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A Novel Preparation of Bicyclo[3.2.2]nonanes and Bicyclo[4.2.2]decanes Substituted at the Bridgeheads

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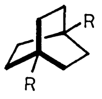
Synopsis. A novel preparation of 1,5-disubstituted bicyclo[3.2.2]nonanes and 1,6-disubstituted bicyclo[4.2.2]decanes based on the one-pot reaction of [3.2.2]- and [4.2.2]propellanecarboxylic acids with 2 equiv. of lead tetraacetate, followed by catalytic hydrogenation, is described.

The bicyclo[n.2.2]alkanes, having substituents on each bridgehead carbon atom, are of importance as models for examining through–bond and/or through–space orbital interactions and as a key intermediate for the synthesis of paddlanes.[1] Syntheses of the 1,4-disubstituted bicyclo[2.2.2]octanes (**1**) have been described.[2] However, only a few methods have been worked out for the higher homologues, bicyclo[3.2.2]nonanes and bicyclo[4.2.2]decanes substituted at the bridgeheads.[2a,3] We have found that the oxidative decarboxylation of [4.2.2]propellanecarboxylic acid (**5**) with lead tetraacetate (Pb(IV)) gives rise to the formation of the cyclopropylcarbinyl type tricyclic acetate (**7**) in high efficiency.[4] Since the oxidation of highly strained bicyclo[*n*.1.0]alkanes with Pb(IV) proceeds with exclusive internal bond cleavage of cyclopropane ring,[5] it may be reasonable to expect the formation of 1,6-disubstituted bicyclo[4.2.2]decane derivatives such as **9** by the reaction of **7** with Pb(IV). In this connection, we wish to report a novel preparation of 1,5-disubstituted bicyclo[3.2.2]nonanes (**2a**, **b**) and 1,6-disubstituted bicyclo[4.2.2]decanes (**3a**, **b**) based on the one-pot reaction of [3.2.2]- and [4.2.2]propellanecarboxylic acids (**4**) and (**5**) with Pb(IV), comprising two successive oxidations by Pb(IV), *i.e.*, oxidative decarboxylation of **4** and **5**, affording the strained tricyclic acetates (**6**) and (**7**), and subsequent oxidative cleavage of internal cyclopropane bond of **6** and **7** leading to the unsaturated diacetates (**8**) and (**9**), followed by catalytic hydrogenation (Scheme 1).



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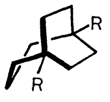
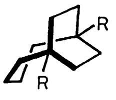


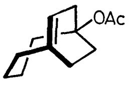
2a R=OAc
2b R=OH



3a R=OAc
3b R=OH

The reaction of **7** with Pb(IV) was examined. When **7** was treated with 1.2 equiv. of Pb(IV) in benzene at 80 °C for 14 h, the bridgehead diacetate (**9**) was obtained as a major product in 76% yield along with 6-acetoxybicyclo[4.2.2]dec-1(8)-ene (**10**)[6] (17%).[7] The structure of **9** was elucidated by the presence of a two-proton singlet at δ 5.83 ppm in the ^{1}H NMR spectrum and the ^{13}C NMR spectrum which showed only seven signals involving a two-carbon doublet at δ 131.56 ppm in the off-resonance decoupled spectrum. No detectable amounts of the triacetates from internal bond cleavage and/or the external bond cleavage products were formed.

The direct preparation of **9** from [4.2.2]propellanecarboxylic acid (**5**) by an one-pot procedure involving two successive Pb(IV) oxidations was attempted. When the reaction of **5** with 2.5 equiv. of Pb(IV) in benzene was carried out at 80 °C for 20 h, the expected product (**9**) was obtained in 58% yield together with **10** in 13% yield.



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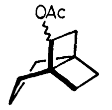

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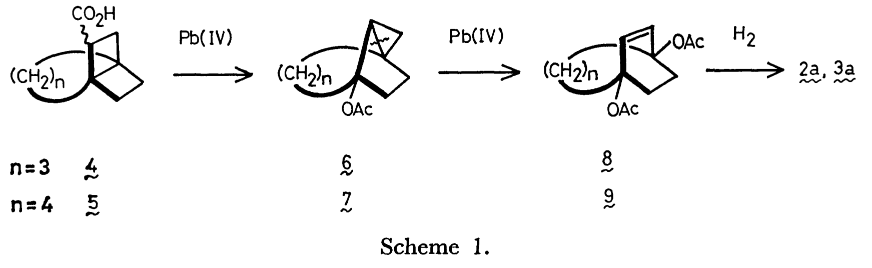
In order to prepare 1,5-disubstituted bicyclo[3.2.2]nonanes, the reaction of [3.2.2]propellanecarboxylic acid (**4**) with 1.2 equiv. of Pb(IV) was examined. After 1 h, the bridgehead diacetate (**8**) was obtained as a major product in 47% yield along with the unrearranged 6-acetoxy[3.2.2]propellane (**11**) in 11% yield, while the tricyclic acetate (**6**) could not be detected even in a shorter reaction time. Similarly, the structure of **8** was determined by the ^{1}H NMR (a two-proton singlet at δ 6.04 ppm) and ^{13}C NMR spectra (seven signals involving a two-carbon doublet at δ 132.54 ppm in the off-resonance spectrum). In view of the fact that a considerable amount (30%) of the unreacted acid (**4**) was recovered, it can be assumed that **8** was formed by rapid oxidation of unstable intermediate (**6**) by Pb(IV) as in the case of **7**.

The catalytic hydrogenation of **8** and **9** over Pd/C gave **2a**, mp 72—73 °C, and **3a**,[6] mp 100—102 °C, respectively, in quantitative yields. The reductive cleavage of the diacetates (**2a**) and (**3a**) by lithium



Scheme 1.

aluminum hydride afforded the corresponding diols (**2b**), mp 139—140 °C, and (**3b**), mp 158—160 °C, in moderate yields.

Experimental

*Reaction of the Acetate (**7**) with Pb(IV).* A mixture of 91 mg (0.47 mmol) of **7**,4) 25 mg (0.32 mmol) of pyridine, and 250 mg (0.56 mmol) of lead tetraacetate in 5 ml of benzene was heated at 80 °C with stirring under nitrogen for 14 h. After filtration, the filtrate was washed with 1 mol dm^{-3} hydrochloric acid, sodium hydrogencarbonate solution, and water, and then dried over anhydrous sodium sulfate (Na_2SO_4). Evaporation of the solvent gave 109 mg of light brown oil. The products were analyzed by GLC (10% FFAP and 5% SE-30 columns) and separated by silica-gel column chromatography.

9 (76%); IR 3030, 1715, 1225, 1040, 1000 cm^{-1}; MS *m/e* 252 (M^+); ^{1}H NMR (CCl_4) δ 1.10—2.60 (m, 18H, s at 1.92), 5.83 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 22.31 (q), 23.24 (t), 29.84 (t), 40.41 (t), 81.36 (s), 131.56 (d), 170.16 (s). Found: C, 66.54; H, 7.99%. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99%.

*Reaction of [4.2.2]Propellanecarboxylic Acid (**5**) with Pb(IV).* A mixture of 504 mg (2.6 mmol) of **5**,4) 119 mg (1.5 mmol) of pyridine, and 2.88 g (6.5 mmol) of Pb(IV) in 40 ml of benzene was heated at 80 °C for 20 h. 606 mg of light brown oil was obtained by a similar work-up to that described above. The products were analyzed and separated as above.

*Reaction of [3.2.2]Propellanecarboxylic Acid (**4**) with Pb(IV).* A mixture of 2.40 g (14 mmol) of **4**,3) 670 mg (8.5 mmol) of pyridine, and 8.36 g (17 mmol) of Pb(IV) in 120 ml of benzene was heated at 80 °C for 1 h. The same work-up as above gave 1.89 g of a product mixture, 860 mg (30%) of unreacted **4** being recovered by acidification of the sodium hydrogencarbonate washings followed by ether extraction. The products were analyzed and separated as above.

8 (47%); IR 3030, 1715, 1230, 1190, 1010 cm^{-1}; MS *m/e* 238 (M^+); ^{1}H NMR (CCl_4) δ 1.60—2.35 (m, 16H, s at 1.91), 6.04 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 20.80 (t), 22.08 (q), 28.87 (t), 34.25 (t), 80.82 (s), 132.54 (d), 169.95 (s). Found: C, 65.50; H, 7.63%. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61%.

11 (11%; a mixture of epimers); IR 1725, 1220, 1020 cm^{-1}; MS *m/e* 180 (M^+); ^{1}H NMR (C_6D_6) δ 1.28—2.64 (m, 15H), 4.80 (t, 0.5H), 5.20 (t, 0.5H). Found: C, 73.03; H, 9.09%. Calcd for $C_{11}H_{16}O_2$; C, 73.30; H, 8.95%.

*Catalytic Hydrogenation of **8** and **9**.* **8** and **9** were hydrogenated under atmospheric pressure of hydrogen over 5% Pd/C catalyst in methanol solvent to give **2a** and **3a**,6) respectively, in quantitative yields. Pure samples of **2a** and **3a** were obtained by recrystallization from hexane–ether.

2a; mp 72—73 °C; IR 1715, 1235, 1200, 1000, 970 cm^{-1}; MS *m/e* 180 (M^+-AcOH); ^{1}H NMR (CCl_4) δ 1.60—2.40 (m, s at 1.92); ^{13}C NMR ($CDCl_3$) δ 20.02 (t), 22.35 (q), 30.65 (t), 38.54 (t), 82.51 (s), 170.04 (s). Found: C, 64.88; H, 8.52%. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39%.

3a; mp 100—102 °C; IR 1715, 1230 cm^{-1}; MS *m/e* 252 (M^+-2), 134 (M^+-2AcOH); ^{1}H NMR (CCl_4) δ 1.20—2.60 (m, s at 1.88); ^{13}C NMR ($CDCl_3$) δ 22.02 (q), 22.90 (t), 30.97 (t), 38.70 (t), 83.56 (s), 169.33 (s). Found: C, 65.76; H, 8.71%. Calcd for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72%.

*Lithium Aluminum Hydride Reduction of **2a** and **3a**.* To a suspension of 1.5 equiv. of lithium aluminum hydride in ether was added dropwise a solution of **2a** or **3a** in the same solvent, the mixture being stirred at room temperature for 2 h. Water and then 1 mol dm^{-3} hydrochloric acid were added carefully. The organic layer was separated and washed with saturated sodium chloride solution and dried over Na_2SO_4. The aqueous layer was extracted with chloroform, the chloroform extracts being washed with saturated sodium chloride solution and dried (Na_2SO_4). Evaporation of both solvents gave **2b** and **3b** as white solids in 60—65% yields which were recrystallized from ether.

2b; mp 139—140 °C; IR 3250, 1030 cm^{-1}; MS *m/e* 156 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.50—2.20 (m). Found: C, 69.11; H, 10.36%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

3b; mp 158—160 °C; IR 3250, 1060, 980 cm^{-1}; MS *m/e* 170 (M^+); ^{1}H NMR ($CDCl_3$) δ 1.40—2.20 (m). Found: C, 70.34; H, 10.71%. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66%.

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7) The by-product **10** may be formed by the action of acetic acid generated during the course of reaction.6)