Thermal Rearrangement of Allylic Amine-imides and Related Topics

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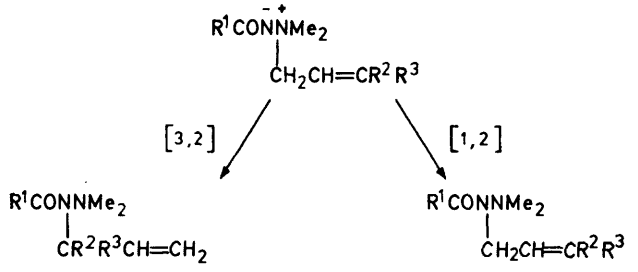
Deuterium reduction (Pd–$BaSO_4$) of *NN*-dimethylpropargylammoniobenzamidate to *N*-(2,3-dideuterioallyl)dimethylammoniobenzamidate and thermal rearrangement of the latter to *N*-(1,2-dideuterioallyl)-*N'N'*-dimethylbenzohydrazide validates a concerted [3,2] rearrangement for unsubstituted allyl groups in this series. Thermolysis of related hydrazinium halides gives the dialkylhydrazides.

THERMAL reactions of amine-imides derived from carboxylic acids (inner salts of amido-ammonium compounds, or *N*-ammonioamidates) have been studied extensively in recent times. Depending on the substituents present in the compounds, the reactions observed have included Curtius-type rearrangements with formation of the corresponding isocyanate (or, by trimerisation, isocyanurate) and tertiary amine, alkene formation with elimination of the corresponding dialkylhydrazide, isomerisation involving migration of an allylic or benzylic group from the cationic to the anionic nitrogen atom, and in some instances competition between alternative pathways.[1] For cases involving allylic migration, more than one product is possible and more than one mechanistic pathway has been suggested.



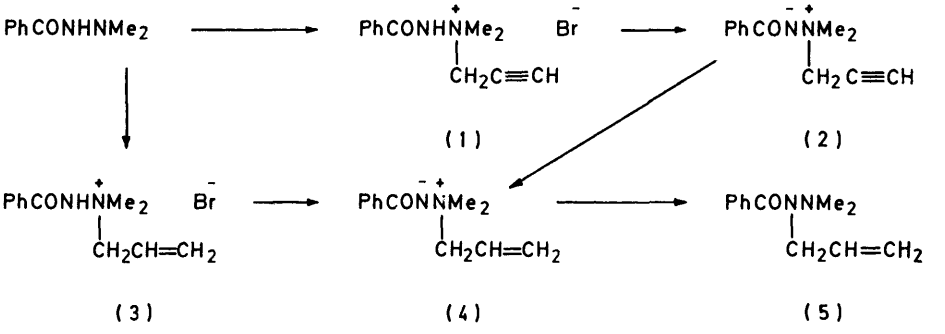
A concerted [3,2] rearrangement has been suggested for the unsubstituted allyl case (R^1 = Ph, R^2 = R^3 = H), implying allylic inversion.[2] A [1,2] rearrangement has been reported for three cases bearing γ-allylic substituent(s) and in one of these (R^1 = Me, R^2 = H, R^3 = Ph) a prior [3,2] rearrangement was excluded on the grounds that the product of such a reaction rearranged too slowly at 170° to account for formation of the reported product. A radical dissociation–recombination mechanism was suggested [3] in line with earlier hypothesis [4] and supported by observation of a chemically induced dynamic nuclear polarisation (CIDNP emission) of the allylic methylene protons in the [1,2] rearrangement product during generation from the above mentioned 3-phenylpropenyl compound at 180°. Interpretation of these data [3] has been complicated by indications that in the cases where R^1 = R^3 = Me, R^2 = H and where R^1 = Me, R^2 = H, R^3 = Ph, reaction products have included compounds resulting both from rearrangement with allylic retention and from rearrangement with allylic inversion.[5,6] Similar findings have more recently been reported for related carbamoylamine-[7] and ethoxycarbonylamine-imides.[8] Rationalisations based on competition between concerted and radical mechanisms or on competitive recombination reactions of radicals produced by dissociation of these amine-imides have been mooted previously.[1,7] In this regard CIDNP results should be interpreted with caution; the technique leaves undetected any non-radical pathway for product formation whilst failure to observe CIDNP does not necessarily exclude involvement of a radical process in the reaction.[9] The work now reported provides evidence that a concerted [3,2] mechanism is operative in the unsubstituted allyl case referred to above; we comment also on a propargylic analogue and on thermolysis of related hydrazinium halides.

Treatment of *N'N'*-dimethylbenzohydrazide with propargyl bromide gave the hydrazinium salt (1) which was readily deprotonated to the amine-imide (2). The latter compound is reported to show CIDNP emission on thermal decomposition but product structures were not assigned.[10] We noted extensive decomposition at *ca.* 140° to give tarry material (as in the case of the phenylcarbamoyl analogue [7]) and did not pursue the matter as our major purpose lay elsewhere, but successful rearrangement of the acetyl analogue has been claimed.[5] By contrast, thermal decomposition of the salt (1) at 145° gave propargyl bromide, *N'N'*-dimethylbenzohydrazide, *N*-benzoyl-*N'N'N'*-trimethylhydrazinium bromide, which probably arises from transmethylation of the first-formed hydrazide by (1), and a minor unidentified compound. Thermolysis of the salt (3) and, at higher temperature, of *N*-benzoyl-*N'N'N'*-trimethylhydrazinium iodide also gave the dimethylhydrazide.

Amine-imides are reductively cleaved to the corresponding amide and tertiary amine, and of greater interest for the sequel was the discovery that (2) could be reduced to the allylic compound (4), albeit in poor yield, by careful hydrogenation using 5% Pd–$BaSO_4$ as catalyst. Compound (4), also available by way of the salt (3), readily rearranged to (5) at 120—140°, as previously noted.

Initially we were interested in establishing whether a prior N→O allyl migration might be involved as an intermediate step in the overall N→N migration. This was excluded by carrying out an allyl migration of this type on a pyrazolidin-3-one template in which the cationic nitrogen and (by delocalisation) anionic oxygen atoms were *anti* to each other.

The question of a concerted [3,2] mechanism or of a radical dissociation–recombination mechanism for the rearrangement (4)→(5) was next considered. Rearrangement occurred readily at 120—140° and was easily monitored by n.m.r. spectroscopy. No CIDNP emission was observed for rearrangement in *o*-dichlorobenzene at 140°, but its absence is not definitive for a concerted rearrangement. Accordingly, (2) was reduced hydrolysed, the former to *p*-bromophenacyl alcohol and the latter to benzamide. This is in marked contrast with the formation of the stable amine-imides from the acylhydrazinium salts under similar conditions.



with deuterium to give (6) and rearrangement of the latter was monitored by n.m.r. spectroscopy; within the limits of detection, this gave (7) only, with no sign of the isomer from a [1,2] rearrangement and no sign of deuterium scrambling, providing good evidence for a concerted [3,2] process.

Baldwin and his co-workers [3] had noted that allylic amine-imides in which the anionic charge was localised (through alkyl substitution) underwent concerted [3,2] rearrangement easily and this is evidently the case with related systems such as sulphimides.[11] Coincidentally studying allylic compounds with γ-substituent(s), they proposed that delocalisation of anionic charge (by acyl substitution) would shift the rearrangement mechanism from concerted to homolytic dissociation–recombination. Whilst this is clearly an important factor, a survey of available results would suggest that the change in mechanistic pathway occurs within the class of amine-imides derived from carboxylic acids, with the shift to a radical mechanism occurring with increasing γ-allylic substitution. This factor would make the concerted [3,2] process increasingly unattractive sterically relative to the homolytic dissociation–recombination mechanism with the substituted allylic radical coupling at the more reactive site.[12] Such an interpretation, based on competition between concerted and radical mechanisms, is consistent with recent studies on a number of pentadienyl amine-imides.[8]

Lastly we have prepared the salts *p*-bromophenacyltriethylammonium and benzamidodimethylsulphonium bromide from *p*-bromophenacyl bromide and *N*-bromobenzamide respectively. When treated with aqueous sodium hydroxide solution, each of these is readily

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded with Varian A60 and Bruker WP60 instruments (tetramethylsilane as internal reference); i.r. data are reported for KBr discs or liquid films.

N-Benzoyl-N′N′-dimethyl-N′-propargylhydrazinium Bromide (1).—A solution of *N′N′*-dimethylbenzohydrazide [13] (16.4 g, 0.1 mol) and propargyl bromide (11.5 g, 0.1 mol) in absolute ethanol (50 ml) was stirred overnight at room temperature. A crystalline deposit of the *salt* (1) (25.6 g, 91%) formed after adding ether and scratching. An analytical sample had m.p. 142.5—144° (with gas evolution) (from propan-2-ol) (Found: C, 50.85; H, 5.25; Br, 28.35. $C_{12}H_{15}BrN_2O$ requires C, 50.9; H, 5.3; Br, 28.25%); $\nu_{max.}$ 1 680 cm^{-1}; δ(D_2O) 3.85 (6 H, s).

Thermolysis of the Salt (1)—The salt (1) (10 g, 0.035 mol) was heated at 145° (oil-bath) for 2 h under a stream of dry nitrogen. The effluent gas was passed in turn through a condenser, a cold trap maintained at −23°, and a further trap containing aqueous cuprammonium hydroxide solution. A brown precipitate formed in the latter trap, indicating the evolution of a terminal acetylenic compound; the condensate in the former trap had an i.r. spectrum identical with that of propargyl bromide.

The black residual oil containing non-volatile thermolysis products was dissolved in boiling propan-2-ol (50 ml). Cooling and addition of a small amount of ether precipitated *N-benzoyl-N′N′N′-trimethylhydrazinium bromide* (2.5 g, 30%) as a buff solid; an analytical sample had m.p. 184—186° (decomp.; sample inserted at 170°) (from propan-2-ol) (Found: C, 45.7; H, 5.9; Br, 30.85. $C_{10}H_{15}BrN_2O$ requires C, 46.35; H, 5.8; Br, 30.9%). The structure was confirmed by conversion to trimethylammoniobenzamidate, m.p. 169—170° (from 1-bromopropane), identical (mixed m.p. and i.r. spectrum) with an authentic sample.[14]

T.l.c. of the ether–propan-2-ol filtrate showed four spots corresponding to the salt (1) (R_F 0.54), *N*-benzoyl-*N′N′N′*-trimethylhydrazinium bromide (R_F 0.17), *N′N′*-dimethylbenzohydrazide (R_F 0.70), and an unknown compound (R_F 0.84). The filtrate was evaporated, water (25 ml) was added, and the mixture was extracted with chloroform (3 × 10 ml). The chloroform solution was dried (Na_2SO_4) and evaporated and the residual oil was triturated with a small amount of ether to give *N′N′*-dimethylbenzohydrazide (1.8 g, 30%), m.p. 105—106°, mixed m.p. 106—107°. The

ether washings contained (t.l.c.) the unknown compound (R_F 0.84), but in insufficient quantity for identification.

Thermolysis of N-*Benzoyl*-N′N′N′-*trimethylhydrazinium Iodide*.—The iodide [14] (3.5 g, 0.008 mol) was heated at 190—200° (oil-bath) under nitrogen for 15 min. Water was added and the mixture was extracted with chloroform. The chloroform solution after drying and evaporation gave an oil which on trituration with ether gave *N′N′*-dimethylbenzohydrazide (0.8 g, 60%), m.p. and mixed m.p. 105—106° This was apparently (t.l.c.) the only product in the ether washings.

NN-*Dimethylpropargylammoniobenzamidate* (2).—A solution of the salt (1) (10 g, 0.035 mol) in water (25 ml) was treated with excess 2M-sodium carbonate solution. Extraction with chloroform (3 × 20 ml), drying (Na_2CO_3), and evaporation gave *compound* (2) (7.2 g, quantitative) as a solid which crystallized from 1-bromopropane as needles, m.p. 100—102° (Found: C, 71.2; H, 6.8; N, 14.0. $C_{12}H_{14}N_2O$ requires C, 71.3; H, 6.95; N, 13.85%); $\nu_{max.}$ 1 600 cm^{-1}; $\delta(CDCl_3)$ 3.48 (6 H, s).

Compound (2) gave an intractable black tar when heated at 140° under nitrogen.

Hydrogenation of Compound (2) ⟶ (4).—A solution of (2) (1.0 g, 0.005 mol) in propan-2-ol (25 ml) was reduced at atmospheric pressure and room temperature with hydrogen using 5% Pd–$BaSO_4$ catalyst (0.1 g). The reaction was terminated after 2 h (hydrogen uptake, 120 ml corrected to s.t.p., 0.0054 mol). The catalyst was filtered off and the filtrate was saturated with dry hydrogen chloride. After standing overnight, the crystalline hydrochloride of (4) (0.4 g, 34%) was collected and treated with 6M-sodium hydroxide (2 ml). The mixture was extracted with chloroform (3 × 5 ml). The chloroform solution was dried (Na_2CO_3) and evaporated to give (4) (0.25 g, 24%), m.p. 86—88°, identical (i.r. spectrum) with the sample prepared below.

N-*Allyl*-N′-*benzoyl*-NN-*dimethylhydrazinium Bromide* (3).—A solution of *N′N′*-dimethylbenzohydrazide (20 g, 0.12 mol) and allyl bromide (23 g, 0.2 mol) in absolute ethanol (300 ml) deposited the *bromide* (3) after stirring for 24 h at room temperature. Crystallization from ethanol gave prisms, m.p. 149—151° (Found: Br, 28.05. $C_{12}H_{17}BrN_2O$ requires Br, 28.05%); $\nu_{max.}$ 1 680 cm^{-1}; $\delta(D_2O)$ 3.80 (6 H, s).

N′N′-Dimethylbenzohydrazide (8.2 g, 0.05 mol) and allyl toluene-*p*-sulphonate (11.0 g, 0.05 mol) in chloroform (100 ml) (48 h; room temperature) gave the *hydrazinium-toluene*-p-*sulphonate* (14.0 g, 73%) which precipitated on addition of ether and crystallized from propan-2-ol as needles, m.p. 152—155° (Found: C, 60.6; H, 6.4. $C_{19}H_{24}N_2O_4S$ requires C, 60.65; H, 6.4%).

Thermolysis of the bromide (3) and work-up essentially as for the case of the trimethyl analogue above gave *N′N′*-dimethylbenzohydrazide (64%) as the only solid product isolable by chloroform extraction.

N-*Allyldimethylammoniobenzamidate* (4).—The salt (3) (2.3 g, 0.08 mol) was triturated with sodium hydroxide (1 g in 5 ml water) and the oily mixture was extracted with chloroform (4 × 10 ml). The chloroform solution was dried (Na_2CO_3) and evaporated to give *compound* (4) as an oil which solidified (1.48 g, 75%) on trituration with ether. An analytical sample had m.p. 86—88° (from 1-bromopropane) (Found: C, 70.55; H, 7.8; N, 13.7. $C_{12}H_{16}N_2O$ requires C, 70.6; H, 7.85; N, 13.7%); $\nu_{max.}$ 1 600 cm^{-1}; $\delta(CDCl_3)$ 3.32 (6 H, s).

N-*Allyl*-N′N′-*dimethylbenzohydrazide* (5).—Compound (4) (5.0 g, 0.024 mol) was heated at 140° for 18 h *in vacuo* in a sealed tube to give a brown oil (5.0 g) which was distilled to give the *hydrazide* (5) as an oil (3.8 g, 76%), b.p. 158° at 7 mmHg, n_D^{25} 1.5329 (Found: C, 70.7; H, 8.0; N, 13.9. $C_{12}H_{16}N_2O$ requires C, 70.6; H, 7.85; N, 13.7%); $\nu_{max.}$ 1 640 cm^{-1}; $\delta(CDCl_3)$ 2.50 (6 H, s). The i.r. spectra of the crude and distilled products were identical.

N′N′-*Diallylbenzohydrazide*.—Allyl bromide (48 g, 0.4 mol) was added during 30 min to a solution of benzohydrazide [14] (13.6 g, 0.1 mol) in ethanolic sodium ethoxide [from sodium (4.6 g, 0.2 g atom) and absolute ethanol (75 ml)]. The mixture was boiled for 2 h and then evaporated *in vacuo*. The residual solid was extracted with boiling butanone, filtered, and the filtrate chilled to yield N′N-*diallylbenzohydrazide* (7.5 g, 35%) as a buff solid which crystallized from butanone as plates, m.p. 115—116° (Found: C, 72.05; H, 7.55; N, 12.85. $C_{13}H_{16}N_2O$ requires C, 72.2; H, 7.4; N, 12.95%); $\nu_{max.}$ 1 640 cm^{-1}.

In a similar preparation in which triethylamine (0.2 mol) was substituted for sodium ethoxide and the work-up was modified the yield of this product was 23%.

1-*Allyl*-1,4-*dimethyl*-3-*oxopyrazolidinium Toluene*-p-*sulphonate*.—A solution of 1,4-dimethylpyrazolidin-3-one [15] (2.3 g, 0.02 mol) and allyltoluene-*p*-sulphonate (4.2 g, 0.02 mol) in ether (50 ml) was allowed to stand for one week at room temperature. The gummy solid that separated was crystallized from propan-2-ol to give 1-*allyl*-1,4-*dimethyl*-3-*oxopyrazolidinium toluene*-p-*sulphonate monohydrate* (1.3 g, 20%) as needles, m.p. 82—84° (Found: C, 52.35; H, 7.1; S, 9.05. $C_{15}H_{24}N_2O_5S$ requires C, 52.3; H, 7.0; S, 9.3%); $\nu_{max.}$ 1 725 cm^{-1}; $\delta(D_2O)$ 3.85 and 3.82 (3 H, d), 2.66 (3 H, s), and 1.66 and 1.56 (3 H, d).

2-*Allyl*-1,4-*dimethylpyrazolidin*-3-*one*.—A solution of 1,4-dimethylpyrazolidin-3-one (4.6 g, 0.04 mol) and allyl bromide (4.8 g, 0.04 mol) in ether (50 ml) was stirred overnight at room temperature. Evaporation gave a yellow glass which was dissolved in water. After washing with chloroform (3 × 20 ml), the aqueous solution was evaporated to give the quaternary bromide as a glass, $\delta(D_2O)$ 3.85 and 3.82 (3 H, d) and 1.66 and 1.56 (3 H, d); basification of the sample caused the former to shift upfield to δ 3.35 and 3.32 (the latter moved upfield by 0.05 p.p.m.), consistent with formation of the amine-imide.

Accordingly the glassy bromide was treated with excess triethylamine and the resulting mixture was heated at 150° (oil-bath) for 30 min. Water (50 ml) was added and the mixture was extracted with chloroform (3 × 20 ml). The chloroform solution was dried (Na_2CO_3) and evaporated and the residue was distilled to give 2-*allyl*-1,4-*dimethylpyrazolidin*-3-*one* as an oil (3.4 g, 74% based on 1,4-dimethylpyrazolidin-3-one), b.p. 110—115° at 30 mmHg (Found: C, 59.1; H, 8.9; N, 18.2. $C_8H_{14}N_2O$ requires C, 62.35; H, 9.1; N, 18.2%); $\nu_{max.}$ 1 700 cm^{-1}; $\delta(CDCl_3)$ 2.51 (3 H, s), and 1.2 and 1.1 (3 H, d).

N-(2,3-*Dideuterioallyl*)*dimethylammoniobenzamidate* (6) *and Thermal Rearrangement thereof*.—Compound (2) (1.0 g, 0.05 mol) was reduced with deuterium (deuterium uptake, 125 ml corrected to s.t.p., 0.0055 mol) in the manner described previously using hydrogen to give the hydrochloride of (6) (0.3 g, 26%) followed by the *amine-imide* (6) (0.2 g, 20%), m.p. 86—88°. The ^1H n.m.r. spectrum of (6) (not deuterium decoupled) showed $\delta(CDCl_3)$ 7.8 (2 H, m), 7.2 (3 H, m), 5.25br (1 H), 4.15br (2 H), and 3.4 (6 H, s).

A small sample of (6) was thermally rearranged (2 h) in an n.m.r. tube. The ^1H n.m.r. spectrum of the resulting hydr-

azide (7) (not deuterium decoupled) showed δ($CDCl_3$) 7.4 (5 H, m), 5.3br (2 H), 4.1br (1 H), and 2.5 (6 H, s).

p-*Bromophenacyltriethylammonium Bromide and Hydrolysis thereof.*—A solution of *p*-bromophenacyl bromide (2.8 g, 0.001 mol) and triethylamine (1.1 g, 0.001 mol) in benzene (20 ml) was stirred overnight to give the quaternary *salt* (2.9 g, 72%) as needles. Crystallization from water and then from propan-2-ol gave needles, m.p. 194—195° (decomp., sample inserted at 180°) (Found: C, 44.4; H, 5.6; Br, 42.05. $C_{14}H_{21}Br_2NO$ requires C, 44.35; H, 5.55; Br, 42.25%); $\nu_{max.}$ 1 690 cm^{-1}.

A solution of the salt (2.0 g, 0.0005 mol) in 50% sodium hydroxide solution (25 ml) was stirred for 15 min and then extracted with chloroform (3 × 10 ml). Drying (Na_2SO_4) and evaporation of the chloroform solution gave an oil which solidified on trituration with light petroleum (b.p. 30—60°). Crystallization from ethanol gave *p*-bromophenacyl alcohol (0.42 g, 42%) as plates, m.p. 135—136° (mixed m.p. 136—137°).

Benzamidodimethylsulphonium Bromide and Hydrolysis thereof.—A solution of dimethyl sulphide (3.1 g, 0.05 mol) in carbon tetrachloride (50 ml) was added dropwise to a stirred solution of freshly prepared *N*-bromobenzamide [16] (10.0 g, 0.05 mol) in acetone (50 ml) at −23° at such a rate that the temperature did not rise above −15°. The orange solution was diluted with light petroleum (b.p. 30—60°) to give a yellowish solid which was collected and crystallized from propan-2-ol to give the ternary *salt* as needles (6.4 g, 48%), m.p. 124—125° (decomp., sample inserted at 115°) (Found: C, 41.7; H, 4.75; Br, 30.65. $C_9H_{12}BrNOS$ requires C, 41.25; H, 4.7; Br, 30.5%); $\nu_{max.}$ 1 675 cm^{-1}.

A solution of the salt (2.6 g, 0.01 mol) in 10% sodium hydroxide solution (25 ml) slowly (15 min) deposited benzamide (1.2 g, 100%), m.p. and mixed m.p. 128—129°.

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