Synthesis of Substituted 8,11-Dioxa(3,4-benzo)-[4.3.3]propellanes

by J. Jamrozik and P. Szlachcic

Department of Organic Chemistry, Jagiellonian University, Ingardena 3, 30-060 Kraków, Poland
E-mail: jamrozik@chemia.uj.edu.pl

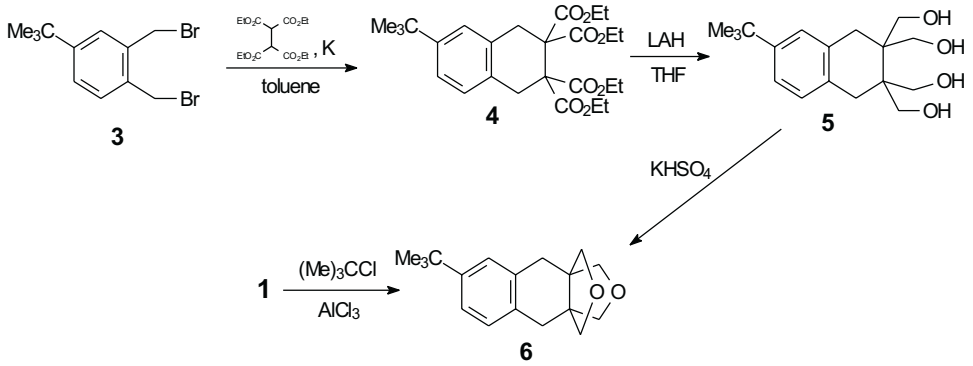
(Received June 8th, 2001; revised manuscript August 23rd, 2001)

The synthesis of three new mono-substituted 8,11-dioxa(3,4-benzo)-[4.3.3]propellanes is described. The method of synthesis of propellanes depends on the substituent, which we want to introduce. The structure of the compounds was determined by chemical and spectral evidences. Some aspects of the conformation of the compounds were studied.

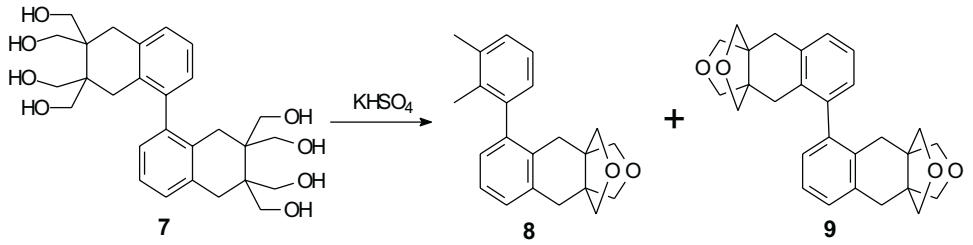
Key words:

Another reaction is an electrophilic aromatic substitution with the *tert*-butyl cation generated from *tert*-butyl chloride with catalytic amount of aluminium chloride. In spite of the fact that carbocation is a strong electrophile, this reaction does not occur. Also in other cases of electrophilic substitution unreacted propellane **1** remained. The aromatic ring is relatively hindered by the tetrahydrofuran rings binding by conjoining bond with boat-shaped cyclohexane [9].

The propellane **6** was, however, obtained from *tert*-butyl-o-xylene. The reaction pathway was similar to the one described in reference [7,8]. The reaction of *tert*-butyl--*o*-xylene with N-bromosuccinimide yields 3,4-bis(bromomethyl)-*tert*-butylbenzene **3** [10]. The reaction of **3** with 1,1,2,2-tetrakis(ethoxycarbonyl)ethane gave **4**, which was reduced with $LiAlH_4$ to tetraol **5**. Then the last reaction of **5** with $KHSO_4$ gave propellane **6**. The ^1H NMR spectrum of the propellane **6** (Experimental) is very similar to the spectrum of the corresponding propellane **2** and is also in good agreement with proposed structure.

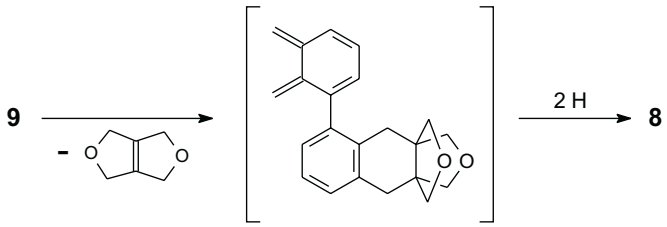


We have previously reported the preparation of bis-propellane **9** [9]. All of the tetrahydrofuran rings have envelope conformation. However, in one of the mono(propellane) parts the oxygen atoms are disordered occupying alternative positions (X-ray analysis) [9]. It probably promotes the process of dehydratation of octaol **7** also to mono(propellane) **8**. The compound **8** was isolated from the mixture by means of high-vacuum sublimation [11].

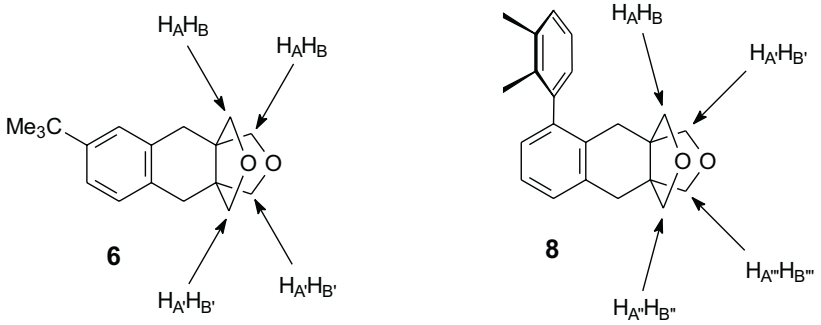


Mono-propellane **8** is probably produced in the first step by the retro *Diels-Alder* reaction [12] of **9** according to the scheme given below.

The next step is connected with addition of hydrogen to double bonds of **10** and aromatization of the system.



The propellane structure of the end-product **8** was suggested by its NMR spectrum (Experimental). Thus the ^{1}H NMR spectrum of the propellane **6** contained the characteristic proton signals corresponding to two AB system of eight geminal non-equivalent tetrahydrofuran protons ($2H_AH_B$, $2H_{A'}H_{B'}$). On the contrary, the ^{1}H NMR spectrum of the propellane **8** exhibited four different groups of proton signals originating from four AB proton systems (H_AH_B, $H_{A'}H_{B'}$, $H_{A''}H_{B''}$, $H_{A'''}H_{B'''}$). The appearance of the different signals is connected with the non-planar aryl rings arrangement.



On the basis of the investigation reported, it can be expected that the method synthesis of substituted propellane **1** depends on the substituents, which we want to introduce.

EXPERIMENTAL

Melting points (uncorrected): Boetius hot-stage microscope. IR spectra were recorded with a Bruker JFS 48 spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AMX 500 spectrometer (500 MHz proton frequency). Chemical shifts are referenced to internal TMS. MS spectra were recorded with a Finnigan MAT 44S spectrometer (EI, 70eV).

8,11-Dioxa[3,4-(2'-nitro-benzo)]-[4.3.3]propellane (2): Sulphuric acid (0.4 g, 98%) was added with stirring to nitric acid (0.2 g, 70%) in a small flask. **1** (0.2 g, 1 mmol) was added in small portions to prepared solution of acids. Then the mixture was heated for 1 hour in 60°C. The reaction mixture was poured into ice. Resulting solid was filtered, washed with water and crystallized from ethanol to give 0.21 g (89%) of yellow solid. ^{1}H NMR ($CDCl_3$), δ: 2.86 (broad s, 4H, CH_2), 3.52/3.74 (AB, J = 9.1 Hz, 4H,

OCH_2), 3.56/3.75 (AB, J = 9.1 Hz, 4H, OCH_2), 7.29 (d, J_{ortho} = 8.2 Hz, 1H, arom.H), 8.00 (d, J_{meta} = 2.1 Hz, 1H, arom.H), 8.08 (dd, J_{ortho} = 8.2 Hz, J_{meta} = 2.3 Hz, 1H, arom.H); ^{13}C NMR ($CDCl_3$), δ: 35.5, 35.7, 58.2, 58.3, 78.2, 78.3, 122.3, 123.0, 128.9, 138.6, 144.7, 147.1,. MS (EI): m/z (%) = M^+ 261 (6), 243 (100). HRMS (EI): 261.0992, calculated for $C_{14}H_{15}NO_4$: 261.1001.

6-*tert*-Butyl-2,2,3,3-tetrakis(ethoxycarbonyl)tetralin (4): 1,1,2,2-Tetrakis(ethoxycarbonyl)ethane (6 g, 19 mmol) was dissolved in anhydrous toluene (200 ml). Potassium (1.48 g, 38 mmol) was added and mixture was stirred for 22 h in 100°C. Then solution of 3,4-bis(bromomethyl)-*tert*-butylbenzene (6 g, 19 mmol) in 1,2-dimethoxyethane (75 ml) was added. After addition reaction mixture was stirred for 140 h in 100–115°C. 2-Propanol was added and then reaction mixture was poured into water. Organic layer was washed with water and dried over $MgSO_4$. Toluene was removed. Remaining yellow oil was chromatographed on Silica Gel with chloroform. 6.3 g (70%); IR (KBr, cm^{-1}): 2967, 2866, 1745 (C=O), 1730 (C=O), 1510, 1476, 1437, 1391, 1366, 1303, 1269, 1230, 1198, 1034; ^{1}H NMR ($CDCl_3$), δ: 1.19–1.23 (m, 12H, $OCH_2C\mathbf{H_3}$), 1.27 (s, 9H, *tert*-butyl), 3.47 (s, 2H, CH_2), 3.53 (s, 2H, CH_2), 4.13–4.25 (m, 8H, $OC\mathbf{H_2}CH_3$), 6.99 (d, J_{ortho} = 8.1 Hz, 1H, arom.H), 7.06 (d, J_{meta} = 1.7 Hz, 1H, arom.H), 7.13 (dd, J_{ortho} = 8.1 Hz, J_{meta} = 1.7 Hz, 1H, arom.H); ^{13}C NMR ($CDCl_3$), δ: 13.7, 31.3, 34.2, 34.3, 35.0, 57.5, 57.7, 61.6, 123.3, 124.9, 127.8, 129.5, 132.1, 148.8, 169.9, 170.0. MS (EI): m/z (%) = M^+ 476 (20), 283 (100). HRMS (EI): 476.2419, calculated for $C_{26}H_{36}O_8$: 476.2411.

6-*tert*-Butyl-2,2,3,3-tetrakis(hydroxymethyl)tetralin (5): A solution of **4** (1.32 g, 2.8 mmol) in anhydrous THF (50 ml) was added dropwise into a solution of $LiAlH_4$ (9 ml of 1M, 9 mmol) in anhydrous THF. Then a mixture was heated under reflux for 150 hours. Then water was added and the mixture was acidified to pH = 8 with 10% sulphuric acid solution and heated for 3 hours. A white solid was filtered off. The solvent was evaporated and the residue washed with methanol. White powder; 0.41 g (47%); m.p. 217–218°C; IR (KBr, cm^{-1}): 3262 (broad, O-H), 2961, 2898, 1615, 1581, 1510, 1481, 1462, 1437, 1393, 1359, 1262, 1235, 1103, 1078, 1049, 1010, 971, 822, 803, 764; ^{1}H NMR (CD_3OD), δ: 1.27 (s, 9H, *tert*-butyl), 2.59 (s, 2H, CH_2), 2.62 (s, 2H, CH_2), 3.52/3.79 (AB, J = 11.3 Hz, 4H, OCH_2), 3.53/3.80 (AB, J = 11.3 Hz, 4H, OCH_2), 6.99 (d, J_{ortho} = 8.0 Hz, 1H, arom.H), 7.09 (d, J_{meta} = 1.7 Hz, 1H, arom.H), 7.13 (dd, J_{ortho} = 8.0 Hz, J_{meta} = 2.0 Hz, 1H, arom.H); ^{13}C NMR (DMSO-d_6), δ: 29.9, 30.7, 31.2, 33.9, 42.6, 60.8, 122.4, 125.2, 128.6, 131.6, 134.0, 147.4. Anal. Calcd for $C_{18}H_{28}O_4$ (308.42): C, 70.10; H, 9.15. Found C, 70.22; H, 9.38; MS (EI): m/z (%) = M^+-H_2O 290 (4), M^+-$2H_2O$ 272 (40), 57 (100).

8,11-Dioxa[3,4-(2′-*tert*-butyl-benzo)]-[4.3.3]propellane (6): $KHSO_4$ (0.7 g) and **5** (154 mg, 0.5 mmol) was triturated in mortar. Then it was heated for 2 hours in 180°C. Resulting black solid was triturated in mortar and heated under reflux with chloroform. Solution was filtered and solvent removed under reduced pressure. Remaining solid was sublimed (1 mmHg, 100°C) to give white crystalline product; 58 mg (43%); m.p. 98–99°C; IR (KBr, cm^{-1}): 3061, 2961, 2916, 2841, 1613, 1501, 1469, 1362, 1271, 1076, 1034, 935, 815, 715, 627; ^{1}H NMR ($CDCl_3$), δ: 1.31 (s, 9H, *tert*-butyl), 2.71 (s, 2H, CH_2), 2.73 (s, 2H, CH_2), 3.54/3.70 (AB, J = 8.9 Hz, 4H, OCH_2), 3.55/3.71 (AB, J = 8.9 Hz, 4H, OCH_2), 7.02 (d, Jortho = 7.8 Hz, 1H, arom.H), 7.11 (d, J_{meta} = 1.7 Hz, 1H, arom.H), 7.19 (dd, J_{ortho} = 7.8 Hz, J_{meta} = 2.0 Hz, 1H, arom.H); ^{13}C NMR ($CDCl_3$), δ: 31.5, 34.4, 35.1, 35.9, 58.4, 78.5, 78.6, 123.5, 125.2, 127.8, 133.7, 136.3, 149.9. Anal. Calcd for $C_{18}H_{24}O_2$ (272.39): C, 79.37; H, 8.88. Found C, 79.11; H, 9.24; MS (EI): m/z (%) = 272 M^+ (54), 257 (100).

2,3-Dimethyl-2′,3′-{8″,11″-dioxa[4.3.3]propella(3″,4″)}biphenyl (8): $KHSO_4$ (0.68 g) and 7 (0.26 g, 0.5 mmol) was triturated. Then it was heated for 2 hours in 200°C. Resulting black solid was triturated and heated under reflux with chloroform. Solution was filtered and solvent removed under reduced pressure. Remaining solid was sublimed (1 mmHg) to give two products: first compound **8** in 95°C and second compound **9** in 200°C. Compound **8**: colourless crystals (ethanol); 56 mg (35%); m.p. 164–165°C; IR (KBr, cm^{-1}): 3059, 3020, 2957, 2934, 2925, 2841, 1145, 1092, 1065; ^{1}H NMR ($CDCl_3$), δ: 1.97 (s, 3H, 2-CH_3), 2.34 (s, 3H, 3-CH_3), 2.46/2.50 (AB, J = 14.8 Hz, 2H, 2'-CH_2), 2.79/2.83 (AB, J = 14.6 Hz, 2H, 3'-CH_2), 3.26–3.74 (4 AB, J = 9 Hz, 8H, OCH_2), 6.90–7.26 (m, 6H, arom.H); ^{13}C NMR ($CDCl_3$), δ: 16.7, 20.5, 31.8, 36.1, 58.1, 58.5, 77.5, 77.6, 79.27, 79.29, 125.1, 125.9, 127.2, 127.4, 128.1, 128.8, 134.8, 136.8, 136.9, 140.6, 141.6. Anal. Calcd for $C_{22}H_{24}O_2$ (320.43): C, 82.47; H, 7.55. Found C, 82.18; H, 7.43; MS (EI): m/z (%) = 320 M^+ (60), 259 (100).

REFERENCES

1. Tobe Y., *Propellanes, Carbocyclic Cage Compounds*, Weinheim 1992, p.125.
2. Jamrozik J. and Żesławski W., *Polish J. Chem*., **70**, 1365 (1996).
3. Jamrozik J. and Szlachcic P., *Polish J. Chem*., **74**, 1363 (2000).
4. Schlüter A.D., Bothe H. and Gosau J.M., *Makromol. Chem*., **192**, 2497 (1991).
5. Dreyer D.L., Bennet R.D. and Basa S.C., *Tetrahedron*, **32**, 2367 (1976).
6. Fritz H. and Fisher O., *Tetrahedron*, **20**, 1737 (1964).
7. Jamrozik J., *Monatsh. Chem*., **111**, 643 (1980).
8. Jamrozik J., Jamrozik M., Ściborowicz P. and Żesławski W., *Monatsh. Chem*., **126**, 587 (1995).
9. Grochowski J., Jamrozik J., Serda P. and Żesławski W., *Liebigs Ann*., 1123 (1995).
10. Volz W. and Voss J., *Phosphorus, Sulfur Silicon Relat. Elem.*, **53**, 429 (1990).
11. Żesławski W., PhD. Thesis, Jagiellonian University, Kraków (1995).
12. Ripoll J.L., Vallee Y., Khalid M. and Hakiki A., *J. Heterocyclic Chem.*, **29**, 1867 (1992).