Naphthalen-1,4-imine Derivatives with Bridgehead Substituents

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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 tetrachlorobenzyne 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 1,4dihydronaphthalen-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-1,4imines with substituents at the 1- and 4-positions have not been isolated (except for some more highly substituted examples 4), and previous attempts to add benzyne to 1,2,5-trisubstituted pyrroles gave only 2naphthylamine 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 tetrafluorobenzyne 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 tetrachlorobenzyne 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 $MeC \equiv NMe (m/e 56)$ 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 pathways 10].

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 benzvne must be generated by aprotic

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.

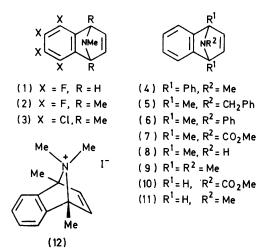
G. Wittig and W. Behnisch, Chem. Ber., 1958, 91, 2358; G. Wittig and B. Reichel, ibid., 1963, 96, 2851.

⁴ E. Wolthuis and A. De Boer, *J. Org. Chem.*, 1965, **30**, 3255; E. Wolthuis, W. Cady, R. Roon, and B. Weidenaar, *ibid.*, 1966, 81, 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.

diazotisation, since other routes using organometallic intermediates are precluded by the nature of the Nsubstituent. Another advantage of the group NCO₂R is the possibility of its easy transformation into NH or NMe in basic reaction conditions.¹⁵



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

⁸ Preliminary communication, M. Ahmed and J. M. Vernon, J.C.S. Chem. Comm., 1976, 462. ⁹ Cf. L. J. Kricka and J. M. Vernon, J.C.S. Perkin I, 1972,

904.

P. L. Coe and A. J. Uff, *Tetrahedron*, 1971, 27, 4065.
R. M. Acheson and J. M. Vernon, J. Chem. Soc., 1961, 457;

1963, 1008.

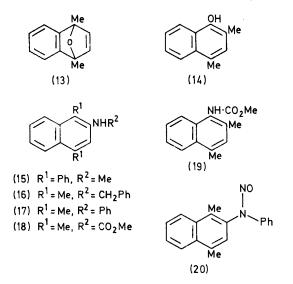
N. W. Gabel, J. Org. Chem., 1962, 27, 301.
R. Kitzing, R. Fuchs, M. Joyeux, and H. Prinzbach, Helv.

Chim. Acta, 1968, 51, 888. 14 R. C. Bansal, A. W. McCulloch, and A. G. McInnes, Canad. J.

Chem., 1969, 47, 2391; 1970, 48, 1472. ¹⁵ Cf. G. M. L. Cragg, R. G. F. Giles, and G. H. P. Roos, J.C.S. Perkin I, 1975, 1339.

satisfactorily (in three steps from pyrrole itself) than before (from benzyne and N-methylpyrrole).³

Treatment of the adduct (7) with methanolic sulphuric acid gave an isomer, m.p. 171-172 °C, with nonequivalent methyl groups (n.m.r.) and N-H as well as C=O absorption (i.r. spectrum). Two structures were considered for this new compound, (18) and (19), the former precedented by other 2-naphthylamine derivatives (15)-(17) ⁵ and the latter by rearrangement of the 1,4-oxide (13) to the 1-naphthol (14).¹⁶ The



1-naphthylcarbamate derivative (19) was synthesised independently in three steps from 1,3-dimethylnaphthalene; its m.p. (135 °C) was decisively different from that of the compound of m.p. 171—172 °C, although spectra of the two were scarcely distinguishable. Thus rearrangement of compound (7) is shown to give the 2-naphthylcarbamate (18).

Having shown that several 1,4-disubstituted derivatives of 1,4-dihydronaphthalen-1,4-imine are isolable and stable under ordinary conditions, we also reexamined one of the systems of Wolthuis et al.⁵ The primary adduct (6) appeared to offer the best chance for isolation, since the N-phenyl group should reduce the sensitivity to rearrangement. So we tried generation of benzyne by aprotic diazotisation in the presence of 2,5-dimethyl-1-phenylpyrrole; the n.m.r. spectrum of the crude reaction mixture after removal of solvents was interpretable in terms of a 1.5:1 molar ratio of the adduct (6) and its rearranged isomer (17), together with unchanged pyrrole and other products. After extraction of the mixture with cold mineral acid, only the 2naphthylamine (17) was recoverable from the acidic extract and the pyrrole from the acid-insoluble fraction. Alternatively, chromatographic work-up also separated these two components of the mixture but destroyed the adduct (6), in which we were chiefly interested. However, chromatography enabled the isolation of a by-

¹⁶ M. Fetizon and N. T. Anh, *Bull. Soc. chim. France*, 1965, 3208.

product, which had otherwise remained unnoticed. This was identified from analysis and i.r. and mass spectra as the nitrosoamine (20); the true molecular ion is seen only in the mass spectrum obtained by chemical ionisation. The nitrosoamine (20) is probably formed as a by-product of the benzyne reaction by nitrosation of the secondary amine (17) with isopentyl nitrite; it was also prepared independently by this same route.

EXPERIMENTAL

I.r. spectra were recorded for liquid films or Nujol mulls, and calibrated with polystyrene. ¹H N.m.r. spectra were recorded at 60 MHz for solutions in carbon tetrachloride with tetramethylsilane as internal standard. Mass spectra were recorded at 70 eV.

5,6,7,8-Tetrachloro-1,4-dihydro-1,4,9-trimethylnaphthalen-1,4-imine (3).-n-Butyl-lithium in n-hexane (2M; 20 ml) was added slowly with stirring to hexachlorobenzene (11.4 g)in dry ether (800 ml) cooled at -70 °C. 1,2,5-Trimethylpyrrole ¹⁷ (4.4 g) was added, and the mixture was allowed to warm to room temperature and stirred overnight. Water was added, and the ether laver was separated and shaken with aqueous sulphuric acid (2M). The acid layer was separated and basified with sodium hydroxide and reextracted with ether. The ether layer was washed with water, dried (Na₂SO₄), and evaporated. Sublimation of the residue at 160 °C (bath) and 0.2 mmHg gave a yellow solid, and recrystallisation of this from carbon tetrachloride-methanol gave the adduct (3) (3.0 g, 23%), m.p. 182-184 °C (Found: C, 48.3; H, 3.5; N, 4.3. C₁₃H₁₁Cl₄N requires C, 48.3; H, 3.4; N, 4.3%), τ 3.50 (2 H, s, 2- and 3-H), 8.05 (3 H, s, NCH₃), and 8.24 (6 H, s, CH₃), m/e 321/323/325 (M⁺, 4/5/2%), 320/322/324 (M - H, 4/5/3), 306/308/310 (M - Me, 4/5/2), 295/297/299 (M - C₂H₂, 16/20/9), 294/296/298 (8/11/6), 286/288/290 (3/3/1), 230/232/

234 (3/3/1), 108 (6), 57 (5), 56 (MeC=NMe, 100), and 42 (10). The adduct (3) (0.5 g) was heated at 210 °C in a slow stream of nitrogen. Evolution of acetylene was shown by passing the exit gases through ammoniacal copper(1) chloride. Sublimation of the residue *in vacuo* returned some of the adduct (3) (0.1 g), m.p. and mixed m.p. 181-184 °C, but no other products were isolated.

Methyl 2,5-Dimethylpyrrole-1-carboxylate.—The following procedure is preferable to one requiring the use of potassium metal.^{11,12} 2,5-Dimethylpyrrol-1-yl-lithium was prepared by dropwise addition of redistilled 2,5-dimethylpyrrole¹⁸ (20 g) in dry ether (50 ml) to n-butyl-lithium in n-hexane (0.24m; 85 ml) at -70 °C under dry nitrogen. The solution was allowed to warm to 0 °C, and methyl chloroformate (20 g) in ether (30 ml) was added during 0.5 h with stirring at 0 °C. The mixture was stirred further for 2 h at room temperature and set aside overnight. Water (50 ml) was added to dissolve the precipitated solid, and the ether layer was separated, washed again with water, dried (Na₂SO₄), and distilled under reduced pressure. Methyl 2,5-dimethyl-pyrrole-1-carboxylate (24 g, 78%) was obtained, b.p. 70-72 °C at ca. 2 mmHg, m.p. 40 °C (lit.,¹² 38 °C).

Benzyne Addition to Methyl 2,5-Dimethylpyrrole-1-carboxylate.—Anthranilic acid (7.0 g) and isopentyl nitrite (6.6 g) ¹⁷ J. M. Patterson and S. Soedigdo, J. Org. Chem., 1968, **33**, 2057.

¹⁸ D. M. Young and C. F. H. Allen, Org. Synth., Coll. Vol. II, 1943, p. 219.

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 (Na₂SO₄) 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. C₁₄H₁₅NO₂ requires C, **73.3**; H, **6.6**; N, **6.1%**), ν_{max} 1 **713** br 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 $(M - C_2H_2, 54)$, 170 $(M - CO_2Me, 87)$, 129 (170 - MeCN, 100), 128 (86), and 56, m^* 98 (170 \longrightarrow 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, Me group). The mixture was cooled, diluted with water, and extracted with ether. The extract was washed several times with water, dried (K₂CO₃), 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. C₁₂H₁₃N requires C, 84.2; H, 7.65; N, 8.2%; M, 171.1048], $\nu_{\rm max}$ (CCl₄) 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 - H, 28), 156 (M - Me, 38), 155 (11), 145 $(M - C_2H_2)$ 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 (MeC≡NH, 52), m* 98.8 (171 ---> 130).

1,4-Dihydro-1,4-dimethyl-1,4-N-methyliminonaphthalene

(9) and its Methiodide (12).—The adduct (7) (1.5 g) in dry

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

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 (Na₂SO₄), 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. C₁₄H₁₈IN requires C, 51.4; H, 5.5; N, 4.3%), τ (D₂O) 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, NCH₃), and 8.02 (6 H, s, CH₃).

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, CH₃), 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-(1,4dimethyl-2-naphthyl)carbamate (18) as needles, m.p. 171-172.5° (Found: C, 73.1; H, 6.1; N, 5.7. C₁₄H₁₅NO₂ 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 (CDCl₃) 1.9–2.9 (5 H, m, ArH), 3.55br (1 H, NH), 6.27 (3 H, s, OCH₃), 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 ($M - CO_2Me$, 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. $C_{14}H_{15}NO_2$ requires C, 73.3; H, 6.6; N, 6.1%), v_{max} 3 270 (N-H) and 1 700 cm⁻¹ (C=O), τ (CDCl₃) 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 $(M - CO_9Me, 43)$, 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 2,5dimethyl-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 (K₂CO₃), 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–dichloromethane (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, CH_a). Then pentane-dichloromethane (3: 2 v/v; 1 l) eluted a yellow oil (2.5 g), which afforded 1,4-dimethyl-N-phenyl-2naphthylamine (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-Nphenyl-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. $C_{18}H_{16}N_2O$ requires C, 78.2; H, 5.8; N, 10.1%), v_{ma} 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 (4N). 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 (K_2CO_3), 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).

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