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Studies on Seven-Membered Heterocyclic Compounds Containing Nitrogen. XII. Schmidt Reaction of Seven-Membered Heterocyclic Ketones

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It has been reported that the Schmidt reaction of benzo-fused, six-membered heterocyclic ketones (I, X=O[1], NH[2], or NMe[3]) chiefly gave the lactam (II) rather than the isomer (III) by the migration of the alkyl chain. The present authors assumed that the double bond character between the heteroatom and the aryl group of I might bring a strain, so that the aryl migration was restricted. In view of this, the strain might, more or less, be removed and the aryl migration would predominate in the corresponding seven-membered ketones (IV, X=O[4] or NH[5]). The idea was confirmed from the reactions below, and we wish to report a mechanism having an intermediate of a carbonium ion for the Schmidt reaction.

The seven-membered ring ketone (IV, X=O) gave two isomeric lactams (V, X=O, and VI, X=O) in a ratio of 7 : 3. The nitrogen analog (IV, X=NH) of the ring ketone as well as its N-tosyl derivative[5] afforded unexpected benzimidazole derivative (VII) along with a small amount of eight-membered lactam (V, X=NH). The structure of VII was determined by elementary analysis, molecular weight (by mass spectrum), and NMR and UV spectra. From the evidence for the formation of VII from IV (X=NH), a carbonium ion (A or B), which depends on the migratory aptitude of the alkyl chain and the benzene ring, should be an intermediate for the Schmidt re-

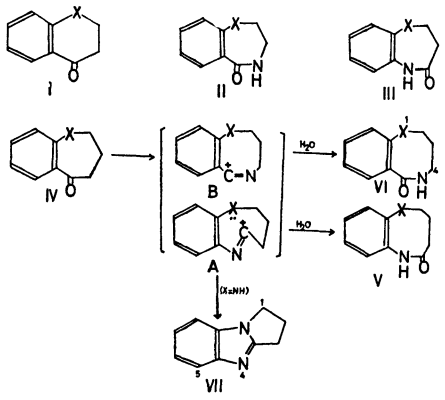

Fig. 1.

1) D. Evans and I. M. Lockhalt, *J. Chem. Soc.*, **1965**, 4806.
2) W. S. Johnson, E. L. Woroch, and B. G. Buell, *J. Amer. Chem. Soc.*, **71**, 1901 (1949).
3) J. A. C. Allison, J. T. Braunholtz, and F. G. Mann, *J. Chem. Soc.*, **1954**, 403.
4) G. Fontaine and P. Maitte, *C. R. Acad. Sci. Paris*, **258**, 4583 (1964).
5) G. R. Proctor and R. H. Thomson, *J. Chem. Soc.*, **1957**, 2312.

action as shown in Fig. 1.

In the Schmidt reaction of IV (X=O), the lactam (V, X=O) was a dominant product and was considered to be formed by the addition of water molecule to the intermediate (A, X=O), in which the benzene ring migrated, the minor isomeric lactam (VI, X=O), being formed from the intermediate (B, X=O), in which the alkyl migration occurred. The nitrogen analog (IV, X=NH) also seemed to facilitate the migration of benzene ring to give the intermediate (A, X=NH). In this case, however, the lone pair of electrons on the nitrogen atom was considered to attack the carbonium ion to give VII. A normal product, the lactam VI (X=NH) could also be detected in a minor extent, which might indicate the formation of intermediate (B, X=NH) followed by the addition of water molecule.

Experimental

The ratio of the reaction product was determined by estimating two kinds of the methylene proton signals (δ(TMS) in $CDCl_3$, 2.90—3.80, $NHCH_2$, and 2.10—2.60, $COCH_2$) using a Hitachi High-resolution NMR Spectrometer. The chemical shifts (δ in $CDCl_3$) of the signals in the following compounds were also referred: benzoylmethylamine (2.93, d, NCH_3), acetoanilide (2.10, s, $COCH_3$), *o*-aminobenzoylmethylamine (2.94, d, NCH_3), *o*-methoxyacetoanilide (2.10, s, $COCH_3$).

The Schmidt reaction of I (X=NH or NMe) was re-investigated using NMR spectra, and it was found that the tendency of the migration of alkyl chain was the same as that of litertures.[2,3] The characteristic chemical shifts (δ in $CDCl_3$) of the products are follows: 2,3,4,5-tetrahydrobenzo[*f*]-1,4-diazepin-5-one (3.30—3.80, m, $CONHCH_2$ and $C_6H_4NHCH_2$), 2,3,4,5-tetrahydrobenzo[*b*]-1,4-diazepin-4-one (2.68, t, $COCH_2$, 3.30—3.80, m, $NHCH_2$), 1-methyl-2,3,4,5-tetrahydrobenzo[*f*]-1,4-diazepin-5-one (3.30, broad s, $NHCH_2$ and $NMeCH_2$), 1-methyl-2,3,4,5-tetrahydrobenzo[*b*]-1,4-diazepin-4-one (2.50, t, J=6 Hz, $COCH_2$, 3.51, t, J=6 Hz, $NMeCH_2$).

*2,3,4,5-Tetrahydro-6*H-*benzo*[b]-*1,4-oxazocin-5-one (V, X=O) and 2,3,4,5-tetrahydro-*6H-*benzo*[b]-*1,5-oxazocin-6-one (VI, X=O).* To a stirred mixture of 0.75 g of 2,3,4,5-tetrahydrobenzo[*b*]-oxepin-5-one (IV, X=O) and 10 g of trichloroacetic acid, maintained at 55—60 °C, was added 0.50 g of sodium azide in the period of 1 hr. After being stirred for 6 hr at the same temperature, ice was added and the resulting mixture was neutrallized by adding 20% aqueous solution of sodium hydroxide. Sodium sulfate formed was removed by filtration and the aqueous solution was extracted with chloroform. Drying over anhydrous sodium sulfate and evaporation of chloroform left a residue, which was washed with ether to give 0.80 g of crude crystals. The crystals were found to be a mixture of V and VI in a ratio of 7 : 3 from the NMR spectrum. Recrystallization from benzene gave 0.30 g of V (X=O) as colorless needles of mp 157—159 °C. IR (KBr): 1670 cm^{-1} (lactam C=O); NMR (δ in $CDCl_3$): 1.70—2.20 (2H, m, C-3), 2.20—2.60 (2H, m, C-4), 4.22 (2H, t, J= 7 Hz, C-2), 6.80—7.80 (4H, m, Ar), 8.76 (1H, broad s, NH). Found: C, 67.60; H, 6.29; N, 8.21%. Calcd for $C_{10}H_{11}O_2N$: C, 67.78; H, 6.26; N, 7.91%. The isomeric lactam, VI (X=O), was not isolated, but the signal at δ 2.90—3.20 ($NHCH_2$) in the crude product proved its contamination.

*1,2-Dihydro-3*H-*pyrrolo*[*1,2-*a]*benzimidazole (VII) and 1,2,3,4,5,6-hexahydrobenzo*[b]-*1,4-diazepin-5-one (V, X=NH).* To a stirred solution of 1.0 g of 1-tosyl-2,3,4,5-tetrahydrobenzo-[*b*]azepin-5-one (IV, X=NTs) in 5 ml of concentrated sulfuric acid was added 0.31 g of sodium azide in a small portions at a room temperature. After being stirred for 2.5 hr, the mixture was worked up as above to give 0.45 g of crude crystals. Recrystallization from cyclohexane yielded 0.21 g of VII as colorless crystals of mp 108—110 °C. No carbonyl absorptions were found in the IR spectrum. NMR (δ in $CDCl_3$): 2.00—3.10 (4H, m, C-2 and C-3), 3.91 (2H, t, J=7 Hz, C-1), 7.10 (3H, m, C-6, -7, and -8), 7.60 (1H, m, C-5). UV: λ_{max} (in phosphate buffer, pH 8.0) nm (ε), 243 (5300), 248 (4900), 266 (3800), 271 (5100), 278 (5200), quite similar to that of 1-methylbenzimidazole.[6] Mass spectrum: *m/e*, 158 (M^+). Found: C, 76.20; H, 6.53; N, 18.06%. Calcd for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71%. Judging from the weak absorption of lactam grouping at 1660 cm^{-1}, the crude product was found to contain a small amount of V (X=NH). The absence of signals at δ 3.30—3.60 region indicates that the crude product includes no such compound as VI (X=NH) in it.

Further investigations of the effect of the above-mentioned double bond character on the migratory aptitude and of the extensive possibility of the mechanism are in progress.

6) DMS UV Atlas of Organic Compounds. Vol. V. H-11/T-1. Butterworths, London.