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CUBYL-CAGED SYSTEMS: REGIOCHEMICAL STEERING OF CATIONIC REARRANGEMENTS BY DISTAL GROUPS

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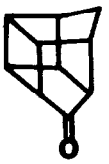
Summary: Novel carbonium ion rearrangements of substituted 1,3-bishomocubanones 3 & 4 to tricyclo(4.2.0.$0^{3,8}$)octane and bicyclo(3.2.1)octane ring systems are reported.

Sometime back, we delineated an interesting transformation of 1,3-bishomocubanone 1 to the tricyclic brendane derivative 2 via a regiospecific fragmentation of the Schmidt reaction intermediate e.g. 13 followed by a Cyclobutyl→Cyclopropyl carbinyl→Homoallylic carbonium ion rearrangement[1]. In order to further exploit the synthetic utility of 1→2 change, as a viable route to 9-keto-norsnoutanes and congeners, it was deemed interesting to carry out Schmidt reaction on pentacyclic keto ketals 3 and 4. Herein, we wish to report that distal ketal functionality in 3 and 4 and 5-bromo substituent in 4 alters the regioselectivity of the Schmidt fragmentation and unfolds novel rearrangement pathways to difficultly accessible[2] tricyclo(4.2.0.$0^{3,8}$)oct-4-ene (bis-nortwistane skeleton) and mechanistically interesting bicyclo(3.2.1) octa-3,6-diene frameworks.



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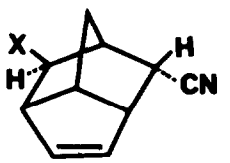
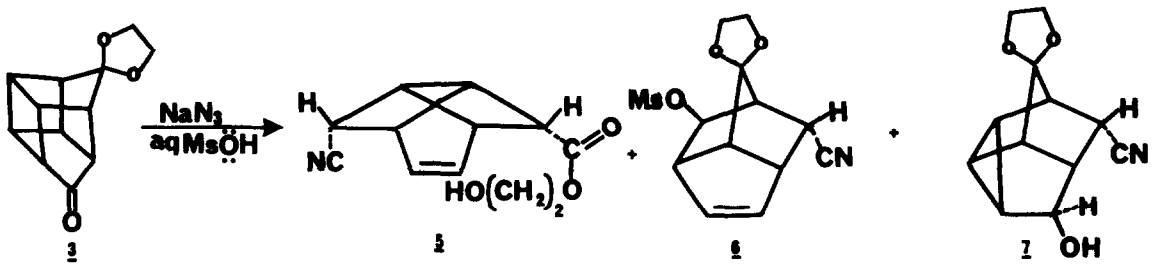
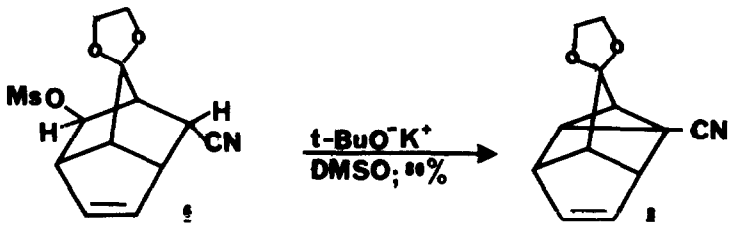


2

Reaction of pentacyclo(5.3.0.$0^{2,5}$.$0^{3,9}$.$0^{4,8}$)deca-6,10-dione-6-ethylene ketal 3[3] with sodium azide (1 equivalent) in methanesulphonic acid (0°,5 min) led to a complex mixture of products from which compounds 5, 6 and 7 could be isolated in 16, 10 and 5% yield, respectively, by silica gel column chromatography. The structure of the major product bearing the tricyclo(4.2.0.$0^{3,8}$) oct-4-ene frame 5, mp 72°, follows from its spectral characteristics: $C_{12}H_{13}O_3N$ M^+ 219, ir(KBr): 3500(-OH), 2240(C≡N), 1730 and 1200 cm^{-1}(ester); ^1H nmr(100 MHz, $CDCl_3$):δ 6.4(2H,m,olefinic), 4.1(2H,m), 3.7(2H,m), 3.4(4H,m), 2.8(2H,m),

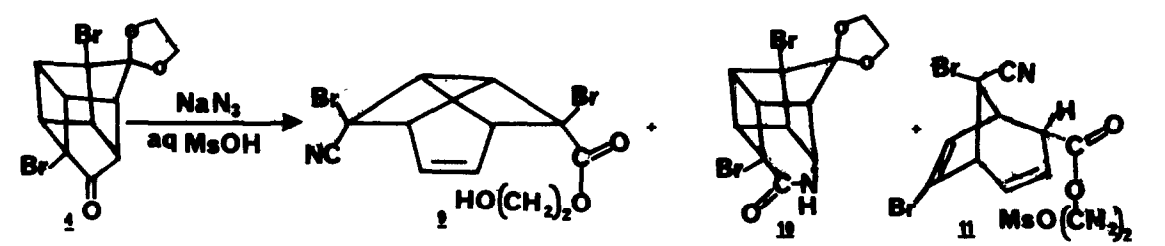


2.0(1H,s,-OH); ^{13}C nmr($CDCl_3$): δ 170.42(O-C=O), 130.04 and 128.92(olefinic), 118.24 (C≡N), 65.19, 59.94, 43.56, 39.5, 38.33(2C), 37.13, 29.88. The diagnostic and structurally revealing feature was the presence of an ethylene glycolate moiety (hydroxyl and carbonyl absorption in the ir; δ 4.1 & 3.7, 4H, typical A_2B_2 spectrum; δ 65.19 & 59.94, oxygen bearing C's) which showed participation by distal ketal oxygen in a fragmentation process (vide infra). Structure of the brendane type compound 6 was forthcoming from its spectral data[4] and more



convincingly from its conversion to δ-cyclene derivative 8[4] through a base catalysed 1,3-elimination reaction. The structure of the third and minor product 7 could also be derived from its spectral characteristics[4] and in particular the ^{13}C nmr spectrum which clearly exhibited resonances at δ 21.24 and 24.43 due to two shielded cyclopropane C's.

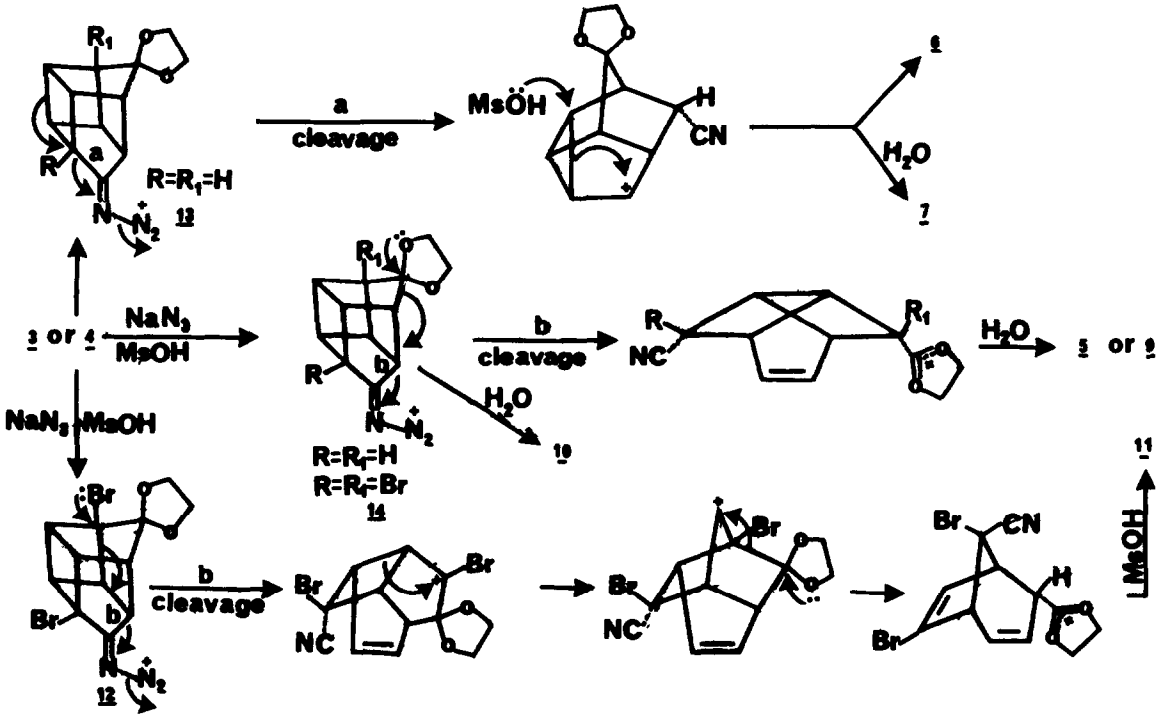
Reaction of 5,9-dibromopentacyclo(5.3.0.0^{2,5}.0^{3,9}.0^{4,8})deca-6,10-dione 6-ethylene ketal 4[3] with NaN_3 (1 equivalent) in methanesulphonic acid (0°, 5 min) furnished a complex mixture of products. Chromatographic separation on silica gel column resulted in the isolation of 9, 10 and 11 in 35, 20 and <5% yield, respectively. The bisnortwistane skeleton of 9 was indicated[4] by the presence of characteristic ethylene glycolate moiety and resonances due to two olefinic protons and two olefinic C's in the ^{1}H and ^{13}C nmr spectra, respectively. The pentacyclic lactam was formulated[4] as 10 mainly on the basis of the



doublet signal due to NH proton in the ^{1}H nmr spectrum, which ruled out the other regioisomeric structure. The third and minor product appeared to be a product of deep seated structural change as it exhibited three olefinic proton signals in the ^{1}H nmr and four olefinic C's (3 doublets and 1 singlet) in the ^{13}C nmr spectrum. Incisive analysis of the spectral data[4], comparison of ^{1}H and ^{13}C nmr data with known bicyclo(3.2.1)octa-3,6-dienes[5] and more notably, its close resemblance with a similar product obtained by us[6] in some other study, firmly established its structure as 11.

The plausible mechanism for the formation of brendane derivative 6 and tricyclo(4.2.0.$0^{3,8}$)oct-4-ene 5 and 9 type products is shown in Scheme I. Formation of 11 seems to be initiated by participation of the distal bromine in Schmidt intermediate 12 followed by a series of cationic rearrangements (Scheme I). It is significant that in unsubstituted 1,3-bishomocubanone 1, only brendane type product is encountered (cleavage of bond 'a' in 13)[1]; in keto ketal 3 both brendane and tricyclo(4.2.0.$0^{3,8}$)oct-4-ene products are formed (cleavage of both bonds 'a' and 'b') and in dibromo-keto ketal 4 only bisnortwistane products (cleavage of bond 'b' in 14) result. This could be attributed to the dominant influence of distal ketal and bromine groups, which seem to get attentuated due to strong through bond transmission present in

S C H E M E I



cubyl systems. It is conceivable that regio-preference for either 'a' or 'b' cleavage is also determined, to some extent, by the geometry of the Schmidt intermediates (12, 13, 14) which in turn could be influenced by the substituent in its vicinity of C_9. We are looking into this possibility.

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References and Notes:

1. G. Mehta, P.N. Pandey, R. Usha and K. Venkatesan, Tetrahedron Letts., 4209 (1976).

2. The tricyclo(4.2.0.$0^{3,8}$)oct-4-ene system has been rarely reported in literature, see, K.V. Scherer, R.S. Lunt III and G.A. Ungefung, Tetrahedron Letts., 1199 (1965); M. Oda, R. Breslow and J. Pecorao, ibid. 4419 (1972). The rearrangement sequence reported here constitutes a simple and direct entry to this tricyclic ring system.

3. N.B. Chapman, J.M. Key and K.J. Toyne, J. Org. Chem., 35, 3860 (1970).

4. Selected physical data and assignments: 6: mp 185°; ν (KBr):2250(C≡N), 1350 & 1180cm^{-1}(-OMs); ^{1}H nmr($CDCl_3$):δ6.4(1H,dd,J_1=3.5Hz,J_2=5Hz),6.1(1H,dd,J_1=2.5Hz, J_2=5Hz),4.6(1H,s,CH-OMs),4.0(4H,m,-OCH$_2$CH$_2$O-),3.36(1H,dd,J_1=5Hz,J_2=7Hz),3.0(3H, s,-SO_2-CH_3),2.6-3.2(5H,m); ^{13}C nmr($CDCl_3$):δ137.36 & 135.42(olefinic),118.17(C≡N) 117.7(C=O) 79.24(C-OMs),65.64,64.76,55.26,51.9,50.9,42.1,38.55,32.75. 7: mp 135°; ν(KBr):3350(OH)&2245cm^{-1}(C≡N); ^{1}H nmr($CDCl_3$):δ4.62(1H,brs,CHOH),3.94(4H,m,-OCH$_2$-CH$_2$O-),3.14(1H,m),2.44(2H,m),2.3-1.88(4H,m),1.62(1H,m); ^{13}C nmr($CDCl_3$):δ125.33 (C=O),119.5(C≡N),75.16(C-OH),65.6,64.7,46,43.37,43.05,35.06,32.33,24.44,21.24. 8:ν(neat):2250cm^{-1}(C≡N); ^{1}H nmr($CDCl_3$):δ6.22(2H,m),3.94(4H,m,-OCH$_2$CH$_2$O-),3.28 (1H,brs),3.16(1H,brs),2.28(2H,m),1.96(1H,brs). 9: M^+ 377,$C_{12}H_{11}O_3NBr_2$;ν(neat): 3500(OH),2250(C≡N),1742 & 1300cm^{-1}(-OC=O); ^{1}H nmr($CDCl_3$):δ6.38(2H,m),4.16(2H,m), 3.92-3.26(6H,m),2.4(1H,s,OH); ^{13}C nmr($CDCl_3$):δ167.37(-OC=O,s),131.45 & 129.1 (olefinic,d's),116(C≡N,s),67(t),60.4(t),59.5(s),50.9(d),49(d),48.3(d),47.4(d), 44.6(s). 10: mp 292-95°(decomp.);ν(KBr):3200(NH),1690cm^{-1}(NH-C=O); ^{1}H nmr(DMSO-d_6):δ8.86(1H,NH,d,J=6Hz),4.32-3.64(5H,m),3.5-2.76(4H,m); ^{13}C nmr(DMSO-d_6):δ164.5 (NHC=O),115.8(C=O),66.1,65.16,62.64,61.12,52.13,47.73,46.44,46.15. 11: M^+ 455, $C_{13}H_{13}O_5NSBr_2$;ν(neat):2250(C≡N)1750(-OC=O),3100 & 1610(olefinic),1360 & 1180cm^{-1} (-OMs); ^{1}H nmr($CDCl_3$):δ6.4(1H,m),6.18(1H,d,J=3-4Hz),5.44(1H,d with st,J=10Hz), 4.40(4H,s),4(1H,m),3.58(1H,m),3.34(1H,d,J=7Hz),3.04(3H,s); ^{13}C nmr($CDCl_3$):δ167 (-OC=O,s),133.8(s,olefinic),131.5,127.7,121.5(olefinic,d's),115.6(C≡N,s),67.22 (t),66.1(Br-C-CN,s),63.4(t),54.54(d),51.37(d),37.9(q),28.65(d).

5. J.B. Stothers, J.R. Swenson and C.T. Tan, Can. J. Chem., 53, 581 (1975).

6. X-ray crystal structure of a derivative bearing close structural relationship to 11 has been carried out. G. Mehta, S.C. Suri, K. Sambasiva Rao, C. Chan& T.S. Cameron, manuscript under preparation.

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