Reactions of Carbamyl (Urethanyl) Radicals: Intramolecular Aromatic Additions

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The irradiation of benzyl *N*-bromo-*N*-methylcarbamates affords products due to Ar_1-5 cyclisation. It has been demonstrated that the intramolecular aromatic cyclisation is regiospecific and is not strongly influenced by electronic effects.

N-Halogenocarbamates have been shown to readily add to olefins, by a homolytic process.[1] In view of the higher yields of 1,2-adducts than obtained from the corresponding *N*-halogenocarboxamides, it has been suggested[2] that the carbamyl radical is more electrophilic than the amidyl radical. In contrast to the well-documented intramolecular aromatic addition reactions of amidyls,[3] there are no reports on the reaction of carbamyl radicals with aromatic substrates. While carbamates[4] have been shown to undergo intramolecular aromatic photoacylation, this process does not involve radical generation on the nitrogen of the carbamyl moiety. This communication reports on the intramolecular aromatic addition of carbamyl radicals with the spin density on nitrogen which were formed by irradiation of the labile *N*-bromo derivatives.

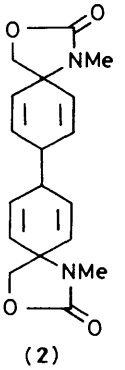
Irradiation of benzyl *N*-bromo-*N*-methylcarbamate (**1b**), prepared from benzyl *N*-methylcarbamate (**1a**) and t-butyl hypobromite,[5] in the presence of an excess of the bromine atom trap, 3,3-dimethylbut-1-ene[6], afforded a modest yield of the spiro compound (**2**), the structure of which was established by ^{1}H n.m.r. and mass spectral analysis (molecular ion at *m/z* 328). An i.r. absorption at 1 755 cm^{-1} was indicative of a five-membered cyclic carbamate. It is proposed that photolysis of (**1b**) leads to the carbamyl radical which undergoes Ar_1-5 cyclization to form the spiro radical (**3a**); dimerisation of these species affords (**2**).

It was expected from analogous amidyl cyclisations,[7] that a *para*-methoxy group as in *p*-methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1c**) would promote Ar_1-5 cyclisation firstly, through its *para*-directing effect in electrophilic reactions, and secondly as a result of its facility to eliminate the methyl group leading to the formation of a dienone. Irradiation of (**1c**) in the presence of 3,3-dimethylbut-1-ene afforded the spiro compound (**4**) (27% yield).

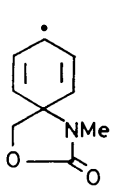
Since it has been proposed[2] that the carbamyl radical is electrophilic, the influence of an aryl methoxy group on the intramolecular cyclisation was investigated further by irradiating *m*-methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1d**) in the presence of 3,3-dimethylbut-1-ene. The reaction mixture afforded mainly the parent carbamate (**1e**) together with the spin compound (**5**), the structure of what was deduced from its mass and ^{1}H n.m.r. spectra. The mass spectrum had a molecular ion at *m/z* 353, fragments at *m/z* 274 (doublet), 242 (doublet) and a base peak at *m/z* 137 due to (M − Br), [M − (Br + NCH_3)] and [M − (2Br + CH_3NCO)] fragmentation respectively. In the n.m.r. spectrum the protons of the methoxy group resonated as a broad unresolved singlet. The NMe signal was a pair of singlets at δ 2.58 and 2.67 of relative area 4:6, respectively. The two resonances at δ 4.8—4.88 attributed to the methylene protons, were less well resolved. Although these different signals could be attributed to different configurations it is proposed that they are due to different conformers since all efforts to separate the compound were unsuccessful. The cyclohexadienyl protons resonated as a multiplet at δ 4.25 and a doublet at δ 6.55. The lowfield resonance is attributed to 4-H. The mode of formation of the dibromocyclohexadiene (**5**) is rationalised in Scheme 1.

$MeN(X)CO_2R$

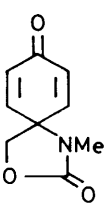
(**1**) a; X = H, R = $PhCH_2$
b; X = Br, R = $PhCH_2$
c; X = Br, R = *p*-$MeOC_6H_4CH_2$
d; X = Br, R = *m*-$MeOC_6H_4CH_2$
e; X = H, R = *m*-$MeOC_6H_4CH_2$
f; X = Br, R = *m*-$MeOC_6H_4$



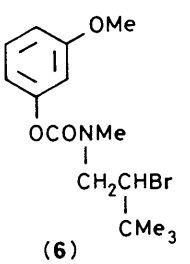
(**2**)



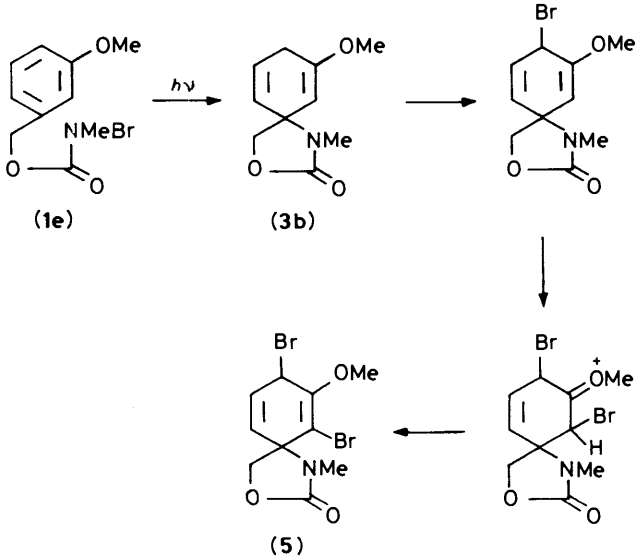
(**3a**)



(**4**)



(**6**)



(**1e**) (**3b**) (**5**)

Scheme 1.

The large amounts of the parent carbamates (**1a**) and (**1e**) recovered in these reactions is in all probability due to the sensitivity of the *N*-bromocarbamates to moisture and/or traces of acidic impurities since it was found that the *N*-bromocarbamate (**1b**) was reduced to the carbamate (**1a**) after 40 h in the dark when stored in dry benzene.

The formation of a dimer from benzyl *N*-bromo-*N*-methylcarbamate (**1b**) and the failure of *m*-methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1d**) to react likewise is probably due to differences in the energies and reactivities of the intermediate cyclohexadienyl radicals (**3a**) and (**3b**). Since steric hindrance by the methoxy substituent would not be expected to prevent dimerisation, we propose that the *m*-methoxy substituent raises the energy of the SOMO of (**3b**) and thus increases its nucleophilicity which allows it to more effectively abstract bromine from its unchanged *N*-bromocarbamate.

These intramolecular aromatic cyclisations of carbamyl radicals demonstrate the difference between the reactions of carbamyl and amidyl radicals. Neither 3-phenylpropionamide nor 2-phenoxyethanamide underwent intramolecular aromatic substitution when irradiated in the presence of t-butyl hypoiodite.[3]

In an attempt to induce *ortho*-substitution *m*-methoxyphenyl *N*-bromo-*N*-methylcarbamate (**1f**) was irradiated in an excess of 3,3-dimethylbut-1-ene. The reaction mixture contained the intermolecular adduct, *m*-methoxyphenyl *N*-(2-bromo-3,3-dimethylbutyl)-*N*-methylcarbamate (**6**), but no products due to intramolecular aromatic addition could be detected. The adduct (**6**) had a non-first-order ^{1}H n.m.r. spectrum which has recently been elucidated.[8]

These results support the proposal[2] that carbamyl radicals are electrophilic, but also demonstrate that the intramolecular aromatic cyclisation reaction is regiospecific and is not strongly influenced by electronic effects.

E.s.r. studies[9] have shown that the carbamyl radical exists in the π-electronic state and MNDO calculations[8] on methyl carbamate indicate significant π-bond orders in the functionality.

The rigid geometry of the π-ground state radical would be expected to preclude reaction at the 1-position in a substrate such as (**1b**). Since reaction does occur, it is proposed that the energy difference between the Π- and Σ-states is small so that a significant amount of state mixing occurs which allows reaction at the 1-position *via* a radical containing greater Σ character in the transition state. An alternative rationalisation would be that a significant amount of twisting[10,11] of the Π-state carbamyl radical occurs in the transition state for reaction to take place at the 1-position. The failure of the carbamyl radical to react at the 2-position to form a 5- or 6-membered ring is in all probability due to the rigidity of the carbamyl system which prevents effective orbital overlap.

The large A_N values observed in the e.s.r. spectra of carbamyl radicals (14—15.6 G),[12] which are significantly larger than those of Π-state lactaminyls (11.2 G),[10] may reflect decreased interaction with the carbonyl, which would be compatible with increased Σ-Π mixing.

Experimental

M.p.s were determined on a Kofler hot-stage and are uncorrected. I.r. spectra were recorded with a Perkin-Elmer i.r. spectrophotometer, Model 297 and n.m.r. spectra with a 60 MHz Perkin-Elmer R12A spectrometer with TMS as internal reference.

N-Bromocarbamates.—These were synthesised as previously described.[8]

Benzyl N-*bromo*-N-*methylcarbamate* (**1b**). Benzyl *N*-methylcarbamate (**1a**) (1.50 g, 9.09 mmol) afforded benzyl *N*-bromo-*N*-methylcarbamate (**1b**) (2.22 g); $\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1}; δ($CDCl_3$) 3.32 (3 H, s), 5.08 (2 H, s), and 7.28 (5 H, s) (Found: Br, 32.1. Calc. for $C_9H_{10}BrNO_2$: Br, 32.79%).

p-*Methoxybenzyl* N-*bromo*-N-*methylcarbamate* (**1c**). *p*-Methoxybenzyl *N*-methylcarbamate (2.00 g, 10.26 mmol) afforded *p*-methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1c**) (3.07 g); $\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1}; δ($CDCl_3$) 3.32 (3 H, s), 3.72 (3 H, s), 5.02 (2 H, s), 6.82 (2 H, d, *J* 7.8 Hz), and 7.28 (2 H, d, *J* 7.8 Hz) (Found: Br, 29.1. Calc. for $C_{10}H_{12}BrNO_3$: Br, 29.20%).

m-*Methoxybenzyl* N-*bromo*-N-*methylcarbamate* (**1d**). *m*-Methoxybenzyl *N*-methylcarbamate (1.50 g, 7.60 mmol) afforded *m*-methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1d**) (2.01 g); $\nu_{max.}$($CHCl_3$) 1 700 cm^{-1}; δ($CDCl_3$) 3.38 (3 H, s), 3.72 (3 H, s), 5.14 (2 H, s), and 6.55—7.55 (4 H, m) (Found: Br, 27.74. Calc. for $C_{10}H_{12}BrNO_3$: Br, 29.20%).

m-*Methoxyphenyl* N-*bromo*-N-*methylcarbamate* (**1f**). *m*-Methoxyphenyl *N*-methylcarbamate (1.00 g, 5.53 mmol) afforded *m*-methoxyphenyl *N*-bromo-*N*-methylcarbamate (**1f**) (1.42 g); $\nu_{max.}$($CHCl_3$) 1 725 cm^{-1}; δ($CDCl_3$) 3.45 (3 H, s), 3.65 (3 H, s), and 6.45—7.50 (4 H, m) (Found: Br, 27.1. Calc. for $C_9H_{10}BrNO_3$: Br, 30.77%).

Photolysis of N-*Bromocarbamates.*—(a) Benzyl *N*-bromo-*N*-methylcarbamate (**1b**) (2.00 g, 8.20 mmol) and 3,3-dimethylbut-1-ene (6.89 g, 82 mmol) in dry benzene (50 ml), irradiated for 1.5 h, afforded a brown oil which was separated by chromatography on silica gel plates ($CHCl_3$) into benzyl *N*-methylcarbamate (**1a**) (0.89 g, 5.39 mmol, 65%) and *N'*,*N'*-dimethyl-4,4-bi[cyclohexa-2,5,dienespiro-4'-1',3'-oxazolidine]-2',2'-dione (**2**) (0.46 g, 1.40 mmol, 17%) as a solid which was recrystallized from benzene–light petroleum (b.p. 40—60 °C), m.p. 176—182 °C (decomp.); M^+ 328, *m/z* 298, 225, 164, 134, and 91; $\nu_{max.}$($CHCl_3$) 1 755 cm^{-1}; ($CDCl_3$) 2.65 (6 H, s), 3.05 (2 H, s br), 4.04 (4 H, s), and 5.50—6.40 (8 H, m) (Found: C, 65.6; H, 6.0; N, 8.3. Calc. for $C_{18}H_{20}N_2O_4$: C, 65.8; H, 6.1; N, 8.5%).

(b) *p*-Methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1c**) (3.07 g, 11.2 mmol) and 3,3-dimethylbut-1-ene (9.41 g, 112 mmol) in dry benzene (50 ml), irradiated for 0.5 h, afforded a brown oil which was separated by repetitive chromatography on silica gel plates (benzene) into *p*-methoxybenzyl *N*-methylcarbamate (1.01 g, 5.18 mmol, 46%) and *N*-methylcyclohexa-2,5-dienespiro-4'-1',3'-oxazolidin-2'-one (**4**) 0.55 g, 3.07 mmol, 27%) which was recrystallized from benzene–light petroleum (40—60 °C), m.p. 125—126.5 °C; M^+ 179, *m/z* 149, 121, 106, and 93; $\nu_{max.}$($CHCl_3$) 1 765, 1 685, 1 640, and 1 400 cm^{-1}; δ($CDCl_3$) 2.72 (3 H, s), 4.32 (2 H, s), 6.44 (2 H, d, *J* 9.0 Hz), and 6.94 (2 H, d, *J* 9.0 Hz) (Found: C, 60.4; H, 5.0; N, 8.3. Calc. for $C_9H_9NO_3$: C, 60.3; H, 5.1; N, 7.8%).

The n.m.r. spectrum of the crude oil was shown, by integration of the CH_2 resonances, to consist of *p*-methoxybenzyl *N*-methylcarbamate (69%) and the spirodienone (**4**), (31%).

(c) *m*-Methoxybenzyl *N*-bromo-*N*-methylcarbamate (**1d**) (2.01 g, 7.34 mmol) and 3,3-dimethylbut-1-ene (6.72 g, 80 mmol) in dry benzene (50 ml), irradiated for 0.5 h, afforded a brown oil which was separated by chromatography on silica gel plates [ether–hexane (4:1)] into *m*-methoxybenzyl *N*-methylcarbamate (**1e**) (0.62 g, 3.18 mmol, 43%) and 2,4-dibromo-3-methoxy-*N'*-methylcyclohexa-2,5-dienespiro-4'-1',3'-oxazolidin-2-one (**5**) (0.41 g, 1.16 mmol, 16%) as a solid which was recrystallized from benzene–light petroleum (b.p. 40—60 °C, m.p. 164.5 °C; M^+ 353, *m/z* 274/272, 244/242, 193, 164, and 137; $\nu_{max.}$ ($CHCl_3$) 1 760, 1 680, 1 640, and 1 400 cm^{-1}; δ($CDCl_3$) 2.58 and 2.67 (3 H, d), 3.68 (3 H, s), 3.90—4.60 (2 H, m), 4.8 and 4.88 (2 H, d), 6.55 (1 H, d) (Found: C, 34.1; H, 3.2; N, 3.9. Calc. for $C_{10}H_{11}NO_3Br_2$: C, 34.0; H, 3.1; N, 4.0%).

(d) *m*-Methoxyphenyl *N*-bromo-*N*-methylcarbamate (**1f**) (1.42 g, 5.46 mmol) and 3,3-dimethylbut-1-ene (4.60 g, 55 mmol) in dry benzene (50 ml), irradiated for 3.5 h, afforded a brown oil which was separated by chromatography on silica gel plates (CH_2Cl_2) into *m*-methoxyphenyl *N*-methylcarbamate (0.85 g, 4.70 mmol, 86%) and *m*-methoxyphenyl *N*-(2-bromo-3,3-dimethylbutyl)-*N*-methylcarbamate (0.36 g, 1.05 mmol, 19%) as an oil which was further purified by chromatography on silica gel plates (benzene); M^+ 344/342, *m/z* 150 and 106; $\nu_{max.}(CHCl_3)$ 3 025, 1 720, and 1 600 cm^{-1}; $\delta(CDCl_3)$ **1**.12 (9 H, s), 2.78—3.58 (5 H, m), 3.80 (3 H, s), 4.15—4.68 (1 H, m), 6.18—6.96 (3 H, m), 7.32—7.78 (1 H, m). The n.m.r. spectrum of a sample purified by repetitive chromatography did not lead to a simple first-order spectrum.

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