

A New Approach to Dehydrocamphenilone and Camphenilone

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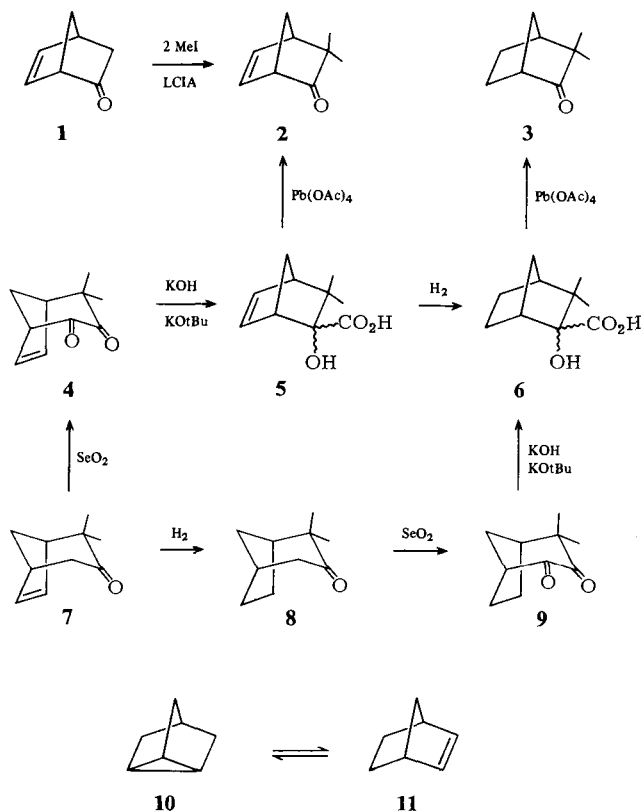
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Eine neue Darstellung von Dehydrocamphenilone und Camphenilone

Benzilsäureumlagerung von Dehydrocarbocamphenilone (4) ergibt die α -Hydroxysäure 5, welche mit Bleitetraacetat oxidativ zu Dehydrocamphenilone (2) decarboxyliert wird. Die gleiche Reaktionsfolge führt von Carbocamphenilone (9) zu Camphenilone (3).

Although dehydrocamphenilone (2) and camphenilone (3) are simple compounds, their synthesis is not trivial. *Dworan* and *Buchbauer*^{1a)} have just described a route to 2, which involves



geminal dimethylation of norbornenone (**1**) with an excess of methyl iodide in the presence of the strong base lithium cyclohexylisopropylamide (LCIA) in refluxing tetrahydrofuran. Although this reaction looks straightforward, it may be expected to give monomethylated and dimethylated bicyclic ketones, and also rearranged tricyclic ketones, because of the greater thermodynamic stability of nortricyclene (**10**) vs. isomeric norbornene (**11**) (ratio **10**:**11** = 77:23 at equilibrium²). In any event, **2** could only be isolated by preparative GC from a complex reaction mixture^{1a}.

We here describe a simple approach to **2**, which does not require preparative GC for isolation. Oxidation of bicyclic ketone **7**³ with SeO₂ yielded dehydrocarbobcamphenilone (**4**)⁴. Similarly, carbocamphenilone (**9**) was obtained by SeO₂ oxidation of **8**⁴. Benzilic acid rearrangement of the α -diketones **4** and **9** was carried out with the *Gassman* base/solvent system⁵ (3 KOtBu + H₂O in diethyl ether), which gave the α -hydroxycarboxylic acids **5** and **6** in an exothermic reaction. Finally, oxidative decarboxylation with lead tetraacetate⁶ yielded the corresponding ketones **2** and **3**. Camphenilone (**3**), which is less strained, was formed in 73% yield, whereas dehydrocamphenilone (**2**) was formed in 36% yield.

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Experimental Part

2,2-Dimethylbicyclo[3.2.1]oct-6-en-3-one (**7**) was prepared as described³ and converted into α -diketone **4**⁴.

2-Hydroxy-5,6-didehydrocamphenilic acid (5): Dehydrocarbobcamphenilone (**4**) (1.5 g, 9.1 mmol) in absol. ether (10 ml) was stirred with potassium *tert*-butoxide (6.03 g, 54 mmol). After addition of water (0.29 ml, 16 mmol) at room temperature an exothermic reaction ensued and a brown solid was precipitated. After 3 h the reaction mixture was acidified with dil. H₂SO₄ and extracted with ether. The combined organic phase was washed with water and dried (Na₂SO₄). The ether was evaporated leaving a solid, which was sublimed *in vacuo*, yielding **5** (1.0 g, 60%). – 90 MHz ¹H NMR (CDCl₃): δ = 0.92 (s, 3H, CH₃), 1.23 (s, 3H, CH₃), 1.55 (dt, 1H), 2.2 (m, 1H), 2.44 (m, 1H) and 3.14 (m, 1H) (bridgehead H's), 6.11 (q, 1H) and 6.44 (q, 1H) (olefinic H's). The signal of the OH protons is obscured.

2-Hydroxycamphenilic acid (6): **5** (108 mg, 0.59 mmol) was dissolved in ethyl acetate (6 ml), 30 mg of Pd on charcoal (10%) being added. Hydrogenation with hydrogen at room temperature and the usual work up gave **6** in quantitative yield. – 90 MHz ¹H NMR (CDCl₃): δ = 1.01 (s, 3H, CH₃), 1.04 (s, 3H, CH₃), 1.33 (m, 4H), 1.78 (m, 2H); 2.22 (m, 1H) and 2.42 (m, 1H) (bridgehead H's).

Dehydrocamphenilone (2): **5** (370 mg, 2.0 mmol) in CHCl₃ (20 ml) and lead tetraacetate (900 mg, 2.0 mmol) (washed twice with ether) were stirred at room temperature. After 4 h ethylene glycol (5 ml) was added and the mixture was stirred for a further 15 min. After addition of water the organic phase was washed with aqueous NaHCO₃, water, and dried (MgSO₄). The solvent was evaporated leaving a yellow oil which was distilled in a Kugelrohr apparatus, giving **2** (100 mg, 36%). – 90 MHz ¹H NMR (CDCl₃): δ = 1.05 (s, 3H, CH₃), 1.16 (s, 3H, CH₃), 2.1 (m, 2H, CH₂), 2.77 (m, 1H) and 3.03 (m, 1H) (bridgehead H's), 6.08 (br q, 1H) and 6.58 (q, 1H) (olefinic H's). – MS (70 eV): *m/e* = 136 (28%, M⁺), 108 (31), 93 (80), 91 (36), 77 (36), 70 (100), 66 (36), 65 (15), 42 (29), 39 (34).

2,4-Dinitrophenylhydrazone: 90 MHz ^1H NMR (CDCl_3): δ = 1.15 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 2.02 (m, 2H), 2.72 (br, 1H) and 3.78 (br, 1H) (bridgehead H's); 6.12 (q, 1H) and 6.51 (q, 1H) (olefinic H's), 7.92, 8.27, 9.11 (3H, aromatic H's), 11.11 (br, 1H, NH).

$\text{C}_{15}\text{H}_{16}\text{N}_4\text{O}_4$ (316.3) Calcd. C 56.96 H 5.06 N 17.72 Found C 56.54 H 4.94 N 17.23

Camphenilone (3): Oxidative decarboxylation of **6** (200 mg, 1.8 mmol) was analogous to that of **5**, giving **3** (110 mg, 73%). – 90 MHz ^1H NMR (CDCl_3): δ = 1.01 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.22–2.11 (m, 6H), 2.22 (br, 1H) and 2.55 (m, 1H) (bridgehead H's). – IR (CHCl_3): 1735 cm^{-1} .

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