

Naphthalen-1,4-imine Derivatives with Bridgehead Substituents

By John M. Vernon,* Munir Ahmed, and John M. Moran, Department of Chemistry, University of York, Heslington, York YO1 5DD

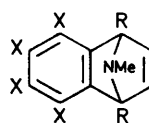
1,4-Dihydro-1,4-dimethylnaphthalen-1,4-imine derivatives have been prepared *via* cycloaddition of benzyne to methyl 2,5-dimethylpyrrole-1-carboxylate and of tetrachlorobenzene to 1,2,5-trimethylpyrrole. 2-Naphthylamine derivatives have been isolated from the reaction of benzyne with 2,5-dimethyl-1-phenylpyrrole.

BENZYNE adds to *N*-substituted pyrroles to give 1,4-dihydronaphthalen-1,4-imines^{1,2} and in some cases also rearranged 2:1 adducts.^{3,4} The 1:1 adducts undergo an acid-catalysed rearrangement to 1-naphthylamine derivatives.^{1,3} However, 1,4-dihydronaphthalen-1,4-imines with substituents at the 1- and 4-positions have not been isolated (except for some more highly substituted examples⁴), and previous attempts to add benzyne to 1,2,5-trisubstituted pyrroles gave only 2-naphthylamine derivatives (15)–(17).⁵ The apparent instability of the primary adducts (4)–(6) in the absence of acid and the unexpected formation of 2-naphthylamines called for further study.

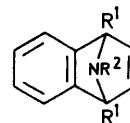
The adduct (1) of tetrafluorobenzene and *N*-methylpyrrole is relatively difficult to aromatise to the corresponding 1-naphthylamine derivative,⁶ although the analogous adduct (2) with bridgehead substituents was too unstable for proper characterisation.⁷ We prepared the naphthalen-1,4-imine (3) by generation of tetrachlorobenzene in the presence of 1,2,5-trimethylpyrrole.⁸ The symmetrical structure (3) is clearly shown by the n.m.r. spectrum, by the absence of N–H absorption in i.r. and n.m.r. spectra, and by the loss of acetylene and the prominence of the nitrilium ion MeC^+NMe (*m/e* 56) in the mass spectrum.⁹ The adduct (3), like (1), was unaffected by cold aqueous acid, and unlike (4)–(6) it survived the reaction conditions for aryne generation by an organometallic route. Acetylene was evolved when the adduct (3) was heated at 210 °C, but other products were not identified [*cf.* the thermal decomposition of the adduct (1) at 325 °C by several different pathways¹⁰].

A second way to reduce the sensitivity of the naphthalen-1,4-imine system to rearrangement is to incorporate an electron-withdrawing *N*-substituent. In particular, *N*-alkyloxycarbonyl derivatives of pyrrole show an enhanced reactivity as heterocyclic dienes,^{11–14} and their corresponding 1:1 adducts with benzyne show no tendency to react further with benzyne.^{1,2} In such cases benzyne must be generated by aprotic

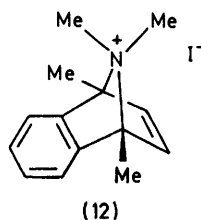
diazotisation, since other routes using organometallic intermediates are precluded by the nature of the *N*-substituent. Another advantage of the group NCO_2R is the possibility of its easy transformation into NH or NMe in basic reaction conditions.¹⁵



- (1) X = F, R = H
 (2) X = F, R = Me
 (3) X = Cl, R = Me



- (4) R¹ = Ph, R² = Me
 (5) R¹ = Me, R² = CH₂Ph
 (6) R¹ = Me, R² = Ph
 (7) R¹ = Me, R² = CO₂Me
 (8) R¹ = Me, R² = H
 (9) R¹ = R² = Me
 (10) R¹ = H, R² = CO₂Me
 (11) R¹ = H, R² = Me



(12)

We therefore added benzyne to methyl 2,5-dimethylpyrrole-1-carboxylate and separated the Diels–Alder adduct (7) chromatographically from unchanged pyrrole. The n.m.r. spectrum and loss of acetylene in the mass spectrum were again characteristic of the structure (7). With hot methanolic potassium hydroxide the adduct (7) gave 1,4-dihydro-1,4-dimethylnaphthalen-1,4-imine (8), a colourless oil with n.m.r. spectrum uniquely fitting the bridged structure (8) and appropriate peaks for the molecular ion (*m/e* 171) and for the fragment ion MeC^+NH^+ (*m/e* 42) in the mass spectrum.⁹ Reduction of the adduct (7) with aluminium lithium hydride gave the 1,4,*N*-trimethyl compound (9), also an oil, which was characterised as the crystalline methiodide (12). The same procedure was applied to the adduct (10) derived from methyl pyrrole-1-carboxylate to obtain the *N*-methylnaphthalen-1,4-imine (11) much more

* Preliminary communication, M. Ahmed and J. M. Vernon, *J.C.S. Chem. Comm.*, 1976, 462.

¹ Cf. L. J. Kricka and J. M. Vernon, *J.C.S. Perkin I*, 1972, 904.

² P. L. Coe and A. J. Uff, *Tetrahedron*, 1971, 27, 4065.

³ R. M. Acheson and J. M. Vernon, *J. Chem. Soc.*, 1961, 457; 1963, 1008.

⁴ N. W. Gabel, *J. Org. Chem.*, 1962, 27, 301.

⁵ R. Kitzing, R. Fuchs, M. Joyeux, and H. Prinzbach, *Helv. Chim. Acta*, 1968, 51, 888.

⁶ R. C. Bansal, A. W. McCulloch, and A. G. McInnes, *Canad. J. Chem.*, 1969, 47, 2391; 1970, 48, 1472.

⁷ Cf. G. M. L. Cragg, R. G. F. Giles, and G. H. P. Roos, *J.C.S. Perkin I*, 1975, 1339.

¹ L. A. Carpino and D. E. Barr, *J. Org. Chem.*, 1966, 31, 764.

² G. Kaupp, J. Perreten, R. Leute, and H. Prinzbach, *Chem. Ber.*, 1970, 103, 2288.

³ G. Wittig and W. Behnisch, *Chem. Ber.*, 1958, 91, 2358; G. Wittig and B. Reichel, *ibid.*, 1963, 96, 2851.

⁴ E. Wolthuis and A. De Boer, *J. Org. Chem.*, 1965, 30, 3255; E. Wolthuis, W. Cady, R. Roon, and B. Weidenaar, *ibid.*, 1966, 31, 2009.

⁵ E. Wolthuis, D. V. Jagt, S. Mels, and A. De Boer, *J. Org. Chem.*, 1965, 30, 190.

⁶ D. D. Callander, P. L. Coe, J. C. Tatlow, and A. J. Uff, *Tetrahedron*, 1969, 25, 25.

⁷ H. Heaney and S. V. Ley, *J.C.S. Perkin I*, 1974, 2698.

separately dissolved in tetrahydrofuran (20 ml) were added dropwise in parallel over 20 min to the pyrrole (7.8 g) in tetrahydrofuran (20 ml), which was stirred and heated at 90–95 °C (bath) under reflux. The mixture was then refluxed for 30 min, allowed to cool, and shaken with added ether and water; the ether layer was separated (initially both layers were so dark that it was difficult to recognise the interface) and further washed with aqueous sodium hydrogen carbonate, and then repeatedly with water until the washings were colourless. It was dried (Na_2SO_4) and evaporated, leaving an oil, the n.m.r. spectrum of which indicated that it contained the starting pyrrole and its benzyne adduct (7) (ca. 1.5 : 1 molar ratio) together with isopentyl alcohol and other material. Isopentyl alcohol and most of the unchanged pyrrole were removed by fractional distillation *in vacuo*. The residue was chromatographed on silica gel (40 g), from which pentane (300 ml) eluted more of the unchanged pyrrole (total recovery 1.5 g), and pentane-ether (9 : 1 v/v; 500 ml) eluted the adduct (7) (2.8 g, 24%) as an oil, which was further purified by short-path distillation *in vacuo*, b.p. 120–140 °C (bath) at 0.5 mmHg. In another experiment with equimolar proportions of benzyne precursors and methyl 2,5-dimethylpyrrole-1-carboxylate and the same work-up procedure, the yield of adduct (7) was only 7% and recovery of the pyrrole was 74%. Hexagonal crystals of the adduct (7) were obtained by dissolving crude material in methanol, adding charcoal, then filtering and concentrating the filtrate, and cooling. A sample for analysis was further recrystallised from pentane; m.p. 52–53 °C (Found: C, 73.1; H, 6.85; N, 6.1. $\text{C}_{14}\text{H}_{15}\text{NO}_2$ requires C, 73.3; H, 6.6; N, 6.1%), ν_{max} 1 713br cm^{-1} (C=O), τ 2.8–3.2 (4 H, m, ArH), 3.48 (2 H, s, 2- and 3-H), 6.55 (3 H, s, OCH_3), and 7.97 (6 H, s, CH_3), *m/e* 229 (M^+ , 56%), 203 ($M - \text{C}_2\text{H}_2$, 54), 170 ($M - \text{CO}_2\text{Me}$, 87), 129 (170 – MeCN, 100), 128 (86), and 56, m^* 98 (170 \rightarrow 129).

1,4-Dihydro-1,4-dimethylnaphthalen-1,4-imine (8).—Potassium hydroxide (5.6 g) was dissolved in water (5 ml) and diluted to 25 ml with methanol. The adduct (7) (2.3 g) was added, and the solution was refluxed for a total of 30 h (samples removed at intermediate times were worked up as described below and analysed by n.m.r. spectroscopy which showed incomplete reaction of the NCO_2Me group). The mixture was cooled, diluted with water, and extracted with ether. The extract was washed several times with water, dried (K_2CO_3), and evaporated; short-path distillation of the residue at 90 °C (bath) and 0.2 mmHg afforded the naphthalen-1,4-imine (8) (1.3 g, 42%) as a colourless oil, which was stored under nitrogen as it gradually darkened in air [Found: C, 83.2; H, 7.7; N, 8.0%; *M* (mass spectrum), 171.1015. $\text{C}_{12}\text{H}_{13}\text{N}$ requires C, 84.2; H, 7.65; N, 8.2%; *M*, 171.1048], ν_{max} (CCl_4) 3 190br,w (N–H), 3 075, 2 970, 2 930, 2 875 (C=O absent), 1 455, 1 445, 1 380, 1 355, 1 245, 1 130, 1 005, and 850 cm^{-1} , τ 2.9–3.4 (4 H, m, ArH), 3.45 (2 H, s, 2- and 3-H), 7.44 (1 H, s, NH, exchangeable in D_2O), and 8.30 (6 H, s, CH_3), *m/e* 171 (M^+ , 52%), 170 ($M - \text{H}$, 28), 156 ($M - \text{Me}$, 38), 155 (11), 145 ($M - \text{C}_2\text{H}_2$, 56), 144 (39), 141 (23), 131 (15), 130 (100), 129 (43), 128 (26), 127 (11), 115 (38), 77 (18), 72 (13), 71.5 (12), 51 (12), and 42 ($\text{MeC}\equiv\text{NH}$, 52), m^* 98.8 (171 \rightarrow 130).

1,4-Dihydro-1,4-dimethyl-1,4-N-methyliminonaphthalene (9) and its Methiodide (12).—The adduct (7) (1.5 g) in dry

ether (50 ml) was stirred overnight with aluminium lithium hydride (0.5 g). Aqueous sodium hydroxide (2.5M; 20 ml) was added. The ether layer was separated, washed with water, dried (Na_2SO_4), and evaporated to leave the *N*-methyl compound (9) as a discoloured oil, which reacted exothermically on addition of methyl iodide. Recrystallisation of the resulting solid from anhydrous methanol afforded the methiodide (12), m.p. 88 °C (decomp.) (Found: C, 50.6; H, 5.5; N, 4.3. $\text{C}_{14}\text{H}_{18}\text{IN}$ requires C, 51.4; H, 5.5; N, 4.3%), τ (D_2O) 2.3–2.7 (4 H, m, ArH), 3.01 (2 H, s, 2- and 3-H), 6.81 and 7.40 (each 3 H, s, NCH_3), and 8.02 (6 H, s, CH_3).

Reduction of the adduct (10) in the same way with aluminium lithium hydride gave the *N*-methyl compound (11) as an oil, showing no N–H i.r. band, τ 2.8–3.4 (6 H, m, ArH and =CH), 6.12 (2 H, t, 1- and 4-H), and 8.10 (3 H, s, CH_3), and which gave a methiodide, m.p. 108–109 °C (decomp.) (from methanol) [lit.,³ 106 °C (decomp.)].

Aromatisation of the Adduct (7).—The adduct (7) (1.5 g) reacted violently on addition of a few drops of methanolic sulphuric acid (2M). The oil obtained was dissolved in ether and washed with aqueous sodium hydrogen carbonate and with water. Evaporation of the dried (K_2CO_3) extract gave a sludge from which was obtained a sticky solid (0.3 g). This was triturated with ice-cold acetone and sucked dry, then washed with pentane and sucked dry, and then recrystallised twice from methanol to give methyl *N*-(1,4-dimethyl-2-naphthyl)carbamate (18) as needles, m.p. 171–172.5° (Found: C, 73.1; H, 6.1; N, 5.7. $\text{C}_{14}\text{H}_{15}\text{NO}_2$ requires C, 73.3; H, 6.6; N, 6.1%), ν_{max} 3 330 (N–H), 1 695 and 1 682 cm^{-1} (C=O), τ (CDCl_3) 1.9–2.9 (5 H, m, ArH), 3.55br (1 H, NH), 6.27 (3 H, s, OCH_3), and 7.38 and 7.52 (each 3 H, s, CH_3), *m/e* 230 (16%), 229 (M^+ , 100), 197 (46), 196 (13), 182 (16), 170 ($M - \text{CO}_2\text{Me}$, 40), and 128 (19).

Methyl *N*-(2,4-Dimethyl-1-naphthyl)carbamate (19).—2,4-Dimethyl-1-naphthylamine¹⁹ (1.0 g) in dry ether (10 ml) was treated with methyl chloroformate (1.0 g). Water was added, and the ether layer was separated, washed with aqueous hydrochloric acid and with water, and dried (K_2CO_3). The acidic extract on basification returned unchanged naphthylamine (0.3 g). Evaporation of the ethereal layer gave a solid (0.8 g) which was recrystallised from methanol (charcoal) to give the *N*-1-naphthylcarbamate (19), m.p. 127 °C. Successive recrystallisation raised the m.p. to 135 °C (Found: C, 73.0; H, 6.7; N, 5.95. $\text{C}_{14}\text{H}_{15}\text{NO}_2$ requires C, 73.3; H, 6.6; N, 6.1%), ν_{max} 3 270 (N–H) and 1 700 cm^{-1} (C=O), τ (CDCl_3) 2.0–2.75 (4 H, m, ArH), 2.90 (1 H, s, 3-H), 3.53br (1 H, s, NH), 6.35 (3 H, s, OCH_3), and 7.43 and 7.69 (each 3 H, s, CH_3), *m/e* 230 (18%), 229 (M^+ , 100), 197 (53), 170 ($M - \text{CO}_2\text{Me}$, 43), and 128 (12).

Benzyne Addition to 2,5-Dimethyl-1-phenylpyrrole.—Anthranilic acid (6.4 g) and isopentyl nitrite (6.0 g) were separately dissolved in tetrahydrofuran (solutions 25 ml each) and added dropwise in parallel over 30 min to 2,5-dimethyl-1-phenylpyrrole (8.8 g) in tetrahydrofuran (10 ml), which was stirred and heated at 100 °C (bath) under reflux. The mixture was then refluxed further for 40 min, concentrated, diluted with ether, and shaken with aqueous sodium hydroxide (2M). The ether layer was separated, washed with water, dried (K_2CO_3), and evaporated to leave an oil (11 g), which was redissolved in pentane-dichloromethane (1 : 1 v/v) and chromatographed on basic alumina (250 g; activity I). Pentane (4 l) and pentane-dichloro-

¹⁹ R. Adams and H. H. Gibbs, *J. Amer. Chem. Soc.*, 1957, **79**, 170.

methane (9 : 1 v/v; 1 l) eluted 2,5-dimethyl-1-phenylpyrrole (3.8 g), m.p. 48 °C (from pentane) (lit.,⁵ 50 °C), τ 2.5—3.1 (5 H, m, ArH), 4.32 (2 H, s, 3- and 4-H), and 8.05 (6 H, s, CH₃). Then pentane-dichloromethane (3 : 2 v/v; 1 l) eluted a yellow oil (2.5 g), which afforded 1,4-dimethyl-*N*-phenyl-2-naphthylamine (17) (2.1 g), m.p. 95 °C (from light petroleum) (lit.,⁵ 95 °C), τ 2.0—3.5 (11 H, m, ArH), 4.81br (1 H, s, NH), and 7.49 and 7.61 (each 3 H, s, CH₃). Further elution with dichloromethane (1 l) gave a darker yellow oil (0.8 g), which was redissolved in methanol and boiled with activated charcoal; the solution was filtered and evaporated and the recovered oil partially crystallised; the solid was separated, triturated with light petroleum, and sucked dry; recrystallisation from light petroleum (b.p. 94—105 °C) and then from absolute ethanol gave 1,4-dimethyl-*N*-nitroso-*N*-phenyl-2-naphthylamine (20) (0.2 g, 1.5%) as brown prisms, m.p. 113—124 °C. Pale yellow crystals, though still with unsharp m.p. 117—124 °C (decomp.), were obtained after repeated recrystallisation (twice more from petroleum and four times from ethanol) (Found: C, 78.6; H, 5.5; N, 9.6. C₁₈H₁₆N₂O requires C, 78.2; H, 5.8; N, 10.1%), ν_{\max} . 1595 cm⁻¹ (N=O), τ (CDCl₃) 1.8—2.9 (9 H, m, ArH), 3.21 (1 H, s, 3-H), and 7.39 and 7.73 (each 3 H, s, CH₃), *m/e* 317, 305, 277 (*M* + 1), 275, and 247 (*M* + 1 - NO) (by chemical ionisation in the presence of methane). The mass spectrum obtained by electron impact was apparently that of the decomposition product (17); *m/e* 247 (*M*⁺, 100%), 246 (45), 231 (31), 230 (51), 170 (*M* - Ph, 28), 128 (34), 115 (40), and 77 (27).

The n.m.r. spectrum of the crude product mixture before chromatography was recorded and analysed, taking

account of characteristic features (in particular, chemical shifts for non-aromatic hydrogen atoms) of the spectra recorded independently for pure samples of three components of the mixture (above). It was assumed that 2 : 1 adducts of benzyne and 2,5-dimethyl-1-phenylpyrrole were absent, since so much of the latter remained unchanged. The n.m.r. spectrum of the 1 : 1 adduct (6) was obtained by difference: τ 2.5—3.3 (9 H, m, ArH), 3.49 (2 H, s, 2- and 3-H), and 8.37 (6 H, s, CH₃), consistent with the spectra of analogous compounds (7)—(9) and (12). Relative intensities of peaks in the n.m.r. spectrum of the crude product mixture showed the formation of the products (6), (17), and (20) (in 25, 16, and 5% yield, respectively, based on anthranilic acid), together with the unchanged pyrrole (58%) and isopentyl alcohol.

In a separate experiment the crude product mixture from benzyne addition was obtained as before, then redissolved in ether and extracted twice with ice-cold aqueous hydrochloric acid (4*N*). The acid extracts were separated, immediately basified with ice-cold aqueous sodium hydroxide, and then re-extracted with ether. The ether layer was separated, washed with water, dried (K₂CO₃), and evaporated to leave a brown oil, the n.m.r. spectrum of which showed it to contain 2,5-dimethyl-1-phenylpyrrole and the rearranged adduct (17) but none of the unrearranged adduct (6).

We thank the Department of Chemistry, University of Victoria, B.C., Canada, for research facilities (to J. M. V.) and Dr. D. McGillivray for some of the mass spectra.

[6/2127 Received, 18th November, 1976]