Cyclopropannelation of the Bicyclo[3.3.0]octane Framework. On the Chemical Significance of *exo*-Positioned Substituents[1)]

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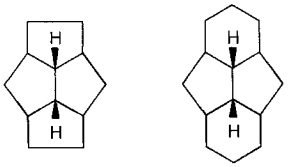
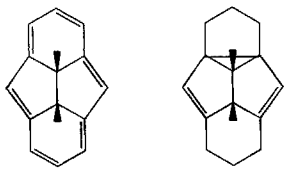
To facilitate the synthesis of tetracycles containing the framework **2**, the reaction of the tetrabromide **8** with cyanide and bis(phenylsulfonyl)methane under various conditions was investigated. Instead of the expected twofold bridging, novel cyclopropa derivatives were obtained. Product formation is a consequence of the stereochemistry of the starting material **8**, with the *exo* configuration of the bromomethyl substituents being the crucial factor.

Tetraquinanes **1**[2)] and the homologous tetracycle **2** are potential sources for the synthesis of novel, cyclic conjugated π systems. The introduction of additional double bonds has been accomplished in the synthesis of the [12]annulene **3** which we have published recently[3)]. Moreover, derivatives comprising the framework **2** have served as building blocks for bridged semibullvalenes of structure type **4**[3,4)].



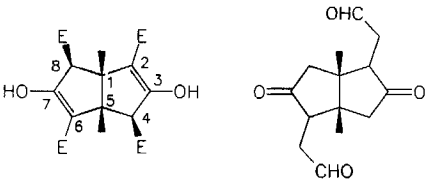
1 **2**



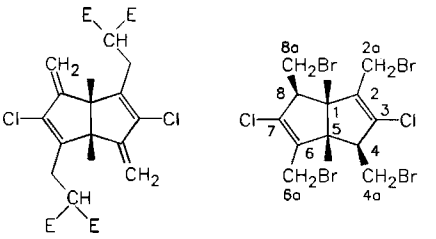
3 **4**

The readily available bicyclo[3.3.0.]octane skeleton **5**[5)] appears to be an appropriate starting material for the attempted synthesis of **1** and **2**. The main problem in the conversion of **5** and of similar molecules into the target compounds **1** and **2**, however, is the bridging cyclization of the centers attached to C-2/8 and C-4/6. The substituents at the centers C-4 and C-8 of e.g. **8** prefer the thermodynamically favored *exo* configuration; thus, due to the large distance, an approach of C-2a and C-8a and C-4a and C-6a, respectively, is prevented [2,3,6)]. Ring closures are only achieved if the substituents are forced into the thermodynamically less favored *all-endo* configuration, or alternatively, if endocyclic double bonds are introduced into the skeleton.

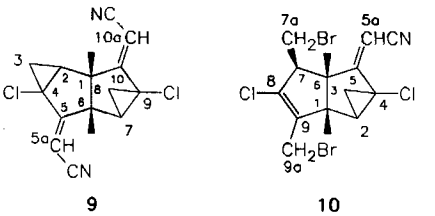
Examples for the application of both concepts are the cyclization of the dialdehyde-diketone **6** to a tetraquinane precursor via the corresponding enol[6)], and the ring closure



5 (E = CO_2Me) **6**



7 (E = CO_2Me) **8**



9 **10**

of **7**[3)]. Compound **7** includes exocyclic double bonds which are epoxidized regio- and stereoselectively yielding a bis(oxirane) with *endo*-configurated CH_2 groups.

Starting from compound **8**, whose synthesis has been described earlier[3)], we have investigated alternative synthetic approaches towards molecules with the framework **2**. Herein, we describe how the sterically demanding bridging of positions 2a/8a and 4a/6a is avoided and different products are formed instead.

Results and Discussion

First, we have investigated the behavior of the tetrabromide **8** in a Kolbe nitrile synthesis[7)]. Partial (or complete)

  0009–2940/91/0808–1827 $ 3.50+.25/0

exchange of the bromo substituents by cyano groups should, in principle, provide intermediates which, in a step similar to the Thorpe-Ziegler reaction [8], allow a modified cyclization. When **8** is treated with four equivalents of potassium cyanide in boiling ethanol or in DMSO at room temperature, the unexpected tetracyclic compound **9** is isolated in 70% yield, besides unreacted bromide. The configuration of the product has been confirmed by NMR spectroscopy and X-ray analysis. The structure of **9** in the crystalline state is shown in Figure 1.

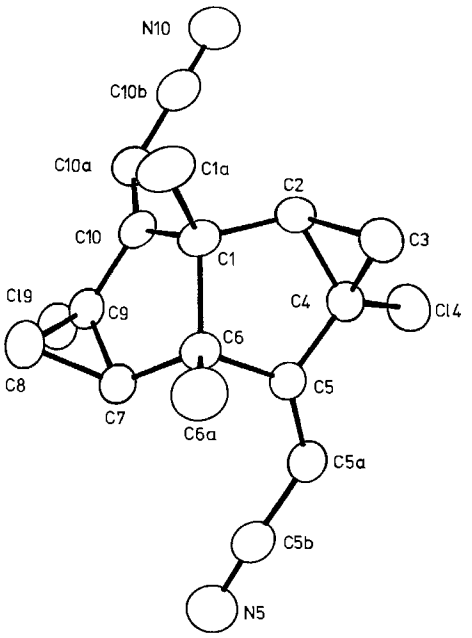


Figure 1. Crystal structure of **9**

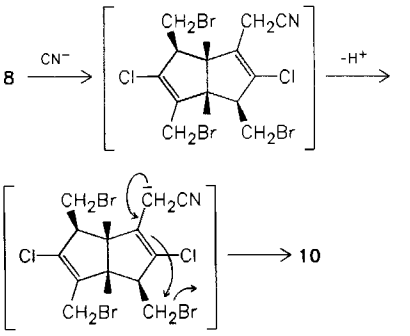
Noteworthy is not only the *exo* configuration of the cyclopropane moieties, but also the *endo* configuration of the cyano groups. The C_2 symmetry of the molecule is also reflected in the simple ^{1}H-NMR spectrum which shows one singlet at $\delta = 1.26$ for the methyl groups, three double doublets at $\delta = 1.12$, 1.66, and 2.97, arising from the cyclopropane protons, and one singlet at $\delta = 5.73$ due to the olefinic protons.

To further investigate the formation of **9** we varied the reaction conditions by using an acetone/DMSO mixture at -15 °C. Besides precursor **8** and product **9**, we obtained the tricyclic system **10** in a yield of 35%. The same result is found when using acetone as solvent. The addition of DMSO is necessary because it increases the solubility of potassium cyanide, thus decreasing the reaction time [9].

From the exclusive formation of **9** and **10** we propose the reaction mechanism depicted in Scheme 1.

First, an allylic methylene group suffers a bromide-cyanide exchange followed by a deprotonation by cyanide acting as a base. Thereby, the first tricyclic compound is formed under hydrogen bromide elimination. The second ring closure takes place similarly. Remarkably, the reaction is diastereoselective not only with respect to the *exo* position of

Scheme 1

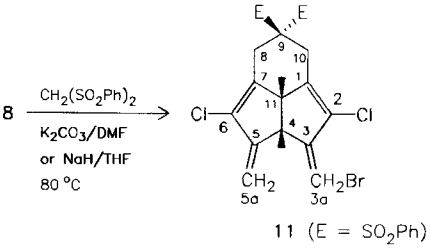


the cyclopropane ring, but also with respect to the *endo* configuration of the cyano groups.

A second synthetic sequence starting from **8** is the twofold alkylation of **8** by using the C_1 building block bis(phenylsulfonyl)methane instead of diethyl malonate, as described recently [3]. The probable advantage of this reaction is the facile removal of the phenylsulfonyl groups in the synthesis of **2**.

The treatment of **8** with the sodium or potassium salt of bis(phenylsulfonyl)methane in THF or DMF does not lead to the dialkylated system, which is obtained when using malonic ester as C_1 nucleophile; instead, the tricyclic compound **11** is formed in 30% yield (Scheme 2).

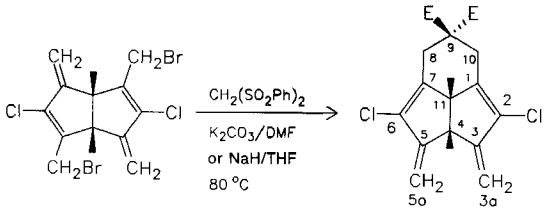
Scheme 2



This result is especially astonishing since, as described previously, a ring closure is only possible if the substituents adopt an *endo* position. We suppose that after an initial alkylation of an allylic position 2a (6a), hydrogen bromide is eliminated at the neighboring substituent 8a (4a), leading to a bromopentadiene moiety. After subsequent deprotonation, the bis(phenylsulfonyl)methane unit attacks this diene system in an S_N2' reaction, substituting bromide and yielding the final product. This proposal is supported by the synthesis of **13**, when **12** (obtained from **8** by twofold hydrogen bromide elimination) is treated in the same manner (Scheme 3).

The reaction of the bis(diene) **13** with an appropriate reactant in a homo Diels-Alder reaction as crucial step represents an attractive possibility for the synthesis of compounds containing an indenoazulene framework. We, therefore, have investigated whether the synthesis of **13** can be simplified by dehydrobromination of **11**. Surprisingly, the treat-

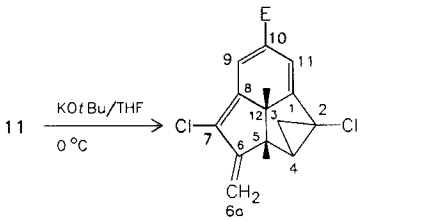
Scheme 3



12 13 (E = SO_2Ph)

ment of **11** with potassium *tert*-butoxide in THF yields the strained tetracyclic compund **14** containing a cyclopropane ring (Scheme 4). It is obvious that under these reaction conditions, the *gem*-bis(phenylsulfonyl)methylene moiety does not persist. Instead, benzenesulfinic acid is eliminated to yield a phenylsulfonylethylene followed by a deprotonation-substitution sequence leading to cyclopropane formation.

Scheme 4



14 (E = SO_2Ph)

With **14**, a second possible and thus attractive starting material for cycloadditions is available.

The reactivity of the bis(diene) **13** and the quasi-homodecapentaene **14** towards activated olefins is presently under investigation.

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Experimental

Commercial solvents: Purified according to standard procedures. – Melting points: Not corrected. – ^1H NMR: Bruker AC 200 (200 MHz) and AM 400 (400 MHz). – ^{13}C NMR: Bruker AM 200 (50 MHz) and AM 400 (100 MHz). – MS: Varian MAT CH 7A.

4,9-Dichloro-5,10-bis(cyanomethylene)-1,6-dimethyltetracyclo[4.4.0.0^{2,4}0^{7,9}]decane (**9**): Tetrabromide **8** (600 mg, 1 mmol) was added in portions to a boiling solution of potassium cyanide (300 mg, 4 mmol) in 100 ml of aqueous ethanol (80%) over a time period of 0.5 h. After ca. 1 h, potassium bromide precipitated as colorless crystals. The mixture was heated to reflux for 2 h and then allowed to cool, whereupon the product crystallized as a fine light brown precipitate. It was removed by filtration, washed several times with water and recrystallized from ethanol to afford 216 mg (68%) of **9** as colorless plates; m.p. 205°C. – ^1H NMR (200MHz, $CDCl_3$, 20°C): δ = 1.12 (dd, J_{AX} = 5 Hz, J_{BX} = 6.6 Hz, 2H, 2-H, 7-H); 1.26 (s, 6H, 2 CH_3); 1.66, 2.97 (2 dd, J_{AB} = 9.2 Hz, J_{BX} = 6.6 Hz, J_{AX} = 5.0 Hz, 4H, 3/8-H_a, 3/8-H_b); 5.73 (s, 2H, 2 CHCN). – ^{13}C NMR (50 MHz, $CDCl_3$, 20°C): δ = 20.63 (2 CH_3); 23.71 (C-3/8); 41.06 (C-2/7); 47.69 (C-1/6); 56.24 (C-4/9); 93.22 (C-5/10a); 115.79 (CN); 175.17 (C-5/10). – MS (70 eV): *m/z* (%) = 306 (9.60) [M^+]; 269 (100) [M^+ – Cl]; 234 (29.7) [M^+ – 2 Cl]; 233 (49.6) [M^+ – Cl – HCl].

$C_{16}H_{14}Cl_2N_2$ (305.2) Calcd. C 62.97 H 4.62 N 9.18
Found C 62.90 H 4.58 N 9.13

7,9-Bis(bromomethyl)-4,8-dichloro-5-cyanomethylene-1,6-dimethyltricyclo[4.3.0.0^{2,4}]nona-8-ene (**10**): **8** (600 mg, 1 mmol) was dissolved in a mixture of acetone/DMSO (1:1) (10 ml); sodium cyanide (200 mg, 4 mmol) was added, and the reaction mixture was stirred at –15°C for 6 h. The solvent was evaporated and the residue chromatographed on silica gel [30 × 2 cm, petroleum ether/ethyl acetate (4:1)]. The tricyclic system was obtained in the second fraction. After evaporation of the solvent, the resulting colorless residue was recrystallized from ethanol to afford 140 mg (31%) of **10** as colorless needles; m.p. 134°C. – ^1H NMR (200 MHz, $CDCl_3$, 20°C): δ = 1.29, 1.36 (2s, 6H, 2 CH_3); 1.27–1.31 (dd, X part of ABX system, 1H, 2-H); 1.65, 2.72 (2dd, J_{AB} = 9.3 Hz, J_{AX} = 6.2 Hz, J_{BX} = 5.2 Hz, 2H, 3-H_a, 3-H_b); 3.58 (d, X part of ABX system, 1H, 7-H); 3.71–3.91 (m, 2H, 7-CH_2Br); 4.12 (AB system, 2H, J_{AB} = 10.6 Hz, 9-CH_2Br); 5.64 (s, 1H, CHCN). – ^{13}C NMR (50 MHz, $CDCl_3$, 20°C): δ = 18.01, 18.29 (2CH_3); 21.61, 24.88 (C-3, C-7a); 30.98 (C-9a); 41.94 (C-2); 47.51, 55.57, 59.23 (C-1, C-6, C-4); 59.34 (C-7); 93.36 (C-5a); 116,14 (CN); 133.79 (C-8); 139.37 (C-9); 180.86 (C-5). – MS (70 eV): *m/z* (%) = 404 (5.03) [M^+ – Cl]; 360 (47.3) [M^+ – Br]; 280 (64.5) [M^+ – 2 Br – H].

$C_{15}H_{15}Br_2Cl_2N$ (439.9) Calcd. C 40.95 H 3.44 N 3.18
Found C 41.02 H 3.47 N 3.16

3-Bromomethyl-2,6-dichloro-4,11-dimethyl-5-methylene-9,9-bis(phenylsulfonyl)tricyclo[5.3.1.0^{4,11}]undeca-1,6-diene (**11**). – *Method A:* A mixture of bis(phenylsulfonyl)methane (600 mg, 2.0 mmol), potassium carbonate (300 mg, 2.4 mmol), and tetrabromide **8** (600 mg, 1.0 mmol) in DMF (0.5 ml/mmol K_2CO_3) was stirred at 80°C under argon until the reaction was complete (ca. 4 h). The reaction mixture was concentrated and the residue dissolved in CH_2Cl_2 and chromatographed on silica gel [30 × 2 cm, petroleum ether/ethyl acetate (4:1)]. Concentration of the eluate, followed by recrystallization (EtOH) of the residue, afforded the pure product **11** (229 mg, 35%) as colorless needles; m.p. 172°C.

Method B: The solid bis(phenylsulfonyl)methane (600 mg, 2.0 mmol) was added to a suspension of NaH (53 mg, 2.2 mmol) in dry THF (6 ml). After hydrogen evolution had ceased, **8** (600 mg, 2 mmol) in 4 ml of dry THF was added, and the reaction mixture was heated at 80°C under argon until the reaction was complete (ca. 3 h).The reaction mixture was concentrated and the residue dissolved in CH_2Cl_2 and chromatographed on silica gel [30 × 2 cm, petroleum ether/ethyl acetate (4:1)]. Concentration of the eluate, followed by recrystallization (EtOH) of the residue, afforded the pure product **11** (229 mg, 35%) as colorless needles; m.p. 172°C.

Method C: Analogously to method B, except that dry DMF was used as solvent. – ^1H NMR (200 MHz, $CDCl_3$, 20°C): δ = 0.95, 1.35 (2s, 6H, 2 CH_3); 3.14–3.82 (m, 7H, 8/10-H_2 3-H, CH_2Br); 4.93, 5.28 (2 s, 2H, =CH_2); 7.5–7.8 (m, 6H, 4 *m*-H, 2 *p*-H; 7.95–8.3 (2d, 4H, 4 *o*-H). – ^{13}C NMR (50 MHz, $CDCl_3$, 20°C): δ = 15.57, 19.33 (2 CH_3); 25.48, 26.08 (C-8, C-10); 31.39 (C-3a); 51.32, 61,16 (C-4, C-11); 61.49 (C-3); 86.16 (C-9); 105.97 (C-5a); 126.19 (C-1/7); 128.63–136.01 (Ph-C); 141.34 (C-2/6); 160.73 (C-5). – MS (70 eV): *m/z* (%) = 593 (15.1) [M^+ – Cl]; 487 (6.10) [M^+ – SO_2Ph).

$C_{27}H_{25}BrCl_2O_4S_2$ (628.4) Calcd. C 51.61 H 4.01 S 10.21
Found C 51.56 H 4.00 S 10.21

Table 1. Atomic coordinates and equivalent thermal parameters B_{eq} [Å^2] of **9**; $B_{eq} = (4/3)\,[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab(\cos\gamma)\beta(1,2) + ac(\cos\beta)\beta(1,3) + bc(\cos\alpha)\beta(2,3)]$

Atom	x	y	z	B
C19	0.62658(6)	0.5597(1)	0.68222(7)	3.90(2)
C14	0.87362(7)	0.0410(1)	0.56240(9)	4.28(2)
N10	0.5292(2)	0.0351(5)	0.3732(3)	4.54(8)
N5	0.9640(2)	0.7119(5)	0.6834(3)	4.72(8)
C9	0.6627(2)	0.5568(4)	0.5527(3)	2.64(7)
C10	0.6425(2)	0.4059(4)	0.4817(3)	2.52(6)
C1	0.7092(2)	0.3907(4)	0.4003(3)	2.48(6)
C6	0.7882(2)	0.5113(4)	0.4530(3)	2.40(6)
C7	0.7505(2)	0.6235(4)	0.5362(3)	2.82(7)
C2	0.7468(2)	0.2098(5)	0.4043(3)	2.69(7)
C4	0.8355(2)	0.2108(4)	0.4745(3)	2.71(7)
C5	0.8555(2)	0.3857(4)	0.5148(3)	2.29(6)
C1a	0.6661(2)	0.4342(5)	0.2818(3)	3.76(8)
C6a	0.8305(2)	0.6199(5)	0.3704(3)	3.47(8)
C10a	0.5751(2)	0.3032(5)	0.4908(3)	3.24(8)
C10b	0.5508(2)	0.1553(5)	0.4240(3)	3.40(8)
C5a	0.9219(2)	0.4192(5)	0.5961(3)	2.89(7)
C5b	0.9438(2)	0.5844(5)	0.6422(3)	3.27(8)
C8	0.6700(2)	0.7254(5)	0.4945(3)	3.45(8)
C3	0.8272(2)	0.1819(5)	0.3506(3)	3.33(8)

2,6-Dichloro-4,11-dimethyl-3,5-dimethylene-9,9-bis(phenylsulfonyl)tricyclo[5.3.1.0^{4,11}]undeca-1,6-diene (**13**): A solution of **12** (400 mg, 1.0 mmol) and bis(phenylsulfonyl)methane (600 mg, 2.0 mmol) in DMF (3 ml) was treated with potassium carbonate (300 mg, 2.4 mmol) at 80°C for 3 h. Then the solvent was evaporated and the residue chromatographed on silica gel [30 × 2 cm, petroleum ether/ethyl acetate (4:1)]. After evaporation of the solvent from the eluate, the colorless solid was recrystallized from ethanol to afford the pure product **13** (200 mg, 37%) as colorless needles; m.p. 180°C. – ^{1}H NMR (200 MHz, $CDCl_3$, 20°C): δ = 1.03, 1.36 (2s, 6H, 2 CH_3); 3.26–3.72 (AB system, 4H, 8/10-H_2); 5.07, 5.18 (2s, 4H, 2 =CH_2); 7.51–7.77 (m, 6H, 4 *m*-H, 2 *p*-H); 8.04–8.18 (2d, 4H, 4 *o*-H). – ^{13}C NMR (50 MHz, $CDCl_3$, 20°C): δ = 15.82, 23.97 (2 CH_3); 26.03 (C-8/10); 52.59, 60.61 (C-4, C-11); 87.37 (C-9); 105.77 (C-3a/5a); 128.20 (C-1/7); 128.67, 129.20, 131.51, 133.92, 134.89, 135.20, 135.37, 135.91 (Ph-C); 141.05 (C-2/6); 156.37 (C-3/5). – MS (70 eV): *m/z* (%) = 511 (11.9) [M^+ – Cl]; 405 (23.2) [M^+ – SO_2Ph].

$C_{27}H_{24}Cl_2O_4S_2$ (547.5) Calcd. C 59.23 H 4.42 S 11.71
Found C 59.19 H 4.39 S 11.74

2,7-Dichloro-5,12-dimethyl-6-methylene-10-phenylsulfonyltetracyclo[6.3.1.0^{2,4}.0^{5,12}]dodeca-7,9,11-triene (**14**): To a stirred solution of **12** (126 mg, 0.2 mmol) in THF (2 ml), a 1 M solution of potassium *tert*-butoxide (0.2 ml) was added dropwise at 0°C under argon. The reaction was monitored by TLC. After complete conversion, a saturated aqueous solution of ammonium chloride (1 ml) was added. The reaction mixture was extracted several times with ether. The combined organic layers were dried (Na_2SO_4); the solvent was removed in vacuo, and the solid residue was purified by recrystallization (EtOH) to afford the pure product **14** (50 mg, 62%) as yellow microcrystals, m.p. 186°C. – ^{1}H NMR (200 MHz, $CDCl_3$, 20°C): δ = 0.85, 1.16 (2s, 6H, 2 CH_3); 1.39–1.47 (m, X part of ABX system, 1H, 4-H); 1.61–1.68, 2.45–2.52 (2m, J_{AB} = 9.2 Hz, J_{AX} = 6.7 Hz, J_{BX} = 5.1 Hz, 2H, 3-H_a, 3-H_b); 5.18–5.53 (s, 2H, =CH_2); 5.90, 7.20 (2s, 2H, 11-H/9-H); 7.49–7.70 (m, 3H, 2 *m*-H, 1 *p*-H); 7.89–8.05 (d, 2H, 2 *o*-H). – ^{13}C NMR (50 MHz, $CDCl_3$, 20°C)): δ = 18.13, 22.33 (2 CH_3); 22.52 (C-3); 47.38, 51.76, 55.76 (C-2, C-5, C-12); 48.49 (C-4); 110.86 (C-11); 111.26 (C-6a); 122.73 (C-9); 127.85, 129.40, 132.63, 133.60 (Ph-C); 139.80, 141.89, 144.22 (C-8, C-7, C-1); 156.86, 157.27 (C-6, C-10). – MS (70 eV): *m/z* (%) = 404 (4.38) [M^+]; 228 (3.34) [M^+ – Cl – SO_2Ph].

$C_{21}H_{18}Cl_2O_2S$ (405.3) Calcd. C 62.23 H 4.48 S 7.91
Found C 62.28 H 4.46 S 7.90

Crystal Structure Determination of Compound **9**[10]: The data were collected with an Enraf-Nonius CAD4 diffractometer, Cu-K_α radiation, λ = 1.5405 Å, graphite monochromator. The structure was solved by direct methods (MULTAN)[11]. The carbon atoms were refined anisotropically, and the hydrogen atoms were refined in the "riding mode" with fixed isotropic thermal parameters, t_{max} = 1.26, t_{min} = 0.80. $C_{16}H_{14}N_2Cl_2$; M_r = 305.2; crystal size: 0.42 × 0.20 × 0.15 mm; T = 293 K; monoclinic; space group $P2_1/c$; a = 15.4836(10), b = 7.8288(14), c = 12.1603(6) Å; β = 98.602(5)°; V = 1457.5 Å^3; Z = 4; D = 1.391 g/cm^3; data collection mode ω-2θ; μ(Cu-K_α) = 39.4 cm^{-1}. 2482 reflections (±h, +k, +l), 1997 reflections with $I \geq 3\sigma(I)$; 8 refined parameters; R = 0.042, R_w = 0.045 [$w = 1/\sigma^2(F_o)$]; residual electron density: 0.29 e Å^{-3}. Atomic coordinates and equivalent thermal parameters are listed in Table 1.

CAS Registry Numbers

8: 134053-12-6 / **9**: 133984-97-1 / **10**: 133984-98-2 / **11**: 133984-99-3 / **12**: 133985-00-9 / **13**: 133985-01-0 / **14**: 133985-02-1 / $(PhSO_2)_2CH_2$: 3406-02-8

[1] Dedicated to Professor *Wolfram Grimme* on the occasion of his 60th birthday.
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