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Furan Derivatives. VII. Synthesis of Cyclohepta[*cd*]benzofurans

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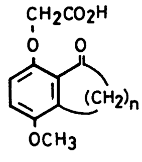
Synopsis. 7-Methoxy-3,4-dihydrocyclohepta[*cd*]benzofuran and 7-methoxycyclohepta[*cd*]benzofuran were synthesized.

Benzofurans are readily synthesized by heating (2-acylphenoxy) acetic acids with sodium acetate in acetic anhydride.[1] In the previous paper,[2] we applied the reaction to acids **1a**, **1b**, and **1c** which had a cyclic ketone (n=2, 3, and 4). The five-membered cyclic ketone **1a** gave no furan **5a**, and the six-membered cyclic ketone **1b** afforded a furan **5b** and a lactone in 1:1 ratio. However, the seven-membered cyclic ketone **1c** produced almost a furan **5c**. Royer *et al.*[3] early reported that a seven-membered cyclic ketone was more effective for furan-ring formation than a six-membered cyclic ketone. The facile furan-ring formation of **1c** is attributed to flexibility of the seven-membered cyclic ketone.[2,4] For the furan-ring formation, an anion such as **8** attacks the carbonyl carbon atom from the upper side of the carbonyl plane.[5] If the carbonyl plane is fixed in the same plane with the benzene ring, the furan-ring formation would be difficult. We introduced double bonds in the seven-membered cyclic ketone to reduce flexibility of the ring and to examine whether the furan-ring formation is possible or not. In this paper, the reaction of acids **3a** and **4a** with sodium acetate in acetic anhydride is reported. However, we abandoned synthesis of **2a** because a ketone **2b** was thermally unstable and polymerized easily. The results are summarized along with the reaction of the related acid **1c** in Table 1.

The acid **3a** produced a furan **6** in 93% yield and the corresponding lactone was not detected. The facile furan-ring formation suggests that seven-membered cyclic ketone in **3a** is still flexible and the carbonyl group can take a favorable conformation for the attack of an anion. We are particularly interested in the furan-ring formation from the acid **4a** as the seven-membered cyclic ketone is fully unsaturated and considered to be rigid. Indeed, the acid **4a** gave easily a furan **7** in 81% yield. It shows that the carbonyl group is yet flexible. The furan **7** is an interesting new class of compound because it has both structures and properties of benzofuran and benzoheptafluvene. The furan **7** is not so stable and polymerizes during storage. Thus, the furan-ring formation was very easy in spite of the additional double bonds in the seven-membered cyclic ketone.



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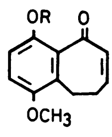

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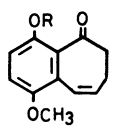

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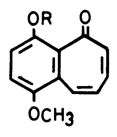

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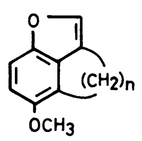

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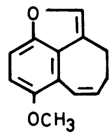

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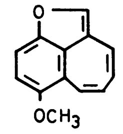

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1, 5 a) $n = 2$
b) $n = 3$
c) $n = 4$

2, 3, 4 a) $R = CH_2CO_2H$
b) $R = H$

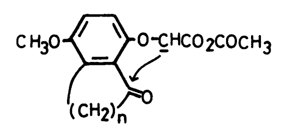

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Table 1. Reaction of acids **1c**, **3a**, and **4a** with sodium acetate in acetic anhydride[a]

Compound	Product	Yield/%
1c	**5c**	89[b]
	lactone	3[c]
3a	**6**	93[b]
	lactone	0[d]
4a	**7**	81[b]

a) Reactions were carried out at 150 °C for 1 h. b) Isolated yield. c) Lactone was initially produced but it was hydrolyzed to the starting material during isolation procedure. d) Lactone was not produced.

Experimental

The column chromatography was performed on silica gel. ^1H and ^{13}C NMR spectra were determined at 90 MHz on a JEOL JNM-FX 90Q FT NMR spectrometer.

*(1-Methoxy-5-oxo-6,7-dihydro-5*H*-benzocyclohepten-4-yloxy)-acetic Acid (3a).* A mixture of **3b** (4.11 g; prepared from **8**[2] through four steps[6]), ethyl bromoacetate (8.22 g), potassium phosphate (12.0 g), and acetone (50 ml) was refluxed for 10 h. The mixture was poured into ice-water, acidified with 6 M hydrochloric acid (1 M=1 mol dm^{-3}), and extracted with ether. The ethereal layer was washed, dried, and evaporated. The residue was dissolved in ethanol and saponified with a 2 M potassium hydroxide solution. The alkaline solution was acidified with 6 M hydrochloric acid and the resulting acid was extracted with ether. The ethereal layer was washed, dried, and evaporated. The residue was chromatographed and eluted with benzene(9)-ether(1) to give **3a** (2.20 g, 42%), colorless needles from acetone, mp 129—130 °C. IR (KBr) ν_{max} 1770, 1750 (COOH), 1685, and 1670 cm^{-1} (CO). ^1H NMR (CD_3COCD_3) δ=2.34—2.56 (2H, m), 2.89—3.05 (2H, m), 3.82 (3H, s), 4.69 (2H, s), 6.17 (1H, dt, J=6 and 12 Hz), 6.73 (1H, d, J=12 Hz), and 7.05 (2H, s). ^{13}C NMR (CD_3COCD_3) δ=25.5 (t), 47.6 (t), 56.8 (q), 68.7 (t), 114.6 (d), 116.4 (d), 125.1 (s), 125.3 (d),

132.5 (s), 132.7 (d), 149.4 (s), 152.7 (s), 170.2 (s), and 204.4 (s). Found: C, 63.98; H, 5.48%. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38%.

*(1-Methoxy-5-oxo-5*H*-benzocyclohepten-4-yloxy)acetic Acid (4a).* The compound **4a** (40%) was prepared from **4b** (synthesized from **8**[2] through three steps[7]) in a manner similar to synthesis of **3a**, colorless prisms from acetone, mp 150—151 °C. IR (KBr) ν_{max} 1770 (COOH) and 1640 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$) δ=3.95 (3H, s), 4.85 (2H, s), and 6.64—8.06 (6H, m). ^{13}C NMR ($CDCl_3$) δ=56.7 (q), 68.7 (t), 113.2 (d), 116.7 (d), 126.7 (s), 127.1 (d), 129.8 (s), 129.9 (d), 134.1 (d), 134.9 (d), 149.3 (s), 152.7 (s), 170.2 (s), and 191.5 (s). Found: C, 64.39; H, 4.68%. Calcd for $C_{14}H_{12}O_5$: C, 64.61; H, 4.65%.

*7-Methoxy-3,4-dihydrocyclohepta[*cd*]benzofuran (6).* A mixture of **3a** (1.0 g), acetic anhydride (15 ml), and sodium acetate (4.6 g) was heated at 150 °C for 1 h. The mixture was poured into ice-water (200 ml), stirred for 5 min to decompose excess acetic anhydride, and extracted with ether. The ethereal layer was washed three times with a 0.5 M potassium carbonate solution (30 ml) and then with water, dried, and evaporated. The residue was chromatographed and eluted with benzene to give **6** (0.71 g, 93%), colorless oil, bp 112—115 °C (0.7 Torr). ^{1}H NMR ($CDCl_3$) δ=2.40—2.60 (2H, m), 2.70—2.90 (2H, m), 3.83 (3H, s), 6.10 (1H, dt, J=7 and 12 Hz), 6.83 (1H, d, J=9 Hz), 6.95 (1H, d, J=12 Hz), 7.23 (1H, d, J=9 Hz), and 7.29 (1H, s). ^{13}C NMR ($CDCl_3$) δ=24.3 (t), 28.2 (t), 57.1 (q), 109.4 (d), 109.8 (d), 119.9 (s), 122.2 (s), 123.8 (d), 127.8 (s), 131.2 (d), 140.4 (d), 150.5 (s), and 152.2 (s). Found: C, 77.80; H, 6.10%. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04%.

*7-Methoxycyclohepta[*cd*]benzofuran (7).* The compound **7** (81%) was prepared from **4a** in a manner similar to synthesis of **6**, yellow oil, bp 128—130 °C (1 Torr (1 Torr=133.322 Pa)). ^{1}H NMR ($CDCl_3$) δ=3.72 (3H, s), 5.19—6.35 (4H, m), 6.56 (1H, d, J=9 Hz), 6.86 (1H, d, J=9 Hz), and 6.91 (1H, s). ^{13}C NMR ($CDCl_3$) δ=56.9 (q), 111.7 (d), 111.8 (d), 123.1 (s), 125.0 (s), 125.6 (d), 125.6 (d), 126.7 (d), 127.0 (d), 131.6 (s), 138.5 (d), 150.5 (s), and 151.6 (s). Found: C,78.78; H, 5.20%. Calcd for $C_{13}H_{10}O_2$: C, 78.77; H, 5.08%.

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