The Rearrangement of Glycicyl *N*-Phenylcarbamate

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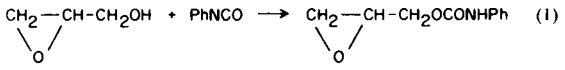
The thermal rearrangement of glycicyl *N*-phenylcarbamate yields 3-phenyl-4-hydroxymethyl-2-oxazolidone and not 3-phenyl-5-hydroxytetrahydro-1,3-oxazin-2-one as reported previously.

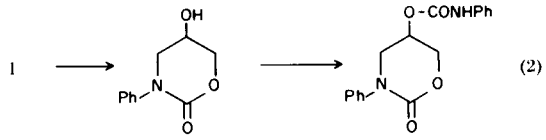
Glycidol reportedly reacts with phenyl isocyanate at room temperature on the hydroxyl function to yield the carbamate (I) exclusively (1). Rearrangement of I occurs readily at elevated temperatures to yield a compound



(1)

I

m.p. 109.5-110.5°, which is claimed to be the tetrahydro-oxazinone II. With phenyl isocyanate, II forms a carbanilate (III), m.p. 175-175.5°.



(2)

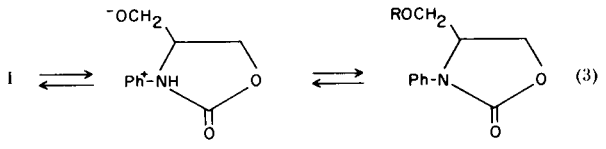
II III

We have attempted to repeat this sequence and found that reaction 1 does not proceed at all well uncatalyzed at room temperature. At elevated temperatures, the product is contaminated with other materials in which the epoxide ring is no longer intact. Catalysis by tertiary amines or quaternary ammonium halides (2,3) resulted in less of I and more of the rearranged products. Only with organometallic catalysts, such as phenylmercuric acetate (4), could excellent yields of pure I be obtained. The structure of I was confirmed by NMR and IR spectral data.

The rearrangement of recrystallized I at 130° proceeds rather more slowly than reported (1), requiring in excess of five hours for complete reaction, and the crude reaction product crystallizes with some difficulty. Acids such as boron trifluoride etherate, phosphoric and trifluoroacetic acids failed to catalyze the rearrangement. Amines (triethylamine, pyridine, triethylenediamine), however, greatly accelerate the rearrangement to a readily crystallized white solid, m.p. 110-112°, which yields a carbanilate, m.p. 179-180°, on treatment with phenyl isocyanate. Although the melting points and solubility properties of these materials agree with those reported for II and III, our evidence indicates that the literature structures are incorrect.

Our spectral data suggest that the rearrangement product contains a primary hydroxyl group and is most probably the oxazolidone IVa, eq. 3. Thus the infrared spectrum shows oxazolidone ring absorption at 9.62 μ (5,6) as well as the hydroxyl and carbonyl absorptions. The NMR spectrum of IVa in DMSO-d_6 shows a well-defined triplet for a single proton at 5.15 ppm (J = 5.3) (7) and an associated two-proton complex doublet centered at 3.52 ppm (J = 5.3). Treatment of this solution with acidified deuterium oxide causes collapse of the hydroxyl triplet to a sharp singlet at 3.8 ppm (presumably HOD) and the methylene multiplet to a broad singlet at 3.52 ppm. These results are to be expected for the hydroxymethyl function of IVa, but not for the secondary hydroxyl of II.

The location of the hydroxymethyl group at the 4-position of the oxazolidone ring as shown in IV requires clarification. Iwakura and Taneda (1) claimed the preparation of the 5-substituted compound Vb (m.p. 156.2-157.5°) (eq. 4) and showed it to be different from the carbanilate, IVb, m.p. 175°. Also, the methylene/methine



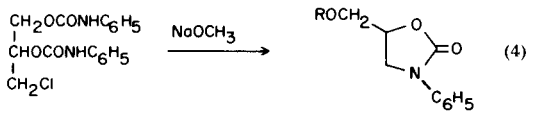
(3)

IVa, R = H
b, R = PhNHCO

proton resonances of the ring system of IV are closely bunched at 4.3-4.8 ppm. This correlates better with the less common 4-substituted oxazolidones studied by Herweh, Foglia and Swern (8) than for the more widely spaced resonances of the 5-substituted compounds.

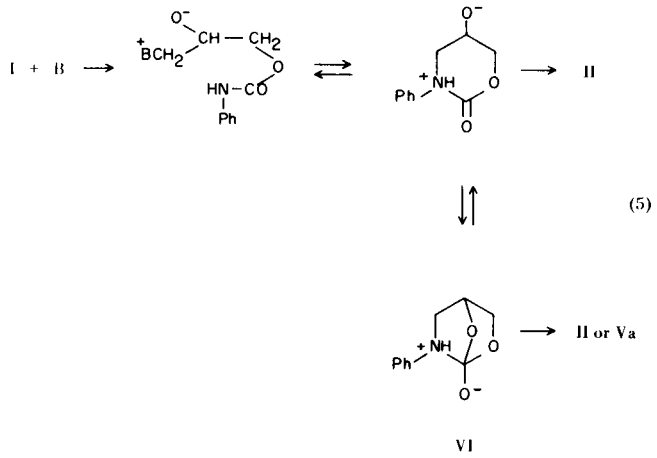
The predominance of IVa as the rearrangement product suggests a mechanism involving an intramolecular displace-

ment by the carbamate nitrogen (9) on the secondary carbon of the epoxide, eq. 3. The more facile formation of the five-membered ring (10) predominates over formation of the six-membered oxazine, II, which would result from attack at the less hindered primary carbon of the epoxide. The absence of appreciable Va precludes any substantial participation of external bases (3) in the epoxide ring opening (eq. 5) or a major contribution of intermediates such as VI (11) to the reaction course.



(4)

Va, R = H
b, R = $CONHC_6H_5$



(5)

VI

Attempts to prepare the 5-substituted compound directly using quaternary ammonium salt catalysis (2) were unsuccessful. Apparently under all the catalytic conditions we examined, reaction at the primary hydroxyl group of glycidol precedes any reaction at the oxirane function.

EXPERIMENTAL

Glycidyl *N*-Phenylcarbamate (I).

To a refluxing solution of 14.8 g. (0.2 mole) of freshly distilled glycidol and 100 mg. of phenylmercuric acetate in 200 ml. of dry benzene was added a solution of 23.8 g. (0.2 mole) of phenyl isocyanate in 30 ml. of dry benzene at a sufficient rate to maintain gentle reflux. After 10-20 minutes the reaction was complete. Removal of solvent at reduced pressure afforded a nearly quantitative yield of I, a white solid, m.p. 60-62°; IR (5%, chloroform), 2.92 μ, 3.0 μ (NH), 5.81 (C=O), 10.7, 11.8 (oxirane ring); NMR (DMSO-d_6), δ = 9.90 ppm (s, 1, N*H*), 7.0-7.8 (m, 5, ArH), 3.8-4.7 (m, 2, CH_2O), 3.25 (m, 1, C*H*), 2.8 (m, 2, CH_2).

3-Phenyl-4-hydroxymethyl-2-oxazolidone (IVa).

The above experiment was repeated except with 100 mg. of tetraethylammonium bromide (4) as catalyst. Carbamate formation was complete in 30 minutes by IR. Reflux was continued overnight. On cooling the reaction solution to room temperature, there was obtained 28.7 g. (0.15 mole, 75%) of white solid, m.p. 110-112°, recrystallized from 4:1 benzene/chloroform, m.p. 112-115°; NMR (DMSO-d_6), δ = 7.0-7.8 ppm (m, 5, Ar*H*), 5.15 (t, 1, O*H*), 4.3-4.7 (m, 3, C*H*, CH_2), 3.52 (m, 2, CH_2OH); IR (10% $CHCl_3$), 2.8 μ 2.95 μ (OH), 5.85 (C=O), 9.65 (oxazolidone ring).

3-Phenyl-4-(*N*-phenylcarbamoyloxymethyl)-2-oxazolidone (IVb).

The triethylamine catalyzed reaction of 6 g. (0.05 mole) of phenyl isocyanate and 9.65 g. (0.05 mole) of IVa in 200 ml. of refluxing benzene required 90 minutes for completion. On cooling the reaction mixture, IVb precipitated and was filtered. The yield was 14.3 g. (0.046 mole, 92%) of white solid, m.p. 179-180°; NMR (DMSO-d_6), δ = 10.8 ppm (s, 1, N*H*), 7.0-7.7 (m, 10, Ar*H*), 4.2-5.0 (m, 5, C*H*, CH_2); IR (5%, dioxane) 5.71, 5.80 μ (C=O).

Rearrangement of I.

Recrystallized I (1.0 g.) was heated to 125° and one drop of triethylamine added to the melt. The infrared spectrum of a sample withdrawn five minutes after addition of the catalyst showed complete rearrangement. The reaction mixture was cooled, dissolved in hot benzene/chloroform and cooled. There was obtained 0.8 g. of white solid, IVa, m.p. 112-114°. A small second crop of fine white crystals, m.p. 105-165°, was predominantly the carbanilate IVb.

Similarly, rearrangement of I was complete in 5 minutes in refluxing pyridine. In refluxing dioxane for 2 hours with trifluoroacetic acid, little change occurred. With boron trifluoride etherate in refluxing benzene for two hours, some degradation was apparent. There was isolated only a red oil which could not be crystallized. Heating I without catalyst for 5-24 hours at 130° caused formation of a mixture of IVa and IVb, which could be crystallized only with some difficulty.

Reaction of 1.0 g. (5.5 mmoles) of I with 0.7 g. (4.6 mmoles) of methyl *N*-phenylcarbamate with one drop of triethylamine at 100° for 15 minutes gave, after crystallization from benzene/chloroform, 0.8 g. of pale yellow crystals of IVa, m.p. 111-113°. No Va or Vb were detected (9a).

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