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# Stereoselective Preparation of Six Diastereomeric Quatercyclopropanes from Bicyclopropylidene and Some Derivatives

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*Dedicated to the memory of Dr. Burkhardt Knieriem*

**Abstract:** Diastereomeric *meso*- and *d*,*l*-bis(bicyclopropylidenyl) (**5**) were obtained upon oxidation with oxygen of a higher-order cuprate generated from lithiobicyclopropylidene (**4**) in 50 and 31% yield, respectively. Their perdeuterated analogues *meso*-[$D_{14}$]- and *d*,*l*-[$D_{14}$]-**5** were obtained along the same route from perdeuterated bicyclopropylidene [$D_8$]-**3** (synthesized in six steps in 7.4% overall yield from [$D_8$]-THF) in 20.5% yield each. Dehalogenative coupling of 1,1-dibromo-2-cyclopropylcyclopropane (**6**) gave a mixture of all possible stereoisomers of 1,5-dicyclopropylbicyclopropylidene **16** in 69% yield, from which (*Z*)-*cis*-**16** was separated by preparative gas chromatography (26% yield). The crystal structure of *meso*-**5** looks like a superposition of the crystal structures of two outer bicyclopropylidene units (**3**) and one inner s-*trans*-bicyclopropyl unit, whereas the two outer cyclopropyl moieties adopt a *gauche* orientation with respect to the cyclopropane rings at the inner bicyclopropylidene units in (*Z*)-*cis*-**16**. Birch reduction with lithium in liquid ammonia of *meso*-**5** and *d*,*l*-**5** gave two pairs of diastereomeric quatercyclopropanes *trans*,*trans*-(*R**,*S**,*R**,*S**)-**17**/*cis*,*trans*-(*R**,*S**,*R**,*R**)-**18** and *trans*,*trans*-(*R**,*S**,*S**,*R**)-**19**/*cis*,*trans*-(*R**,*S**,*S**,*S**)-**20** in 97 and 76% yield, respectively, in a ratio 9:1 for every pair. The latter diastereomer was also obtained as the sole product by Birch reduction of (*Z*)-*cis*-**16** in 96% yield. Under the same conditions, tetradecadeuterio analogues *trans*,*trans*-[$D_{14}$]-(*R**,*S**,*R**,*S**)-**17**/*cis*,*trans*-[$D_{14}$]-(*R**,*S**,*R**,*R**)-**18** (8:1) and *trans*,*trans*-[$D_{14}$]-(*R**,*S**,*S**,*R**)-**19**/*cis*,*trans*-[$D_{14}$]-(*R**,*S**,*S**,*S**)-**20** (12:1) were prepared from *meso*-[$D_{14}$]-**5** and *d*,*l*-[$D_{14}$]-**5** in 37 and 63% yield, respectively. Reduction of *meso*-**5** with diimine gave the *cis*,*cis*-quatercyclopropane (*S**,*S**,*R**,*R**)-**21** as the main product (58% yield) along with the *cis*,*trans*-diastereomer (*S**,*S**,*R**,*S**)-**18** (29% yield). Thus, five of the six possible diastereomeric quatercyclopropanes were obtained from *meso*-**5**, *d*,*l*-**5**, and (*Z*)-*cis*-**16**. The X-ray crystal structure analyses of *trans*,*trans*-(*R**,*S**,*R**,*S**)-**17** and *cis*,*cis*-(*S**,*S**,*R**,*R**)-**21** revealed for the both an unusual conformation in which the central bicyclopropyl unit adopts an s-*trans*-(antiperiplanar) orientation with $\phi = 180.0°$, and the two terminal bicyclopropyl moieties adopt a synclinal conformation with $\phi = 49.8$ and 72.0°, respectively. In solution the vicinal coupling constants $\langle {}^3J_{H,H} \rangle$ in *trans*,*trans*-(*R**,*S**,*R**,*S**)-[$D_{14}$]-**17**, *trans*,*trans*-(*R**,*S**,*S**,*R**)-[$D_{14}$]-**19**, *trans*,*cis*-(*R**,*S**,*R**,*R**)-[$D_{14}$]-**18** and *trans*,*cis*-(*R**,*S**,*S**,*S**)-[$D_{14}$]-**20** were found to be 4.1, 4.7, 5.9 and 5.9 Hz, respectively. This indicates a predominance of the all-*gauche* conformer in (*R**,*S**,*R**,*S**)-**17** and a decreasing fraction of it in this sequence of the other diastereomers.

**Keywords:** bicyclopropylidenes · C–C coupling · conformation analysis · lithiation · small-ring systems

## Introduction

Remarkably, nature not only produces a large variety of biologically active and structurally interesting compounds with single cyclopropyl moieties,[1–3] but also brings forward products which contain fatty acid residues with four and even five consecutive cyclopropane rings.[4]

One example is the antifungal nucleoside FR-900848 **1**, which was isolated as a natural product from *Streptoverticillum fervens* in 1990,[5] the other is U-106305 **2**, a cholesteryl ester transfer protein inhibitor from the fermentation broth of *Streptomyces sp*. UC 11136.[6] In both compounds the consecutive oligocyclopropane moieties are all-*trans*-configured.

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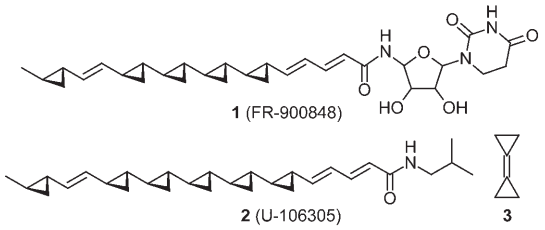
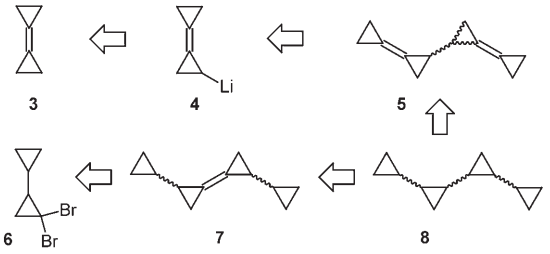



It comes as no surprise that several synthetically oriented groups around the world have invested a considerable amount of work into the development of feasible syntheses of these two compounds.[7–10] The total synthesis of FR-900848 **1**[11,12] and U-106305 **2**[12,13] was achieved in 1996 by Barrett et al., and the key step for the stereoselective assembly of the quatercyclopropane moiety was the enantioselective Simmons–Smith-type cyclopropanation of 2-butene-1,4-diol as developed by Charette et al.[14] The higher acyclic and even cyclic *syn*-all-*trans*-oligocyclopropyl-1,*n*-dimethanol derivatives have been prepared not only as precursors to the natural products **1** and **2** but also out of interest in their conformational behavior.[15] Having gained some experience with the conformational analysis of bicyclopropyl early on,[16,17] we were intrigued by the conformational features of the quater- and quinquecyclopropane units in **1** and **2**. We therefore set out to prepare as many as possible of the six diastereomers of unsubstituted quatercyclopropane as model compounds and study their structural and conformational properties. In view of the fact that the tetrasubstituted alkene bicyclopropylidene (**3**),[18] which already contains two cyclopropyl groups with a stereoselectively reducible double bond between them, can easily be deprotonated with *n*-butyllithium in tetrahydrofuran at 0 °C,[19] we anticipated it to be a feasible building block for the construction of stereoisomeric quatercyclopropanes.

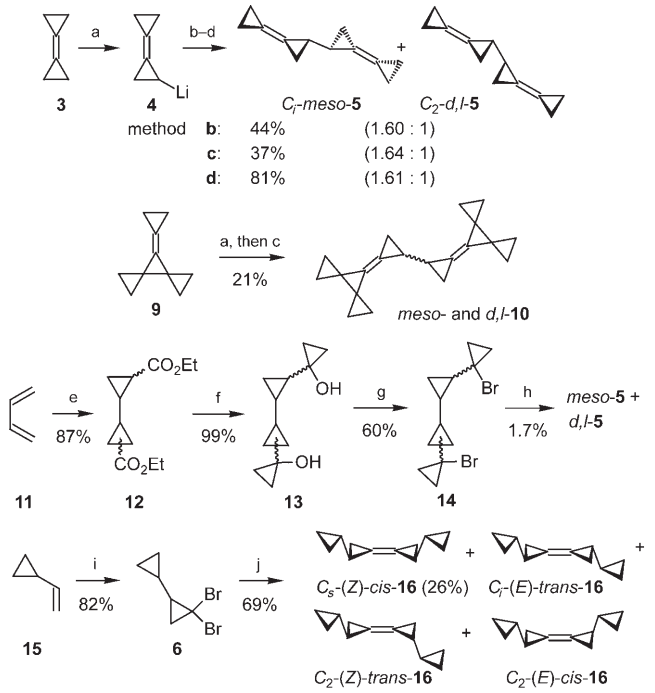
## Results and Discussion

The concept was to subject lithiobicyclopropylidene (**4**), formed upon deprotonation of (**3**) with *n*-butyllithium almost quantitatively,[19] to some sort of homocoupling, if necessary via some other organometallic intermediate derived from **4**, adopting one of the established procedures,[20] and thus convert it into a bis(bicyclopropylidenyl) (**5**), which would contain the four cyclopropane rings necessary for the target compounds (Scheme 1). Alternatively, another bicyclopropylidene derivative **7** with four cyclopropyl groups should be accessible by the highly efficient dimerization of bromocoppercyclopropylidenoids[21] generated from dibromocyclopropanes, in this case 2,2-dibromobicyclopropyl **6**, by treatment with *n*-butyllithium in tetrahydrofuran in the presence of cupric chloride. The resulting bicyclopropylidene **7** just as the bis(bicyclopropylidenyl) (**5**), by *trans*- or *cis*-stereoselective reduction of the double bonds would yield various diastereomeric quatercyclopropanes **8**.




Scheme 1. Retrosynthetic considerations concerning quatercyclopropanes **8** to be prepared from bicyclopropylidene (**3**) and dibromobicyclopropyl **6**.

The oxidative coupling of two lithiobicyclopropylidene molecules (**4**) was indeed accomplished under different conditions (Scheme 2). For instance, transmetallation of **4** with anhydrous magnesium bromide solution, followed by treatment with cupric chloride at −78 °C (cf. ref. [22]) afforded a 1.6:1 mixture of *meso*- and *d*,*l*-bis(bicyclopropylidenyl) (**5**) in 44 % yield (Scheme 2). A similar result was achieved upon oxidation with oxygen of a higher-order cuprate[20a] generated from lithiobicyclopropylidene (**4**) and cuprous cyanide adopting a published procedure,[23] upon which the




Scheme 2. Preparation of the diastereomeric bis(bicyclopropylidenyl)s *meso*-**5** and *d*,*l*-**5** as well as *meso*-**10** and *d*,*l*-**10** under various conditions and as cupric chloride-assisted dehalogenative dimerization of 1,1-dibromo-2-cyclopropylcyclopropane (**6**). a) *n*BuLi, THF, 0 °C, 1 h; b) $MgBr_2$, $Et_2O$, −78→20 °C, 1 h, then $CuCl_2$, −78→20 °C, 2.5 h; c) CuCN, −100→−40 °C, 0.5 h, then $O_2$, −78 °C, 0.5 h; d) $[CuIBu_3P]_4$, −78 °C, 1 h, then $O_2$, −78 °C, 1 h; e) $N_2CHCO_2Et$, $[Rh(OAc)_2]_2$ (0.3 mol %), $CH_2Cl_2$, −5→0 °C, 12.5 h; f) EtMgBr, $Ti(OiPr)_4$, $Et_2O$, 20 °C; g) $Ph_3P{\cdot}Br_2$, Py, $CH_2Cl_2$, −30→20 °C, 24 h; h) *t*BuOK, DMSO, 20 °C, 24 h; i) $CHBr_3$, KOH (pellets), TEBACl, $CH_2Cl_2$, 20–25 °C, 2 h; j) $CuCl_2$, THF, −100 °C, slow addition of *n*BuLi over 1 h, then −100→20 °C, 2 h.

bisspirocyclopropanated bicyclopropylidene **9**[24] gave a mixture of the corresponding dehydrodimers *meso*- and *d*,*l*-**10** in 21% yield. The higher-order cuprate generated from lithiobicyclopropylidene (**4**) and tetrakis[iodo(tri-*n*-butylphosphine)copper(I)] $[CuIBu_3P]_4$ could be oxidatively dimerized to give a 1.6:1 mixture of *meso*-**5** and *d*,*l*-**5** in 81% yield (Scheme 2). An attempted alternative approach to bis(bicyclopropylidenyl) of type **5** utilizing the Kulinkovich reaction[25] turned out unfruitful. Although the twofold reductive cyclopropanation of the diester **12** prepared from butadiene (**11**) by twofold cyclopropanation with ethyl diazoacetate, worked perfectly well, and the conversion of the biscyclopropanol **13** to the dibromide **14** also gave a reasonable yield (60%), the twofold dehydrobromination of **14** yielded only 1.7% of a mixture of *meso*-**5** and *d*,*l*-**5** (Scheme 2).

The tetraspirocyclopropanated bis(bicyclopropylidenyl)s *meso*-**10** and *d*,*l*-**10** can be separated by simple column chromatography on silica gel (see Experimental Section). As *meso*-**5** crystallized well from its 20% ethereal solution at −20°C, it could be separated from the *d*,*l*-diastereomer and purified very easily, while the purification of the *d*,*l*-diastereomer *d*,*l*-**5** with this method was a little more tedious. Alternatively, the bis(bicyclopropylidenyl)s *meso*-**5** and *d*,*l*-**5** were separated quite well by column chromatography on silica gel impregnated with 5% of silver nitrate,[26] however, some material was lost due to partial decomposition. Dehalogenative coupling of the known 1,1-dibromo-2-cyclopropylcyclopropane (**6**)[27] under modified conditions[28] based on those of Neuenschwander et al.[21] gave a mixture of all four possible diastereomers (Scheme 2) in 69% yield, from which only (*Z*)-*cis*-**16** could be separated and isolated in pure form by preparative gas chromatography (26% yield).

While the *meso*-diastereomer *meso*-**5** with s-*trans* orientation of the two bicyclopropylidenyl groups possesses $C_i$ symmetry, *d*,*l*-**5** has $C_2$ symmetry. Since three diastereomers of **16** could not be isolated in pure form, their structures could not be unequivocally assigned on the basis of the NMR spectra of the mixture. Only the single isolated diastereomer was assigned the (*Z*)-*cis*-configuration as determined by an X-ray crystal structure analysis (Figure 1). A crystal structure analysis was also performed for *meso*-**5** (Figure 1).

In the crystal, the hydrocarbon *meso*-**5** adopts a $C_i$-symmetrical conformation with an s-*trans*-orientation of the central bicyclopropyl unit (*antiperiplanar* conformation with $\phi = 180$ and 179.4° in the two independent molecules, respectively). The parent bicyclopropyl also has such a conformation in the crystal,[30] whereas in the gas phase[17,31] and in the liquid[16,32] the *synclinal* (*gauche*) conformer predominates. From a structural point of view, *meso*-**5** is essentially a linked combination of the structures of bicyclopropylidene (**3**)[18b] and of bicyclopropyl.[30a] Thus, the structures of both bicyclopropylidene units in *meso*-**5** are actually undistorted in comparison with the parent bicyclopropylidene (**3**),[18b] and the bond length **h** between the two bicyclopropylidenes in *meso*-**5** [1.494(1) Å] is essentially the same as the central bond length in bicyclopropyl [1.4924(4) Å], as measured at 100 K.[30a] Apparently, no additional electronic interactions

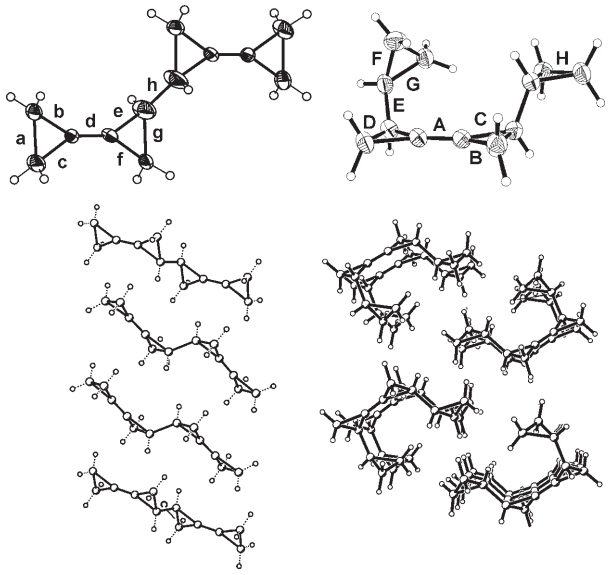
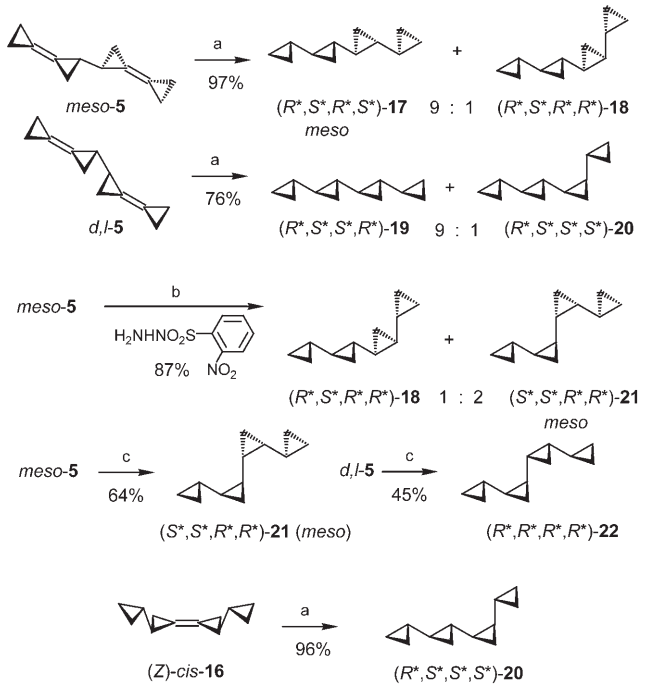



Figure 1. Structures of *meso*-bis(bicyclopropylidenyl) (*meso*-**5**, top left), 1,5-dicyclopropylbicyclopropylidene [(*Z*)-*cis*-**16**, top right)] and fractions of their molecular packing (bottom) in the crystals.[29] Bond lengths [Å] (mean values based on assumed $C_i$ symmetry for *meso*-**5** and $C_s$ symmetry for (*Z*)-*cis*-**16**). *meso*-**5**: **a** = 1.5332(12), **b** = 1.4617(12), **c** = 1.4657(12), **d** = 1.3045(12), **e** = 1.4689(12), **f** = 1.4664(12), **g** = 1.5371(12), **h** = 1.4938(12). (*Z*)-*cis*-**16**: **A** = 1.303(2), **B** = 1.477(3), **C** = 1.479(3), **D** = 1.546(3), **E** = 1.494(3), **F** = 1.503(3), **G** = 1.504(3), **H** = 1.500(2).

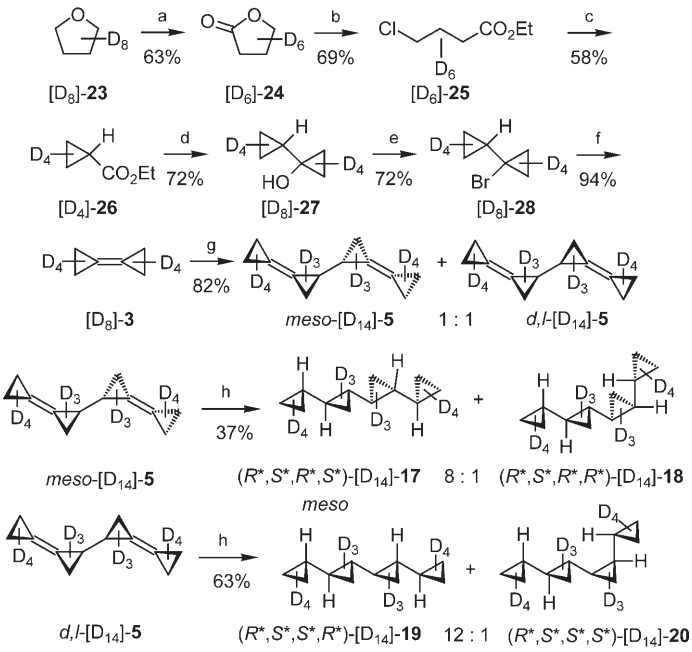
in comparison with those existing in bicyclopropyl can be attributed to *meso*-**5** on the basis of its X-ray crystal structural data. For (*Z*)-*cis*-**16** the situation is different. As in *meso*-**5**, the distance **E** between the cyclopropyl and bicyclopropylidene moieties [1.494(3) Å], the bond lengths within the terminal cyclopropanes and that of the double bond are very close to those found in bicyclopropyl and in bicyclopropylidene (**3**), respectively. However, the distal (with respect to the double bond) bond **D** in the bicyclopropylidene fragment of (*Z*)-*cis*-**16** is slightly longer [1.546(3) Å, measured at 230 K] than the corresponding one in bicyclopropylidene (**3**) [1.534(2) Å, measured at 245 K], and the proximal bonds **B** and **C** are slightly longer too [1.478(3) vs 1.467(1) Å]. These structural changes cannot easily be explained by an electronic influence of the terminal cyclopropane rings (cf. [33]). Only one of the two terminal cyclopropyl groups adopts an s-*trans*- (*antiperiplanar*) conformation with $\phi = 178.8$° with respect to the adjacent three-membered ring of the bicyclopropylidene core, while the other ring adopts a *gauche* (*synclinal*) orientation with $\phi = 47.5$°. As was mentioned above, such differences in conformation have remarkably little effect on the geometrical parameters of the molecule.

Birch reduction of *meso*-bis(bicyclopropylidenyl) (*meso*-**5**) with lithium in liquid ammonia proceeds diastereoselectively and in almost quantitative yield to give the two diastereomeric quatercyclopropanes *trans*,*trans*-(*R**,*S**,*R**,*S**)-**17** and *cis*,*trans*-(*R**,*S**,*R**,*R**)-**18** in a ratio of 9:1 (Scheme 3). On the other hand, reduction of *meso*-**5** with diimine, in situ generated from 2-nitrobenzenesulfonyl hydrazide,[34] gave




Scheme 3. Reduction of bis(bicyclopropylidenyl)s *meso*-**5** and *d*,*l*-**5**, as well as of (*Z*)-*cis*-**16** under various conditions. a) Li, liq. $NH_3$, −78 °C, 1.5 h, then MeOH, −78→20 °C; b) 2-nitrobenzenesulfonyl hydrazide (8.7 equiv), MeOH, 20 °C, 5 h; c) $H_2$, Pd/$BaSO_4$ (2 mol %), MeOH, 20 °C, 16–44 h.




Scheme 4. Preparation of *meso*- (*meso*-[$D_{14}$]-**5**) and *d*,*l*- (*d*,*l*-[$D_{14}$]-**5**) perdeuteriobis(bicyclopropylidenyl)s as well as their Birch reduction. a) $Ca(OCl)_2$ (2 equiv), MeCN/AcOH (3:2), 0→20 °C, 22 h; b) $SOCl_2$, 80 °C, 3 h, then EtOH, 20→78 °C, 1.5 h at 78 °C; c) EtONa, EtOH, 20→78 °C, 1 h at 78 °C, then aq. 10 M $H_2SO_4$, 0 °C; d) $C_2D_5MgBr$, $Ti(OiPr)_4$, $Et_2O$, 20 °C, 1 h, then aq. 10 % $H_2SO_4$, 0 °C, 1 h; e) $Ph_3P{\cdot}Br_2$, Py, $CH_2Cl_2$, −15→20 °C, 48 h; f) *t*BuOK, DMSO, 20 °C, 48 h; g) *n*BuLi, THF, 20 °C, 1 h, then CuCN, −100→−40 °C, 0.5 h, then $O_2$, −78 °C, 0.5 h; h) Li, liq. $NH_3$, −78 °C 1.5 h, then MeOH, −78→20 °C.

the *cis*,*cis*-quatercyclopropane (*S**,*S**,*R**,*R**)-**21** as the main product (58 % yield, isolated by preparative gas chromatography) along with the *cis*,*trans*-diastereomer (*R**,*S**,*R**,*R**)-**18** (29 % yield). Thus, as three of the six possible diastereomeric quatercyclopropanes were obtained from *meso*-**5**, the other three ought to be accessible analogously from *d*,*l*-bis(bicyclopropylidenyl) (*d*,*l*-**5**). Indeed, Birch reduction of the latter was accomplished with the same diastereoselectivity (9:1) to give the quatercyclopropanes *trans*,*trans*-(*R**,*S**,*S**,*R**)-**19** and *cis*,*trans*-(*R**,*S**,*S**,*S**)-**20**, however, in lower isolated yield (76 %). The minor component of this mixture—the quatercyclopropane *cis*,*trans*-(*R**,*S**,*S**,*S**)-**20**—was also obtained as the sole product by Birch reduction of (*Z*)-*cis*-2,2′-dicyclopropylbicyclopropylidene (*Z*)-*cis*-**16** in 96 % yield (Scheme 3).

With the purpose to separate and more easily determine the vicinal H,H-coupling constants between cyclopropyl groups in quatercyclopropanes, the perdeuteriobis(bicyclopropylidenyl)s *meso*-[$D_{14}$]- and *d*,*l*-[$D_{14}$]-**5** were also prepared, applying the procedure c discussed above (see Scheme 2), from perdeuteriobicyclopropylidene [$D_8$]-**3**. The latter was obtained from perdeuterated γ-butyrolactone (prepared from perdeuteriotetrahydrofuran) according to an established protocol[24a,b] (Scheme 4). Thus, [$D_8$]-THF ([$D_8$]-**23**) was oxidized to [$D_6$]-γ-butyrolactone ([$D_6$]-**24**) in 63 % yield adopting a published procedure.[35] This was converted by a known method[36] into ethyl [$D_4$]-cyclopropanecarboxylate ([$D_4$]-**26**) in two steps in 40 % overall yield. Reductive cyclopropanation with perdeuterated ethylmagnesium bromide (prepared in two steps from commercially available [$D_5$]-ethanol, see Experimental Section) followed by conversion to the bromide and subsequent dehydrobromination according to an established protocol[24a,b] furnished perdeuteriobicyclopropylidene [$D_8$]-**3** in 49 % yield over three steps (Scheme 4).[37] Finally, [$D_8$]-**3** was converted into a 1:1 mixture of *meso*-[$D_{14}$]-**5** and *d*,*l*-[$D_{14}$]-**5** which were separated by column chromatography on silica gel impregnated with 5 % of silver nitrate.

Under the same conditions as applied for the Birch reduction of the diastereomeric bis(bicyclopropylidenyl)s, the perdeuterated analogues *meso*-[$D_{14}$]-**5** and *d*,*l*-[$D_{14}$]-**5** gave the tetradecadeuterated quatercyclopropanes *trans*,*trans*-(*R**,*S**,*R**,*S**)-[$D_{14}$]-**17** and *cis*,*trans*-(*R**,*S**,*R**,*R**)-[$D_{14}$]-**18** (8:1) in 37 % yield as well as *trans*,*trans*-(*R**,*S**,*S**,*R**)-[$D_{14}$]-**19** and *cis*,*trans*-(*R**,*S**,*S**,*S**)-[$D_{14}$]-**20** (12:1) in 63 % yield (Scheme 4).

In the *trans*,*trans*-quatercyclopropane (*R**,*S**,*R**,*S**)-**17**, as disclosed by X-ray crystal structure analysis at 150 K, the bonds **a**, **c**, **d** and **g** are virtually of the same lengths as the corresponding bonds in unsubstituted cyclopropane,[30a] while the bonds **b**, **e** and **f** are slightly longer. The bonds between the cyclopropane moieties **d** [1.496(2) Å] and **h** [1.491(3) Å] are essentially the same as the corresponding one in bicyclopropyl [1.4924(4) Å].[30a] In contrast to this, in

the *cis*,*cis*-quatercyclopropane (*S**,*S**,*R**,*R**)-**21**, as disclosed by X-ray crystal structure analysis at 113 K, the bonds **B**, **F** and **G** are also of the same lengths as the bonds in unsubstituted cyclopropane,[30a] however, the bonds **A**, **C** and **E** are slightly shorter. Moreover, the bonds between the cyclopropane moieties **D** [1.481(2) Å] and **H** [1.480(3) Å] are definitely shorter than the corresponding one in bicyclopropyl [1.4924(4) Å].[30a] This indicates a change in hybridization of the involved carbon atoms in (*S**,*S**,*R**,*R**)-**21**, but the reason for this change compared to bicyclopropyl is not clear.

In the crystal, both the *trans*,*trans*-quatercyclopropane (*R**,*S**,*R**,*S**)-**17** and the *cis*,*cis*-quatercyclopropane (*S**,*S**,*R**,*R**)-**21** adopt a remarkable conformation in which the two central cyclopropyl groups are in an s-*trans* (*antiperiplanar*) orientation with $\phi = 180.0°$ just as in crystalline bicyclopropyl,[30a] and the two terminal cyclopropyl groups each are in *gauche* (*synclinal*) orientations with respect to their nearest neighbors with $\phi = 49.8$ and 72.0°, respectively (Figure 2). These conformations must result from energetic

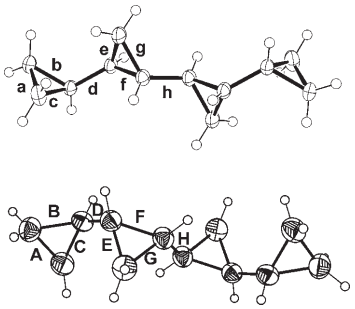



Figure 2. Structures of quatercyclopropanes *trans*,*trans*-(*R**,*S**,*R**,*S**)-**17** (top) and *cis*,*cis*- (*S**,*S**,*R**,*R**)-**21** (bottom) in the crystal.[29] Bond lengths [Å] in (*R**,*S**,*R**,*S**)-**17** (mean values based on assumed $C_i$ symmetry): **a** = 1.498(3), **b** = 1.505(2), **c** = 1.500(3), **d** = 1.496(2), **e** = 1.504(3), **f** = 1.507(2), **g** = 1.502(2), **h** = 1.491(3). Bond lengths [Å] in (*S**,*S**,*R**,*R**)-**21** (mean values based on assumed $C_i$ symmetry): **A** = 1.480(2), **B** = 1.493(2), **C** = 1.488(2), **D** = 1.481(2), **E** = 1.487(2), **F** = 1.499(2), **G** = 1.496(2), **H** = 1.480(3).

compromises between intramolecular van der Waals interactions between hydrogen atoms or simply from crystal packing effects. It is noteworthy that such a conformation has never been observed in the solid state for either of the quater- or quinquecyclopropane derivatives along the routes to FR-900848 (**1**) (all-*gauche* conformation[10b,12]) and to U-106305 (**2**) (*gauche*/*trans*/*gauche*/*gauche* conformation[13c]), or the macrocyclic compounds containing a quinquecyclopropane fragment (predominating *trans*/*trans*/*gauche*/*trans* conformation[15a]).

In solution, the *synclinal* conformation of bicyclopropyl is known to be more stable than the *antiperiplanar* one by 150–160 cal mol$^{-1}$,[16b,38] as derived from, for example, the temperature dependence of the vicinal spin-spin coupling constant $\langle^3J_{H,H}\rangle$ in 2,2,3,3,2′,2′,3′,3′-octadeuteriobicyclopropyl (4.42 Hz at +70 decreasing to 4.21 at −65 °C).[16] At 25 °C in $CD_2Cl_2$ the value of $\langle^3J_{H,H}\rangle$ for (*R**,*S**,*R**,*S**)-[$D_{14}$]-**17** was found to be equal to 4.1 Hz. This corroborates that at least for the outer bicyclopropyl units in this *meso*-quatercyclopropane the proportion of the *gauche* conformers is even more prevalent than in parent bicyclopropyl. On going from *trans*,*trans*-(*R**,*S**,*R**,*S**)-[$D_{14}$]-**17** via *trans*,*trans*-(*R**,*S**,*S**,*R**)-[$D_{14}$]-**19** and *trans*,*cis*-(*R**,*S**,*R**,*R**)-[$D_{14}$]-**18** to *trans*,*cis*-(*R**,*S**,*S**,*S**)-[$D_{14}$]-**20** the predominance of this conformer decreases, as seen from the corresponding $\langle^3J_{H,H}\rangle$ values which were equal to 4.1, 4.7, 5.9 and 5.9 Hz, respectively. However, in contrast to the case of bicyclopropyl,[16] these values practically do not change, at least not systematically, on raising or lowering temperature, but an up-field shift of the $^1$H signals was observed upon decreasing the temperature.

In order to gage the reasons for the different conformational preferences of the diastereomeric quatercyclopropanes **17**–**22** in the solid states and in solutions, their geometries were optimized at the B3LYP/6-31G(d) level of theory starting with the geometry of the lowest energy conformer in each case, as obtained by MMFF force field calculations.[39] In all but one case, the s-*trans* conformation of each two adjacent cyclopropane rings with a maximum deviation of ±6.5° came out to be energetically preferred. Only for the *trans*,*cis*-isomer **18** was a *gauche* orientation of the two central cyclopropanes with a torsional angle of $\phi = 82°$ predicted to be more stable. The energies of the *meso*-*trans*,*trans* **17** and the *d*,*l*-*trans*,*trans* isomer **19** were found to be very similar and the lowest among those of all diastereomers (Table 1). To check whether the predicted preference for the

Table 1. Computed energy differences ($\Delta E$ in kcal mol$^{-1}$ relative to the energy of the all-s-*trans* conformer of **19**) for six diastereomeric quatercyclopropanes **17**–**22** for geometries optimized from two different starting geometries and at different levels of theory.

| Compound | B3LYP/6-31G(d) | | | MP2(fc)/6-31G(d)// B3LYP/6-31G(d) | | |
|---|---|---|---|---|---|---|
| | all-s-*trans* | all-*gauche* | *g*,*g*,*t*[a] | all-s-*trans* | all-*gauche* | *g*,*g*,*t*[a] |
| **17** | 0.0 | 0.3 | | 0.1 | −2.1 | |
| **18** | 1.0[b] | 5.7 | 1.4 | −0.6[b] | 2.3 | −1.1 |
| **19** | 0.0 | 0.5 | | 0.0 | −1.9 | |
| **20** | 1.3 | 4.0 | 3.1 | 0.6 | 1.1 | 0.6 |
| **21** | 2.6 | 7.3 | | 1.9 | 3.8 | |
| **22** | 2.5 | 7.6 | | 1.6 | 4.4 | |

[a] *gauche*,*gauche*,s-*trans* conformer. [b] s-*trans*,*gauche*,s-*trans* conformer.

s-*trans* conformations were artefacts produced by the MMFF force field,[40,41] all-*gauche* conformations with $\phi =$ 48° were used as starting geometries for the optimization at the same level of theory. For all six diastereomers **17**–**22**, the all-*gauche* conformations were calculated to be of higher energy than the corresponding optimized all-s-*trans* conformer. Many of the torsional angles $\phi$ increased during optimization to values of 55–60° and even up to 84°.

Since this is in sharp contrast to the experimental results on the basis of vicinal coupling constants $\langle^3J_{H,H}\rangle$, single point energies for all optimized structures were also computed at the MP2(fc)/6-31G(d) level of theory.[42] By this

method, at least for the *meso-trans,trans*-**17** and the *d,l-trans,trans*-**19**, the all-*gauche* conformers were predicted to be the more stable ones. The larger value of this differences (about 2 kcal mol$^{-1}$) compared with the expected value (ca. 0.5 kcal mol$^{-1}$ for three *gauche* conformations) supports the higher prevalence of the *gauche* conformations in **17** and **19** as predicted by the NMR experiments. The larger energy difference for the two conformations of **18** than that for **20** was reproduced at this level of theory as well, still being in disagreement with the observed coupling constants. Since the larger $\langle^3J_{H,H}\rangle$ values measured for **18** and **20** suggested a higher s-*trans* conformer contribution, the geometry of the respective *gauche,gauche*,s-*trans* conformations were optimized, and the energies calculated as before. Indeed, these conformations were predicted to be more favorable than the all-*gauche* conformation at the MP2(fc)/6-31G(d)//B3LYP/6-31G(d) level of theory. For **18**, this conformation corresponds to the lowest-energy conformer found.

## Experimental Section

**General aspects**: Bicyclopropylidene (**3**),[24b] 7-cyclopropylidenedispiro-[2.0.2.1]heptane (**9**),[24a] 2-nitrobenzenesulfonyl hydrazide[34] and tetrakis-[iodo(tri-*n*-butylphosphine)copper(I)] ([$CuIBu_3P]_4$)[43] were prepared according to previously published procedures. Pentane for column chromatography was shaken with conc. sulfuric acid for 12 h, then with a 0.5 N solution of $KMnO_4$ in 3 M $H_2SO_4$ for 24 h, washed with a diluted aq. solution of oxalic acid, aq. 5% $NaHCO_3$ solution, dried ($MgSO_4$) and distilled from $P_4O_{10}$. Anhydrous diethyl ether and THF were obtained by distillation from sodium/benzophenone, $CH_2Cl_2$, DMSO and pyridine from $CaH_2$, ethanol and methanol from the corresponding magnesium alkoxides. Oxygen was dried by passing it through a glass tube packed with $P_4O_{10}$ on glass wool, ammonia was recondensed through a glass column packed with KOH pellets. All other chemicals were used as commercially available (Merck, Acros, BASF, Bayer, Clariant, Degussa AG, and Hüls AG). All operations in anhydrous solvents were performed under argon in flame-dried glassware. Organic extracts were dried over $MgSO_4$. The compositions of solvent mixtures are given as volume per volume. $^1$H and $^{13}$C NMR spectra were recorded at 250, 270, 300, 500, 600 ($^1$H), and 50.3, 62.9, 75.5, 100.6 MHz [$^{13}$C, additional DEPT (Distortionless Enhancement by Polarization Transfer)] on Inova 600, Inova 500, Mercury 300, Bruker AM 250, Unity 200 and Mercury 200 instruments, respectively, in $CDCl_3$ or $CD_2Cl_2$ solutions, $CHCl_3/CDCl_3$ or $CH_2Cl_2/CD_2Cl_2$ as internal references; $\delta$ in ppm, $J$ in Hz. Mass spectra (EI) were measured with Varian MAT 112 and Finnigan MAT 95 spectrometers at 70 eV, DCI with $NH_3$. 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. GC analyses were performed with a Varian CP-3380 instrument using a 25 m capillary column with CP-Sil-5-CB. Preparative GC separations were performed on Intersmat 130 and Varian Aerograph 920 instruments (20% SE 30 on Chromosorb W-AW-DMCS, 1200×8.2 mm column, or 15% OV101 on Chromosorb W-AW-DMCS, 1500×9.4 mm column).

**1,1-Dibromo-2-cyclopropylcyclopropane (6)**:[27] To a vigorously stirred pre-cooled (−10 °C) solution of vinylcyclopropane (35.0 g, 514 mmol), $CHBr_3$ (227.46 g, 78.7 mL, 900 mmol) and benzyltriethylammonium chloride (TEBACl, 1.14 g, 4.1 mmol) in anhydrous $CH_2Cl_2$ (500 mL) was added in three portions KOH (pellets, 196.0 g, 3.49 mol), and the resulting mixture was stirred for 2 h maintaining the temperature at 20–25 °C by external cooling. Pentane (500 mL) was added and, after stirring for an additional 0.5 h, the mixture was filtered through a pad of Celite (0.5 cm) and silica gel (1 cm), then concentrated under reduced pressure. Distillation under reduced pressure furnished dibromide **6** (101.6 g, 82%) as a colorless liquid with b.p. 77–78 °C (20 mbar) [lit.:[27] yield 51%, b.p. 76 °C (14 Torr)]. Its NMR spectra were identical to the reported ones.[27]

**Preparation of bis(bicyclopropylidenyl)s *meso*-5, *d,l*-5, *meso*-10 and *d,l*-10**

**General procedure GP 1**: *n*BuLi (15 mmol as a solution in hexane) and the respective hydrocarbon **3** or **9** (15 mmol) were mixed in anhydrous THF (40 mL) at −78 °C. After having been stirred at 0 °C for 1 h, the solution was cooled to −100 °C, and CuCN (7.5 mmol) or [$CuIBu_3P]_4$ (1.88 mmol) was added in one portion. The mixture was allowed to warm to −40 °C over a period of 15 min, and stirred at this temperature for an additional 15 min until a clear solution had formed. After this, the reaction mixture was recooled to −78 °C, and a slow stream of oxygen was passed through the mixture with stirring for 0.5 h. The mixture was allowed to warm to 0 °C, diluted with pentane (40 mL) and poured into ice-cold water. The organic phase was washed with sat. aq. $NH_4Cl$ solution and brine (50 mL each), dried and carefully concentrated under reduced pressure at 0 °C. The product was purified as indicated below.

***meso*-Bis(bicyclopropylidenyl) (*meso*-5) and *d,l*-bis(bicyclopropylidenyl) (*d,l*-5)**: a) Column chromatography ($R_f$ = 0.57, 30 g silica gel, 3.5×12 cm column, hexane) of the residue (825 mg) obtained from bicyclopropylidene (**3**) (1.03 g, 1.20 mL, 12.8 mmol), *n*BuLi (13.0 mmol, 7.9 mL of a 1.64 M solution in hexane) and CuCN (560 mg, 6.25 mmol) in THF (50 mL) according to GP 1 gave a 1.6:1 mixture of *meso*-**5** and *d,l*-**5** (375 mg, 37%) as a wax.

b) Column chromatography ($R_f$ = 0.57, 30 g silica gel, 3.5×12 cm column, hexane) of the residue (1.34 g) obtained from bicyclopropylidene (**3**) (504 mg, 0.59 mL, 6.29 mmol), *n*BuLi (6.30 mmol, 3.84 mL of a 1.64 M solution in hexane) and [$CuIBu_3P]_4$ (1.235 g, 786 μmol) in THF (50 mL) according to GP 1 gave a 1.6:1 mixture of *meso*-**5** and *d,l*-**5** (404 mg, 81%) as a wax. This was taken up with diethyl ether (2.3 mL), and the resulting solution was allowed to stand at −20 °C over two days. The formed precipitate was quickly filtered off while the mixture was still cold to give *meso*-**5** (189 mg, 38%) as a colorless solid, m.p. 49–52 °C. Evaporation of the mother liquor furnished a sample enriched in *d,l*-**5**, an analytical sample of which was obtained by preparative GC at 100 °C.

In another run, the 1.6:1 mixture of *meso*-**5**/*d,l*-**5** (329 mg) was separated by column chromatography on silica gel impregnated with 5% of silver nitrate (30 g of silica gel, 3×15 cm column, hexane/$Et_2O$ 150:1) to give pure *meso*-**5** (95 mg) and *d,l*-**5** (88 mg).

c) The reaction mixture which was obtained from dibromide **14** (15.36 g, 48.1 mmol) and *t*BuOK (11.9 g, 106 mmol) in DMSO (200 mL) according to GP 4 (24 h stirring at ambient temperature, see below) was poured into ice-cold water (200 mL) and extracted with hexane (3×100 mL). The combined organic phases were washed with water (3×100 mL), dried and carefully concentrated under reduced pressure at 0 °C. Column chromatography of the residue ($R_f$ = 0.57, 10 g silica gel, 2×10 cm column, hexane) gave a 1:1 mixture of *meso*-**5** and *d,l*-**5** (130 mg, 1.7%) as a wax. *meso*-**5**: $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 2.01–1.96 (m, 2H; 2CH), 1.41–1.20 (m, 8H; 4$CH_2$), 1.10–0.69 (m, 4H; 2$CH_2$); $^{13}$C NMR (50.3 MHz, $CDCl_3$): $\delta$ = 113.7 (2C), 110.2 (2C), 16.3 (2 CH), 7.2 (2$CH_2$), 3.0 (2$CH_2$), 2.8 (2$CH_2$).

*d,l*-**5**: $^1$H NMR (200 MHz, $CDCl_3$): $\delta$ = 1.90–1.78 (m, 2H; 2CH), 1.40–1.27 (m, 4H; 2$CH_2$), 1.16–0.97 (m, 8H; 4$CH_2$); $^{13}$C NMR (50.3 MHz, $CDCl_3$): $\delta$ = 112.9 (2C), 110.7 (2C), 17.0 (2CH), 9.9 (2$CH_2$), 3.0 (4$CH_2$).

***meso*-2,2′-Bis[(dispiro[2.0.2.1]hept-7-ylidene)cyclopropyl] (*meso*-10) and *d,l*-2,2′-bis[(dispiro[2.0.2.1]hept-7-ylidene)cyclopropyl] (*d,l*-10)**: Column chromatography ($R_f$ = 0.27, 5 g silica gel, 1.5×6.5 cm column, hexane) of the residue (227 mg) obtained from 7-cyclopropylidenedispiro-[2.0.2.1]heptane (**9**) (275 mg, 2.08 mmol), *n*BuLi (2.08 mmol, 1.27 mL of a 1.64 M solution in hexane) and CuCN (93 mg, 1.04 mmol) in THF (20 mL) according to GP 1 gave a 1:1 mixture of *meso*-**10** and *d,l*-**10** (57 mg, 21%) as a wax. The two diastereomers were separated by twofold column chromatography (34 g flash silica gel, 3×11 cm column, hexane). *meso*-**10**: colorless oil; $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 1.86–

1.78 (m, 2H; 2CH), 1.20–0.80 (m, 20H; 10 $CH_2$); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): $\delta$ = 120.6 (2C), 106.6 (2C), 15.9 (2C), 15.8 (2C), 15.3 (2CH), 8.5 ($2CH_2$), 8.45 ($2CH_2$), 8.3 ($2CH_2$), 8.0 ($2CH_2$), 6.5 ($2CH_2$).

*d*,*l*-**10**: colorless oil, $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 1.76–1.68 (m, 2H; 2CH), 1.30–0.76 (m, 20H; $10CH_2$); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): $\delta$ = 121.1 (2C), 106.2 (2C), 16.6 (2CH), 15.9 (2C), 15.7 (2C), 8.8 ($2CH_2$), 8.7 ($2CH_2$), 8.22 ($2CH_2$), 8.2 ($2CH_2$), 8.1 ($2CH_2$); MS (DCI): *m*/*z* (%): 298/297 (12/55) [$M$+$NH_4^+$+$NH_3$], 281/280 (20/100) [$M$+$NH_4^+$], 264/263 (2/10) [$M$+H]$^+$, 248 (4), 247 (15).

***meso*-Tetradecadeuteriobis(bicyclopropylidenyl) (*meso*-[$D_{14}$]-5) and *d*,*l*-tetradeca-deuteriobis(bicyclopropylidenyl) (*d*,*l*-[$D_{14}$]-5)**: Column chromatography (20 g silica gel, 2.0×20 cm column, hexane) of the residue obtained from octadeuteriobicyclopropylidene ([$D_8$]-**3**) (2.0 mL, 19.37 mmol), *n*BuLi (38.78 mmol, 15.7 mL of a 2.47 M solution in hexane) and CuCN (867 mg, 9.69 mmol) in THF (50 mL) according to GP 1, but the mixture of [$D_8$]-**3** and *n*BuLi was stirred at ambient temperature for 1 h, gave a 1:1 mixture of *meso*-[$D_{14}$]-**5** and *d*,*l*-[$D_{14}$]-**5** (1.36 g, 82%) as a wax. The composition of this mixture was determined by GC in comparison with non-deuterated analogues. Repeated column chromatography (30 g silica gel impregnated with 5% $AgNO_3$, 2.8×14 cm column, hexane/$Et_2O$ 150:1) gave pure *meso*-[$D_{14}$]-**5** (352 mg) and *d*,*l*-[$D_{14}$]-**5** (123 mg).

*meso*-[$D_{14}$]-**5**: colorless oil; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ = 113.6 (2C), 110.0 (2C), 15.6 (t, $J$ = 24.8 Hz, 2CH), 6.4 (p, $J$ = 24.8 Hz, $2CH_2$), 2.1 (p, $J$ = 24.8 Hz, $2CH_2$), 1.9 (p, $J$ = 24.8 Hz, $2CH_2$); MS (EI): *m*/*z* (%): 170 (3) [$M^+$−D], 154 (9) [$M^+$−$CD_2$−D], 152 (18) [$M^+$−$CD_2$−2D], 150 (16), 138 (42) [$M^+$−$C_2D_4$−D], 136 (100) [$M^+$−$C_2D_4$−2D], 126 (57), 122 (71) [$C_9D_7^+$], 110 (18), 98 (85) [$C_7D_7^+$], 84 (31) [$C_6D_6^+$], 82 (38) [$C_5D_{11}^+$], 70 (29) [$C_5D_5^+$], 54 (28), 42 (46).

*d*,*l*-[$D_{14}$]-**5**: colorless oil; $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ = 112.8 (2C), 110.6 (2C), 16.2 (t, $J$ = 24.8 Hz, 2CH), 9.1 (p, $J$ = 24.8 Hz, $2CH_2$), 2.16 (p, $J$ = 24.8 Hz, $2CH_2$), 2.12 (p, $J$ = 24.8 Hz, $2CH_2$).

**Diethyl bicyclopropyl-2,2′-dicarboxylate (12)**: This compound was prepared applying the previously reported protocol,[44] but with $[Rh(OAc)_2]_2$ as a catalyst.[45] A 100 mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar, a thermometer and a reflux condenser cooled with dry ice, was charged with a solution of butadiene (**11**) (8.12 g, 13.1 mL, 150.1 mmol) in anhydrous dichloromethane (50 mL) and dirhodium tetraacetate (199 mg, 450 μmol, 0.3 mol%). Under stirring was added ethyl diazoacetate (17.14 g, 15.8 mL, 150.2 mmol) at −5 to 0 °C over a period of 0.5 h. The same portion ethyl diazoacetate was added over a period of 12 h at this temperature. The reaction mixture was filtered through a pad of silica gel and concentrated under reduced pressure. The residue was distilled in vacuo to give **12** (29.60 g, 87%) as a mixture of isomers. **12**: colorless liquid; b.p. 99–102 °C (2 mbar) [lit.[43] 110–115 °C (3 Torr)]; $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 4.20–3.95 (m, 4H; $2OCH_2$), 1.75–1.55 (m, 1H; *c*Pr-H), 1.55–1.30 (m, 3H; *c*Pr-H), 1.30–1.12 (m, 6H; $2CH_3$), 1.12–0.85 (m, 3H; *c*Pr-H), 0.85–0.60 (m, 1H; *c*Pr-H); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): $\delta$ = 173.4, 172.7, 172.4, 171.9, 171.8 (C), 60.3, 60.2, 60.1 ($CH_2$), 23.5, 23.2, 22.8, 22.7, 20.0, 19.97, 19.8, 19.5, 19.2, 19.1, 19.0, 18.7, 18.6, 18.5 (CH), 14.1, 14.0, 13.9, 13.8 ($CH_3$), 15.4, 14.8, 13.7, 12.9, 12.8, 12.5 ($CH_2$).

**(*Z*)-*cis*-2,2′-Dicyclopropylbicyclopropylidene [(*Z*)-*cis*-16]**: To a solution of 1,1-dibromo-2-cyclopropylcyclopropane (**6**) (3.60 g, 15.0 mmol) in anhydrous THF (30 mL), anhydrous $CuCl_2$ (202 mg, 1.5 mmol) was added in one portion, and the resulting slurry was cooled to −100 °C. *n*BuLi (15.0 mmol, 5.77 mL of a 2.60 M solution in hexane) was added dropwise at this temperature over a period of 1 h. The resulting mixture was stirred at this temperature for an additional 1 h, then allowed to warm to room temperature over 1 h. The reaction mixture was diluted with $Et_2O$ (100 mL) and then poured into an ice-cold mixture of sat. aq. $NH_4Cl$ solution (100 mL). The aqueous layer was extracted with the same solvent (2×50 mL), the combined organic phases were washed with $H_2O$ (1×50 mL), brine (1×50 mL), dried and concentrated under reduced pressure at 0 °C to give crude **16** (1.63 g, 69%) as a mixture of four stereoisomers from which (*Z*)-*cis*-**16** (603 mg, 26%) was isolated by preparative gas chromatography. (*Z*)-*cis*-**16**: oil, $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 1.64–1.55 (m, 2H), 1.26–1.16 (m, 2H), 1.00–0.82 (m, 4H), 0.45–0.25 (m, 4H; $CH_2$), 0.25–0.08 (m, 4H; $CH_2$); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): $\delta$ = 114.0 (2C), 18.10 (2CH), 11.8 (2CH), 7.8 ($2CH_2$), 3.4 ($2CH_2$), 2.0 ($2CH_2$).

**Hexadeuterio-γ-butyrolactone ([$D_6$]-24)**: To a vigorously stirred solution of $Ca(OCl)_2$ (71.0 g, 497 mmol) in $H_2O$ (400 mL) was added dropwise a solution of octadeuteriotetrahydrofuran ([$D_8$]-**23**) (19.7 g, 20 mL, 246 mmol) in a 3:2 mixture of MeCN and AcOH (250 mL) at 0 °C over a period of 30 min, and the mixture was stirred at ambient temperature for an additional 22 h. The reaction mixture was diluted with water (400 mL) and extracted with $CH_2Cl_2$ (4×200 mL). The combined extracts were washed with sat. aq. $NaHCO_3$ solution and $H_2O$ (200 mL each), dried and concentrated using a 100 cm rectification column. The residue was distilled under reduced pressure to give [$D_6$]-**24** (14.45 g, 63%) as a colorless liquid, b.p. 75 °C (14 mbar). $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ = 177.8 (C), 67.7 (p, $J$ = 23.5 Hz, $CD_2$), 27.0 (p, $J$ = 20.5 Hz, $CD_2$), 21.1 (p, $J$ = 20.8 Hz, $CD_2$).

**Ethyl 4-Chlorohexadeuteriobutanoate ([$D_6$]-25)**: Lactone [$D_6$]-**24** (26.5 g, 288 mmol) was stirred under reflux in thionyl chloride (35.97 g, 22.0 mL, 302 mmol) for 3 h, and the mixture then cooled to ambient temperature. Anhydrous EtOH (14.62 g, 18.5 mL, 317 mmol) was added dropwise at this temperature, and the reaction mixture was stirred under reflux for 1.5 h again, cooled to ambient temperature and concentrated under reduced pressure at 0 °C. Distillation of the residue under reduced pressure furnished [$D_6$]-**25** (30.7 g, 69%) as a colorless liquid, b.p. 74–75 °C (22 mbar). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 4.08 (q, $J$ = 7.2 Hz, 2H; $OCH_2$), 1.21 (t, $J$ = 7.2 Hz, 3H; $CH_3$); $^{13}C$ NMR (75.5 MHz, $CDCl_3$): $\delta$ = 172.7 (C), 60.5 ($CH_2$), 43.3 (p, $J$ = 21.2 Hz, $CD_2$), 32.2 (p, $J$ = 20.4 Hz, $CD_2$), 27.0 (p, $J$ = 19.8 Hz, $CD_2$), 14.1 ($CH_3$).

**Ethyl 2,2,3,3-tetradeuteriocyclopropanecarboxylate ([$D_4$]-26)**: To a stirred solution of sodium ethanolate [prepared from Na (5.03 g, 219 mmol) in anhydrous EtOH (60 mL)] was added dropwise [$D_6$]-**25** (30.7 g, 196 mmol) over a period of 1.5 h, and the resulting mixture was stirred under reflux for 1 h. After cooling to 0 °C, the reaction mixture was carefully brought to pH ≈6 by adding a 10 M aq. $H_2SO_4$ solution, diluted with $H_2O$ (100 mL) and extracted with benzene (2×100 mL). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (2×100 mL), brine (100 mL), dried and concentrated at ambient pressure applying a 10 cm Vigreux column. The residue was distilled at ambient pressure with a 10 cm Vigreux column to give [$D_4$]-**26** (13.6 g, 58%) as a colorless liquid, b.p. 133 °C. $^1H$ NMR (250 MHz, $CDCl_3$): $\delta$ = 4.13 (q, $J$ = 7.1 Hz, 2H; $OCH_2$), 2.47 (s, 1H; CH), 1.17 (t, $J$ = 7.1 Hz, 3H; $CH_3$); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): $\delta$ = 174.9 (C), 60.3 ($CH_2$), 14.2 ($CH_3$), 12.5 (CH), 7.5 (p, $J$ = 25.1 Hz, 2 $CD_2$); MS (EI): *m*/*z* (%): 119 (6) [$M^+$ (from $C_3D_5CO_2Et$)], 118 (10) [$M^+$], 91 (22), 90 (21), 74 (46) [$M^+$−$C_2H_5O$ (from $C_3D_5CO_2Et$)], 73 (100) [$M^+$−$C_2H_5O$], 46 (17), 45 (31) [$C_2H_5O^+$].

**Preparation of [1,1′;2′,1″;2″,1‴]quatercyclopropane-1,1‴-diol (13) and [$D_8$]-1-cyclopropylcyclopropanol ([$D_8$]-27)**

**General procedure GP 2**: To the well stirred solution of the respective diester **12** or ester [$D_4$]-**26** (80 mmol) and titanium tetraisopropoxide (20 mol% for each ethoxycarbonyl group) in anhydrous diethyl ether (100 mL), was added the indicated quantity of ethylmagnesium bromide at 20–25 °C over a period of 2 h. After stirring for an additional 1 h at the same temperature, the reaction mixture was cooled to −5 °C, and the reaction quenched by careful addition of 250 mL of ice-cold 10% aq. sulfuric acid while the temperature was maintained between −5 and 0 °C. The mixture was stirred at 0 °C for an additional 1 h, the ethereal phase was washed with sat. aq. $NaHCO_3$ (2×100 mL), brine (100 mL), dried and concentrated under reduced pressure to give crude **13** or [$D_8$]-**27** which were used without further purification.

**[1,1′;2′,1″;2″,1‴]Quatercyclopropane-1,1‴-diol (13)**: From the diester **12** (18.1 g, 80 mmol), $Ti(OiPr)_4$ (9.07 g, 9.5 mL, 32 mmol, 40 mol%) and EtMgBr (336 mmol, 96.8 mL of a 3.47 M solution in $Et_2O$), was obtained according to GP 2 a mixture of isomeric diols **13** (15.6 g, 99%) as an yellow oil.

**1-(2,2,3,3-Tetradeuteriocyclopropyl)-2,2,3,3-tetradeuteriocyclopropanol ([$D_8$]-27)**: From the ester [$D_4$]-**26** (13.6 g, 115 mmol), $Ti(OiPr)_4$ (6.542 g, 6.85 mL, 23.0 mmol, 20 mol%) and $C_2D_5MgBr$ [prepared in anhydrous $Et_2O$ (100 mL) from magnesium (7.82 g, 322 mmol) and $C_2D_5Br$ (32.90 g,

21.5 mL, 288 mmol) which in turn was prepared from the less expensive $C_2D_5OH$ according to a published procedure[46] in 57% yield], was obtained according to GP 2 [$D_8$]-**27** (8.78 g, 72%) as a yellow oil.

**Preparation of quatercyclopropane dibromide 14 and bromide [$D_8$]-28**

**General procedure GP 3**: To a solution of triphenylphosphane (26.23 g, 100 mmol) in anhydrous dichloromethane (100 mL) was added bromine (15.98 g, 5.15 mL, 100 mmol) under vigorous stirring at −30 to −15 °C over a period of 0.5 h. After an additional 15 min of stirring, a mixture of the respective diol (47.5 mmol) or alcohol (95 mmol) and anhydrous pyridine (7.52 g, 95 mmol) was added dropwise at −15 °C over a period of 1 h. The reaction mixture was stirred at ambient temperature for the indicated time and worked up as indicated below.

**1,1‴-Dibromo [1,1′;2′,1″;2″,1‴]quatercyclopropane (14)**: The reaction mixture obtained from diol **13** (15.60 g, 80 mmol), $Ph_3P$ (44.6 g, 170 mmol), $Br_2$ (27.08 g, 8.7 mL, 170 mmol) and pyridine (13.40 g, 13.7 mL, 170 mmol) according to GP 3 (24 h stirring at ambient temperature) was concentrated under reduced pressure. The residue was vigorously stirred with pentane (400 mL), the solids were filtered off, and the solution concentrated under reduced pressure. This operation was repeated twice with 300 and 200 mL of pentane, respectively, to give a crude mixture of isomeric dibromides **14** (15.36 g, 60%) as a yellow oil, which was used without further purification.

**1-Bromo-1-(2,2,3,3-tetradeuteriocyclopropyl)-2,2,3,3-tetradeuteriocyclopropane ([$D_8$]-28)**: All the volatile material from the reaction mixture, which was obtained from the cyclopropanol [$D_8$]-**27** (8.78 g, 82.7 mmol), $Ph_3P$ (23.9 g, 91.0 mmol), $Br_2$ (13.88 g, 4.46 mL, 86.8 mmol) and pyridine (6.87 g, 7.02 mL, 86.8 mmol) according to GP 3 (after 48 h of stirring at ambient temperature), was "bulb-to-bulb" distilled into a cold trap (−78 °C) at first under water-aspirator vacuum and 30 °C oil bath temperature, then under further reduced pressure (0.1 Torr) with a 120 °C oil bath. The distillation was continued until the temperature in the reaction flask reached 90 °C. The receiver flask was allowed to warm up to 20 °C, and the solvent was removed by distillation at ambient pressure using a 10 cm Vigreux column. The residue was distilled under reduced pressure to give [$D_8$]-**28** (10.0 g, 72%) as a colorless liquid, b.p. 65 °C (120 mbar). $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta = 36.7$ (C), 20.1 (CH), 13.7 (p, $J = 24.5$ Hz, $2CD_2$), 5.3 (p, $J = 25.1$ Hz, $2CD_2$).

**Preparation of bis(bicyclopropylidenyl)s *meso*-5, *d,l*-5 and octadeuteriobicyclopropylidene ([$D_8$]-3)**

**General procedure GP 4**: To a vigorously stirred solution of potassium *tert*-butoxide (60 mmol) in anhydrous DMSO (100 mL) was added dropwise the respective dibromide (25 mmol) or bromide (50 mmol). The temperature was maintained between 20 and 25 °C with a water bath. The reaction mixture was stirred at ambient temperature for the indicated time and worked up as indicated below.

**Octadeuteriobicyclopropylidene ([$D_8$]-3)**: All the volatile material from the reaction mixture, which was obtained from bromide [$D_8$]-**28** (10.0 g, 59.1 mmol) and *t*BuOK (7.99 g, 71.2 mmol) in DMSO (80 mL) according to GP 4 (48 h of stirring at ambient temperature), was "bulb-to-bulb" distilled to a cold trap (−78 °C) at first under water-aspirator vacuum and 30 °C oil bath temperature, then under further reduced pressure (0.1 Torr) with a 50 °C oil bath. The receiver flask was allowed to warm up to 20 °C, its contents was washed with three 10 mL portions of ice-cold water and transferred into a pre-weighed glass bottle containing some molecular sieve 4 Å, to yield of [$D_8$]-**3** (4.89 g, 94%), a colorless liquid of 95% purity (according to GC analysis). $^{13}$C NMR (62.9 MHz, $CDCl_3$): $\delta = 110.2$ (2C), 2.1 (p, $J = 24.7$ Hz, $4CD_2$).

**Preparation of quatercyclopropanes by Birch reduction**

**General procedure GP 5**: A 50 mL, three-necked, round-bottomed flask equipped with a magnetic stirring bar, a thermometer and a reflux condenser cooled with dry ice was charged with liquid ammonia (30 mL). Ammonia was dried by stepwise addition of lithium in milligram quantities until a persisting blue color had appeared. Then lithium (3–4 equiv per double bond) was added in one portion, and the mixture was stirred until the lithium had completely dissolved. A solution of the respective diene or monoene (0.5–1 mmol) in diethyl ether or THF was added dropwise at −78 °C, and the reaction mixture was stirred at this temperature for an additional 1.5 h. The reaction was quenched by addition of several drops of MeOH to the mixture, allowed to warm up to −35 °C and diluted with hexane (10 mL). After careful evaporation of the ammonia, ice-cold water (10 mL) was added to the residue, and the reaction mixture was extracted with pentane (3 × 10 mL). The combined extracts were dried, filtered through a pad of silica gel and concentrated under reduced pressure.

**(1′*R**,2′*S**,1″*R**,2″*S**)-Quatercyclopropane [(*R**,*S**,*R**,*S**)-17] and (1′*R**,2′*S**,1″*R**, 2″*R**)-quatercyclopropane [(*R**,*S**,*R**,*R**)-18]**: From a solution of *meso*-**5** (100 mg, 0.632 mmol) in $Et_2O$ (6 mL) and Li (26.3 mg, 3.79 mmol) in liq. $NH_3$ (30 mL) was obtained a 9:1 mixture (100 mg, 97%) of (*R**,*S**,*R**,*S**)-**17** and (*R**,*S**,*R**,*R**)-**18** according to GP 5 as a colorless oil. (*R**,*S**,*R**,*S**)-**17**: $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 0.76$–0.68 (m, 2H), 0.52–0.44 (m, 4H), 0.32–0.22 (m, 4H), 0.10–0.02 (m, 4H), −0.02 to −0.08 (m, 4H); $^{13}$C NMR (50.3 MHz, $CDCl_3$): $\delta = 18.7$ (2CH), 18.1 (2CH), 12.1 (2CH), 8.2 ($2CH_2$), 3.0 ($2CH_2$), 2.8 ($2CH_2$).

(*R**,*S**,*R**,*R**)-**18**: $^1$H NMR: cannot be unequivocally attributed. $^{13}$C NMR (62.9 MHz, $CDCl_3$): $\delta = 19.9$ (CH), 19.8 (CH), 19.1 (CH), 15.5 (CH), 12.1 (CH), 10.1 ($CH_2$), 9.6 (CH), 8.6 ($CH_2$), 4.8 ($CH_2$), 4.5 ($CH_2$), 3.0 ($CH_2$), 2.5 ($CH_2$).

**(1′*R**,2′*S**,1″*S**,2″*R**)-Quatercyclopropane [(*R**,*S**,*S**,*R**)-19] and (1′*R**,2′*S**,1″*S**,2″*S**)-quatercyclopropyl [(*R**,*S**,*S**,*S**)-20]**: From a solution of *d,l*-**5** (76 mg, 0.480 mmol) in THF (2 mL) and Li (20.0 mg, 2.88 mmol) in liq. $NH_3$ (20 mL) was obtained a 9:1 mixture (59.0 mg, 76%) of (*R**,*S**,*S**,*R**)-**19** and (*R**,*S**,*S**,*S**)-**20** according to GP 5 as a colorless oil. (*R**,*S**,*S**,*R**)-**19**: $^1$H NMR (250 MHz, $CDCl_3$): $\delta = 0.80$–0.68 (m, 2H), 0.57–0.47 (m, 4H), 0.32–0.23 (m, 4H), 0.12–0.01 (m, 4H), 0.00 to −0.05 (m, 4H); $^{13}$C NMR (62.9 MHz, $CDCl_3$): $\delta = 18.8$ (2CH), 18.0 (2CH), 12.1 (2CH), 8.0 ($2CH_2$), 3.0 ($2CH_2$), 2.8 ($2CH_2$). Unfortunately, attempted separation of enantiomers of **19** by preparative HPLC on a Chiralcel OD-H column, eluent hexane/ethanol 95:5, UV detector JASCO MD-2010, was unsuccessful.[47]

For the NMR data of hydrocarbon (*R**,*S**,*S**,*S**)-**20** see below.

**(1′*R**,2′*S**,1″*R**,2″*S**)-2,2,3,3,2′,3′,3′,1″,3″,3″,2‴,2‴,3‴,3‴-Tetradecadeuterioquatercyclopropane {(*R**,*S**,*R**,*S**)-[$D_{14}$]-17} and (1′*R**,2′*S**,1″*R**,2″*R**)-2,2,3,3,2′,3′,3′,1″,3″,3″,2‴,2‴,3‴,3‴-tetradecadeuterioquatercyclopropane {(*R**,*S**,*R**,*R**)-[$D_{14}$]-18}**: From a solution of *meso*-[$D_{14}$]-**5** (352 mg, 2.04 mmol) in THF (7 mL) and Li (85 mg, 12.25 mmol, 3 equiv) in liq. $NH_3$ (30 mL), and after purification by column chromatography (50 g of silica gel, 3 × 14 cm column, pentane) was obtained a 8:1 mixture (133 mg, 37%) of (*R**,*S**,*R**,*S**)-[$D_{14}$]-**17** and (*R**,*S**,*R**,*R**)-[$D_{14}$]-**18** according to GP 5 as an oil. (*R**,*S**,*R**,*S**)-[$D_{14}$]-**17**: $^1$H NMR (600 MHz, $CD_2Cl_2$): $\delta = 0.70$ (d, $J = 4.1$ Hz, 2H; CH), 0.46 (d, $J = 4.1$ Hz, 2H; CH); $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta = 18.2$ (2CH), 17.3 (t, $J = 24.0$ Hz, $2CD_2$), 11.6 (2CH), 7.4 (p, $J = 24.4$ Hz, $2CD_2$), 2.1 (p, $J = 24.4$ Hz, $2CD_2$), 1.9 (p, $J = 24.5$ Hz, $2CD_2$).

(*R**,*S**,*R**,*R**)-[$D_{14}$]-**18**: $^1$H NMR (600 MHz, $CD_2Cl_2$): $\delta = 0.64$ (d, $J = 5.9$ Hz, 2H; CH), 0.49 (d, $J = 5.9$ Hz, 2H; CH).

**(1′*R**,2′*S**,1″*S**,2″*R**)-2,2,3,3,2′,3′,3′,1″,3″,3″,2‴,2‴,3‴,3‴-Tetradecadeuterioquatercyclopropane {(*R**,*S**,*S**,*R**)-[$D_{14}$]-19} and (1′*R**,2′*S**,1″*S**,2″*S**)-2,2,3,3,2′,3′,3′,1″,3″,3″,2‴,2‴,3‴,3‴-tetradecadeuterioquatercyclopropane {(*R**,*S**,*S**,*S**)-[$D_{14}$]-20}**: From a solution of *d,l*-[$D_{14}$]-**5** (123 mg, 0.71 mmol) in THF (3 mL) and Li (30 mg, 4.3 mmol, 3 equiv) in liq. $NH_3$ (15 mL), and after purification by column chromatography (50 g of silica gel, 1.2 × 14 cm column, pentane) was obtained a 12:1 mixture (80 mg, 63%) of (*R**,*S**,*S**,*R**)-[$D_{14}$]-**19** and (*R**,*S**,*S**,*S**)-[$D_{14}$]-**20** according to GP 5 as a colorless oil. (*R**,*S**,*S**,*R**)-[$D_{14}$]-**19**: $^1$H NMR (600 MHz, $CD_2Cl_2$): $\delta = 0.70$ (d, $J = 4.7$ Hz, 2H; CH), 0.47 (d, $J = 4.7$ Hz, 2H; CH); $^{13}$C NMR (75.5 MHz, $CDCl_3$): $\delta = 18.4$ (2 CH), 17.2 (t, $J = 24.0$ Hz, 2CD), 11.6 (2CH), 7.2 (p, $J = 24.4$ Hz, $2CD_2$), 2.12 (p, $J = 24.4$ Hz, $2CD_2$), 1.95 (p, $J = 24.6$ Hz, $2CD_2$).

(*R**,*S**,*S**,*S**)-[$D_{14}$]-**20**: $^1$H NMR (600 MHz, $CD_2Cl_2$): $\delta = 0.63$ (d, $J = 5.9$ Hz, 2H; CH), the signals partly overlap with the signals of the major diastereomer.

**(1′*R**,2′*S**,1″*S**,2″*S**)-Quatercyclopropane [(*R**,*S**,*S**,*S**-20)]**: From a solution of (*Z*)-*cis*-**16** (241 mg, 1.50 mmol) in $Et_2O$ (10 mL) and Li (42 mg, 6.0 mmol, 4 equiv) in liq. $NH_3$ (50 mL) and after purification by

column chromatography (50 g of silica gel, 1.2×14 cm column, pentane) was obtained (*R**,*S**,*S**,*R**)-**20** (238 mg, 96%) as the sole product according to GP 5 as an oil. $^1$H NMR (250 MHz, $CDCl_3$): $\delta$=0.88–0.78 (m, 2H), 0.76–0.60 (m, 2H), 0.59–0.35 (m, 4H), 0.34–0.21 (m, 4H), 0.20–0.12 (m, 2H), 0.08–0.00 (m, 2H), −0.06 to −0.13 (m, 2H); $^{13}$C NMR (63.9 MHz, $CDCl_3$): $\delta$=20.4 (CH), 19.7 (CH), 19.3 (CH), 15.6 (CH), 12.3 (CH), 10.0 ($CH_2$), 9.7 (CH), 8.6 ($CH_2$), 4.8 ($CH_2$), 4.4 ($CH_2$), 2.85 ($CH_2$), 2.80 ($CH_2$).

**Catalytic hydrogenation of bis(bicyclopropylidenyl)s *meso*-5 and *d*,*l*-5**

**General procedure GP 6**: A stirred suspension of palladium on barium sulfate in MeOH was pre-hydrogenated for 30 min (hydrogen pressure 1 bar). The respective bis(bicyclopropylidenyl) was added, and the reaction mixture was stirred under the same pressure of hydrogen for the indicated time until the theoretically necessary volume of $H_2$ had been consumed. The reaction mixture was filtered through a pad of Celite and concentrated under reduced pressure.

**(1′*S**,2′*S**,1″*R**,2″*R**)-Quatercyclopropane [(*S**,*S**,*R**,*R**)-21]**: From *meso*-**5** (60.0 mg, 0.379 mmol) and 10% Pd/$BaSO_4$ (8.1 mg, 7.61 μmol, 2 mol%) in MeOH (5 mL) was obtained (*S**,*S**,*R**,*R**)-**21** (39.5 mg, 64%) according to GP 6 as a colorless oil; 17 mL of hydrogen had been consumed. (*S**,*S**,*R**,*R**)-**21**: $^1$H NMR (250 MHz, $CDCl_3$): $\delta$ = 0.98–0.35 (m, 12H), 0.24–0.12 (m, 4H), 0.02 to −0.06 (m, 2H); $^{13}$C NMR (62.9 MHz, $CDCl_3$): $\delta$=18.9 (2 CH), 15.7 (2CH), 10.0 (2$CH_2$), 9.5 (2CH), 4.6 (2$CH_2$), 4.3 (2$CH_2$); MS (DCI): *m*/*z* (%): 180 (17) $[M+NH_4]^+$, 163 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{12}H_{18}$ (162.3): C 88.82, H 11.18; found: C 88.62, H 11.26.

**(1′*R**,2′*R**,1″*R**,2″*R**)-Quatercyclopropane [(*R**,*R**,*R**,*R**)-22]**: From *d*,*l*-**5** (80.0 mg, 0.506 mmol) and 10% Pd/$BaSO_4$ (10.7 mg, 10.1 μmol, 2 mol%) in MeOH (10 mL) was obtained (*R**,*R**,*R**,*R**)-**22** (37.0 mg, 45%) according to GP 6 as a colorless oil; 23 mL of hydrogen had been consumed. (*R**,*R**,*R**,*R**)-**22**: $^1$H NMR (250 MHz, $CDCl_3$): $\delta$=0.98–0.35 (m, 12H), 0.26–0.10 (m, 4H), 0.04 to −0.06 (m, 2H); $^{13}$C NMR (62.9 MHz, $CDCl_3$): $\delta$=19.6 (2CH), 15.5 (2CH), 9.71 (2CH), 9.69 (2$CH_2$), 4.6 (2$CH_2$), 4.2 (2$CH_2$); MS (DCI): *m*/*z* (%): 180 (17) $[M+NH_4]^+$, 163 (100) $[M+H]^+$; elemental analysis calcd (%) for $C_{12}H_{18}$ (162.3): C 88.82, H 11.18; found: C 88.70, H 11.06.

**(1′*R**,2′*S**,1″*R**,2″*R**)-Quatercyclopropane [(*R**,*S**,*R**,*R**)-18] and (1′*S**,2′*S**,1″*R**,2″*R**)-quatercyclopropane [(*S**,*S**,*R**,*R**)-21]**: To a stirred solution of *meso*-**5** (180 mg, 1.14 mmol) in methanol (15 mL) was added in one portion 2-nitrobenzenesulfonyl hydrazide (2.151 g, 9.90 mmol, 8.7 equiv), and the resulting mixture was stirred at ambient temperature for 5 h. The reaction mixture was diluted with hexane (90 mL) and poured into ice-cold water (90 mL). The organic phase was washed with brine (2×90 mL), dried, filtered through a pad of silica gel and concentrated under reduced pressure to give a 1:2 mixture (160 mg, 87%) of (*R**,*S**,*R**,*R**)-**18** and (*S**,*S**,*R**,*R**)-**21** as a colorless oil. A sample of (*S**,*S**,*R**,*R**)-**21** for X-ray crystal structure analysis was isolated by preparative gas chromatography. Its NMR data were identical to those reported above.

**Crystal structure determinations**: Suitable single crystals of hydrocarbons *meso*-**5**, (*Z*)-*cis*-**16**, (*R**,*S**,*R**,*S**)-**17**, and (*S**,*S**,*R**,*R**)-**21** were grown *in situ* on the diffractometer in a Lindeman capillary, for *meso*-**5**, (*R**,*S**,*R**,*S**)-**17** and (*S**,*S**,*R**,*R**)-**21** with the help of the Optical Heating and Crystallization Device (OHCD), which uses a miniature zone melting procedure with focused IR-laser light.[48] The device was mounted on a four circle Nicolet R3m/V [*meso*-**5**, (*R**,*S**,*R**,*S**)-**17**, (*S**,*S**,*R**,*R**)-**21**] or Bruker SMART CCD 6000 [(*Z*)-*cis*-**16**] diffractometer, and the crystal formation detected using graphite monochromated $Mo_{K\alpha}$ radiation. Correction for the cylindrical shape of the crystals (0.5 mm diameter) was applied for *meso*-**5** and (*S**,*S**,*R**,*R**)-**21**. The structures were solved by direct methods and refinements on $F^2$ were performed with the Bruker AXS SHELXTL program suite (Version 5.10). The hydrogen atoms were located in the difference Fourier maps and refined isotropically. The parameters of the crystal data collections and structure refinements are compiled Table 2.

Table 2. Crystal and data collection parameters for compounds *meso*-**5**, (*Z*)-*cis*-**16**, *trans*,*trans*-(*R**,*S**,*R**,*S**)-**17** and *cis*,*cis*-(*S**,*S**,*R**,*R**)-**21**.

| Compound | *meso*-**5** | (*Z*)-*cis*-**16** | (*R**,*S**,*R**,*S**)-**17** | (*S**,*S**,*R**,*R**)-**21** |
|---|---|---|---|---|
| formula | $C_{12}H_{14}$ | $C_{12}H_{16}$ | $C_{12}H_{18}$ | $C_{12}H_{18}$ |
| molecular mass | 158.23 | 160.25 | 162.27 | 162.27 |
| crystal size [mm] | ∅0.5 | 1.00×0.20×0.20 | ∅0.3 | ∅0.5 |
| crystals | triclinic | monoclinic | triclinic | monoclinic |
| space group | $P\bar{1}$ | $P2_1/c$ | $P\bar{1}$ | $P2_1/n$ |
| $a$ [Å] | 5.0649(10) | 12.890(2) | 4.949(2) | 5.1770(10) |
| $b$ [Å] | 10.551(2) | 5.0530(8) | 6.664(3) | 7.585(2) |
| $c$ [Å] | 13.384(3) | 15.092(2 | 8.209(3) | 12.498(3) |
| $\alpha$ [°] | 75.370(2) | 90 | 72.28(3) | 90 |
| $\beta$ [°] | 79.332(2) | 99.08(2) | 81.30(3) | 96.86(3) |
| $\gamma$ [°] | 80.893(3) | 90 | 71.96(3) | 90 |
| $V$ [Å$^3$] | 675.4(2) | 970.7(4) | 244.69(17) | 487.3(2) |
| $Z$ | 3 | 4 | 1 | 2 |
| $F$(000) | 258 | 352 | 90 | 180 |
| $\rho$ [g cm$^{-3}$] | 1.167 | 1.097 | 1.101 | 1.106 |
| $\mu$ [mm$^{-1}$] | 0.065 | 0.061 | 0.061 | 0.060 |
| $T$ [K] | 113(2) | 230(1) | 150(2) | 113(2) |
| $\Theta_{max}$ [°] | 30 | 26 | 25 | 25 |
| refl. collected | 6604 | 6860 | 838 | 2059 |
| refl. independent | 3921 | 1895 | 838 | 853 |
| $R_{int}$ | 0.0218 | 0.0406 | 0.0315 | 0.0524 |
| w$R_2$(all data) | 0.1192 | 0.1652 | 0.1195 | 0.0957 |
| $R_1$ [$I$=2σ($I$)] | 0.0408 | 0.0540 | 0.0451 | 0.0364 |
| no. parameters refined | 247 | 173 | 55 | 91 |
| GOOF | 1.018 | 1.037 | 1.064 | 1.099 |
| largest diff. peak and hole [e Å$^{-3}$] | 0.570 and −0.209 | 0.168 and −0.196 | 0.158 and −0.165 | 0.115 and −0.148 |

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[1] Reviews: a) J. Salaün, M. S. Baird, *Curr. Med. Chem.* **1995**, *2*, 511–542; b) J. Salaün, *Top. Curr. Chem.* **2000**, *207*, 1–67; c) L. A. Wessjohann, W. Brandt, T. Thiemann, *Chem. Rev.* **2003**, *103*, 1625–1647.

[2] Some latest examples, see: a) F. Brackmann, M. Es-Sayed, A. de Meijere, *Eur. J. Org. Chem.* **2005**, 2250–2258; b) M. Kordes, M. Brands, M. Es-Sayed, A. de Meijere, *Eur. J. Org. Chem.* **2005**, 3008–3016; c) F. Brackmann, H. Schill, A. de Meijere, *Chem. Eur. J.* **2005**, *11*, 6593–6600.

[3] For some recent unusual examples see: a) E. Rössner, A. Zeeck, W. A. König, *Angew. Chem.* **1990**, *102*, 84–85; *Angew. Chem. Int.*

  

*Ed. Engl.* **1990**, *29*, 64–65; b) B. Zlatopolskiy, A. de Meijere, *Chem. Eur. J.* **2004**, *10*, 4718–4727; c) A. Asai, A. Hasegawa, K. Ochiai, Y. Yamashita, T. Mizukami, *J. Antibiot.* **2000**, *53*, 81–83; d) O. V. Larionov, A. de Meijere, *Org. Lett.* **2004**, *6*, 2153–2156; e) A. Armstrong, J. N. Scutt, *Chem. Commun.* **2004**, 510–511.

[4] Review: J. Pietruszka, *Chem. Rev.* **2003**, *103*, 1051–1070.

[5] M. Yoshida, M. Ezaki, M. Hashimoto, M. Yamashita, N. Shigematsu, M. Okuhara, M. Kohsaka, K. Horikoshi, *J. Antibiot.* **1990**, 748–754.

[6] M. S. Kuo, R. J. Zielinski, J. I. Cialdella, C. K. Marschke, M. J. Dupius, G. P. Li, D. A. Kloosterman, C. H. Spilman, V. P. Marshall, *J. Am. Chem. Soc.* **1995**, *117*, 10629–10634.

[7] a) C. R. Theberge, C. K. Zercher, *Tetrahedron Lett.* **1995**, *36*, 5495–5498; b) C. R. Theberge, C. K. Zercher, *J. Org. Chem.* **1996**, *61*, 8792–8798; c) W. S. McDonald, C. A. Verbicky, C. K. Zercher, *J. Org. Chem.* **1997**, *62*, 1215–1222.

[8] R. W. Armstrong, K. W. Maurer, *Tetrahedron Lett.* **1995**, *36*, 357–360.

[9] J. R. Falck, B. Mekonnen, J. Yu, J.-Y. Lai, *J. Am. Chem. Soc.* **1996**, *118*, 6096–6097.

[10] a) A. G. M. Barrett, G. J. Tustin, *J. Chem. Soc. Chem. Commun.* **1995**, 355–356; b) A. G. Barrett, K. Kasdorf, G. J. Tustin, D. J. Williams, *J. Chem. Soc. Chem. Commun.* **1995**, 1143–1144, and references therein.

[11] A. G. M. Barrett, K. Kasdorf, *J. Am. Chem. Soc.* **1996**, *118*, 11030–11037.

[12] A. G. M. Barrett, W. W. Doubleday, D. Hamprecht, K. Kasdorf, G. J. Tustin, A. J. P. White, D. J. Williams, *J. Chem. Soc. Chem. Commun.* **1997**, 1693–1700.

[13] a) A. G. M. Barrett, W. W. Doubleday, G. J. Tustin, *Tetrahedron* **1996**, *52*, 15325–15338; b) A. G. M. Barrett, W. W. Doubleday, K. Kasdorf, G. J. Tustin, *J. Org. Chem.* **1996**, *61*, 3280–3288; c) A. G. M. Barrett, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1996**, *118*, 7863–7864.

[14] a) A. B. Charette, H. Juteau, *J. Am. Chem. Soc.* **1994**, *116*, 2651–2652; b) A. B. Charette, S. Prescott, C. Brochu, *J. Org. Chem.* **1995**, *60*, 1081–1083; c) Review: H. Lebel, J.-F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev.* **2003**, *103*, 977–1050.

[15] a) A. G. M. Barrett, D. Hamprecht, R. A. James, M. Ohkubo, P. A. Procopiou, M. A. Toledo, A. J. P. White, D. J. Williams, *J. Org. Chem.* **2001**, *66*, 2187–2196; b) A. G. M. Barrett, R. A. James, G. E. Morton, P. A. Procopiou, C. Böhme, A. de Meijere, C. Griesinger, U. M. Reinscheid, *J. Org. Chem.* **2006**, *71*, 2756–2759.

[16] a) W. Lüttke, A. de Meijere, H. Wolff, H. Ludwig, H. W. Schrötter, *Angew. Chem.* **1966**, *78*, 141–142; *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 123–124; b) A. de Meijere, W. Lüttke, F. Heinrich, *Liebigs Ann. Chem.* **1974**, 306–327; c) M. Spiekermann, B. Schrader, A. de Meijere, W. Lüttke, *J. Mol. Struct.* **1981**, *77*, 1–17.

[17] a) O. Bastiansen, A. de Meijere, *Angew. Chem.* **1966**, *78*, 142–143; *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 124–125; b) O. Bastiansen, A. de Meijere, *Acta Chem. Scand.* **1966**, *20*, 516–521.

[18] Reviews: a) A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Zh. Org. Khim.* **1996**, *32*, 1607–1626; *Russ. J. Org. Chem. (Engl. Transl.)* **1996**, *32*, 1555–1575; b) A. de Meijere, S. I. Kozhushkov, A. F. Khlebnikov, *Top. Curr. Chem.* **2000**, *207*, 89–147; c) A. de Meijere, S. I. Kozhushkov, *Eur. J. Org. Chem.* **2000**, 3809–3822; d) 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.

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

[20] Reviews: a) B. H. Lipshutz, *Synlett* **1990**, 119–128; b) Y. Kai, P. Knochel, S. Kwiatkowski, J. D. Dunitz, J. F. M. Oth, D. Seebach, H. O. Kalinowski, *Helv. Chim. Acta* **1982**, *65*, 137–161.

[21] a) M. Borer, T. Loosli, M. Neuenschwander, *Chimia* **1991**, *45*, 382–386; b) T. Loosli, M. Borer, I. Kulakowska, A. Minder, M. Neuenschwander, P. Engel, *Helv. Chim. Acta* **1995**, *78*, 1144–1165; c) M. Borer, T. Loosli, A. Minder, M. Neuenschwander, P. Engel, *Helv. Chim. Acta* **1995**, *78*, 1311–1324; d) M. Borer, M. Neuenschwander, *Helv. Chim. Acta* **1997**, *80*, 2486–2501; e) R. Huwyler, X. Li, P. Bönzli, M. Neuenschwander, *Helv. Chim. Acta* **1999**, *82*, 1242–1249.

[22] a) H. Gilman, H. H. Parker, *J. Am. Chem. Soc.* **1924**, *46*, 2823; b) A. de Meijere, W. Lüttke, *Chem. Ber.* **1966**, *99*, 2155–2161.

[23] S. I. Kozhushkov, M. Brandl, D. S. Yufit, R. Machinek, A. de Meijere, *Liebigs Ann.* **1997**, 2197–2204.

[24] a) A. de Meijere, S. I. Kozhushkov, T. Späth, N. S. Zefirov, *J. Org. Chem.* **1993**, *58*, 502–505, and references therein; b) A. de Meijere, S. I. Kozhushkov, T. Späth, *Org. Synth.* **2000**, *78*, 142–151; c) in order to check the scope and limitations of this coupling method the bisspirocyclopropanated bicyclopropylidene **9** was converted into a mixture of the dehydrodimers *meso*- and *d*,*l*-**10**.

[25] Reviews: a) O. G. Kulinkovich, A. de Meijere, *Chem. Rev.* **2000**, *100*, 2789–2834; b) B. Breit, *J. Prakt. Chem.* **2000**, *342*, 211–214; c) F. Sato, H. Urabe, S. Okamoto, *Chem. Rev.* **2000**, *100*, 2835–2886; d) F. Sato, H. Urabe, S. Okamoto, *Synlett* **2000**, 753–775; e) A. de Meijere, S. I. Kozhushkov, A. I. Savchenko, in *Titanium and Zirconium in Organic Synthesis* (Ed.: I. Marek), Wiley-VCH, Weinheim **2002**, pp. 390–434; f) O. Kulinkovich, *Eur. J. Org. Chem.* **2004**, 4517–4529.

[26] Review: C. M. Williams, L. N. Mander, *Tetrahedron* **2001**, *57*, 425–447.

[27] a) W. R. Roth, T. Schmidt, H. Humbert, *Chem. Ber.* **1975**, *108*, 2171–2175; b) W. E. Farneth, M. W. Thomsen, *J. Org. Chem.* **1982**, *47*, 4851–4855.

[28] A. de Meijere, M. von Seebach, S. Zöllner, S. I. Kozhushkov, V. N. Belov, R. Boese, T. Haumann, J. Benet-Buchholz, D. S. Yufit, J. A. K. Howard, *Chem. Eur. J.* **2001**, *7*, 4021–4034.

[29] CCDC-606384 (*meso*-**5**), -606106 [(*Z*)-*cis*-**16**], -606385 [*trans*,*trans*-quatercyclopropane (*R**S**R**S**)-**17**] and -606386 [*cis*,*cis*-quatercyclopropane (*S**S**R**R**)-**21**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[30] a) D. Nijveldt, A. Vos, *Acta Crystallogr. Sect. B* **1988**, *44*, 281–289, 289–296, 296–307; b) J. Eraker, C. Rømming, *Acta Chem. Scand.* **1967**, *21*, 2721–2726.

[31] a) K. Hagen, G. Hagen, M. Traetteberg, *Acta Chem. Scand.* **1972**, *26*, 3649–3661; b) O. Bastiansen, M. Traetteberg, *Tetrahedron* **1962**, *17*, 147–154.

[32] For computational studies of this phenomenon see also: a) H. Braun, W. Lüttke, *J. Mol. Struct.* **1976**, *31*, 97–129; b) R. Stölevik, P. Bakken, *J. Mol. Struct.* **1989**, *197*, 137–142; c) K. Kovacević, Z. B. Maksić, *J. Org. Chem.* **1974**, *39*, 539–545; d) J.-Y. Yeh, S. Saebo, *THEOCHEM* **1995**, *334*, 155–163, and references therein.

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

[34] N. J. Cusack, C. B. Reese, A. C. Risius, B. Roozpeikar, *Tetrahedron* **1976**, *32*, 2157–2162.

[35] S. O. Nwaukwa, P. M. Keehn, *Tetrahedron Lett.* **1982**, *23*, 35–38. The yield of non-deuterated **24** was 68%.

[36] S. C. Bunce, R. A. Kent, *Org. Prep. Proced.* **1974**, *6*, 193–196. The yields of non-deuterated compounds **25** and **26** were 85 and 66%, respectively.

[37] Apparently due to significant kinetic effects of the deuterium isotope, the yields in this synthetic sequence were lower than those for the non-deuterated **27** and **28** (99 and 78%, respectively[24]), and almost no lithiation of [$D_8$]-**3** was observed at 0°C (cf. ref. [19]).

[38] H. Braun, W. Lüttke, *J. Mol. Struct.* **1975**, *28*, 391–413.

[39] Spartan '04, Wavefunction Inc., Irvine, CA.

[40] The MMFF force field is not optimized for bicyclopropyl and predicts the s-*trans*-conformation to prevail in the equilibrium conformer.

[41] A previously published force field adjusted for bicyclopropyl to reproduce the preference for the *gauche* conformer in the liquid state, unfortunately could not be implemented in the Spartan program package. Compare E. Osawa, G. Szalontai, A. Tsurumoto, *J. Chem. Soc. Perkin Trans. 2* **1983**, 1209–1216.

  

[42] Gaussian 03, Revision B.04, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, **2003**.

[43] G. B. Kauffman, L. A. Teter, *Inorg. Synth.* **1963**, 7, 9–12.

[44] I. E. Dolgii, E. A. Shapiro, O. M. Nefedov, *Izv. Akad. Nauk SSSR Ser. Khim.* **1979**, 1282–1286; *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1979**, *28*, 1197–1200.

[45] a) A. J. Hubert, A. F. Noels, A. J. Anciaux, P. Teyssie, *Synthesis* **1976**, 600–602; reviews: b) M. P. Doyle, *Chem. Rev.* **1986**, *86*, 919–939; c) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalysts for Organic Synthesis with Diazo Compounds*, Wiley, New York, **1997**.

[46] V. F. Baklan, A. N. Khil′chevskii, V. M. D′yakovskaya, L. S. Sologub, V. P. Kukhar, *Zh. Org. Khim.* **1993**, *29*, 542–545; *Russ. J. Org. Chem. (Engl. Transl.)* **1993**, *29*, 454–456.

[47] We are grateful to Prof. Dr. Y. Okamoto and Dr. C. Yamamoto, Graduate School of Engineering, Nagoya University, Japan, for their performing these experiments.

[48] R. Boese, M. Nussbaumer, in *Correlations, Transformations, and Interactions in Organic Crystal Chemistry* (Eds.: D. W. Jones, A. Katrusiak), Oxford University Press, Oxford, **1994**, pp. 20–37.

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