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REARRANGEMENT AND CYCLIZATION REACTIONS OF α,β-EPOXY DIAZOMETHYL KETONES CATALYZED BY BORON TRIFLUORIDE

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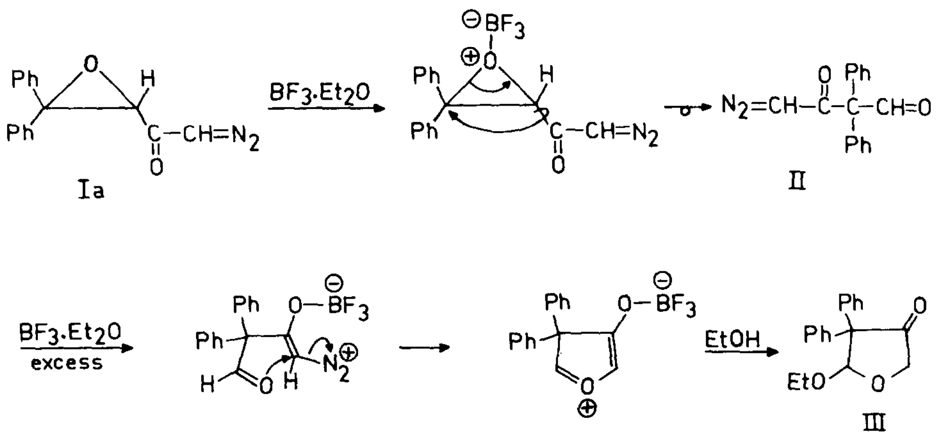
α,β-Epoxy diazomethyl ketones, a class of compounds that recently became available[1,2], possess two functional groups sensitive to acidic reagents. In a previous paper[1] we showed that with proton acids the primary reaction takes place at the diazomethyl ketone moiety, *e.g.* hydrogen chloride in ether produces α,β-epoxy chloromethyl ketones. This communication deals with the reaction of α,β-epoxy diazomethyl ketones with $BF_3.Et_2O$ as acidic reagent. As will be demonstrated in this case the primary reaction occurs chemospecifically at the epoxide function.

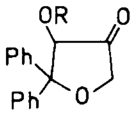
Treatment of the β,β-diphenyl α,β-epoxy diazomethyl ketone Ia with 0.1 equiv. of $BF_3.Et_2O$[3] in dichloromethane[3] at 5° for 60 h gave, after removal of the solvent and recrystallization from ether/pentane, the rearranged diazomethyl ketone II in 80% yield (Scheme I). The identity of this product (m.p. 116-118°) was based on a correct elemental analysis and the following spectral features: IR (KBr), 2880 (O=*C*-*H*), 2105 (N≡N), 1725 (CH=O) and 1625 (N_2CH*C*=*O*) cm^{-1}; NMR (CCl_4), δ 10.00 (s, 1H, C*H*=O), 6.9-7.4 (m, 10 H, C_6H_5) and 4.90 (s, 1H, C*H*=N_2) ppm. The formation of

Scheme I



II can only be explained by an acyl migration in the BF_3-catalyzed rearrangement of the epoxide moiety in the epoxy diazomethyl ketone (Scheme I).

Treatment of the substrate Ia with a slight excess of $BF_3.Et_2O$[3] in dichloromethane[3] at room temperature for 16 h resulted in a oily product (yield 60%, by thick layer chromatography on silica) which did not contain a diazo function anymore. The spectra of this product (m/e 282, $C_{18}H_{18}O_3$ by exact mass measurement; IR (film), 1760 (C=O) cm^{-1}; NMR (CCl_4), δ 1.05 (t, 3H, CH_3), 3.2-4.0 (m, 2H, CH_3CH_2), 4.10 (s, 2H), 5.80 (s, 1H) and 7.1-7.5 (m, 10 H, C_6H_5) ppm) are compatible with the structure III as well as with IVa. Decisive information about the structure[4] was obtained as follows: *i*. Treatment of a solution of the product in methanol with gaseous hydrogen chloride gave a quantitative conversion into the methoxy analogue (NMR (CCl_4), the signals for the ethyl protons are replaced by a methyl singlet at δ 3.40 ppm). Such a transformation is only conceivable with structure III by transacetalization of the cyclic acetal. *ii*. Reduction of the product with lithium aluminum hydride in ether (20°, 16 h) afforded the corresponding alcohol (m.p. 114-115°, yield 80%). In the NMR spectrum of this cyclic alcohol the one proton singlet at δ 5.70 ppm was still present. This is only in accordance with the reduced structure III, because reduction of the carbonyl function in IVa would have led to a doublet for this absorption.



IVa R=Et
IVb R=H

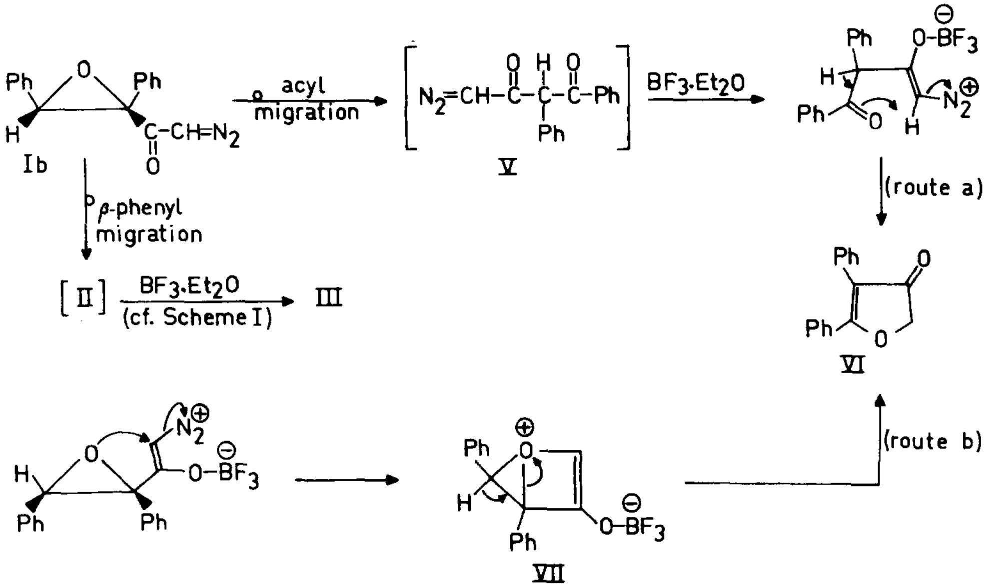
In order to rationalize the formation of III an initial rearrangement of Ia to II is assumed. Subsequently, cyclization of II takes place by a nucleophilic attack[5] of the carbonyl group on the activated diazomethyl function (Scheme I). Reaction of the oxonium ion with ethanol, which is present[3] in the reaction mixture, then produces the observed product III. Strong support for the intermediacy of II during the formation of III is the fact that treatment of II with excess $BF_3.Et_2O$ in dichloromethane[3] results in a high yield of the cyclized product III.

The reaction of the epoxy diazomethyl ketone Ib (Scheme II) with an excess of $BF_3.Et_2O$ in dichloromethane at 0° for 20 h gave two products, III and VI, in a 1:1 ratio (yield 60%). When the reaction was performed at 45° compound VI was the only product isolated (60%). The structure of VI was deduced from its spectra (m/e 236, $C_{16}H_{12}O_2$ by exact mass measurement; IR (film), 1700 (C=O) and 1625 (C=C) cm^{-1}; NMR (CCl_4), δ 7.0-7.7 (m, 10 H, C_6H_5), 4.60 (s, 2H, H_2) ppm) and its conversion into 2,3-diphenylfuran by reduction with lithium aluminum hydride followed by work-up with dilute acid (yield 40%, spectra identical with those reported in lit.[6]).

The product VI was also obtained in a yield of 50% from the reaction of Ib and triethyloxonium fluoroborate in alcohol-free dichloromethane.

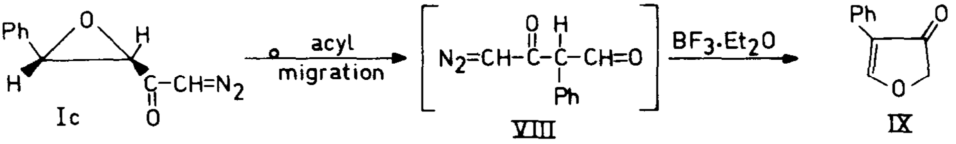
The formation of III from Ib can be explained by a primary rearrangement of the epoxide moiety in which the β-phenyl group migrates[7], followed by a cyclization of the thus-formed diazoketone II to the cyclic ketone III as indicated in Scheme I. For the formation of VI, however, two mechanistic pathways can be envisaged (Scheme II). Firstly (route *a*), by an acyl migration during the epoxide

Scheme II



rearrangement which results in the diazoketone V. Subsequent cyclization by an intramolecular reaction of the β-carbonyl group and the diazomethyl group produces the dihydrofuran-3-one VI as indicated in Scheme II. Secondly (route *b*), by a nucleophilic reaction[8] of the epoxy function with the diazomethyl ketone group activated by BF_3. In view of the energetically rather unfavourable intermediate VII and the results obtained[9] with the substrate Ia, route *a* is strongly favoured. This preference is supported by the observed acyl migration for the epoxy diazomethyl ketone Ic. Treatment of Ic (Scheme III) with an excess $BF_3.Et_2O$ in dichloromethane (20°, 16 h) gave the product IX (m.p. 88-88.5°) in 65% yield. The spectra (IR (KBr), 1690 (C=O) and 1615 (C=C) cm^{-1}; NMR ($CDCl_3$), δ 7.1-7.8 (m, 5H, C_6H_5), 4.60 (s, 2H, H_2) and 8.45 (s, 1H, H_5) ppm) are distinctly different from those of an authentic sample of 5-phenyl-2,3-dihydrofuran-3-one[10] (m.p. 82°, NMR ($CDCl_3$), δ 7.4-7.9 (m, 5H), 4.69 (s, 2H) and 6.07 (s, 1H) ppm) and therefore indicative of structure IX.

Scheme III



The formation of IX can only be explained *via* an acyl migration during the initial epoxide rearrangement (Scheme III). A reaction path analogous to route *b* in Scheme II would have led to 5-phenyl-2,3-dihydrofuran-3-one.

Attempts were made to isolate the intermediate diazoketones II, V and VIII mentioned in the Schemes II and III, by varying the amount of $BF_3.Et_2O$ in the reactions of Ib and Ic, however, they were unsuccessful.

The interesting conclusion from the presented results is that the reaction of epoxy diazomethyl ketones with $BF_3.Et_2O$ proceeds in two discrete steps, the first of which is a rearrangement of the epoxide moiety and the second one an intramolecular cyclization of 1-diazo-2,4-butanediones.

REFERENCES AND NOTES

1. B. Zwanenburg and L. Thijs, Tetrahedron Lett., 1974, 2459.
2. N.F. Woolsey and M.H. Khalil, J. Org. Chem., 38, 4216 (1973).
3. The dichloromethane used contained about 0.3% ethanol as stabilizing agent. Borontrifluoride etherate was carefully distilled prior to use.
4. It should be noted that the reaction of Ia with conc. sulfuric acid in ether yields the product IVb (see ref. 1).
5. *Cf.* the cyclization of 2-alkoxyethyl diazomethyl ketones, J.H. Sperna Weiland, Recl. Trav. Chim. Pays Bas, 83, 81 (1964).
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9. For Ia route *b* would lead to product IVa which, however, was not observed.
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