

A Reinvestigation of the Prévost Reaction with *N*-Allylmorpholine

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Abstract

A reinvestigation of the Prévost reaction of *N*-allylmorpholine (1) with silver(I) benzoate and iodine shows that it gives the 1,3-dibenzoate (2) (11%) through rearrangement, the 1,2-dibenzoate (3) (5%) and (1) (13%).

Ferretti and Tesi¹ reported that the reaction of *N*-allylmorpholine (1) with silver(I) benzoate and iodine (Prévost reaction) gave only the 1,3-dibenzoate (2) which was not isolated but was hydrolysed to 2-morpholinopropane-1,3-diol in 30% overall yield. Although participation of neighbouring amino groups in Prévost reactions appears to be the rule rather than the exception^{1,2} the formation of only the 'rearranged' dibenzoate is surprising since the 1,2-dibenzoate (3) could be expected as a product either through direct addition to the double bond or through an intermediate aziridinium ion (4). We have therefore reinvestigated the reaction.

In our hands, treatment of the alkene (1) with silver(I) benzoate (2 equiv.) and iodine (1 equiv.) gave a mixture of two products which were separated by p.l.c. The major product, which analysed for $C_{21}H_{23}NO_5$, was identified as 2-morpholinopropane-1,3-diyl dibenzoate (2) from its spectral parameters. The symmetrical structure of the dibenzoate was shown by the appearance of only four signals in the aliphatic region of the noise-decoupled ^{13}C n.m.r. spectrum at δ 67.4 (C1 and C3), 62.1 (C5), 61.7 (C2), and 50.3 (C4); assignments were confirmed by high power single frequency proton decoupling experiments.

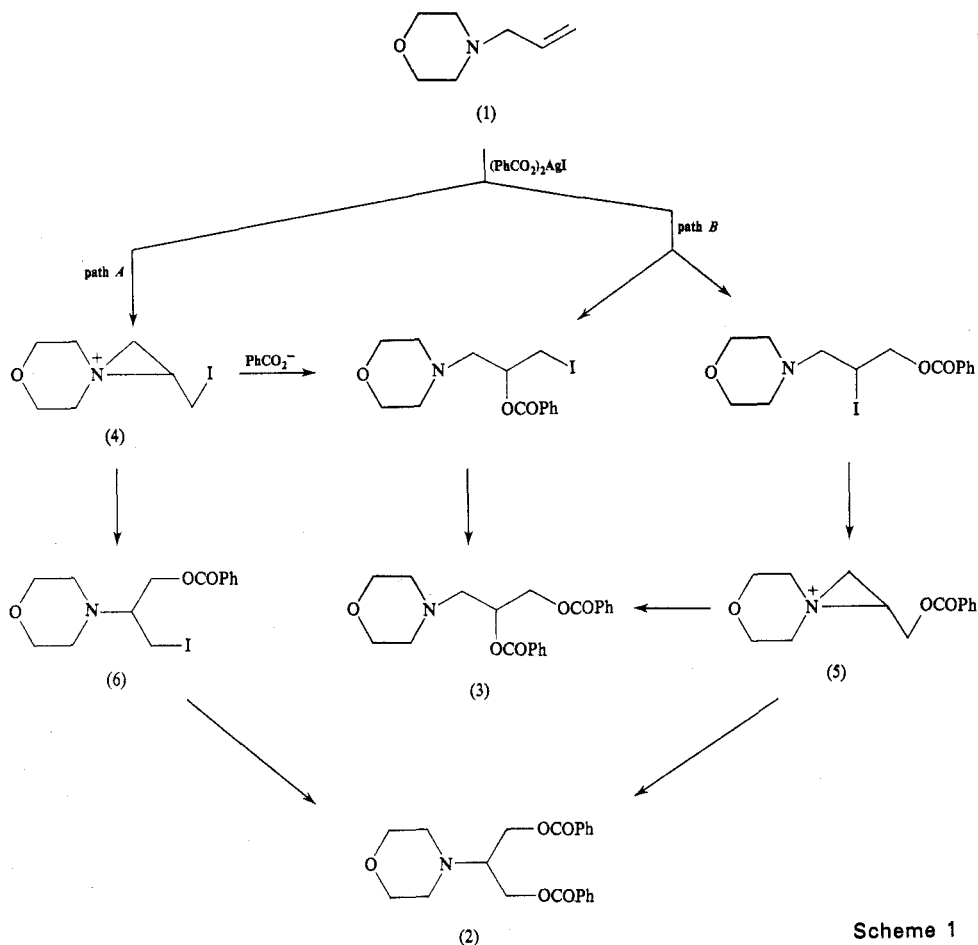
A correct elemental analysis for the minor product, 3-morpholinopropane-1,2-diyl dibenzoate (3), was not obtained but its structure was apparent from its spectral data. Thus, the aliphatic region of the 1H n.m.r. spectrum and the results of double resonance experiments were distinct from those for (2) while the noise-decoupled ^{13}C n.m.r. spectrum showed a total of five aliphatic carbon signals, namely δ 69.5 (C2), 66.8 (C5), 64.6 (C1), 58.7 (C3), and 54.1 (C4).

Formation of the dibenzoates (2) and (3) can be rationalized in two ways (Scheme 1) depending on whether the skeletal rearrangement occurs as a result of the initial electrophilic step (path *A*) or during the subsequent nucleophilic step (path *B*).

¹ Ferretti, A., and Tesi, G., *J. Chem. Soc.*, 1965, 5203.

² Russell, P. B., *J. Am. Chem. Soc.*, 1956, 78, 3115.

Path *A* involves the initial formation of an aziridinium ion (4)* from participation of the neighbouring tertiary amino group and is based on the proposal by Ferretti and Tesi¹ but modified to account for the formation of (3). An alternative pathway (path *B*) may involve the formation of regioisomeric iodo benzoates (cf. allylbenzene³), one of which can subsequently form the aziridinium ion (5)† by neighbouring group participation.



Scheme 1

* Formation of a four-membered azetidinium ion at this or a subsequent stage cannot be discounted.

† A referee has suggested that the aziridinium ion (5) could also be formed from the rearranged iodo benzoate (6). However, such a pathway to (3) involves two skeletal rearrangements. Our attempts to clarify this point by isolation of intermediate iodo benzoates were unsuccessful, since reaction of (1) with thallium(i) benzoate and iodine^{3,4} did not give any iodo benzoates.

³ Cambie, R. C., Hayward, R. C., Roberts, J. L., and Rutledge, P. S., *J. Chem. Soc., Perkin Trans. 1*, 1974, 1858.

⁴ Cambie, R. C., Potter, G. J., Rutledge, P. S., and Woodgate, P. D., *J. Chem. Soc., Perkin Trans. 1*, 1977, 530.

Experimental

General

For general experimental details see ref.⁴ A LAOCOON 3 computer program⁵ was used to simulate ¹H n.m.r. spectra.

Reaction of *N*-Allylmorpholine (1) with Silver(I) Benzoate and Iodine

Iodine (12.0 g, 47.2 mmol) was added to a suspension of dry silver(I) benzoate (21.6 g, 94.5 mmol) in anhydrous benzene (200 ml) at 20° and the mixture was heated to 80° and swirled until the iodine colour was discharged. The mixture was cooled, *N*-allylmorpholine (6.0 g, 47.2 mmol) was added dropwise over 5 min, and the mixture was refluxed for 3 h. Precipitated silver(I) iodide was filtered off from the cooled mixture and the solvent was removed from the filtrate to give a red-brown oil which was percolated through a short column of alumina (CHCl₃). Removal of solvent gave a yellow oil (6.4 g) which darkened upon standing and which contained (t.l.c.) starting alkene (1) and two other more polar compounds in an approximate ratio of 2:1 (¹H n.m.r. analysis). P.l.c. (benzene/ether, 3:2) of a portion of this oil (1.5 g) gave the following compounds.

(i) 2-Morpholinopropane-1,3-diyl dibenzoate (2) (0.44 g), as an oil, b.p. 164° (Kugelrohr) at 0.02 mmHg (Found: C, 68.4; H, 6.5; N, 3.9. C₂₁H₂₃NO₅ requires C, 68.3; H, 6.3; N, 3.8%). ν_{\max} 1720 (CO) and 1600 cm⁻¹ (aryl ring). ¹H n.m.r. δ 2.80, m, 2CH₂N; 3.33, quintet, *J* 6.0 Hz, CH; 3.67, m, 2CH₂O; 4.48, 4.63, 8 lines of the AB part of an ABX system, *J*_{A,B} (calc.) -11.72, *J*_{A,X} (calc.) 5.49, *J*_{B,X} (calc.) 6.37 Hz, 2CH₂OBz; 7.65, m, ArH. Double resonance experiments showed that H2 was coupled to (H1)₂ and (H3)₂. ¹³C n.m.r. δ 50.3, CH₂N; 61.7, C2; 62.1, CH₂O; 67.4, C1, C3; 128.3, *meta*-C; 129.5, *ortho*-C; 129.8, *ipso*-C; 133.0, *para*-C; 166.1, C=O.

(ii) 3-Morpholinopropane-1,2-diyl dibenzoate (3) (0.21 g), as an oil, b.p. 127° (Kugelrohr) at 0.01 mmHg.* ν_{\max} 1720 (CO) and 1600 (aryl ring) cm⁻¹. ¹H n.m.r. δ 2.59 m, 2CH₂N; 2.77, d, *J* 12.0 Hz, CH₂N; 3.68, m, 2CH₂O; 4.56, 4.70, 8 lines of the AB part of an ABX system, *J*_{A,B} (calc.) -11.89, *J*_{A,X} (calc.) 5.15, *J*_{B,X} (calc.) 3.52 Hz, CH₂OBz; 5.58, m, CHOBz; 7.75, m, ArH. Double resonance experiments showed that H2 was coupled to (H1)₂ and (H3)₂. ¹³C n.m.r. δ 54.1, CH₂N; 58.7, C3; 64.6, C1; 66.8, CH₂O; 69.5, C2; 128.3, *meta*-C; 129.6, *ortho*-C; 129.9, *ipso*-C; 133.0, *para*-C; 165.8 and 166.2, C=O.

(iii) Starting alkene (1) (0.18 g) (correct ¹H n.m.r. spectrum).

When the reaction was carried out with *N*-allylmorpholine (0.25 g, 0.2 mmol), silver(I) benzoate (0.45 g, 0.2 mmol) and iodine (0.51 g, 0.2 mmol) in dry ether a red oil (0.60 g) was obtained which contained (2), (3) and (1) in an approximate ratio of 1:1:2. Attempts to carry out the reaction with thallium(I) acetate or thallium(I) benzoate and iodine in dry benzene or with silver(I) acetate and iodine in dry ether gave mainly starting material and unidentified products.

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* Incorrect analyses (e.g. Found: C, 70.4; H, 7.5; N, 3.3%) were obtained.

⁵ Bothner-By, A. A., and Castellano, S. M., in 'Computer Programs for Chemists' (Ed. D. F. DeTar) Vol. 1, Ch. 3, p. 10 (Benjamin: Menlo Park, California, 1968).