3,4,5-Triphenylpyrazoles

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Benzoin reacts with hydrazine hydrochloride in ethanol to give benzil, benzil azine, deoxybenzoin, benzaldehyde, benzonitrile, benzoic acid, ethyl benzoate, desylamine hydrochloride, 3,4,5-triphenylpyrazole, and 3,4,5,6-tetraphenylpyridazine and their hydrochlorides. A mechanism is proposed to account for some of the products, and some reactions of 3,4,5-triphenylpyrazole are described.

SINCE benzoin reacted with hydrazine hydrochloride¹ to give, unexpectedly, 3,4,5-triphenylpyrazole,² the course of the reaction has been investigated.

Together with the pyrazole, its hydrochloride and benzil azine were obtained by fractional crystallization of the product from ethanol and identified by comparison with authentic samples. Removal of the ethanol, and extraction of the residue with ether, gave a yellow oil from which deoxybenzoin separated; the remaining oil on distillation gave a mixture of benzonitrile and ethyl benzoate; finally benzoic acid sublimed to leave a residue which contained benzil. The original yellow oil showed five peaks on g.l.c., which were identified as due to deoxybenzoin, benzil, ethyl benzoate, benzonitrile, and benzaldehyde; the last-named was absent if the oil had been standing sufficiently long for a sublimate of benzoic acid to appear.

The ether-insoluble fraction was extracted with water, giving a mixture of ammonium chloride and 2-amino-2-phenylacetophenone (desylamine) hydrochloride. The latter was converted into desylamine³ which had a base peak with m/e of 106[PhCHNH₂]⁺ and a prominent peak at 105[PhCO]⁺ consistent with scission of the carboncarbon bond. When heated above its melting point desylamine hydrochloride lost hydrogen chloride to give 3,4,5,6-tetraphenylpyrazine (amarone).⁴ Amarone could not, however, be detected in the reaction between benzoin and hydrazine hydrochloride.

That part of the ether-insoluble fraction which did not dissolve in water yielded more 3,4,5-triphenylpyrazole and 3,4,5,6-tetraphenylpyridazine.

The acid-catalysed disproportionation of benzoin gives benzil and deoxybenzoin and also tetraphenylfuran,⁵ hence the formation of benzil, benzil azine, and deoxybenzoin is readily explained. 3,4,5,6-Tetraphenylpyridazine could conceivably arise from the condensation of hydrazine with tetraphenylfuran⁶, or its precursor.⁵

It was feasible that benzoin hydrazone, deoxybenzoin hydrazone, or benzoin azine 1(1) might be involved in the formation of 3,4,5-triphenylpyrazole. Attempted cyclization of benzylidene benzoin hydrazone and of N-benzoyl deoxybenzoin hydrazone (both possible intermediates) was unsuccessful; benzylidene deoxybenzoin whilst condensing with hydrazine to give the pyrazole would appear unlikely as an intermediate since 3,4,5-triphenyl-2-pyrazoline, the major product of the reaction,⁷ could not be detected. Attempts to prepare benzoin azine from benzoin and hydrazine hydrate 8 gave only benzoin hydrazone and lends support to the uncertainty regarding its existence,¹ nor was it isolated in the reaction between benzoin and hydrazine hydrochloride.

α-Benzoin oxime and benzoin azide undergo acidcatalysed rearrangement with the formation of benzonitrile and benzaldehyde,^{9,10} the reaction apparently being facilitated by a group attached to the oxime- or azide-carbon atom, which has greater than usual stability as a cation, for instance [PhCHOH]^{+.11} It is possible, therefore, that benzoin azine is formed initially during the reaction with hydrazine hydrochloride but under the acidic conditions undergoes fission in an analogous manner to the so-called second-order or abnormal Beckmann and abnormal Schmidt rearrangements of abenzoin oxime and benzoin azide, respectively. This would account for the formation of benzonitrile, benzaldehyde and desylamine (4) from the cation (2), while fragmentation of the isomeric cation (3) by an alternative path would explain the formation of 3,4,5-triphenylpyrazole.

N-Alkyl derivatives of 3,4,5-triphenylpyrazole were prepared from the dialkyl sulphates. 1,2-Dibromoethane in presence of potassium carbonate gave a mixture 1,2-bis-(3,4,5-triphenylpyrazolyl)ethane and $1-\beta$ of bromoethyl-3,4,5-triphenylpyrazole. An attempt to prepare 1,3,4,5-tetraphenylpyrazole from iodobenzene by the Ullmann reaction gave a copper complex containing one atom of copper to one of ligand. The same product was obtained when the iodobenzene was omitted. Recently ¹² it has been shown that N-arylation of azoles by unactivated aryl halides fails under Ullmann conditions.

N-Acyl and N-sulphonyl derivatives were obtained from the acid- and sulphonyl-chlorides, respectively, in

⁶ B. Jägersten, Arkiv Kemi, 1968, **30**, 261. ⁷ W. E. Parham and W. R. Hasek, J. Amer. Chem. Soc., 1954, **76**, 799.

⁸ T. Curtis and A. Blumer, J. prakt. Chem., 1895, 52, 132. ⁹ A. F. Ferris, J. Org. Chem., 1960, 25, 12; R. K. Hill, ibid., 1962, 27, 29.

¹⁰ G. Caronna and M. G. Marino, Gazzetta, 1964, 94, 31; R. T. Conley and B. E. Novak, J. Org. Chem., 1961, 26, 692. ¹¹ 'Molecular Rearrangements,' ed. P. de Mayo, John Wiley,

1963, vol. 1, 502.

¹² M. A. Khan and J. B. Polya, J. Chem. Soc. (C), 1970, 85.

¹ J. Van Alphen, Rec. Trav. chim., 1933, 52, 47, 478, 525.

Van Alphen, Rev. 1740. tmm., 1853, 60, 41, 416, 525.
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D. Davidson, M. Weiss, and M. Jelling, J. Org. Chem., 1937, 2000.

^{1960,} **10**, 290.

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pyridine. Phosgene in toluene gave the 1,1'-bistriphenylpyrazolyl ketone and oxalyl chloride the 1,1'-bistriphenylpyrazolyl diketone which when heated above its melting point lost carbon monoxide to give the former.

Electrophilic substitution took place in the *para*position of the benzene ring. Nitration gave 3,4,5-tri*p*-nitrophenylpyrazole which gave *p*-nitrobenzoic acid as the only identifiable solid on oxidation.¹³ Other phenylpyrazoles behave similarly on nitration.¹⁴ Reduction of the nitro-derivative gave the tri-amine, the tri-acetyl derivative of which did not form an azo-dye. Ethanol.—Benzoin (42.2 g.), hydrazine hydrochloride (10.5 g.), and ethanol (400 ml.) were heated under reflux for 5—6 hr.; the insoluble white solid was filtered off and recrystallized to give 3,4,5-triphenylpyrazole hydrochloride (3.0 g.) m.p. 270° (from ethanol) (Found: C, 75.5; H, 5.1; N, 8.1. $C_{21}H_{17}ClN_2$ requires C, 75.8; H, 5.1; N, 8.4%), ν_{max} (KCl) 2200—2800 cm⁻¹. The filtrate deposited a yellow solid which was filtered off and fractionally crystallized from ethanol to yield benzil azine (1.7 g.), m.p. 204° [ν_{max} (KCl) 1690, 1605 cm⁻¹], 3,4,5-triphenylpyrazole (10.2 g.), m.p. 265°, and a residue consisting of a mixture (2.5 g.) of both.



Bromination of 3,4,5-triphenylpyrazole gave a mixture which showed parent peaks in the mass spectrum corresponding to a mono-, a di- and a tri-bromo-derivative. Oxidation ¹³ of the mixture gave benzoic and p-bromobenzoic acids. The mass cracking pattern of the monobromo-derivative failed to distinguish between 3(5)-pbromophenyl-4,5(3)-diphenylpyrazole and 4-p-bromophenyl-3,5-diphenylpyrazole, no peak corresponding to the extrusion of a p-bromobenzonitrile fragment being observed.¹⁵ The p.m.r. spectrum of 3,4,5-triphenylpyrazole showed a chemical shift of 1-2 Hz between the protons of the aromatic ring attached to C-4 on the one hand and to C-3 and C-5 of the pyrazole ring on the other, while the monobromo-derivative had an AA', BB' quartet and a singlet consistent with 4-p-bromophenyl-3,5-diphenylpyrazole. Synthetic confirmation has so far proved unexpectedly difficult.

EXPERIMENTAL

P.m.r. spectra were obtained on a Perkin-Elmer R12 instrument, i.r. spectra on a Perkin-Elmer 157 instrument and mass measurements on an A.E.I. MS9 mass spectrometer. M.p.s were determined on a Kofler hot stage and are uncorrected. Known compounds were identified by comparison (m.p., mixed m.p., i.r.) with authentic specimens.

Reaction of Benzoin and Hydrazine Hydrochloride in ¹³ W. E. Parham, C. Serres, and P. R. O'Connor, J. Amer. Chem. Soc., 1958, **80**, 588. The mother liquor from the reaction mixture was evaporated under reduced pressure and the semisolid residue boiled with ether (150 ml.) and filtered. Evaporation of the filtrate gave a yellow oil (14·0 g.) from which deoxybenzoin (1·5 g.), m.p. 56° [$\nu_{max.}$ (KCl) 1690 cm.⁻¹] was deposited. When no more solid separated out the oil remaining was heated at atmospheric pressure on a water-bath when benzonitrile and ethyl benzoate (4·0 g.) [$\nu_{max.}$ (film) 2220, 1720, and 1110 cm.⁻¹] slowly co-distilled. After distillation was complete a sublimate of benzoic acid (0·4 g.) m.p. 122° gradually appeared leaving a yellow residue of benzil (0·8 g.) m.p. 95—96° (from ethanol), $\nu_{max.}$ (KCl) 1680 cm.⁻¹.

The ether-insoluble fraction was shaken with water (50 ml.), the residue filtered off, dried, and on fractional crystallization from ethanol gave 3,4,5-triphenylpyrazole (2.2 g.) m.p. 265°; concentration of the mother liquor gave 3,4,5,6-tetraphenylpyridazine hydrochloride (0.7 g.) m.p. 210° (Found: C, 79.5; H, 5.4; N, 6.9. $C_{28}H_{21}ClN_2$ requires C, 79.9; H, 5.0; N, 6.65%), $\nu_{max.}$ (KCl) 2040, and 2200– 2800 cm.⁻¹, and 3,4,5,6-tetraphenylpyridazine (32 mg.), m.p. 194° (M, 384); the water-soluble fraction was taken down to dryness under reduced pressure, the residue dissolved in water (50 ml.), basified with ammonia, and extracted with ether (50 ml.). The ether solution was shaken with dilute hydrochloric acid (15 ml.) and the aqueous layer evaporated under reduced pressure till solid commenced to separate. When set aside desylamine hydrochloride (3.1 g.), m.p. 233-234° (dec.) (from ethanol),

¹⁴ W. J. Barry, P. Birkett, and I. L. Finar, J. Chem. Soc. (C), 1969, 1328.

¹⁵ T. Nishiwaki, J. Chem. Soc. (B), 1967, 885.

2808

separated (Found: C, 67.9; H, 5.8; Cl, 13.8; N, 5.8. Calc. for C₁₄H₁₄ClNO, C, 67.9; H, 5.7; Cl, 14.3; N, 5.65%), $\nu_{max.}$ (KCl) 2200–2800, 1690 cm.⁻¹. Desylamine, m.p. 87-89° (from ether) was liberated by ammonia from an aqueous solution of the hydrochloride (Found: C, 79.15; H, 6.05. Calc. for C₁₄H₁₃NO, C, 79.6; H, 6.15%), τ (CDCl₃), 7.7 (2H, s, amino), 4.6 (1H, s, CH), 2.8 (10H, m, Ar) (lit.,3 m.p. 109° and 87-89°).

1-Methyl-3,4,5-triphenylpyrazole.-3,4,5-Triphenylpyrazole (1.5 g.) in dimethyl sulphate (7.5 ml.) was heated on a water-bath for 3 hr., cooled, and diluted with water (50 ml.); the precipitate was filtered off to give the *product* (0.65 g.), m.p. 189-190° (from ethanol) (Found: C, 84.8; H, 5.9; N, 8.8%; *M*, 310. C₂₂H₁₈N₂ requires C, 85.2; H, 5.8; N, 9.0%; M, 310).

1-Ethyl-3,4,5-triphenylpyrazole.-3,4,5-Triphenylpyrazole (1.5 g.) and diethyl sulphate (7.5 ml.) similarly gave the product (0.8 g.), m.p. 135-136° (from ethanol) (Found: C, 85.0; H, 6.0; N, 8.5%; M, 324. C₂₃H₂₀N₂ requires C, 85.2; H, 6.2; N, 8.6%; M, 324).

Reaction of 3,4,5-Triphenylpyrazole and 1,2-Dibromoethane.—3,4,5-Triphenylpyrazole (3.0 g.), 1,2-dibromoethane (15 ml.), and anhydrous potassium carbonate (2.0 g.) were heated under reflux for 36 hr. Excess of 1,2-dibromoethane was removed under reduced pressure and the residue was washed with water, dried, and then washed with ether to give 1,1'-bis-(3,4,5-triphenylpyrazolyl)ethane (1.1 g.), m.p. 211-212° (from chloroform-ethanol) (Found: C, 85.4; H, 5.4; N, 9.0%; M, 618. C₄₄H₃₄N₄ requires C, 84.95; H, 5.5; N, 9.1%; M, 618). The ether washings and mother liquor were combined and concentrated to give 1-β-bromoethyl-3,4,5-triphenylpyrazole as a golden-brown solid (0.8 g.), m.p. 157-158° (from ethanol) (Found: C, 68.6; H, 4.55; N, 6.85%; M, 402. $C_{23}H_{19}^{79}BrN_2$ requires C, 68.5; H, 4.7; N, 6.9%; M, 402), τ (CDCl₃), 6.23 (2H, t, bromomethyl), 5.54 (2H, t, methylene), 2.85 (5H, s, Ar), 2.52 (10H, s, Ar).

Attempted Preparation of 1,3,4,5-Tetraphenylpyrazole.—A mixture of 3,4,5-triphenylpyrazole (3.0 g.), copper bronze (0.6 g.), potassium carbonate (1.5 g.), iodobenzene (3 ml.), nitrobenzene (25 ml.) was heated under reflux for 8 hr. Water (50 ml.) was added to the mixture and the nitrobenzene and iodobenzene were steam distilled off. The solution was filtered and the residue was washed successively with water, ethanol, acetone, and ether and dried in vacuo to give the copper-derivative $(2 \cdot 0 \text{ g.})$ as grey needles, m.p. >320° (Found: C, 69.9; H, 4.05; Cu, 18.4; N, 8.1. C₂₁H₁₅CuN₂ requires C, 70·3; H, 4·2; Cu, 17·7; N, 7·9%).

3,4,5-Tri-p-nitrophenylpyrazole.-3,4,5-Triphenylpyrazole (3.0 g.) was added in small portions to fuming nitric acid (30 ml.) at -10 to -5° and the temperature allowed to rise; it was kept at room temperature for 30 min. before being poured onto crushed ice (50 g.). The precipitate was filtered off and dried to give the trinitro-compound (2·2 g.) as a yellow micro-crystalline solid, m.p. $>350^{\circ}$ (from ethanol) (Found: C, 58.6; H, 3.3; N, 16.3%; M, 431. C₂₁H₁₃N₅O₆ requires C, 58.5; H, 3.0; N, 16.2%; M, 431), v_{max.} (KCl) 1515, 1335 cm.⁻¹.

3,4,5-Tri-p-aminophenylpyrazole.-3,4,5-Tri-p-nitro-

phenylpyrazole $(2 \cdot 0 \text{ g.})$ was reduced with hydrazine hydrate and Raney nickel ¹⁶ to give the triamino-derivative (0.9 g.) as off-white needles, m.p. 277° (from ethanol) (Found: C, 73·3; H, 5·3; N, 20·3%; M, 341. $C_{21}H_{19}N_5$ requires C, 73·9; H, 5·6; N, 20·5%; M, 341), v_{max} . (KCl) 3450 cm.⁻¹. 3,4,5-Tri-p-acetamidophenylpyrazole.—3,4,5-Tri-p-amino-

phenylpyrazole (0.34 g.) was dissolved in acetic anhydride

(10 ml.) by gentle warming; the solution was diluted with water (20 ml.) after 15 min. When set aside the 3,4,5-tri-pacetamido-derivative separated as a grey solid (0.12 g.), m.p. 291-293° (from ethanol) (Found: C, 69.3; H, 5.5; N, 14.7%; M, 467. $C_{27}H_{25}N_5O_3$ requires C, 69.4; H, 5.3; N, 15.0%; M, 467), $\nu_{\text{max.}}$ (KCl) 3220, 1665 cm.⁻¹. Bromination of 3,4,5-Triphenylpyrazole.—Bromine (6 ml.)

was slowly added to 3,4,5-triphenylpyrazole (3.0 g.) and heated on a water-bath until most of the excess of bromine had been expelled. The residue was boiled with ethanol (10 ml.) and the solvent was evaporated to dryness. Recrystallization from 90% ethanol till homogeneous (t.l.c.) gave 4-p-bromophenyl-3,5-diphenylpyrazole (2.0 g.), as needles m.p. 272-273° (Found: C, 67.0; H, 3.95; N, 7.3%; M, 374. $C_{21}H_{15}^{79}BrN_2$ requires C, 67.4; H, 4.0; N, 7·5%; M, 374), τ (DMSO) 2·42 (2H, d, Ar), 2·63 (10H, s, Ar), 2.86 (2H, d, Ar), and 7.5 (1H, s, NH).

1-Acetyl-4-p-bromophenyl-3,5-diphenylpyrazole.-4-p-Bromophenyl-3,5-diphenylpyrazole (0.1 g.) in acetic anhydride (1 ml.) was heated under reflux for ca. 30 min.; the mixture was then cooled and poured onto ice (10 g.). The precipitate was filtered off giving the product (20 mg.), m.p. 284-285° (from aqueous ethanol) (Found: C, 65.9; H, 4.1; N, 6.5. C₂₃H₁₇BrN₂O requires C, 66.2; H, 4.1; N, 6.7%), $\nu_{\rm max.}$ (KCl) 1755 cm. $^{-1}.$

1,1'-Bis-3,4,5-triphenylpyrazolyl Ketone.—(a) 3,4,5-Triphenylpyrazole (3.0 g.) and a 12.5% (w/v) solution of phosgene in toluene (10 ml.), in dry pyridine (30 ml.) was heated under reflux on a water-bath for ca. 1 hr.; the mixture was filtered and then evaporated to dryness under reduced pressure. The residue was washed with water, ethanol, and ether, and then sublimed to yield the ketone $(2.0 \text{ g.}) \text{ m.p.} > 340^{\circ} \text{ (Found: C, 83.8; H, 4.8; N, 9.1%; } M,$ 618. $C_{43}H_{30}N_4O$ requires C, 83.5; H, 4.9; N, 9.0%; M, 618), ν_{max} (KCl) 1750, cm.⁻¹. (b) 1,1'-Bis-3,4,5-triphenyl-pyrazolyl diketone (0.5 g.) was heated to 270—300° until evolution of gas ceased; the residue then sublimed to give 1,1'-bis-3,4,5-triphenylpyrazolyl ketone (0·2 g.), m.p. $>340^{\circ}$, ν_{max.} (KCl) 1750 cm.⁻¹.

1,1'-Bis-3,4,5-triphenylpyrazolyl Diketone.—3,4,5-Triphenylpyrazole (3.0 g.) and oxalyl chloride (2 ml.) in dry pyridine (30 ml.) was heated under reflux on a water-bath for ca. 1 hr.; it was then evaporated to dryness under reduced pressure to give the *diketone* (2.5 g.), m.p. $270-271^{\circ}$ (from benzene) (Found: C, 81.2; H, 4.9; N, 8.4%; M, 646. $C_{44}H_{30}N_4O_2$ requires C, 81.7; H, 4.65; N, 8.7%; M, 646), $v_{max.}$ (KCl) 1750 and 1725 cm.⁻¹.

1-Ethoxycarbonyl-3,4,5-triphenylpyrazole.-3,4,5-Triphenylpyrazole and ethyl chloroformate similarly gave the 1-ethoxycarbonyl-derivative, m.p. 162-163° (from ethanol) (Found: C, 78.3; H, 5.2; N, 7.8%; M, 368. C₂₄H₂₀N₂O₂ requires C, 78.3; H, 5.5; N, 7.6%; M, 368), $v_{\text{max.}}$ (KCl) 1755 and 1200 cm.-1.

1-Tolyl-p-sulphonyl-3,4,5-triphenylpyrazole.-3,4,5-Triphenylpyrazole and toluene-p-sulphonyl chloride similarly gave the 1-tolyl-p-sulphonyl-derivative, m.p. 196-198° (from aqueous ethanol) (Found: C, 74.9; H, 5.2; N, 6.4%; *M*, 450. $C_{28}H_{22}N_2O_2S$ requires C, 74.7; H, 4.9; N, 6.2%; M, 450), $v_{\rm max}$ (KCl) 1170 and 960 cm.⁻¹.

1-Ethoxycarbonyl-3,4,5-tri-p-nitrophenylpyrazole. 3,4,5-Tri-p-nitrophenylpyrazole and ethyl chloroformate similarly gave the 1-ethoxycarbonyl-derivative, m.p. 277-278° (from ethanol) (Found: C, 57.3; H, 3.5; N, 13.9.

¹⁶ R. E. Moore and A. Furst, J. Org. Chem., 1958, 23, 1504.

J. Chem. Soc. (C), 1971

 $\rm C_{24}H_{17}N_5O_8$ requires C, 57·2; H, 3·4; N, 13·9%), $\nu_{max.}$ (KCl) 1755, 1515, 1340, and 1190 cm. $^{-1}$

N-Benzoyldeoxybenzoin Hydrazone.—Ethyl benzoate (1 ml.) and deoxybenzoin hydrazone (1 g.) in ethanol (50 ml.) was heated under reflux for several hours. The product (0.5 g.), m.p. $137-138^{\circ}$ (from ethanol) separated when the solution was concentrated and cooled (Found: C, 80.3; H,

5.7; N, 8.4. $\rm C_{21}H_{18}N_2O$ requires C, 80.25; H, 5.7; N, 8.9%), $\nu_{max.}$ (KCl) 3330 and 1695 cm. $^{-1}.$

The author thanks Mr. F. Daubney for the micro-analysis, Dr. S. M. Aftalion for the mass measurements, and Prof. C. W. Rees for a sample of 3,4,5,6-tetraphenylpyridazine.

[1/483 Received, April 5th, 1971]