **2000**, *72*, 1745–1756.

[12] A. de Meijere, S. I. Kozhushkov, N. S. Zefirov, *Synthesis* **1993**, 681–683.

[13] Prepared by cyclopropanating methylenespiropentane with ethyl diazoacetate, chromatographic separation of *endo*- and *exo*-cycloadducts followed by hydrolysis: a) P. E. Eaton, K. A. Lukin, *J. Am. Chem. Soc*. **1993**, *115*, 11370–11375; b) A. de Meijere, S. I. Kozhushkov, T. Spaeth, N. S. Zefirov, *J. Org. Chem*. **1993**, *58*, 502–505. The starting material, methylenespiropentane, can now be prepared on a large scale by flash vacuum pyrolysis of bicyclopropylidene: c) A. de Meijere, S. I. Kozhushkov, D. Faber, V. Bagutskii, R. Boese, T. Haumann, R. Walsh, *Eur. J. Org. Chem*. **2001**, 3607–3614. The authors are grateful to Dipl.-Chem. V. Bagutskii for his donation of a sample of methylenespiropentane.

[14] a) S. H. Wilen, A. Collet, J. Jacques, *Tetrahedron* **1977**, *33*, 2725–2736. The closest analogue is the recently reported preparation of (*R*)-(−)-spiropentanecarboxylic acid by optical resolution of the racemic acid with (*S*)-1-phenylethylamine: b) K. B. Wiberg, C. G. Oesterle, *J. Org. Chem*. **1999**, *64*, 7763–7767.

[15] For the rules of this nomenclature see: I. Ugi, *Z. Naturforsch.* **1965**, *20B*, 405–409.

[16] S. Bernasconi, A. Comini, A. Corbella, P. Gariboldi, M. Sisti, *Synthesis* **1980**, 385–387.

[17] a) G. Helmchen, H. Völter, W. Schühle, *Tetrahedron Lett.* **1977**, 1417–1420; b) G. Helmchen, G. Nill, D. Flockerzi, W. Schühle, M. S. K. Youssef, *Angew. Chem.* **1979**, *91*, 64–65; *Angew. Chem. Int. Ed. Engl*. **1979**, *19*, 62–63; c) G. Helmchen, G. Nill, D. Flockerzi, M. S. K. Youssef, *Angew. Chem.* **1979**, *91*, 65–66; *Angew. Chem. Int. Ed. Engl*. **1979**, *19*, 63–64.

[18] a) K. Miyazawa, D. S. Yufit, J. A. K. Howard, A. de Meijere, *Eur. J. Org. Chem*. **2000**, 4109–4117; b) K. Miyazawa, *Dissertation*, Universität Göttingen, **1999**.

[19] a) K. A. Lukin, S. I. Kozhushkov, A. A. Andrievsky, B. I. Ugrak, N. S. Zefirov, *J. Org. Chem*. **1991**, *56*, 6176–6179; b) T. Heiner, S. I. Kozhushkov, M. Noltemeyer, T. Haumann, R. Boese, A. de Meijere, *Tetrahedron* **1996**, *52*, 12185–12196.

[20] For a recent review see: L. R. Subramanian, K.-P. Zeller, in *Methods of Organic Chemistry (Houben-Weyl)*, *Vol. E 17a* (Ed.: A. de Meijere), Thieme, Stuttgart, **1997**, pp. 256–308.

[21] J. M. Russo, W. A. Price, *J. Org. Chem*. **1993**, *58*, 3589–3590.

[22] P. K. Kadaba, *Synthesis* **1971**, 316–317.

[23] See: a) O. Repic, P. G. Lee, U. Giger, *Org. Prep. Proced. Int.* **1984**, *16*, 25–30; b) N. S. Zefirov, K. A. Lukin, S. F. Politanskii, M. A. Margulis,

Zh. Org. Khim. **1987**, *23*, 1799 – 1800; N. S. Zefirov, K. A. Lukin, S. F. Politanskii, M. A. Margulis, *J. Org. Chem. USSR (Engl. Transl.)* **1987**, *23*, 1603 – 1604.

[24] a) R. Paulissen, A. J. Hubert, P. Teyssie, *Tetrahedron Lett*. **1972**, 1465 – 1466; b) U. Mende, B. Radüchel, W. Skuballa, H. Vorbrüggen, *Tetrahedron Lett*. **1975**, 629 – 632; c) Review: Yu. V. Tomilov, V. A. Dokichev, U. M. Dzhemilev, O. M. Nefedov, *Usp. Khim*. **1993**, *62*, 847 – 886; Yu. V. Tomilov, V. A. Dokichev, U. M. Dzhemilev, O. M. Nefedov, *Russ. Chem. Rev*. **1993**, *62*, 799 – 838.

[25] W. A. König, *The Practice of Enantiomer Separation by Capillary Gas Chromatography*, Hüthig, Heidelberg, **1987**.

[26] R. Boese, T. Haumann, S. I. Kozhushkov, E. D. Jemmis, B. Kiran, A. de Meijere, *Liebigs Ann.* **1996**, 913 – 919.

[27] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, A. J. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, *Gaussian 98*, *Revision A.9*, Pittsburgh PA, **1998**.

[28] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098 – 3100.

[29] C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785 – 789.

[30] R. G. Parr, W. Yang, *Density Functional Theory of Atoms and Molecules*, Oxford University Press, New York, **1989**.

[31] W. J. Hehre, L. Radom, P. v. R. Schleyer, J. A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley Interscience, New York, **1986**.

[32] S. Grimme, *Chem. Phys. Lett.* **1996**, *259*, 128 – 137.

[33] Planar chiral and arylaliphatic helical molecules have previously been successively treated in the same way. See also: S. Grimme, J. Harren, A. Sobanski, F. Vögtle, *Eur. J. Org. Chem*. **1998**, 1491 – 1509, and references therein.

[34] Significant electronic interactions between neighboring spiroannelated cyclopropane groups have, e.g., been confirmed by photoelectron spectroscopy on [3]- and [4]rotane. See: R. Gleiter, R. Heider, J.-M. Conia, J.-P. Barnier, A. de Meijere, W. Weber, *J. Chem. Soc. Chem. Commun*. **1979**, 130 – 132.

[35] A. de Meijere, A. F. Khlebnikov, R. R. Kostikov, S. I. Kozhushkov, P. R. Schreiner, A. Wittkopp, D. S. Yufit, *Angew. Chem.* **1999**, *111*, 3682 – 3685; *Angew. Chem. Int. Ed. Engl*. **1999**, *38*, 3474 – 3477.

[36] W. Hug, G. Zuber, A. de Meijere, A. F. Khlebnikov, H. J. Hansen, *Helv. Chim. Acta* **2001**, *84*, 1 – 21.

[37] K. A. Lukin, A. Yu. Masunova, B. I. Ugrak, N. S. Zefirov, *Tetrahedron* **1991**, *30*, 5769 – 5780.

[38] N. S. Zefirov, K. A. Lukin, S. I. Kozhushkov, T. S. Kuznetsova, A. M. Domarev, I. M. Sosonkin, *Zh. Org. Khim*. **1989**, *25*, 312 – 319; N. S. Zefirov, K. A. Lukin, S. I. Kozhushkov, T. S. Kuznetsova, A. M. Domarev, I. M. Sosonkin, *J. Org. Chem. USSR (Engl. Transl.)* **1989**, *25*, 278 – 284.

[39] M.-t. Lai, L.-d. Liu, H.-w. Liu, *J. Am. Chem. Soc*. **1991**, *113*, 7388 – 7397.

[40] C. Y. Fiakpui, E. E. Knaus, *Can. J. Chem*. **1987**, *65*, 1158 – 1161.

[41] D. S. Yufit, J. A. K. Howard, S. I. Kozhushkov, A. de Meijere, *Acta Crystallogr. Sect. B* **2001**, in press.

[42] R. Ahlrichs, M. Bär, M. Häser, H. Horn, C. Kölmel, *Chem. Phys. Lett.* **1989**, *162*, 165 – 169.

[43] A. Schaefer, H. Horn, R. Ahlrichs, *J. Chem. Phys.* **1992**, *97*, 2571 – 2577.

[44] a) A. Schaefer, C. Huber, R. Ahlrichs, *J. Chem. Phys.* **1994**, *100*, 5829 – 5835; b) F. Furche, R. Ahlrich, C. Wachsmann, E. Weber, A. Sobanski, F. Vögtle, S. Grimme, *J. Am. Chem. Soc*. **2000**, *122*, 1717 – 1724.

[45] C. Djerassi, *Optical Rotatory Dispersion—Applications to Organic Chemistry*, McGraw Hill, New York, **1960**.

Received: June 26, 2001 [F3373]

  0947-6539/02/0804-0842 $ 17.50+.50/0