Attempted Cycloaddition of *N*-Ethoxycarbonylmethylenenamine to *N*-Ethoxycarbonylazepine: Formation of 4,4'-Bis(ethoxycarbonylamino)-diphenylmethane

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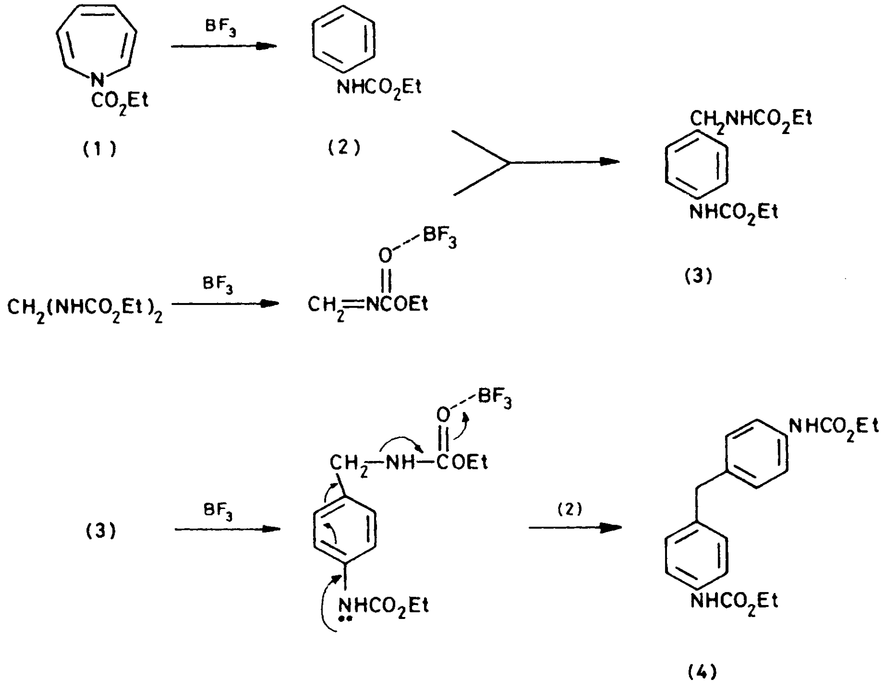
Three products were formed in the boron trifluoride-catalysed reaction of *N*-ethoxycarbonylmethyleneamine with *N*-ethoxycarbonylazepine, *N*-ethoxycarbonylaniline (2), 4-(*N*-ethoxycarbonylaminomethyl)-*N*-ethoxycarbonylaniline (3), and 4,4'-bis-(*N*-ethoxycarbonylamino)diphenylmethane (4). Product (4) was independently synthesised. The mechanisms of formation of the products (2), (3), and (4) were established.

THERMAL (6 + 2) cycloaddition reactions are uncommon, though permitted by either a ($\pi 6_a + \pi 2_s$) or ($\pi 6_s + \pi 2_a$) pathway.[1] Both cycloheptatriene[2] and *N*-ethoxycarbonylazepine[3] (1) undergo a formal (6 + 2) cycloaddition reaction with nitrosobenzene. Since Krow and co-workers[4] noted that *N*-ethoxycarbonylmethyleneamine (NEM) (CH_2=NCO_2Et) undergoes a (6 + 2) cycloaddition to cycloheptatriene, albeit in a step-wise manner, we undertook an investigation of the reaction of NEM with (1).



SCHEME

RESULTS AND DISCUSSION

It has been established that NEM is formed by the boron trifluoride-catalysed fragmentation of bis-(*N*-ethoxycarbonylamino)methane.[4] Accordingly (1) was heated in benzene with bis-(*N*-ethoxycarbonylamino)methane and boron trifluoride–ether. No cycloadducts were detected. The three products (2), (3), and (4) only were formed (Scheme) together with the dimer of (1) (see Experimental section). *N*-Ethoxycarbonylaniline (2) was readily identified and the assignment confirmed by comparison with an authentic sample. The second product had spectra consistent with structure (3). In addition (3) was readily hydrogenated to a hexahydro-derivative. The spectral properties of the latter, which included a u.v. difference spectrum [$\lambda_{max.}$ 250 nm (ε 7 839)], were consistent with a structure derived from (3). The structure (4) was indicated by its spectra, and was confirmed by synthesis from diphenylmethane. Diphenylmethane was nitrated, reduced to the 4,4'-diamine,[5] and converted to the bis-(*N*-ethoxycarbonyl)-derivative by reaction with ethyl chloroformate.[6] This product was identical with compound (4).

The modes of formation of (2)—(4) were investigated. Treatment of (1) with boron trifluoride–ether in benzene effected rapid and quantitative rearrangement (<5 min) into (2) at room temperature. Although mineral acid is known [7] to induce this rearrangement, boron trifluoride catalysis has not been noted hitherto. The rapidity of this rearrangement explains the absence of cycloaddition products. Cycloaddition reactions of (1) are generally slow.[3,8] It seemed probable, then, that the formation of the products (3) and (4) involved (2). Accordingly when (2) was heated with boron trifluoride–ether in either benzene or chloroform with bis-(*N*-ethoxycarbonylamino)methane, (3) and (4) were formed exclusively. In addition, it was noted that, by following the reaction by t.l.c., (3) was formed first, followed slowly by (4). This indicated that boron trifluoride catalysed a reaction of (2) with (3). When, therefore, an equimolar solution of (2) and (3) in either benzene or chloroform was refluxed for 24 h in the presence of boron trifluoride–ether, the diphenylmethane (4) was the only product. No reaction occurred in the absence of boron trifluoride.

On this basis we suggest the mechanism outlined in the Scheme. The mode of fragmentation of bis-(*N*-ethoxycarbonylamino)methane is well established and the boron trifluoride-catalysed cleavage of (3) is formally related. However, this fragmentation may require a suitably oriented activating ring-substituent to be effective.

EXPERIMENTAL

Microanalyses were performed in this Department. Spectra were recorded with a Perkin-Elmer 257 i.r. spectrophotometer for KBr discs, a Unicam SP 800 u.v. spectrophotometer for solutions in ethanol, a Perkin-Elmer R20A 60-MHz ^1H n.m.r. spectrometer, a JEOL FX60 ^{13}C n.m.r. spectrometer, and an A.E.I. MS 902 mass spectrometer. T.l.c. involved the use of Merck silica gel HF_{254} plates. For preparative t.l.c., Merck Kieselgel PF_{254} was used. The eluant in both cases was ethyl acetate–light petroleum (30 : 70). The u.v. extinction coefficient (ε) is expressed in $mol^{-1}\ l\ cm^{-1}$ units.

Boron Trifluoride-catalysed Reaction of (1) *with Bis-*(N-*ethoxycarbonylamino*)*methane*.—A solution of (1) (0.825 g, 0.005 mol), bis-(*N*-ethoxycarbonylamino)methane (0.95 g, 0.005 mol), and freshly distilled boron trifluoride–ether (0.5 ml) in dried benzene (30 ml) was refluxed until no further change was apparent (t.l.c., 24 h). The solution was cooled, washed with water, 5% sodium hydrogencarbonate, dilute hydrochloric acid, and water, and dried with magnesium sulphate. The solvent was removed to give a pale yellow solid (1.35 g) which consisted (t.l.c.) of four compounds, three of which were isolated by preparative t.l.c.; the fourth had the same R_F (0.01) as the dimer [9] of (1) and was not isolated.

The first component was 4-(N-*ethoxycarbonylaminomethyl*)-N-*ethoxycarbonylaniline* (3) (0.3 g, 22%), m.p. 101—102 °C, R_F 0.14 (Found: C, 58.7; H, 7.0; N, 10.6. $C_{13}H_{18}N_2O_4$ requires C, 58.6; H, 6.8; N, 10.5%); $\nu_{max.}$ 3 322, 2 980, 1 690, and 1 595 cm^{-1}; $\lambda_{max.}$ 212 (ε 1 957) and 248 nm (8 370); τ 2.60—3.04 (4 H, q, A_2B_2, *J* 8 Hz, Ph), 3.15 (1 H, br s, NH, disappeared with D_2O), 5.0 (1 H, br s, NH), 5.83 (2 H, d, *J* 7 Hz, CH_2), 5.70—6.15 (4 H, 2 × q, *J* 7.5 Hz, 2 × OCH_2), and 8.62—8.92 (6 H 2 × t, *J* 7.5 Hz, 2 × Me); δ_C 14.61 (q, 2 × Me), 44.63 (t, OCH_2), 61.20 (t, OCH_2), 119.03 (d, Ph), 128.29 (d, Ph), 133.58 (s, Ph), 137.48 (s, Ph), 153.79 (s, C=O), and 156.77 (s, C=O); *m/e* 266 (M^+). Product (3) (0.4 g, 0.001 5 mol) was hydrogenated with PtO_2 (0.1 g) at 50 lb in^{-2} for 120 h. Filtration and evaporation of the solvent afforded the *hexahydro-derivative* (0.39 g, 80%), m.p. 108—110 °C (Found: C, 57.7; H, 8.7; N, 9.9. $C_{13}H_{24}N_2O_4$ requires C, 57.3; H, 8.9; N, 10.3%); $\nu_{max.}$ 3 310, 2 910, 1 680, and 1 540 cm^{-1}; $\lambda_{max.}$ 224 nm (ε 2 160); τ 5.35 (2 H, br s, 2 × NH), 6.00 (4 H, q, *J* 7.5 Hz, 2 × OCH_2), 7.00 (2 H, br s, CH_2N), 8.00—8.60 (10 H, m, 4 × CH_2 + 2 × CH), and 8.20 (6 H, *J* 7.5 Hz, 2 × Me); *m/e* 272 (M^+).

The second component was 4,4′-*bis*-(N-*ethoxycarbonylamino*)*diphenylmethane* (4) (0.08 g, 6%), m.p. 133—134 °C, R_F 0.22 (Found: C, 66.35; H, 6.6; N, 7.8. $C_{19}H_{22}N_2O_4$ requires C, 66.66; H, 6.43; N, 8.20%); $\nu_{max.}$ 3 300, 3 030, 2 910, 1 690, and 1 590; $\lambda_{max.}$ 255 (ε 1 172), 278 (157), and 290sh nm (98); τ 2.95 (8 H, q, Ph), 3.45 (2 H, br s, 2 × NH), 5.90 (4 H, q, *J* 7.5 Hz, 2 × OCH_2), 6.21 (2 H, s, CH_2), and 8.75 (6 H, t, *J* 7.5 Hz, 2 × Me); *m/e* 342 (M^+). Product (4) (0.06 g) was hydrogenated in methanol (25 ml) with PtO_2 (0.01 g) for 100 h at 50 lb in^{-2} and room temperature. The *perhydro-product* (0.05 g, 83%), m.p. 118—120 °C was isolated (Found: C, 64.5; H, 9.85; N, 7.8. $C_{19}H_{34}N_2O_4$ requires C, 64.40; H, 9.70; N, 7.90%); $\nu_{max.}$ 3 300, 2 910, 1 720, and 1 650br cm^{-1}; τ 5.30 (2 H, s, 2 × NH), 5.95 (4 H, q, 2 × CH_2), 6.30 (2 H, s, CH_2), 7.75—8.60 (20 H, m, 8 × CH_2 + 4 × CH), and 8.80 (6 H, t, *J* 8 Hz, 2 × Me); *m/e* 354 (M^+). Product (4) was identical (m.p., mixed m.p., ^1H n.m.r.) with a sample prepared from 4,4′-diaminodiphenylmethane [5] by treatment with ethyl chloroformate in the presence of aqueous sodium hydroxide.[6]

The third product (2) (0.10 g, 8%), m.p. 53—54 °C, mixed m.p. 53—54 °C (lit.,[10] 53 °C), R_F 0.33, was identified as *N*-ethoxycarbonylaniline (Found: C, 65.2; H, 7.0; N, 7.4. Calc. for $C_9H_{11}NO_2$: C, 65.4; H, 6.7; N, 8.5%).

Boron Trifluoride-catalysed Reaction of N-*Ethoxycarbonylaniline* (2) *with Bis-*(N-*ethoxycarbonylamino*)*methane*.—A solution of aniline (2) (0.5 g, 0.003 mol) was treated in the same manner as (1). The same work-up and separation by preparative t.l.c. afforded (2) (0.28 g, 35%), (3) (0.4 g, 50%), and (4) (0.105 g, 13%). No other products were formed.

Boron Trifluoride-catalysed Reaction of N-*Ethoxycarbonylaniline* (2) *with* 4-(N-*Ethoxycarbonylaminoethyl*)-N-*ethoxycarbonylaniline* (3).—A solution of (2) (0.025 g), (3) (0.04 g), and boron trifluoride–ether (0.3 ml) in benzene (7 ml) was heated under reflux 24 h. The usual work-up provided exclusively (4) (0.048 g, 94%).

[0/675 *Received, 8th May*, 1980]

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