

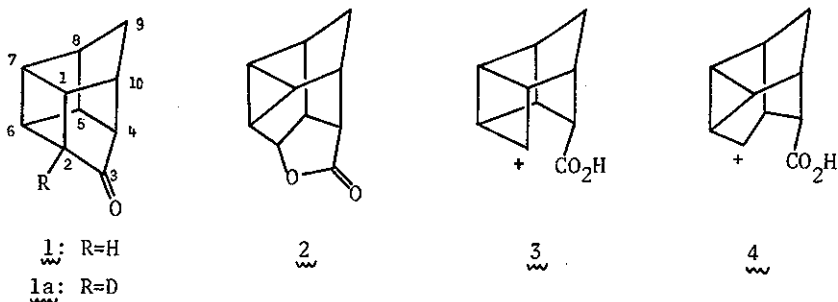
THE BECKMANN REARRANGEMENT OF BISHOMOCUBANONE OXIMES

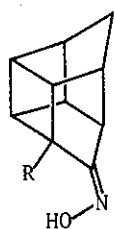
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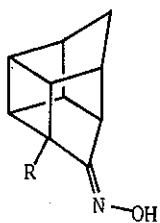
The Beckmann rearrangement of the title compounds gave brendane derivatives (7, 10, 17, 19, 20) through a regiospecific fission of the C₂-C₃ bond and hetero-cage lactams (8, 9) through a concerted rearrangement of intermediates (viii, ix). The product distribution depends on the reaction conditions.

Recently, we have reported that the Baeyer-Villiger oxidation of bishomocubanone (1) affords normal lactones together with a rearrangement lactone (2), and that these lactones are formed mainly via carbocation intermediates (3, 4) through the participation of the most strained C₆-C₇ bond.¹ As an extension of these studies with the aim of synthesizing heterocyclic cage compounds, we have now studied the Beckmann rearrangement² of bishomocubanone oximes (5, 6).

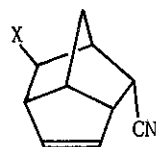




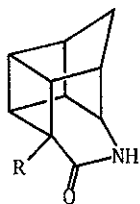
5: R=H
5a: R=D



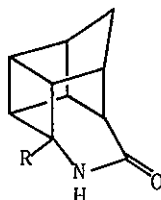
6: R=H
6a: R=D



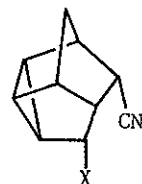
7: X=OCHO
10: X=OH
17: X=OAc
19: X=Cl
20: X=Ph



8: R=H
8a: R=D

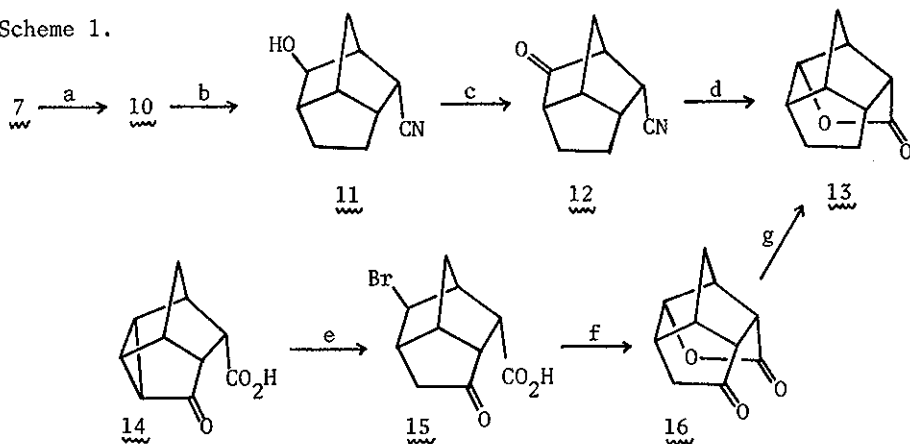


9: R=H
9a: R=D



18: X=OAc
21: X=OH

Scheme 1.



12, mp 168-169°; 15, mp 150-151.5°; 16, mp 208-210°;

a, NaOH, MeOH; b, 10% Pd-C/H₂; c, CrO₃, pyridine;

d, NaBH₄; 10% HCl; e, 47% HBr; f, 10% NaOH;

g, (CH₂SH)₂, BF₃·Et₂O; Raney Ni, EtOH

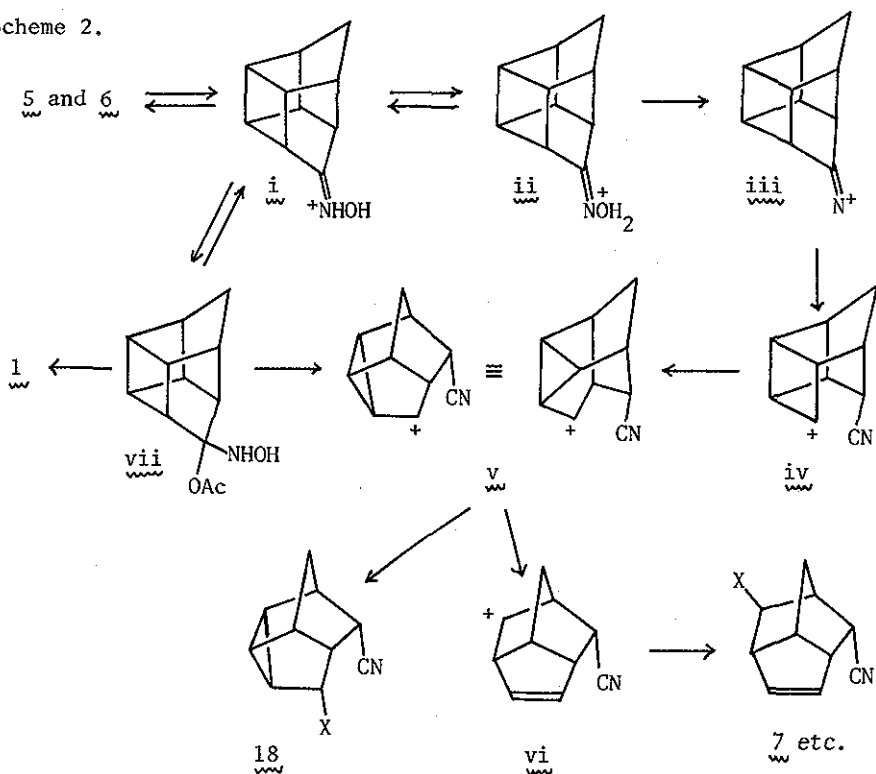
A 1:1 mixture [mp 97-99°; ν (Nujol) 3150 (broad), 1700 cm^{-1} ; m/e 161 (M^+), 144, 66 (base)] of Z- (5) and E-oximes (6) was obtained quantitatively from 1 in the usual way. Since the separation of these isomeric oximes was not achieved, the ratio was determined by pmr analysis in the presence of a shift reagent, $\text{Eu}(\text{dpm})_3$.³

When a formic acid solution of the oximes was refluxed for 5 min, a brendane derivative (7) [mp 51-53°; ν (neat) 2250, 1720, 1600 cm^{-1} ; m/e 189 (M^+), 133 (base), 132, 79, 67; δ (CDCl_3) 4.78 (1H, s), 6.06 (1H, d, J = 6 Hz), 6.36 (1H, dd, J 4, 6 Hz), 8.00 (1H, s)]⁵ was obtained in 95% yield and no traces of lactams (8, 9) were detected. The structure of 7 was established by its conversion into a lactone (13) [mp 187-189°; ν (CHCl_3) 1770, 1760 cm^{-1} ; m/e 164 (M^+), 136, 79 (base); δ (CDCl_3) 4.62 (1H, dd, J = 5, 8 Hz)], which was derived from the known lactone (14)¹ as shown in Scheme 1.

Since the formation of the brendane derivative (7) shows that the regio-specific fission of the $\text{C}_2\text{-C}_3$ bond in both 5 and 6 takes place, we can describe the possible mechanism of this reaction as shown in Scheme 2. The initial protonation and the subsequent dehydration must occur to give an imminium cation intermediate (iii).⁷ Since the bicyclo[2.2.0]hexyl unit in this ring system is strongly electrofugal⁹ as already shown in the mechanism of the Baeyer-Villiger oxidation of 1, a bicyclohexyl cation (iv) and a cyclopropylcarbinyll cation (v)¹ are readily formed. Formic acid ultimately cleaves the cyclopropyl ring of v to give the product 7.

Even acetic acid reacted with the oximes (reflux for 6 hr) in a similar manner to give a 1:1 mixture (40%)¹⁰ of acetates (17, 18) together with 1 (16%). Rather nucleophilic acetic acid could trap the cyclopropylcarbinyll cation (v) to give 18. Compound 1 must have been formed via an adduct (vii),

Scheme 2.



which is in equilibrium with the oximes (5, 6) and their protonated forms (i, ii).¹¹

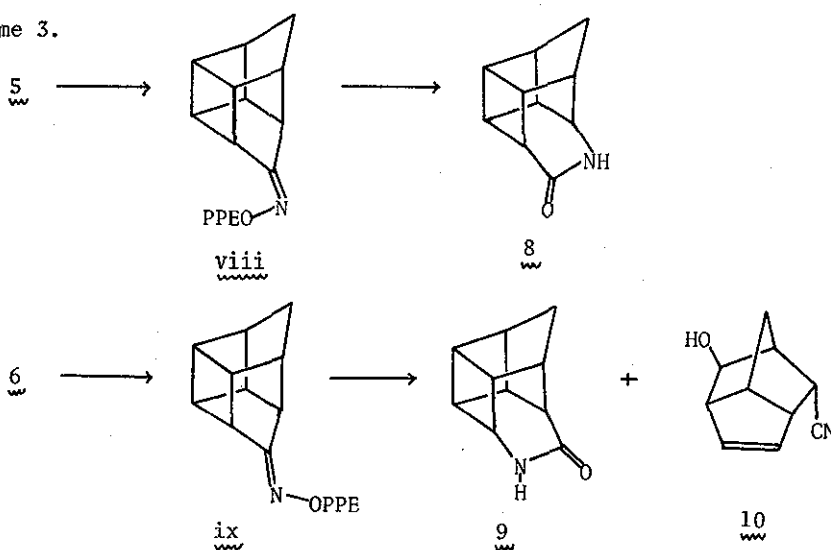
On treatment of a benzene solution of the oximes with $AlCl_3$ (reflux for 3 hr), which usually stabilized cation intermediates, the brendane derivatives, 19 [60%; mp 84-85°; ν (Nujol) 2250, 1600 cm^{-1} ; δ ($CDCl_3$) 4.00 (1H, s), 6.02 (1H, dd, $J = 3, 8$ Hz), 6.30 (1H, dd, $J = 4, 8$ Hz); m/e 181, 179 (M^+), 113 (base)] and 20 [3%; oil; ν (neat) 2240, 1600, 1580, 720, 700 cm^{-1} ; m/e 221 (M^+ , base), 165; δ ($CDCl_3$) 6.05 (1H, d, $J = 6$ Hz), 6.40 (1H, dd, $J = 3, 6$ Hz)], were expectedly obtained.

In contrast with the above results, the reaction of the oximes with PPE (polyphosphoric ester) in $CHCl_3$ (reflux for 2 hr) actually gave desired

lactams, 8 [47%; mp 149-150°; ν (Nujol) 3170, 1670 cm^{-1} ; δ (CDCl_3) 3.78 (1H, t, $J = 6$ Hz); m/e 161 (M^+), 96, 95 (base)] and 9 [11%; mp 161.5-162.5°; ν (Nujol) 3180, 1670 cm^{-1} ; δ (CDCl_3) 3.94 (1H, dd, $J = 6, 12$ Hz); m/e 161 (M^+), 96 (base), 95],¹² though accompanied by the formation of the brendane (10) [7%; mp 144-145°; ν (Nujol) 3425, 2250 cm^{-1} ; δ (CDCl_3) 3.86 (1H, s), 5.96 (1H, d, $J = 6$ Hz), 6.28 (1H, dd, $J = 4, 6$ Hz); m/e 161 (M^+), 79 (base)].

Since the yield of 8 was 47%, the Z-oxime (5) must have been converted almost exclusively to 8, because PPE in an aprotic solvent is least liable to cause the E-Z isomerization of oxime.⁸ Analogously, the origin of 9 and 10 must be the E-oxime (6). The reaction is initiated by the formation of intermediates (viii, ix), not of cationic species. The former (viii) undergoes a subsequent stereospecific rearrangement of the C_3 - C_4 bond to give the lactam (8), whereas the stereospecific rearrangement of the C_2 - C_3 bond in the latter (ix) to the lactam (9) competes with the fragmentation to yield the brendane (10).

Scheme 3.



REFERENCES AND NOTES

- 1) K. Hirao, H. Miura, H. Hoshino, and O. Yonemitsu, Tetrahedron Lett., 1976, 3895.
- 2) L. G. Donaruma and W. Z. Heldt, Org. Reactions, 1960, 11, 1.
- 3) The signals of α -methine protons of oxime groups in 5 and 6 were unambiguously determined by comparing their pmr spectra with those of the deuterated 5a and 6a prepared from the deuterated ketone 1a.⁴
- 4) K. Hirao, E. Abe, and O. Yonemitsu, Tetrahedron Lett., 1975, 4131.
- 5) Recently, Mehta et al.⁶ reported the Schmidt reaction of 1 to brendane derivatives, whose structures were established by X-ray analysis.
- 6) G. Mehta, P. N. Pandey, R. Usha, and K. Venkatesan, Tetrahedron Lett., 1976, 4209.
- 7) The Beckmann rearrangement usually proceeds in a concerted manner without intervention of an imminium ion. However, imminium ions may be discrete intermediates in some cases. Cf. P. T. Lansbury and N. R. Mancuso, J. Am. Chem. Soc., 1966, 88, 1205, and see also ref. 8.
- 8) P. A. Smith, "Molecular Rearrangement," Part I, P. de Mayo, ed., Interscience Publisher, Inc., New York, N. Y., 1963, p 457.
- 9) C. A. Grob and P. W. Schiess, Angew. Chem. Int. Ed. Eng., 1967, 6, 1; C. A. Grob, ibid., 1969, 8, 535.
- 10) The yields of these acetates were determined by the pmr signals of AcO-CH- in the product mixture at 4.68 and 5.60 ppm for 17 and 18, respectively. After hydrolysis of this mixture, alcohols 10 and 21, were separable. Compound 21 [mp 141-142°; ν (Nujol) 3250, 2250 cm^{-1} ; m/e 161 (M^+), 79 (base); δ (CDCl_3) 4.76 (1H, s)] has a characteristic hydroxy methine proton at 4.76 ppm deshielded by a CN group and high-field protons (1.5-2.1 ppm, 5H) assignable to those of a cyclopropane ring and a methylene group.
- 11) This equilibrium, in which 7.1% of the adduct (vii) is present, is established within 2 hr at room temperature. The detail will be published soon.
- 12) The lactams, 8 and 9, were unequivocally characterized by the pmr spectra of deuterated 8a and 9a obtained from 5a and 6a, respectively. The signal of -CH-NH- at 3.94 ppm disappeared in 9a, whereas that at 3.78 ppm remained unchanged in 8a.

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