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Thiele's Ester as a Reagent in Organic Synthesis. Preparation of Pentacyclo[5.4.0.0^{2,5}.0^{3,10}.0^{4,8}]undecane-10-carboxylic Acid

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Abstract. Succinyl cleavage of the C(2)-C(5) σ-bond in dimethyl pentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]decane-2,5-dicarboxylate, **2**, afforded a tetracyclic diester, **3** (22-26%), along with two minor reaction products (**4** and **5**). Dieckmann condensation of **3** produced a mixture of **6a** and **6b** (67%). Wolff-Kishner reduction of the mixture of **6a** and **6b** thereby obtained afforded a mixture of products from which the title compound, **7b**, could be isolated in 63% yield by fractional recrystallization. The structures of **3**, **4** and **7b** were established unequivocally via X-ray crystallographic methods.

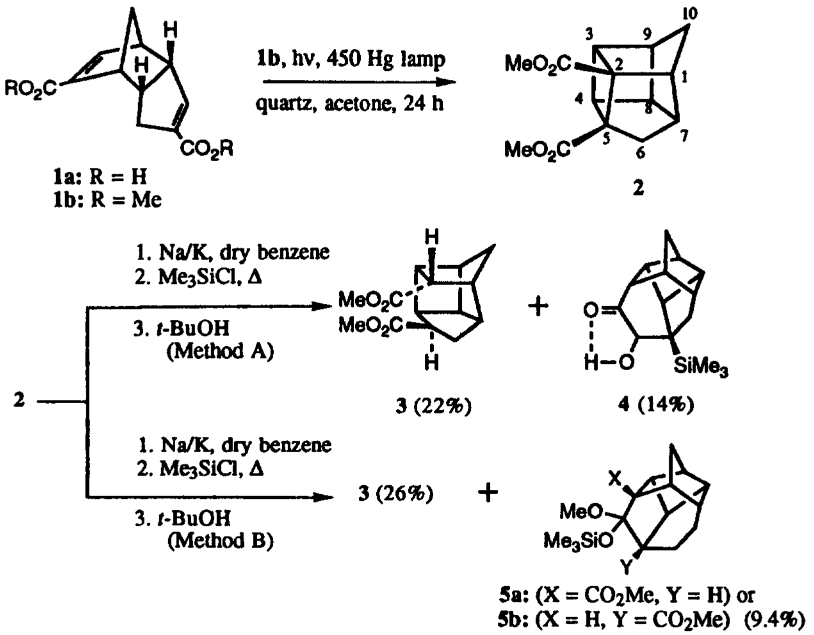
Introduction. At the turn of the century, Thiele[1] reported that carbonation of cyclopentadienylpotassium results in formation of a dimeric material, $C_{14}H_{16}O_4$, mp 210 °C, which subsequently became known as "Thiele's acid" (**1a**). Acid promoted esterification of **1a** with methanol affords the corresponding dimethyl ester ("Thiele's ester, **1b**, mp 85 °C).[1] The structure of **1b** has been established by chemical[2] and by NMR spectroscopic[3] methods.

Compound **1b**, a difunctionalized *endo*-tricyclo[5.2.1.0^{2,6}]tricycloundecane-3,8-diene, is potentially useful as a starting material for the synthesis of novel polycyclic systems. However, this compound has received relatively little attention in this regard.[4] In the present study, we have utilized **1b** to gain synthetic entry into the pentacyclo[5.4.0.0^{2,5}.0^{3,10}.0^{4,8}]undecane ring system. To our knowledge. neither the parent hydrocarbon nor any functionalized derivative of this ring system has been reported previously.[5]

Results and Discussion. Thiele's ester has been reported[2] to undergo facile intramolecular [2 + 2] cyclization when a solution of this compound in acetone is irradiated in a quartz immersion photolysis apparatus by using a 450 W medium pressure Hg lamp. This procedure affords the corresponding pentacyclic cage diester (i.e., dimethyl pentacyclo[$5.3.0.0^{2,5}.0^{3,9}.0^{4,8}$]decane-2,5-dicarboxylate, **2**, Scheme 1) in 66% yield. Our approach to the synthesis of a substituted pentacyclo[$5.4.0.0^{2,5}.0^{3,10}.0^{4,8}$]undecane takes advantage of the fact that the strained C(2)-C(3) σ-bond contained within the succinyl ester moiety [comprised of MeO_2C-C(2)-C(5)-CO_2Me] in **2** can be cleaved selectively by using Na-K alloy in the presence of Me_3SiCl.[6]

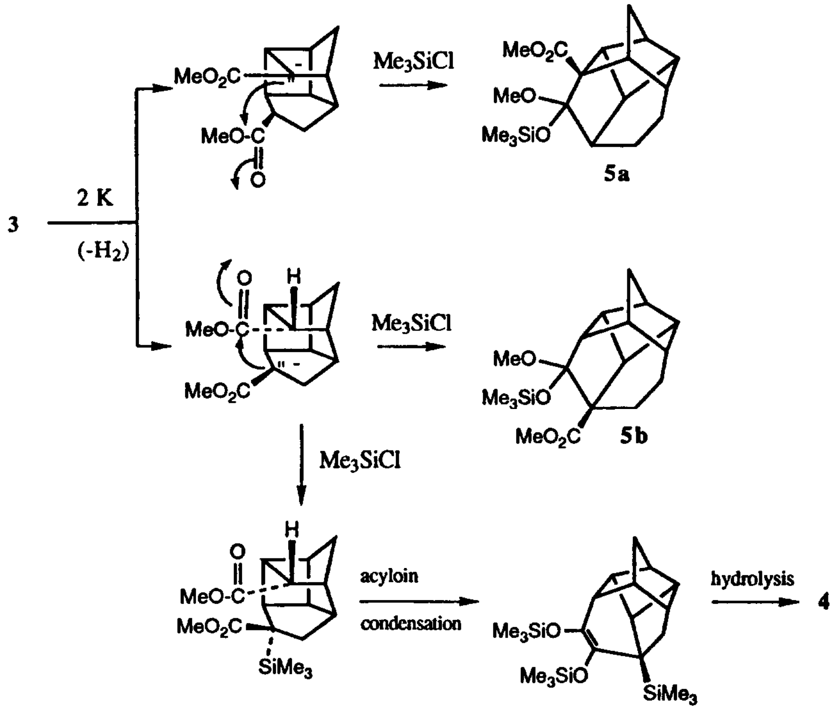
In our hands, Na-K promoted reduction of **2**, performed by using two very similar procedures (Methods A and B, see the Experimental Section), resulted in the desired cleavage of the C(2)-C(5) bond, thereby affording **3** as the major reaction product (Scheme 1). Fractional recrystallization of the material thereby obtained from EtOAc-hexane afforded isomerically pure **3**. The results of single crystal X-ray structural analysis revealed that both the C(2)-CO_2Me and C(5)-CO_2Me bonds in **3** are endo.

Scheme 1



When the reduction of **2** was performed by using Method A, a minor product, **4**, was obtained in addition to **3**. The structure of **4** was established unequivocally via single crystal X-ray crystallographic analysis. A plausible mechanism which accounts for the formation of **4** is shown in Scheme 2. It seems likely that the C(11)-Si bond in **4** results via selective base promoted deprotonation at C(5) in **3**, followed by capture of the resulting enolate anion by Me$_3$SiCl. Subsequent acyloin condensation[7] between the endo CO$_2$Me moieties in the intermediate C-silylated compound followed by hydrolysis leads to the formation of **4**.

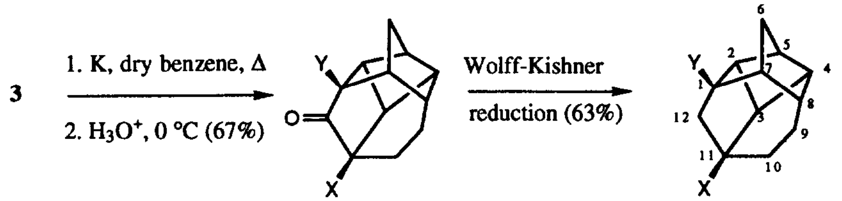
Scheme 2



When **2** was reduced by using the procedure described in Method B, a minor product, **5**, was obtained in addition to **3**. Possible structures for **5** (i.e., **5a** and **5b**, Scheme 1) are suggested on the basis of analysis of its ^{1}H and ^{13}C NMR spectra and on mechanistic grounds. Thus, the ^{1}H NMR spectrum of **5** reveals the presence of a SiMe$_3$ group (δ 1.17, s, 9 H) along with two singlets, δ 3.13 (area 3 H) and 3.61 (area 3H), which correspond to two nonequivalent OCH_3 moieties. In addition, the ^{13}C NMR spectrum of **5** displays an absorbance at δ 110.0 (s), which corresponds to a quaternary carbon atom of the type RR'C(OR)(OR'). It should be noted that Dieckmann condensation of **3** might occur via either of two pathways. Subsequent trapping of the intermediate alkoxide anions by Me_3SiCl would be expected to afford either **5a** or **5b**. We are unable to further differentiate between structures **5a** and **5b** on the basis of available spectral data.

Subsequent treatment of **3** with metallic K resulted in Dieckmann condensation, thereby affording a mixture of two cage β-ketoesters, **6a** and **6b** (67%, Scheme 3). Finally, Wolff-Kishner reduction[8] of this mixture of **6a** and **6b** afforded a mixture of two cage carboxylic acids, **7a** and **7b**. Fractional recrystallization of the product mixture from hexane afforded the title compound, **7b**, in 63% yield. The structure of **7b** was established unequivocally via single crystal X-ray structural analysis.

Scheme 3



6a: X = H, Y = CO_2Me
6b: X = CO_2Me, Y = H

7a: X = H, Y = CO_2H
7b: X = CO_2H, Y = H

Summary and Conclusions. Succinyl cleavage of the C(2)-C(5) σ-bond in dimethyl pentacyclo[$5.3.0.0^{2,5}.0^{3,9}.0^{4,8}$]decane-2,5-dicarboxylate, **2**, afforded a tetracyclic diester, **3** (22-26%), along with two minor reaction products (**4** and **5**, Scheme 1). Dieckmann condensation of **3** produced a mixture of **6a** and **6b** (67%), which subsequently could be converted to a mixture of **7a** and **7b** via Wolff-Kishner reduction. Fractional recrystallization of this product mixture from hexane afforded isomerically pure **7b** (63%). To our knowledge, the foregoing reaction sequence constitutes the first successful synthesis of a substituted pentacyclo-[$5.4.0.0^{2,5}.0^{3,10}.0^{4,8}$]undecane.

Experimental Section

Melting points are uncorrected. Compound **2** was prepared via intramolecular photocyclization of **1b**[1] by using the method described by Dunn and Donohue.[2] High-resolution mass spectra were obtained by personnel at the Midwest Center for Mass Spectrometry, Department of Chemistry, University of Nebraska, Lincoln, NE 68588.

Dimethyl Tetracyclo[5.3.0.0^{3,9}.0^{4,8}]decane-*endo*-2,*endo*-5-dicarboxylate (3).
Method A. Freshly cut Na (800 mg, 22.6 mg-atom) was placed under nitrogen into a flame-dried 500 mL three-neck round bottom flask that had been fitted with a reflux condenser. One of the necks of the reaction vessel was fitted with a rubber septum. Dry toluene (100 mL) was added, and the mixture was heated with vigorous stirring under nitrogen until the Na had become finely dispersed. The mixture then was cooled to room temperature, and the toluene was decanted and was replaced by dry benzene (250 mL). Freshly cut metallic K (4.00 g, 103 mg-atom) was added, and the resulting mixture was heated with vigorous stirring under nitrogen until the Na-K alloy had become finely dispersed. The mixture was cooled to room temperature, and two additional reactants, (i) a solution of 2[2] (6.94 g, 28 mmol) in benzene (50 mL) and (ii) Me_3SiCl (25 mL, excess), were injected sequentially into the reaction vessel. The resulting mixture was refluxed under nitrogen with stirring for 16 h and then was allowed to cool to room temperature. The reaction mixture was filtered under nitrogen to remove unreacted Na-K alloy, and *t*-BuOH (30 mL) was added to the filtrate. The resulting solution was concentrated in vacuo, thereby affording a viscous yellow oil (6.66 g). This material was purified via column chromatography on silica gel by using a 1-4% EtOAc-hexane gradient elution scheme. The first chromatography fraction thereby obtained was concentrated in vacuo, and the residue was recrystallized from EtOAc-hexane. Pure **4** (1.03 g, 14%) was thereby obtained as a colorless microcrystalline solid: mp 175-176 °C; IR (KBr) 3468 (s), 2956 (br, s), 1695 (s), 1260 (s), 1130 (s), 853 cm^{-1} (s); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 9 H), 1.45-1.75 (m, 4 H), 2.50-1.70 (m, 5 H), 2.77 (t, J = 6.0 Hz, 1 H), 2.93 (t, J = 2.5 H, 1 H), 3.59 (d, J = 2.5 Hz, 1 H), 4.04 (br s, 1 H), ^{13}C NMR ($CDCl_3$) δ -3.59 (q), 32.47 (s), 32.86 (t), 34.07 (d), 39.80 (d), 42.13 (t), 43.95 (d), 47.23 (d), 48.03 (d), 49.14 (d), 54.22 (d), 77.89 (d), 214.1 (s); mass spectrum, *m/e* (relative intensity) 282 (molecular ion, 6.7), 247 (3.9), 196 (16.4), 195 (15.3), 181 (11.7), 190 (12.7), 179 (46.7), 172 (10.9), 167 (11.5), 144 (8.9), 129 (11.9), 107 (23.2), 106 (17.8), 103 (12.8), 91 (12.3), 79 (18.7), 75 (59.9), 73 (100.0), 66 (31.3), 65 (13.1), 45 (42.6), 43 (13.0), 41 (10.7), 39 (13.7). Anal. Calcd for $C_{15}H_{22}SiO_2$: C, 68.65; H, 8.45. Found: C, 68.41; H, 8.47. The structure of **4** was established unequivocally via single crystal X-ray structural analysis (*vide infra*).

Further elution of the chromatography column afforded a colorless oil which solidified when cooled and triturated with hexane. Recrystallization of the solid thereby obtained from EtOAc-hexane afforded isomerically pure **3** (1.54 g, 22%) as a colorless microcrystalline solid: mp 73-74 °C; IR (KBr) 2950 (s), 1720 (vs), 1440 (m), 1320 (m), 1310 (w), 1290 (m), 1250 (s), 1230 (s), 1060 cm^{-1} (w); ^{1}H NMR ($CDCl_3$) δ 1.40 (AB, J_{AB} = 10.2 Hz, 1 H), 1.52 (AB, J_{AB} = 10.2 Hz, 1 H), 2.04 (m, 1 H), 2.30 (m, 1 H), 2.52 (m, 3 H), 2.85 (m, 5 H), 3.63 (s, 6 H), ^{13}C NMR ($CDCl_3$) δ 28.01 (t), 37.14 (d), 39.25 (d), 41.60 (t), 42.97 (d), 44.12 (d), 46.25 (d), 44.46 (d), 48.73 (d), 50.98 (d), 51.37 (d), 51.63 (d), 173.2 (s), 173.8 (s), mass spectrum (70 eV), *m/e* (relative intensity) (no molecular ion), 218 (13.1), 190 (20.5), 131 (37.8), 130 (23.7), 125 (100.0), 124 (20.1), 66 (96.4), 65 (34.9). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.20; H, 7.20. Found: C, 67.55; H, 7.26. The fact that the C(2)-CO_2Me and C(5)-CO_2Me bonds in **3** are both endo was established unequivocally via single crystal X-ray structural analysis (*vide infra*).

Method B. To a suspension of Na sand (100 mg, 4.9 mg-atom) in dry benzene (50 mL) under nitrogen was added freshly cut metallic K (550 mg, 141 mg-atom), and the resulting mixture was heated to reflux to form Na-K alloy. The mixture was cooled to room temperature, and a solution of 2[2] (1.1 g, 4.4

mmol) in dry benzene (10 mL) was added, followed by addition of Me_3SiCl (4.0 mL, 31 mmol, excess). The resulting mixture was refluxed under nitrogen with stirring for 16 h and then allowed to cool to room temperature. The reaction mixture was filtered under nitrogen to remove unreacted Na-K alloy, and t-BuOH (5 mL) was added to the filtrate. The filtrate was concentrated in vacuo, thereby affording a yellow oil which was purified via column chromatography on silica gel by using a 1-5% EtOAc-hexane gradient elution scheme. The first fraction afforded **5** (i.e., **5a** or **5b**, 13 mg, 9.4%) as a colorless oil: IR (film) 2953 (vs), 2871 (sh, m), 1717 cm^{-1} (vs). ^1H NMR ($CDCl_3$) δ 1.17 (s, 9 H), 1.33 (AB, J_{AB} = 10.0 Hz, 1 H), 1.46 (A*B*, J_{AB} = 10.0 Hz, 1 H), 1.66 (dd, *J* = 14.0, 4.0 Hz, 1 H), 2.33 (m, 2 H), 2.43-2.64 (m, 5 H), 3.10 (m, 1 H), 3.13 (s, 3 H), 3.61 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 1.79 (q), 36.01 (d), 38.20 (t), 40.18 (d), 41.72 (t), 42.28 (d), 45.67 (d), 45.85 (d), 46.30 (d), 48.50 (d), 51.28 (q), 52.96 (q), 61.23 (s), 110.0 (s), 173.9 (s). Anal. Calcd for $C_{17}H_{26}O_4Si$: M_r 322.1600. Found (high-resolution mass spectrometry): M_r 322.1586.

Further elution of the chromatography column with 5% EtOAc-hexane afforded **3** (290 mg, 26%), whose spectral properties were identical with those reported above for the corresponding compound obtained via Method A.

Dieckmann Condensation of 3. Freshly cut metallic K (39 mg, 1.0 mg-atom) and dry benzene (20 mL) were placed under nitrogen into a flame-dried 30 mL three-neck round bottom flask that had been fitted with a reflux condenser. Dry benzene (20 mL) was added, and the mixture was heated with vigorous stirring under nitrogen until the K had become finally dispersed. The mixture then was allowed to cool to room temperature, and a solution of **3** (500 mg, 2.0 mmol) in dry benzene (5 mL) was added under nitrogen. The resulting mixture was stirred and heated slowly to 70 °C. The reaction mixture was maintained at this temperature for 3 h, during which time all of the K reacted. The reaction mixture then was cooled externally to 0 °C, and the reaction was quenched by careful dropwise addition of cold 4% HCl solution (15 mL) with constant stirring. The quenched reaction mixture was transferred into a separatory funnel, water (30 mL) was added, and the resulting mixture was extracted with ether (2 x 30 mL). The combined extracts were washed sequentially with 20% aqueous $NaHCO_3$ solution (30 mL), brine (50 mL), and water (50 mL). The organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated in vacuo. The residue, a viscous yellow oil (480 mg), was purified by column chromatography on silica gel by using a 1-4% EtOAc-hexane gradient elution scheme. This procedure afforded a colorless oil (290 mg) whose ^{13}C NMR spectrum indicated the presence of at least two compounds (**6a** and **6b**). A single pure compound (either **6a** or its isomer, **6b**) could be obtained via flash column chromatographic purification of this mixture on silica gel by using a 1-4% EtOAc-hexane gradient elution scheme. The material thereby obtained (160 mg, 37%) was a colorless oil: bp 80 °C (0.1 mm Hg); IR (CCl_4) 2950 (s), 2870 (w), 1740 (vs), 1720 (vs), 1450 (w), 1320 (m), 1300 (m), 1270 (s), 1170 (m), 1080 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.41 (*AB*, J_{AB} = 10.8 Hz, 1 H), 1.69 (A*B*, J_{AB} = 10.8 Hz, 1 H), 2.51 (br s, 2 H), 2.59 (m, 2 H), 2.88 (m, 4 H), 3.20 (m, 1 H), 3.67 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 38.12 (d), 40.72 (d), 42.54 (t), 43.82 (t), 44.08 (d), 46.46 (d), 46.59 (f), 50.86 (d), 52.10 (d), 56.81 (d), 61.05 (s), 171.1 (s), 211.9 (s); mass spectrum (70 eV), m/e (relative intensity) 218 (molecular ion, 16.7), 190 (21.8), 131 (32.4), 130 (22.5), 125 (83.9), 124 (17.0), 91 (18.3), 66 (100.0), 39 (32.9). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.34; H, 6.30.

Pentacyclo[5.4.0.0^{2,5}.0^{3,10}.0^{4,8}]undecane-10-carboxylic Acid (7a). To a 50 mL round bottom flask equipped with a reflux condenser were added diethylene glycol (5 mL) and KOH pellets (340 mg, 6.0 mmol). The resulting mixture was heated with stirring until all of the KOH had dissolved. The resulting solution was heated to 80 °C. To this hot solution were added sequentially (i) a mixture of **6a** and **6b** (440 mg, 2.0 mmol) and (ii) hydrazine (1.0 g, 31 mmol). The temperature of the reaction mixture was increased to 100-110 °C, and heating was continued at this temperature with stirring for 5 h. The reaction flask was fitted with a Dean-Stark tube, and water was removed from the reaction mixture by azeotropic distillation during 3 h. The Dean-Stark trap then was removed, and the temperature of the reaction mixture was increased to 200-210 °C. The reaction mixture was heated at this temperature with stirring for 15 h and then was allowed to cool to room temperature. Water (10 mL) was added with stirring, the resulting mixture was cooled externally to 0°C, and the pH of the cooled mixture was adjusted to 5-6 via dropwise addition of 3% aqueous HCl (ca. 5 mL). The resulting mixture was trnasferred into a separatory funnel. Water (20 mL) was added, and the resulting mixture was extracted with ether (2 x 30 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated in vacuo. The residue, a viscous yellow oil (360 mg) was purified via column chromatography on silica gel by using 4% EtOAc-hexane as eluent. A colorless solid was thereby obtained. Recrystallization of this material from hexane afforded pure **7b** (240 mg, 63%) as a colorless microcrystalline solid: mp 138-139 °C; IR (KBr) 2950 (s), 2870 (m), 1680 (vs), 1310 (m), 1280 cm^{-1} (m), ^{1}H NMR ($CDCl_3$) δ 1.42 (m, 2 H), 1.87 [d(*AB*), *J* = 12.0, 4.0 Hz, 2 H], 2.10 (m, 3 H), 2.47 (m, 3 H), 2.72 (m, 2 H), 2.88 (m, 1 H), 11.40 (very broad, 1 H); ^{13}C NMR ($CDCl_3$) δ 34.30 (d), 41.52 (t), 42.08 (t), 42.46 (d), 47.02 (d), 47.77 (d), 50.61 (d), 54.21 (s), 184.1 (s), mass spectrum (70 eV), m/e (relative intensity) 190 (molecular ion, 29.1), 145 (16.4), 105 (93.7), 91 (21.9), 80 (74.0), 79 (100), 78 (20.8), 77 (49.4), 66 (32.1), 65 (20.7), 51 (21.3), 45 (20.2), 41 (22.2), 39 (45.5). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.52. Found: C, 75.76; H, 7.42. The structure of **7b** was established unequivocally via single crystal X-ray structural analysis (*vide infra*).

X-ray Crystal Structures of 3, 4, and 7b.[9] All X-ray data were collected on a R3M/μ update of a Nicolet $P2_1$ diffractometer by using the ω-scan mode with variable scan speed and monochromated Mo Kα radiation. Crystals of 3 and 4 proved to be of very poor quality (broad, multiple peaks were obtained). X-ray data obtained for 3 and 4 provided molecular identification but not suitable refinement.

X-ray Data for 3. Space group $P2_1/c$, a = 11.379 (5), b = 9.795 (5), c = 11.393 (6) Å, b = 115.45 (8) °.

X-ray Data for 4. Space group P1, a = 6.465 (3), b = 9.253 (7), c = 12.971 (6) Å, a = 101.93 (5), b = 101.58 (4), g = 108.85 (4) °, V = 688 (1) Å^3, d_{calc} = 1.267 g-cm^{-3}.

X-ray data for 7b. Space group $P2_1/n$, a = 6.389 (2), b = 11.390 (5), c = 13.250 (4) A, b = 101.94 (2) °. and V = 943.4 (5) Å^3 from a least squares refinement of 25 reflections; Z = 4; d_{calcd} = 1.339 g-cm^{-3}, and $\mu = 0.84$ cm^{-1}. A total of 2162 independent reflections were collected, 1511 of which displayed $I > 3\sigma(I)$. The structure was solved by direct methods, and the model was refined to R = 0.075 with 183 parameters and S = 2.03, $(\Delta/\sigma)_{max} = 0.007$, and $\rho_{max,min}$ = 0.029, -0.27 eÅ^{-3}.

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References and Footnotes

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4. For example, **1a** and **1b** have been used as starting materials to synthesize triquinacene and several triquinacene derivatives. See: (a) Deslongchamps, P.; Cheriyan, U. O.; Lambert, Y.; Mercier, J.-C.; Ruest, L.; Russo, R.; Soucy, P. *Can J. Chem.* **1978,** *56*, 1687. (b) Paquette, L. A.; Kearney, F. R.; Drake, A. F.; Mason, S. F. *J. Am. Chem. Soc.* **1981,** *103*, 5064.

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9. Structure drawings of **3**, **4**, and **7b**, and tables of atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, anisotropic thermal parameters, H-atom coordinates, and isotropic thermal parameters for **7b** (8 pages) are available upon request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CV2 1EW, U. K. Requests should be accompanied by the full literature citation for this article.