Novel Thermal Rearrangements of Tetrahydro-azirinocyclobutabenzofuran Derivatives

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Thermolysis of the 1a,1b,6b,6c-tetrahydro-azirino[2',3': 3,4]cyclobuta[1,2-b][1]benzofurans (3) results in ring transformations to form the benzofuro[2,3-b]pyrroles (5) and their [3,2-b]-isomers (6).

There is a growing interest in the ring-opening reactions of highly strained bicyclopentane ring systems¹ and their heteroanalogues.² Recently, we reported³ that the flash vacuum pyrolysis of the dioxatricyclo-octane derivatives (1) at 550 °C resulted in ring expansion to give the novel 1,4benzodioxocines (2), although even when the compounds (1) were heated in solvents at 250 °C, no reaction occurred. These results prompted us to examine the thermal behaviour of aza-analogues of (1), and we report here that the title compounds (3) gave interesting rearrangement products, although the expected 1,4-benzoxazocines (4) could not be obtained.

The tetrahydro-azirinocyclobutabenzofurans (**3a**—c) were prepared from 1-benzoxepines⁴ by photocyclization followed by treatment with ethoxycarbonylnitrene generated from *N*ethoxycarbonyl-*O*-(*p*-nitrophenylsulphonyl)hydroxylamine.⁵



Scheme 1. Reagents and conditions: i, flash vacuum pyrolysis, ii, toluene or xylene, $160 \,^{\circ}$ C, $8-12 \,$ h; iii, $10\% \,$ HCl, ethanol, room temp.; iv, heat; v, $10\% \,$ NaOH, ethanol.

Heating the compounds (3) (Scheme 1) in toluene or xylene at 160 °C for 8-12 h in a sealed tube resulted in ring transformations to give the benzofuro[2,3-b] pyrroles (5) (40-70%), their [3,2-b]-isomers (6) (5-20%), and the 1,3-oxazin-2-ones (7) (20-30%).† Flash vacuum pyrolysis of (3) at 380 °C also gave the same products (5)-(7), but in lower yields. In neither case was the formation of 1,4-benzoxazocine (4) observed. The products were characterized by their spectral data and the results of the following chemical reactions. Treatment of (5a) $(R^1 = H)$ with 10% HCl in ethanol at room temperature gave the o-(3-pyrrolyl)phenol (8a) in 86% yield, but the compounds (5b,c) $(R^1 = Me)$ did not react under similar conditions. Compounds (6) were readily converted into (7) by further heating; this result clearly indicates that the oxazinones (7) are derived from (6) via N-ethoxycarbonyl-o-(2-pyrrolyl)phenols. presumably Treatment of (7) with 10% NaOH in ethanol afforded the N-unsubstituted o-(2-pyrrolyl)phenols (9) in high yields.

A possible mechanism for the thermolysis is shown in Scheme 2. The ring conversion of (3) into (5) and (6) may proceed *via* initial C-C bond fission in the aziridine ring to the ionic intermediates (10), which may undergo migration of the phenoxy group to give (5). On the other hand, the products (6)might be formed from (10) by a Wagner-Meerwein type phenyl group migration followed by the shift of the phenoxy group. We assume that the difference in thermolysis between (1) and (3) may depend on the different mode of the initial



† Satisfactory elemental analyses and spectral data were obtained for all products. (5b) (oil): i.r. v (CHCl₃) 1705 (C=O) cm⁻¹; ¹H n.m.r. δ (CDCl₃) 1.59 (3H, s, 4-Me), 5.23 (1H, d, J 4 Hz, 3-H), 6.32 (1H, s, 5-H), 6.70 (1H, d, J 4 Hz, 2-H), 6.9-7.4 (4H, m, Ph-H), 1.37 and 4.36 (3H, t, and 2H, q, CO₂Et). The ¹H n.m.r. spectra of (6a-c) measured at room temperature showed complex broad split signals presumably owing to the temperature dependent inversion of the rings. The split signals of (6a) coalesced completely at 110°C to give a simple spectrum: δ, [2H₈]toluene, 5.12 (1H, dd, 3-H), 5.55 (1H, d, 5-H), 5.73 (1H, dd, 4-H), and 6.79 (1H, d, 2-H), 1.23 and 4.23 (3H, t, and 2H, q, CO_2Et), 6.8–8.1 (4H, m, Ar-H); $J_{2,3}$ 4.5, $J_{3,4}$ 2.5, and $J_{4,5}$ 9 Hz. However, (6b) was converted into (7b) at 100-110 °C, and thus the structure of (6b) including the position of the methyl group was inferred from that of (7b): m.p. 106-107 °C; i.r. v (KBr) 1750 (C=O) cm⁻¹; ¹H n.m.r. δ (CDCl₃) 2.48 (3H, s, 4-Me), 6.57 (1H, d, J 4 Hz, 3-H), 7.65 (1H, d, J 4 Hz, 2-H), and 7.4-8.0 (4H, m, Ar-H).

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References

1 For a review, see K. U. Ingold and J. C. Walton, Acc. Chem. Res., 1986, 19, 72.

- R. A. Aitken, J. I. G. Cadogan, I. Gosney, B. J. Hamill, and L. M. McLaughlin, J. Chem. Soc., Chem. Commun., 1982, 1164; H.-D. Martin, H. Höchstetter, and A. Steigel, Tetrahedron Lett., 1984, 25, 297; J. Kurita, K. Iwata, M. Hasebe, and T. Tsuchiya, J. Chem. Soc., Chem. Commun., 1983, 941; J. Kurita, K. Iwata, H. Sakai, and T. Tsuchiya, Chem. Pharm. Bull., 1985, 33, 4572; J. Kurita, H. Sakai, and T. Tsuchiya, J. Chem. Soc., Chem. Commun., 1985, 1769.
- 3 J. Kurita, S. Yamada, H. Sakai, and T. Tsuchiya, J. Chem. Soc., Chem. Commun., 1985, 1254.
- 4 H. Igeta, H. Arai, H. Hasegawa, and T. Tsuchiya, Chem. Pharm. Bull., 1975, 23, 2791.
- W. Lwowski and T. J. Maricich, J. Am. Chem. Soc., 1965, 87, 3630;
 M. Seno, T. Namba, and H. Kise, J. Org. Chem., 1978, 43, 3345.