TRANSANNULAR CYCLIZATIONS OF TETRACYCLO[6.3.0.0.$^{2,6}0^{5,9}$]-UNDECAN-3,11-DIONE TO 4-HETERO-9,10-SECOBIRD-CAGE SYSTEM[1]

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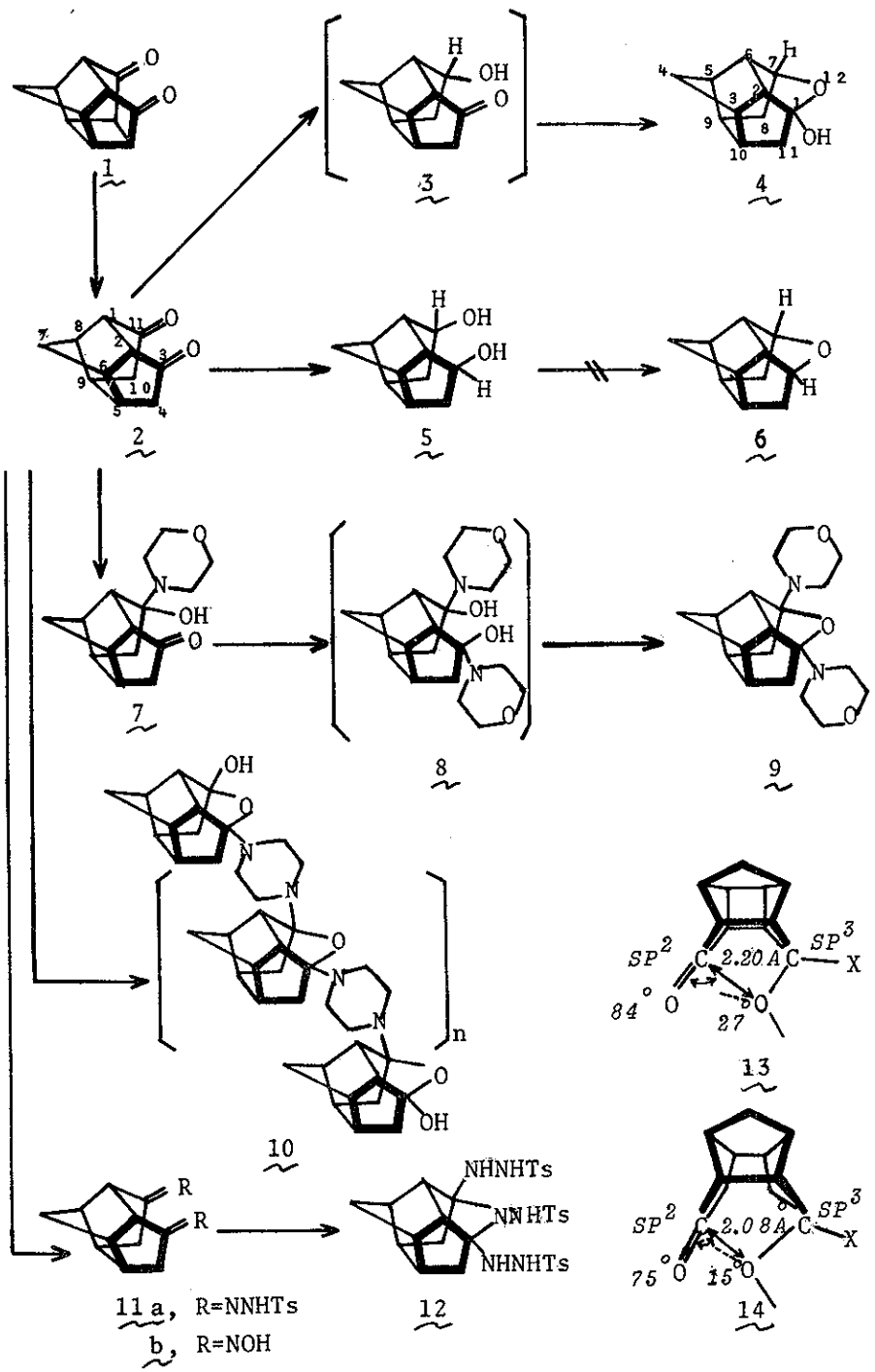
Transannular cyclizations of dione (2) in the title were observed on $NaBH_4$ reduction, and on additions of morpholine, piperazine, and p-toluenesulfonylhydrazine, affording the corresponding 4-oxa- and -aza-9,10-secobird-cage compounds.

We have previously reported a facile synthesis of 4-hetero-bird-cage system via the transannular cyclization of pentacyclo[6.2.1.0.$^{2,7}0.^{4,10}0^{5,9}$]undecan-3,6-dione (1).[2] In this communication we wish to report the transannular cyclizations of tetracyclo[6.3.0.0.$^{2,6}0^{5,9}$]undecan-3,11-dione (2)[3] as a facile route to 4-hetero-9,10-secobird-cage system.

Reduction of 2 with sodium borohydride (1/4 molar equivalent) in refluxing 90% aqueous ethanol for 10 min afforded directly transannularly cyclized product 4 (1-hydroxy-12-oxapentacyclo[5.4.1.0.$^{2,6}0.^{3,10}0^{5,9}$]undecane) in 80% yield, mp 212-214°;†[1] ν_{max}^{KBr} 3360 cm^{-1}; δ($CDCl_3$) 4.60 (1H, t, J=5.5Hz, C_7H), 4.42 (1H, s, OH), 3.0-1.8 (10H, m, other protons), and

†[1] All mps were measured in a sealed tube and are uncorrected. Satisfactory analyses were obtained for all new compounds reported in this communication.


1
2
3
4
5
6
7
8
9
10
11a, R=NNHTs
b, R=NOH
12
13
14
2.20Å
2.08Å
SP2
SP3
84°
27°
75°
15°

1.75 (2H, AB-q, J=11.5Hz, J/Δδ=0.956, C_4Hx2); m/e 178 (M^+).

Reduction of 2 with excess $LiAlH_4$ in ether gave diol 5 in 53% yield, mp 258-261°; ν_{max}^{KBr} 3220 cm^{-1}; δ($CDCl_3$) 5.52 (2H, s, OHx2), 4.34 (2H, broad t, J=ca.6Hz, C_3H and C_{11}H),†2 2.5-1.9 (10H, m, other protons), and 1.52 (2H, AB-q, J=12Hz, J/Δδ= 0.888, C_7Hx2); m/e 180 (M^+). Even on heating at 195° for 5 min 5 did not afford transannularly dehydrated product (6) but a complex olefinic mixture in contrast to the diol from 1, which is known to give 4-oxabird-cage.[2]

Treatment of 2 with an equimolar amount of morpholine in tetrahydrofuran for 5 hr at room temperature afforded 7 (34%), mp 170° dec; ν_{max}^{KBr} 3300 and 1686 cm^{-1}; δ ($CDCl_3$) 3.7 (5H, m, $-CH_2OCH_2-$ and OH), 3.12 (2H, broad s, C_1H and C_2H), 2.8-2.3 (12H, m, $-CH_2NCH_2-$ and protons at $C_{4-6,8-10}$), and 1.70 (2H, AB-q, J=12Hz, J/Δδ=0.522, C_7Hx2); m/e 263 (M^+).

Treatment of 2 with 3 molar excess morpholine in refluxing benzene for 6 hr afforded transannularly cyclized bis-adduct 9 (34%), mp 204-205° dec; ν_{max}^{KBr} 1152 and 1107 cm^{-1}; δ ($CDCl_3$) 3.67 (8H, t, J=4.5Hz, $-CH_2OCH_2-$x2), 2.85 (2H, s, C_2H and C_6H), 2.78 (8H, t, J=4.5Hz, $-CH_2NCH_2-$x2), 2.5-2.2 (4H, m, protons at C_3, C_5, C_9 and C_{10}), 1.92 (4H, s, C_8H and C_{11}H), and 1.70 (AB-q, J=12Hz, J/Δδ=3.750, C_4Hx2).

On refluxing with an equimolar amount of piperazine hexahydrate in ethanol for 5 hr, 2 afforded an oligomer 10 (33%), mp >300°; ν_{max}^{KBr} 3420 and 1625 (broad and weak) cm^{-1}. From analytical data (Found: C, 72.20; H, 8.23; N, 9.79. Calcd for $C_{86}H_{114}N_{10}O_8 \cdot C_2H_5OH$: C, 72.30; H, 8.27; N, 9.58) 10 had n=4, tentatively.

†2 The diol may be a mixture of stereoisomers.

Treatment of 2 with 2 molar equivalent p-tosylhydrazine in refluxing ethanol for 6 hr gave bistosylhydrazone 11a (40%), mp 275° dec; ν_{max}^{KBr} 3042 and 1647 cm^{-1}. However, on the same treatment of 2 with 4 molar excess tosylhydrazine, an aza-bridged product 12 was obtained (60%), mp 165-166°; ν_{max}^{KBr} 3275 cm^{-1}; δ ($CDCl_3$-CF_3COOH) 7.6 (12H, AB-q, J=8.4Hz, $J/\Delta\delta$=0.350, phenyl protons), 3.50 (2H, s, C_2H and C_6H), 3.2-2.6 (8H, m, other protons), 2.50 (9H, s, CH_3x3), and 2.03 (2H, AB-q, J=12Hz, $J/\Delta\delta$=0.800, C_4Hx2).

Similar treatment of 2 with hydroxylamine (4 times equivalent) in 70% aqueous ethanol gave only bisoxime 11b (95%), mp 240-242°; ν_{max}^{KBr} 3220 and 1668 cm^{-1}; δ ($CDCl_3$-CF_3COOH) 4.0-3.46 (2H, m, C_1H and C_2H), 3.42-2.88 (8H, m, other protons), and 3.08 (2H, AB-q, J=12Hz, $J/\Delta\delta$=0.885, C_7Hx2); m/e 206 (M^+).

These results indicate that the transannular cyclization reactivity of 2 is larger than that of 1 where ketol is isolable.[4] Studies on the Dreiding stereomodel indicate also that the distance between the carbonyl carbon and the alcoholic oxygen in 3 is 0.12 Å closer than that in the corresponding ketol from 1 (see 13 and 14).

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