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Phenanthro[4,5-*bcd*]furan Derivatives. V. The Cyclization of (Dibenzofuran-1-yl)acetic Acid Derivatives

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Synopsis. The cyclization of (6-methoxy-1,2,3,4-tetrahydrodibenzofuran-1-yl)acetic acid (**3b**) and (6-methoxy-1,2,3,4,4a,9b-hexahydrodibenzofuran-1-yl)acetic acid (**5**) to the corresponding phenanthro[4,5-*bcd*]furans have been examined. The cyclization of **3b** was difficult, while that of **5** was easy. The difficult cyclization of **3b** has been attributed to strains in the reaction intermediate.

Dendy *et al.*[1] attempted to cyclize the (1,2,3,4-tetrahydrodibenzofuran-1-yl)acetic acids (**3a** and **3b**) to the corresponding phenanthro[4,5-*bcd*]furans (**4a** and **4b**) for the purpose of synthesizing morphenol. All attempts to cyclize **3a** were, however, unsuccessful. **4b** was obtained from Friedel-Crafts reaction of the acid chloride of **3b** but the yield was very low. Dendy *et al.* attributed the failure to ring strain in the products (**4a** and **4b**). 3-(8-Methoxy-4,5-dihydro-3*H*-naphtho-[1,8-*bc*]furan-3-yl)propionic acid (**1**) was readily cyclized by polyphosphoric acid (PPA) to the corresponding phenanthro[4,5-*bcd*]furan (**2**) which has a similar ring skeleton to **4b** in good yield.[2] Therefore, it is improbable that there is great strain in the **4b** molecule. It has previously been reported that the difficult cyclization of **3b** to **4b** may be due to strain in the reaction intermediate (**10**) rather than that of the product (**4b**).[3] Hydrogenation of the carbon-carbon double bond in the furan ring of **3b** would facilitate ready cyclization since the acetic acid side chain would closely approach the benzene ring in molecular terms. Thus, the saturated dibenzofuran derivative (**5**) could be readily cyclized. Consequently the cyclization of **5** to phenanthro[4,5-*bcd*]furan (**6**) has been attempted.

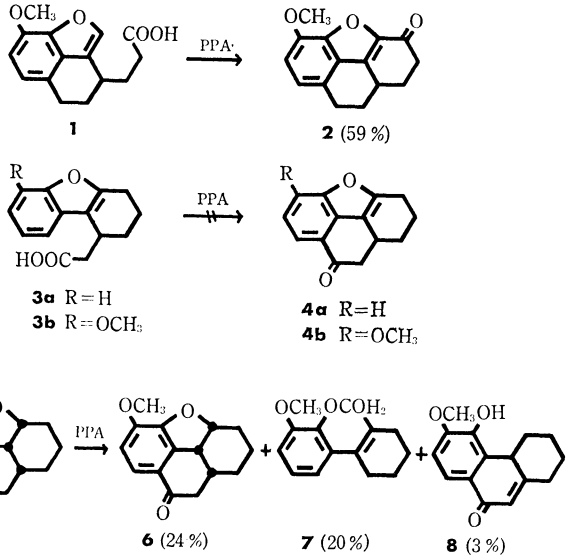

Fig. 1.

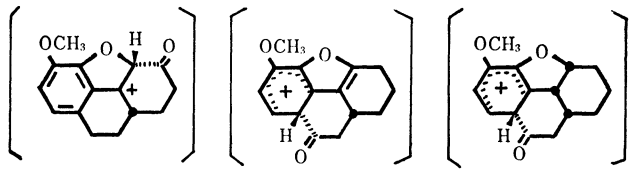

Fig. 2.

The ester (**13**) has been obtained by the Reformatsky reaction of the ketone (**12**). The formation of the ester (**14**) has been reported by Dendy *et al.*,[1] but the IR and NMR spectra of the product here were compatible with the structure of **13**. **13** was hydrogenated in the presence of palladium on charcoal and subsequently hydrolyzed to give **5**. It appears that the configuration of **5** is *cis-syn* as shown, since the furan ring is preferentially hydrogenated from the less hindered face after reduction of the exo-double bond. **5** was heated at 45 °C with PPA, and the desired phenanthro[4,5-*bcd*]-furan (**6**; 24%) was obtained together with a lactone (**7**; 20%) and a hydroxyl ketone (**8**; 3%). Cleavage of the furan ring before the formation of a carbonyl compound yields **7**. Cyclization and subsequent cleavage of the furan ring yields **8**. **5** was heated at 80 °C with PPA and the only product was **8** (40% yield). Under the same conditions (45 and 80 °C), **3b** did not give **4b**, the starting material being recovered. Thus, **5** was cyclized with greater facility than **3b**, as predicted.

These observations suggest that the conformation of the intermediate (**10**) is cup-shaped and possesses a large strain, whereas **11**, the intermediate in the cycliza-

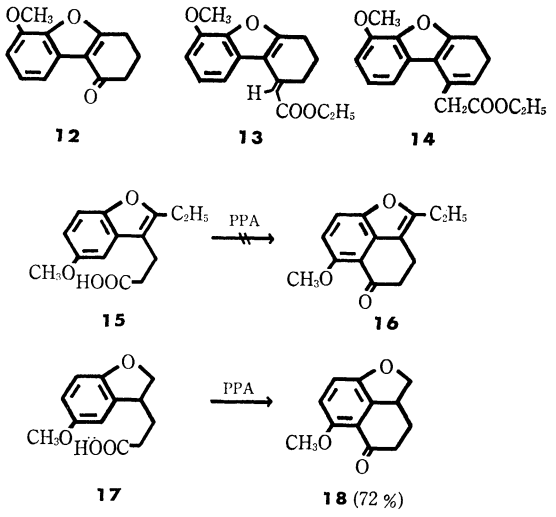

Fig. 3.

tion of **5** to **6**, possesses little strain owing to the saturated furan ring. The strain in the intermediate (**9**) is not large strain as the flexible propionic acid rest of **1** is attached very favorably for the cyclization reaction of **1** to **2**. Support for the above explanation is found in the facts that the cyclization of **15** to **16** is difficult but that of **17** to **18** is easy.[4]

Experimental

*The Cyclization of **5** with Polyphosphoric Acids.* A mixture of **5** (2.0 g) and 20% polyphosphoric acid (160 g) was heated with stirring at 45 °C for 7 h. The mixture was worked up in the usual manner. The resulting oil was chromatographed (benzene–ether 95:5) on silica gel to give three products.

*Loctone (**7**).* 370 mg (20% yield). Colorless prisms from benzene–hexane; mp 81—82 °C. IR (KBr): ν_{max} 1765 (COO–Ar) cm^{-1}. NMR ($CDCl_3$): δ 1.66—1.81 (4H, m), 2.35 (4H, broad s), 2.89 (2H, s), 3.87 (3H, s), 6.82—7.33 (3H, m).

Found: C, 73.52; H, 6.67%. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%.

*5-Hydroxy-6-methoxy-1,2,3,4,4a,9-hexahydrophenanthrene-9-one (**8**).* 60 mg (3% yield). Colorless plates from acetone–benzene; mp 144—145 °C. IR (KBr): ν_{max} 1665 (C=O), 3200, 3440 (OH) cm^{-1}. NMR (CD_3COCD_3): δ 1.28—1.79 (4H, m), 1.83—2.17 (2H, m), 2.39 (1H, dd, J=3 and 12 Hz), 2.83 (1H, dd, J=5 and 12 Hz), 3.12—3.31 (1H, m), 3.92 (3H, s), 6.20 (1H, s), 7.09 (1H, d, J=8 Hz), 7.62 (1H, d, J=8 Hz), 7.73 (1H, s).

Found: C, 73.51; H, 6.48%. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%.

*5-Methoxy-1,2,3,3a,8,9,9a,9b-octahydrophenanthro[4,5-bcd]furan-8-one (**6**).* 440 mg (24% yield). Colorless needles from benzene–hexane; mp 101—102 °C. IR (KBr): ν_{max} 1690 (C=O) cm^{-1}. NMR ($CDCl_3$): δ 1.02—1.30 (3H, m), 1.53—1.70 (2H, m), 1.95—2.18 (1H, m), 2.40—2.75 (1H, m), 2.50 (1H, dd, J=2 and 17 Hz), 2.79 (1H, dd, J=5 and 17 Hz), 3.81 (1H, t, J=7 Hz), 3.94 (3H, s), 5.10 (1H, q, J=8 Hz), 6.83 (1H, d, J=9 Hz), 7.41 (1H, d, J=9 Hz).

Found: C, 73.58; H, 6.77%. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%.

*Ethyl (6-Methoxy-1,2,3,4-tetrahydrodibenzofuran-1-ylidene)-acetate (**13**).* **13** was prepared by Dendy's method.[1] Colorless needles from ethanol; mp 96—97 °C. (**14**, prepared by Dendy *et al.*;[1] mp 97 °C). IR (KBr): ν_{max} 1695 ($COOC_2H_5$). NMR ($CDCl_3$): δ 1.32 (3H, t, J=7 Hz), 1.90—2.15 (2H, m), 2.90 (2H, t, J=6 Hz), 3.21 (2H, dt, J=1 and 6 Hz), 3.98 (3H, s), 4.21 (2H, q, J=7 Hz), 6.30 (1H, t, J=1 Hz), 6.78 (1H, d, J=7 Hz), 7.18 (1H, t, J=7 Hz), 7.38 (1H, d, J=7 Hz).

*(6-Methoxy-1,2,3,4,4a,9b-hexahydrodibenzofuran-1-yl)acetic Acid (**5**).* Ester **13** (3 g) in ethanol (50 ml) was hydrogenated in the presence of 10% palladium on charcoal (3 g) for 15 h at 7 atm and 60 °C. The resulting ester was purified by chromatography (benzene–ether 95:5) on silica gel and hydrolyzed to give 1.6 g (59%) of **5**. Colorless needles from benzene–hexane; mp 79—80 °C. IR (KBr): ν_{max} 1710 (COOH) cm^{-1}. NMR ($CDCl_3$): δ 1.10—2.10 (6H, m), 2.25—2.53 (1H, m), 2.43 (2H, broad s), 3.60 (1H, dd, J=3 and 8 Hz), 3.86 (3H, s), 4.86—5.03 (1H, m), 6.72—6.90 (3H, m).

Found: C, 68.58; H, 6.71%. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92%.

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