ORGANIC AND BIOLOGICAL CHEMISTRY

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The Preparation and Reactions of Some Diazopyrazoles[1]

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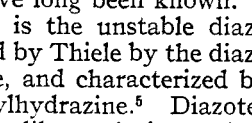
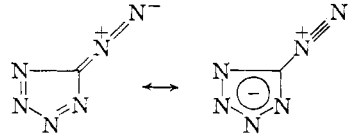
The preparation and reactions of a number of diazopyrazole derivatives have been investigated: 3-benzyl- and 3-benzoyl-4-diazo-5-phenylpyrazole, 3-benzyl- and 3-benzoyl-5-diazo-4-phenylpyrazole, and 4-diazo-3-phenyl-5-pyrazolone. The stability and reactivity of these compounds have been found to vary widely.

The structures of aliphatic diazo compounds can be represented as resonance hybrids of type I, the contribution of other canonical forms to the hybrid being of lesser importance.[3] It would be anticipated that in those cases where the diazo carbon atom is an integral part of a potentially aromatic five-membered ring such diazo compounds might show unusual properties. Doering and DePuy,[4] activated by this view, developed a novel synthetic method leading to the interesting and unusual diazohydrocarbon, diazocyclopentadiene. This is the first example of this type of compound in which the aromatic system is fully carbocyclic; however, analogous compounds with heterocyclic ring systems have long been known. Perhaps the earliest example is the unstable diazotetrazole (II), first prepared by Thiele by the diazotization of 5-aminotetrazole, and characterized by its reduction to 5-tetrazolylhydrazine.[5] Diazotetrazole decomposed slowly in dilute solution and explosively in concentrated solution; although the pure substance has, therefore, never been isolated, several coupling products with substituted hydrazines have been prepared and characterized.[6] Subsequently, Bamberger reported[7] the preparation of several diazoindazoles. In contrast to diazotetrazole, these

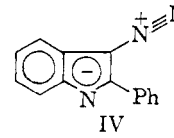


I



II III

compounds exhibited unusual stability; the parent diazoindazole (III),[8] for example, was completely decomposed only after 12 hours in boiling water, or 20 hours in boiling, aqueous, 1 *N* sulfuric acid. The remarkable difference in the stabilities of compounds II and III presaged the results obtained by later investigators. Shortly after 1900 a group of Italian workers[9,10] initiated studies of the diazopyrroles and diazoindoles. The stabilities of the substances prepared, all of which had the diazo group in the 3-position of the nucleus, varied from that of 2-phenyl-3-diazoindole (IV), which decomposed readily in 25% sulfuric acid at room temperature,[9] to that of 2,4,5-triphenyl-3-diazopyrrole (V), which, after 36 hours in boiling 25% sulfuric acid, was partially recovered and partially transformed into an isomer later shown to be VI.[10,11] All of these diazoindazoles, diazoindoles and diazopyrroles are reported to be light-sensitive. Recently, Tedder and Webster[12] have developed



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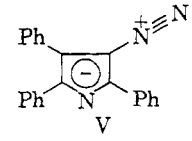

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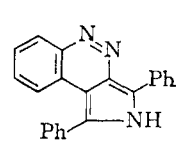
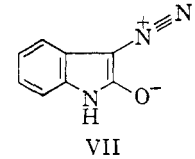


VI



VII

additional methods for the synthesis of 3-diazopyrroles and have investigated their reactions; they were, however, unsuccessful in their attempts to make 2-diazopyrroles. Related to the diazoindoles is the diazoöxide VII[13]; this appears to be the only well-characterized heterocyclic diazoöxide to have

(1) A preliminary communication on this work has appeared: D. G. Farnum and P. Yates, *Chemistry & Industry*, 659 (1960).

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(3) R. Huisgen, *Angew. Chem.*, **67**, 439 (1955).

(4) W. von E. Doering and C. H. DePuy, *J. Am. Chem. Soc.*, **75**, 5955 (1953).

(5) J. Thiele, *Ann.*, **270**, 46 (1892); J. Thiele and J. T. Marais, *ibid.*, **273**, 147 (1893); J. Thiele and H. Ingle, *ibid.*, **287**, 235 (1895).

(6) K. A. Hofman and H. Hock, *Ber.*, **44**, 2946 (1911); F. L. Scott, D. A. O'Sullivan and J. Reilly, *Chemistry & Industry*, 782 (1952).

(7) E. Bamberger, *Ber.*, **32**, 1773 (1899); *cf.* A. Hantzsch, *ibid.*, **35**, 888 (1902).

(8) In formula III and in subsequent, related formulas, resonance hybrids of the type depicted in II are represented in truncated form; *cf.* ref. 24.

(9) A. Angeli and A. D'Angelo, *Atti accad. Lincei rend.*, [5] **13**, I, 259 (1904); V. Castellana and A. D'Angelo, *ibid.*, [5] **14**, II, 145 (1905); V. Castellana and A. D'Angelo, *Gazz. chim. ital.*, **36**, II, 56 (1906); F. Angelico and S. Capuano, *ibid.*, **67**, 633, 710 (1937); *cf.* P. Seidel, *Ber.*, **77B**, 797 (1944).

(10) A. Angeli and G. Marchetti, *Atti accad. Lincei rend.*, [5] **16**, II, 790 (1907); F. Angelico, *ibid.*, [5] **14**, II, 169 (1905); F. Angelico, *ibid.*, [5] **17**, II, 655 (1908); F. Angelico, *Gazz. chim. ital.*, **39**, II, 134 (1909); F. Angelico and C. Labisi, *ibid.*, **40**, I, 411 (1910); F. Angelico and F. Monforte, *ibid.*, **53**, 795 (1923).

(11) The cinnabar-red VI gives blue salts with strong acids, and an indigo-blue ethyl derivative with ethyl iodide in base, presumably a "pseudoazulene" derivative; *cf.* G. V. Boyd, *J. Chem. Soc.*, 1978 (1958).

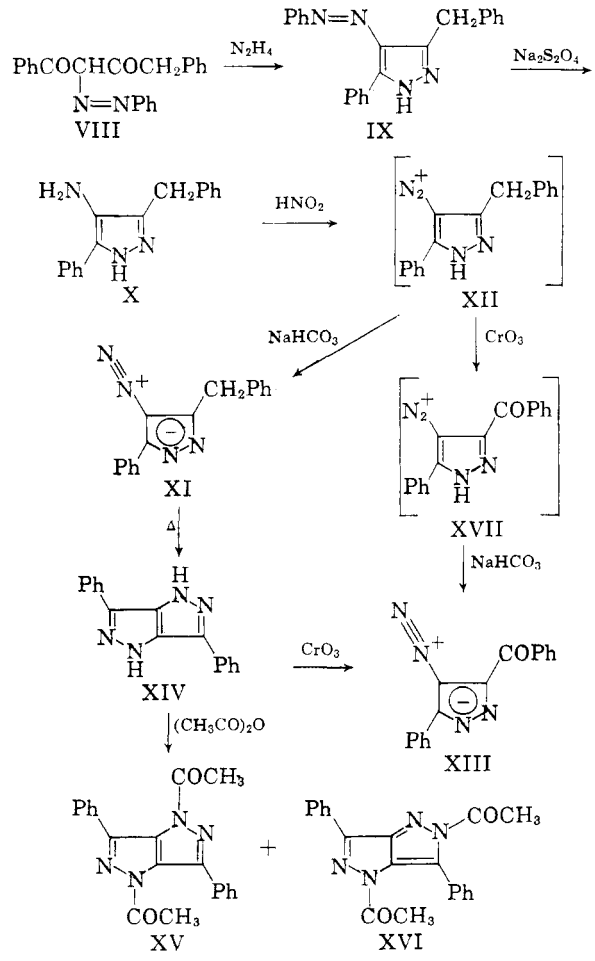
(12) J. M. Tedder and B. Webster, *ibid.*, 3270 (1960).

(13) (a) T. Curtius and H. Lang, *J. prakt. Chem.*, [2] **44**, 544 (1891); J. Thiele, *Ber.*, **44**, 2522 (1911); A. Angeli, *Atti accad. Lincei rend.*, [5] **20**, I, 625 (1911); H. Staudinger and J. Goldstein, *Ber.*, **49**, 1923 (1916). (b) M. P. Cava, R. L. Litle and D. R. Napier, *J. Am. Chem. Soc.*, **80**, 2257 (1958).

been recorded, although the patent literature[14] contains references to pyrazole diazoöxides.[15]

In order to explore further the chemistry of compounds of the general type discussed above we have investigated the preparation and some reactions of several diazopyrazoles,[16] including one which was required for a synthetic purpose in connection with another problem.[17]

Condensation of 1,4-diphenyl-2-phenylazobutane-1,3-dione (VIII) with hydrazine in acetic acid gave 3-benzyl-5-phenyl-4-phenylazopyrazole (IX), whose structure was established on the basis of its elemental analysis, infrared and ultraviolet spectra, and mode of synthesis. Reduction of IX with sodium hydrosulfite afforded 4-amino-3-benzyl-5-phenylpyrazole (X). This was diazotized with sodium nitrite in cold acetic acid and the resulting solution was treated with cold aqueous sodium bicarbonate. The product thus formed, which was purified at temperatures below 40°, was a pale yellow crystalline compound, $C_{16}H_{12}N_4$, which on heating became colorless at *ca.* 100°, but did not melt below 300°. Its infrared spectrum lacked absorption in the NH region and showed a strong band at 4.71 μ, attributable to a diazo group.[18] It is therefore assigned structure XI, 3-benzyl-4-diazo-5-phenylpyrazole, and is considered to be formed *via* the diazonium ion XII. Support for this structural assignment derives from the relationship of XI to 3-benzoyl-4-diazo-5-phenylpyrazole (XIII) (*vide infra*). The loss of color by XI on being heated was found to be due to a facile thermal isomerization, which was most conveniently effected by heating a solution of XI in acetic acid on the steam-bath. The white, crystalline isomer, which did not melt below 300°, and was insoluble in all common organic solvents, showed a band in its infrared spectrum at 3.15 μ but lacked any band in the diazo region. On acetylation with acetic anhydride it was converted to two isomeric diacetyl derivatives, $C_{20}H_{16}N_4O_2$, whose infrared spectra lacked the NH band of their progenitor; the spectrum of the higher-melting isomer possessed a single carbonyl band at 5.76 μ, while that of the lower-melting isomer possessed two carbonyl bands at 5.70 and 5.84 μ. Oxidation of the thermal isomerization product with chromic acid in acetic acid converted it to the diazopyrazole XIII. On the basis of these data it is assigned the pyrazolopyrazole structure XIV and the higher- and the lower-melting diacetyl derivatives are assigned structures XV and XVI, respectively. When the rearrangement XI →XIV was carried out in hot acetic acid, a brief and somewhat variable induction eripod was observed before separation of the highly insoluble



product began, and the reaction then proceeded rapidly to completion. This observation suggests that the transformation proceeds *via* a radical chain pathway; initiation of the reaction might well involve formation of a benzylic radical by hydrogen abstraction.

When the solution containing XII, obtained by the diazotization of X, was treated with chromium trioxide and sulfuric acid before basification with sodium bicarbonate, the product formed was 3-benzoyl-4-diazo-5-phenylpyrazole (XIII), presumably *via* the diazonium ion XVII. The diazopyrazole XIII was obtained as bright yellow needles, m.p. 148–148.5°, with infrared bands at 4.66, 6.08 and 11.15 μ; the 4.66 μ band confirms the presence of the diazo grouping, while the other bands are in full accord with the presence of a benzoyl group attached to a heteroaromatic ring.[19] The structural assignment was corroborated by the reduction of XIII with dilute methanolic potassium hydroxide, which proceeded vigorously at room temperature with the formation of a substance, $C_{16}H_{12}N_2O$, shown to be 3-benzoyl-5-phenylpyrazole (XVIII) by comparison with a sample prepared by chromic acid oxidation of the known 3-benzyl-5-phenylpyrazole (XIX).[20] The diazopyrazole XIII was found to be remarkably stable; after treatment with boiling 50% aqueous

(14) *Cf.* for example, A. W. Nies, U. S. Patent 2,420,791 (1947); *C. A.*, **41**, 5729 (1947).

(15) It may be noted that benzene-1,2-diazoöxide and related compounds represent analogs in the six-membered aromatic series of diazocyclopentadiene and the five-membered diazoheterocycles.

(16) Since the completion of this work, the preparation and characterization of solutions of the parent 3-diazopyrazole have been reported: H. Reimlinger, A. van Overstraeten and H. G. Viehe, *Chem. Ber.*, **94**, 1036 (1961).

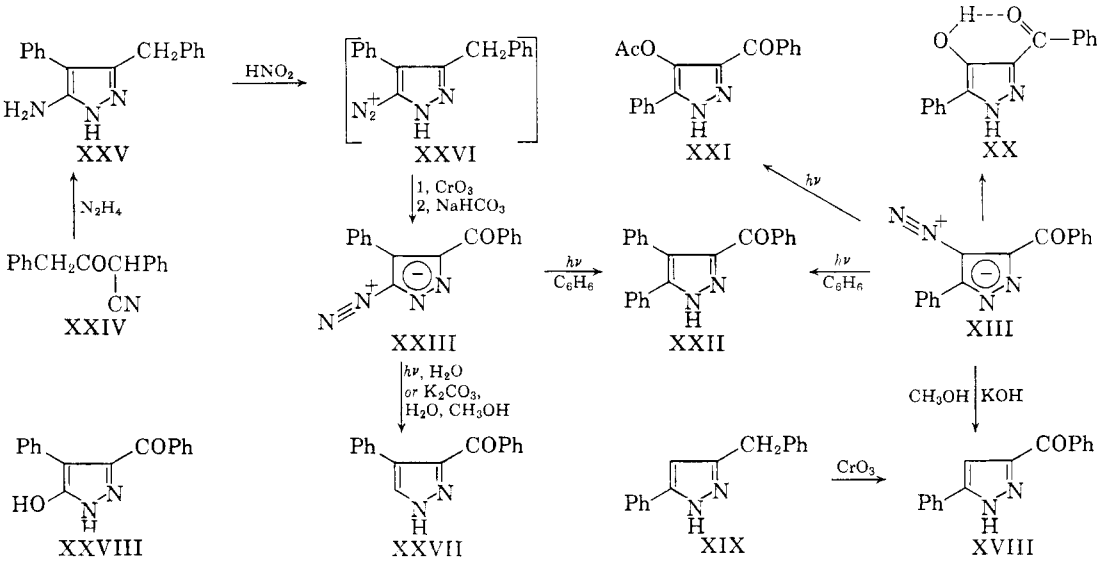
(17) P. Yates and D. G. Farnum, *Tetrahedron Letters*, **No. 17**, 22 (1960).

(18) P. Yates, B. L. Shapiro, N. Yoda and J. Fugger, *J. Am. Chem. Soc.*, **79**, 5756 (1957).

(19) D. G. Farnum and P. Yates, *J. Org. Chem.*, in press.

(20) C. Bülow and H. Grotowsky, *Ber.*, **34**, 1479 (1901).

sulfuric acid for 30 minutes it could be recovered to the extent of 90%. Its unusual thermal stability was demonstrated by the fact that, in contrast to most diazo compounds, it melted without decomposition at 148–148.5°, and visible gas evolution did not occur until the temperature of the melt reached 190–200°. Photolytic decomposition of XIII occurred readily, however. Irradiation of a solution in aqueous acetone with a sun lamp converted it to 3-benzoyl-4-hydroxy-5-phenylpyrazole (XX), which showed bands in its infrared spectrum at 2.97, 3.07, 6.16 and 11.05 μ, dissolved in dilute aqueous sodium hydroxide to give a yellow solution, and gave a blue-green coloration with ethanolic ferric chloride. Photolysis in acetic acid produced the corresponding acetoxy compound XXI, with infrared bands at 2.95, 3.10, 5.75, 6.12, 8.45 and 11.00 μ. When benzene was used as solvent for the photolysis, a quantitative yield of a product, $C_{22}H_{16}N_2O$, was obtained. This is assigned the structure 3-benzoyl-4,5-diphenylpyrazole (XXII) on the basis of the similarity of its spectrum [$\lambda_{max}^{CH_2Cl_2}$ 2.90, 3.10, 6.08 and 11.05 μ, λ_{max}^{EtOH} 256 mμ (log ϵ 4.45)] to that of 3-benzoyl-5-phenylpyrazole (XVIII) [$\lambda_{max}^{CH_2Cl_2}$ 2.98, 6.07 and 11.20 μ; 258 mμ (log ϵ 4.55)], and of the fact that it is identical with the product obtained on photolysis of 3-benzoyl-5-diazo-4-phenylpyrazole (XXIII) (*vide infra*) in benzene solution.



Reaction of the ketonitrile XXIV with hydrazine gave the aminopyrazole XXV, with infrared bands at 2.90, 2.95 and 6.26 μ. Diazotization with sodium nitrite and acetic acid to give the corresponding diazonium ion XXVI followed by oxidation and treatment with aqueous sodium bicarbonate gave the diazopyrazole XXIII, a deep yellow crystalline substance with infrared bands at 4.68, 6.06 and 11.05 μ.[21] Its structure was confirmed by its reduction with aqueous, methanolic potassium carbonate to 3-benzoyl-4-phenylpyrazole (XXVII) identified by direct comparison with an authentic sample. Unlike its isomer XIII, the diazopyrazole XXIII dissolved in hot, 50% aqueous sulfuric acid with gas evolution and was completely decomposed within a few minutes; the expected product, 3-benzoyl-5-hydroxy-4-phenylpyrazole (XXVIII),[17] could not be detected in the reaction mixture, from which no pure product was obtained. Photolysis of XXIII in solution in aqueous acetone also failed to give XXVIII, but gave instead the reduction product XXVII. As noted above, photolysis of XXIII in solution in benzene led to the same product, XXII, as that obtained from the similar reaction with the 4-diazo compound XIII.

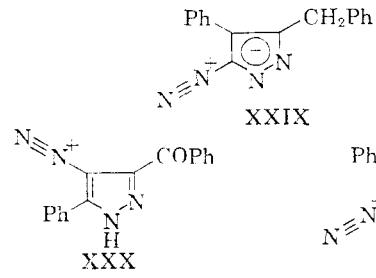
In an attempt to prepare 3-benzyl-5-diazo-4-phenylpyrazole (XXIX), an analog of XI, the solution containing the diazonium ion XXVI was treated directly with aqueous sodium bicarbonate. A thermally unstable, yellow, crystalline solid was obtained which undoubtedly contained XXIX as the major component, since its infrared spectrum exhibited major bands at 4.72, 6.26 and 9.10 μ and lacked other significant absorption. However the high instability of this product prevented its being purified for elemental analysis.

We turn now to some aspects of the relative stabilities and reactivities displayed by the diazopyrazoles whose preparation has been described; as in the case of the other diazoheterocycles discussed earlier, these cover a wide range. Perhaps the most striking contrast is that between the isomeric benzoyl compounds, XIII and XXIII, which is summarized in Table I. In the case of both compounds an important structural feature is the aromatic character common to diazocyclopentadiene and other diazoheterocycles, implied by the representations XIII and XXIII.[8] The importance of these types of contributors to the resonance hybrids in the ground state is reflected in the positions of the bands associated with the

(21) Preliminary work indicates that XXIII can also be obtained by the sequence: ethyl 3-benzoyl-4-phenyl-2-pyrazoline-5-carboxylate[22] → ethyl 3-benzoyl-4-phenylpyrazole-5-carboxylate → 3-benzoyl-4-phenylpyrazole-5-carbonyl azide → 5-amino-3-benzoyl-4-phenylpyrazole → XXIII.

(22) E. P. Kohler and L. L. Steele, *J. Am. Chem. Soc.*, **41**, 1093 (1919).

diazo group in the infrared spectra of these compounds; these bands fall at wave lengths well below those of the bands of most aliphatic diazo compounds, including diazoketones (4.76–4.97 μ),[18] and occur, in fact, within the range (4.33–4.68 μ) observed[23] for aromatic diazonium salts.[24] These contributors would be expected to be of even greater importance in the case of the diazopyrazoles than in that of diazocyclopentadiene, because of the greater electronegativity of the heterocyclic ring. Further stabilization, no doubt, is derived from resonance involving the carbonyl and phenyl groups (*cf.* the positions of the diazo bands at 4.71 and 4.72 μ in the infrared spectra of the benzyl analogs, XI and XXIX, respectively). Thus, steric and other effects dependent upon the presence and position of these substituents both in XIII and XXIII and in the transition states for their decomposition may well be important, or even decisive, in determining the observed difference in stabilities. Such effects could include, for example, (i) partial steric inhibition of resonance involving the adjacent benzoyl and phenyl groups and the pyrazole ring in XXIII (the linear diazo group appears in scale molecular models to make less steric demands than a phenyl group, even when the latter is rotated far from the plane of the pyrazole ring), and (ii) stabilization of XIII relative to XXIII because of greater ionic attraction between the more closely-lying, positively charged diazo group and the negatively charged oxygen atom. It would be premature to conclude, therefore, that this difference necessarily reflects a difference in the stabilities of 3- and 4-diazopyrazoles as such. In any event, it is evident that the incorporation



tization of the known aminopyrazolone XXXII[25] with sodium nitrite in cold dilute sulfuric acid followed by treatment with aqueous sodium bicarbonate. The deep yellow-orange, crystalline product, $C_9H_6N_4O$, was characterized as the diazo-

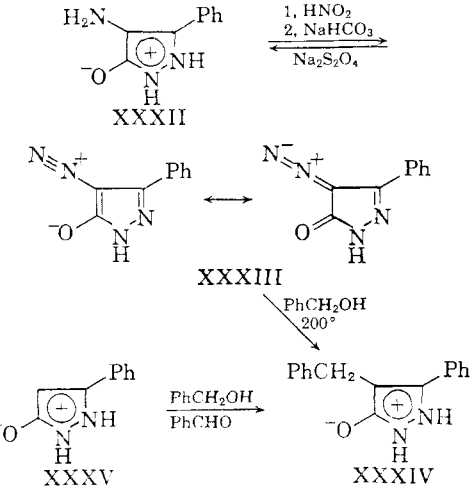


TABLE I

COMPARISON OF PROPERTIES OF COMPOUNDS XIII AND XXIII

	XIII	XXIII
Infrared bands	4.66, 6.08 μ	4.68, 6.06 μ
Thermal stability	M.p. 148–148.5° without dec.; visible dec. 190–200°	M.p. *ca.* 105° with vigorous dec.
Action of boiling 50% aq. H_2SO_4	Recovery of 90% after 30 min.	Rapid and complete decomposition
Reduction by methanol and base	Methanolic KOH required	Rapid reduction with methanolic K_2CO_3
Photolysis in aq. acetone	Solvol. prod. formed	Redn. prod. formed

of the diazo carbon into a potentially aromatic system is not an overriding factor in determining the stability of aliphatic diazo compounds. The resistance of XIII or, more exactly, the corresponding diazonium salt XXX, to solvolysis in aqueous sulfuric acid could reflect steric hindrance to the approach of solvent at the carbon atom bearing the diazo group by the flanking benzoyl and phenyl groups. Such hindrance should be considerably less in XXXI, the protonated species derived from XXIII. Similar differences in steric effects could also cause the difference observed in the ease of reduction of XIII and XXIII. Unfortunately, the facile thermal isomerization of XI prevents a similar comparison with XIII.

Finally, we describe the preparation of a diazooxide in this series. This was obtained by diazooxide XXXIII by its infrared spectrum (bands at 2.95, 4.78 and 5.93 μ) and its reduction with sodium hydrosulfite to its precursor XXXII. It was soluble in dilute aqueous sodium hydroxide and was precipitated unchanged on acidification of the solution; it was unaffected by treatment with boiling methanolic potassium hydroxide for 30 minutes. Its thermal stability was unusual for diazoöxides, which are generally explosive[27]; although it decomposed slowly at its melting point (182–183°), it was recovered to the extent of 90% after 12 hours in boiling xylene. Decomposition could be effected in boiling benzyl alcohol and was complete within four hours, with the formation

(23) (a) M. Aroney, R. J. W. Le Fèvre and R. L. Werner, *J. Chem. Soc.*, 276 (1955); (b) K. B. Whetsel, G. F. Hawkins and F. E. Johnson, *J. Am. Chem. Soc.*, **78**, 3360 (1956).

(24) It is on this basis that representations such as XIII and XXIII are used in the present discussion.

(25) Although this substance was not characterized by elemental analysis in the earlier work[26] because of its extreme sensitivity in solution to air oxidation, it was found in the present work that recrystallization from aqueous methanol containing a trace of sodium bisulfite permitted the preparation of a sample whose elemental composition was in excellent accord with a $C_9H_6N_4O$ formulation.

(26) R. v. Rothenburg, *J. prakt. Chem.*, [2] **52**, 23 (1895).

(27) *Cf.* E. W. Robb, Ph.D. Thesis, Harvard, 1956.

of a product, $C_{16}H_{14}N_2O$, whose melting point and infrared spectrum (bands at 2.98, 3.9 (br) and 6.65 μ) corresponded closely with those recorded[28] for 4-benzyl-3-phenyl-5-pyrazolone (XXXIV).[29] As verification for this structural assignment and also in order to obtain evidence bearing on a possible mode of formation of XXXIV from the diazoöxide, 3-phenyl-5-pyrazolone (XXXV) was boiled for 4 hours in benzyl alcohol in the presence of a trace of benzaldehyde. Reductive benzylation[30] occurred with the formation of XXXIV, identical with the product obtained from XXXIII. Its formation from the latter can then be suggested to occur by initial reduction with benzyl alcohol to give XXXV and benzaldehyde followed by reductive benzylation.

The infrared spectrum of the diazoöxide is of interest; its two intense bands are compared in Table II with the corresponding bands in the solution spectra of some other compounds of the 1,2-diazoöxide type. The diazo stretching band[18]

TABLE II

Compound	Solvent	λ_{max}, μ
4-Diazo-3-phenyl-5-pyrazolone (XXXIII)	CH_2Cl_2	4.78, 5.93
1,2-Naphthalenediazoöxide[a]	$CHCl_3$	4.77, 6.17
2,1-Naphthalenediazoöxide[a]	$CHCl_3$	4.73, 6.17
10-Diazo-9-phenanthrone[b]	CH_2Cl_2	4.84, 6.13
2-Diazo-1-acenaphthenone[c]	$CHCl_3$	4.82, 5.95
3-Diazoöxindole (VII)[b]	CH_2Cl_2	4.78, 5.87

[a] Ref. 31. [b] Ref. 13b. [c] Ref. 18.

of XXXIII falls within the relatively narrow range of the similar bands of the other compounds. Its carbonyl band falls close to the corresponding bands of the two analogs in which the diazoöxide function is situated in a five-membered ring; the bands in the case of the six-membered diazoöxides occur at considerably larger wave lengths. Although it is expected that ring size should influence the position of the carbonyl band in this sense, the shift is too large to be interpreted solely on this basis, at least in the case of XXXIII.[32] However, because of the several variables involved, interpretation in terms of the fine structures of the resonance hybrids appears to be unwarranted at this time.

Experimental[33]

3-Benzyl-5-phenyl-4-phenylazopyrazole (IX).—1,4-Diphenyl-2-phenylazobutane-1,3-dione (VIII), m.p. 113–114° (lit.[20] 113°), $\lambda_{max}(CH_2Cl_2)$ 3.30(broad), 6.06, 6.62 μ, was prepared in quantitative yield from 1,4-diphenylbutane-1,3-dione according to the method of Bülow and Grotowsky.[20]

The phenylazodiketone (10.3 g., 0.030 mole) was dissolved in warm acetic acid (*ca.* 100 ml.), and 95% hydrazine (*ca.* 0.5 ml.) was added dropwise with swirling and intermittent cooling. The red solution was heated gently on the steam-bath for a few minutes, allowed to cool slowly and left overnight at room temperature. The mixture was chilled in the refrigerator and the resulting crystals were collected, washed well with water and dried. The product was thus obtained as deep yellow-orange needles (10.2 g., 100%), m.p. 178.5–179°. Two recrystallizations from 95% ethanol afforded a sample for analysis, m.p. 178–178.5°; λ_{max} (95% EtOH) 340 mμ (log ϵ 4.30), 430 mμ (log ϵ 3.13); $\lambda_{max}(CH_2Cl_2)$ 2.95, 3.20, 6.23, 6.32, 6.70, 6.75 μ.

Anal. Calcd. for $C_{22}H_{18}N_4$: C, 78.08; H, 5.36; N, 16.56. Found: C, 77.84; H, 5.46; N, 16.77.

4-Amino-3-benzyl-5-phenylpyrazole (X).—The phenylazopyrazole IX (4.5 g., 0.013 mole) was slurried in boiling aqueous 80% ethanol (*ca.* 75 ml.), and small portions of powdered sodium hydrosulfite were added to the boiling solution until the orange solid had dissolved and a light yellow solution resulted. The solution was then diluted to *ca.* 150 ml. with hot water, and aniline and ethanol were distilled from the mixture. In a short time, the light yellow, insoluble oil which separated crystallized in the boiling solution. Chilling the mixture to 0° afforded very faintly yellow crystals (3.3 g., 100%), m.p. 137–139°, which were recrystallized several times from aqueous ethanol with treatment with Norit to give a sample for analysis as colorless needles, m.p. 139.5–140°.

Anal. Calcd. for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.86. Found: C, 77.38; H, 6.04; N, 16.86.

3-Benzyl-4-diazo-5-phenylpyrazole (XI).—The aminopyrazole X (1.0 g., 4.0 mmoles) was dissolved in acetic acid (*ca.* 10 ml.), the solution was cooled in an ice-bath, and a solution of sodium nitrite (0.3 g.) in a little water was added dropwise while the reaction mixture was swirled. After 15 minutes, the solution was poured into cold dilute aqueous sodium bicarbonate, and the gummy yellow precipitate was extracted into dichloromethane. The organic extracts were filtered through sodium sulfate and evaporated to dryness at reduced pressure with gentle warming. The yellow, crystalline residue was taken up in a little dichloromethane, and the resultant solution was diluted with hexane to the cloud point, filtered through Norit and chilled to −25°. The diazopyrazole XI was thus obtained as light yellow crystals (700 mg., 70%), turning colorless *ca.* 100°, infusible below 300°. Recrystallization of this product from benzene–hexane at temperatures below 40° yielded a sample for analysis as long, transparent, light yellow flakes, turning colorless *ca.* 100°, infusible below 300°; $\lambda_{max}(CH_2Cl_2)$ 4.71, 6.26, 7.21 μ.

Anal. Calcd. for $C_{16}H_{12}N_4$: C, 73.83; H, 4.65; N, 21.53. Found: C, 73.65; H, 4.73; N, 21.79.

Reaction of XI in Hot Acetic Acid. Formation of XIV.—A solution of XI (100 mg., 0.38 mmole) in acetic acid (*ca.* 2 ml.), was filtered through Norit and then heated on the steam-bath. After an initiation period ranging from 1 to 10 minutes in various runs, colorless needles rapidly separated from the solution. After 15 minutes, the mixture was cooled to room temperature, and the small, white needles which were deposited (100 mg., 100%), infusible below 300°, were collected and dried for analysis; λ_{max} (Nujol) 3.15, 6.25, 6.36, 9.2, 10.06 μ.

Anal. Calcd. for $C_{16}H_{12}N_4$: C, 73.83; H, 4.65; N, 21.53. Found: C, 73.34, 73.36; H, 5.01, 4.79; N, 21.47, 21.19.

This substance was insoluble in most organic solvents. It dissolved in boiling dimethylformamide, but could not be recovered in crystalline form upon cooling these solutions. It was insoluble in cold dilute aqueous sodium hydroxide or in alcohol, but dissolved in alcoholic sodium hydroxide.

Acetylation of XIV. Formation of XV and XVI.—Compound XIV (260 mg., 1.0 mmole) was dissolved in boiling acetic anhydride (*ca.* 10 ml.). When the solution was cooled in the refrigerator, colorless leaflets (300 mg., 87%), m.p. 215–250°, separated. This crude product was digested in dichloromethane, and the insoluble, colorless leaflets (180 mg., 52%), m.p. 267–269°, were recrystallized from nitromethane to give a sample for analysis, m.p. 269–270°; λ_{max} (Nujol) 5.76, 7.95, 10.40 μ.

Anal. Calcd. for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68; N, 16.27; Found: C, 69.75; H, 4.69; N, 15.83.

Evaporation of the dichloromethane extracts afforded a colorless crystalline solid (110 mg., 32%), dec. slowly above 200°, m.p. *ca.* 270°, which, upon recrystallization from benzene–hexane, afforded a sample for analysis, dec. above 200°; λ_{max}(Nujol) 5.70, 5.84, 7.95, 10.28 μ.

(28) P. E. Gagnon, J. L. Boivin and R. J. Paquin, *Can. J. Chem.*, **31**, 1025 (1953).

(29) We thank Professor Paul E. Gagnon, Laval University, for a sample of this compound.

(30) *Cf.* Y. Sprinzak, *J. Am. Chem. Soc.*, **78**, 466 (1956).

(31) P. Yates and E. W. Robb, *ibid.*, **79**, 5760 (1957).

(32) The carbonyl band of the parent compound, 3-pyrazolinone, falls at the same position as the bands of simple *six*-membered cyclic ketones.

(33) Melting points are uncorrected. Infrared bands in the 6 μ region were calibrated against the 6.24 μ band of a polystyrene film, and bands near 5 μ were calibrated against the 5.14 μ band of this substance.

Anal. Calcd. for $C_{20}H_{16}N_4O_2$: C, 69.75; H, 4.68; N, 16.27. Found: C, 69.65; H, 4.69; N, 16.15.

Chromic Acid Oxidation of XIV. Formation of XIII.—A solution of chromium trioxide (140 mg., 1.4 mmoles) in a little water was added to a mixture of XIV (260 mg., 1.0 mmole) and acetic acid (*ca.* 5 ml.). Concentrated sulfuric acid (5 drops) was added, and a small portion of the mixture was removed, heated on the steam-bath, and returned to the mixture. After 2 days at room temperature, the mixture was poured into a large volume of cold water, the resultant slurry was stirred to effect solution of inorganic material, and the deep yellow, crystalline deposit was collected and recrystallized from benzene–hexane. Deep yellow rhombs of XIII (190 mg., 69%), m.p. and mixture m.p. 147.5–148.5°, infrared spectrum identical with that of a sample prepared by the method below, were thus obtained.

3-Benzoyl-4-diazo-5-phenylpyrazole (XIII).—The aminopyrazole X (3 g., 0.012 mole) was dissolved in acetic acid (*ca.* 20 ml.), and a solution of sodium nitrite (1.0 g., 0.015 mole) in a little water was added gradually while the reaction mixture was cooled in an ice-bath. After 5 minutes, a solution of chromium trioxide (6 g., 0.060 mole) in a little water was added, followed by concentrated sulfuric acid (6 ml.) with ice-bath cooling. A small portion of the deep red solution was withdrawn, heated on the steam-bath until chromic sulfate precipitated, then returned to the main reaction mixture. The reaction was moderated with ice-bath cooling for the first hour, then allowed to proceed for 2 days at room temperature. The mixture of green precipitate and red solution was washed into ice-water (*ca.* 400 ml.) and stirred to effect solution of the chromium salts. The insoluble, crystalline, red solid was collected and washed with a little cold water. The "diazonium chromate" thus obtained was decomposed by prolonged stirring in dilute aqueous potassium carbonate. The resulting yellow, crystalline precipitate was collected and washed well with water. Dilution of the mother liquors from the isolation of the "diazonium chromate" to 1.5 l. with cold water caused the precipitation of further product as yellow needles. The total product (2.4 g., 74%) m.p. 147–148.5°, was dissolved in boiling benzene, and the solution was filtered free of a trace of insoluble residue. The filtrate was brought to boiling, diluted with hexane to the cloud point and cooled slowly to 0° to give stout, bright yellow needles, m.p. 148–148.5° (90% recovery). Recrystallization could also be effected from 95% ethanol to give long, slim, bright yellow needles, m.p. 148–148.5°

Recrystallization from benzene–hexane afforded a sample for analysis, m.p. 148–148.5°; λ_{max}(CH_2Cl_2) 4.66, 6.08, 11.15 μ; λ_{max} (Et_2O) 232 mμ (log ϵ 4.38), 250 mμ (log ϵ 4.24), 352 mμ(log ϵ 3.97).

Anal. Calcd. for $C_{16}H_{10}N_4O$: C, 70.06; H, 3.68; N, 20.43. Found: C, 70.22; H, 3.67; N, 20.48.

Reduction of XIII with Sodium Methoxide. Formation of 3-Benzoyl-5-phenylpyrazole (XVIII).—Compound XIII (100 mg., 0.36 mmole) was dissolved in warm methanol (2 ml.), and aqueous 40% potassium hydroxide (3 drops) was added. Vigorous gas evolution was immediately apparent. After 5 minutes at room temperature, gas evolution had ceased, and the solution was poured into water. Vigorous scratching in the resultant solution caused the separation of a faintly yellow crystalline solid (90 mg., 100%), m.p. 169.5–170.5°, λ_{max} (CH_2Cl_2) 2.98, 6.07, 11.20 μ, which was shown to be identical with an authentic sample of 3-benzoyl-5-phenylpyrazole (*vide infra*) by infrared spectral comparison and a mixture melting point determination.

3-Benzyl-5-phenylpyrazole (XIX).—1,4-Diphenylbutane-1,3-dione[20] (4.8 g., 0.020 mole) was dissolved in acetic acid (*ca.* 10 ml.) and 95% hydrazine (2 ml.) was added dropwise while the reaction mixture was swirled. The resultant solution was maintained at room temperature overnight and then poured into dilute aqueous potassium carbonate. The light yellow gummy solid thus obtained was extracted with ether. The ethereal extracts were filtered through sodium sulfate and concentrated on the steam-bath. The boiling solution was diluted with petroleum ether and boiling was continued until crystallization began. Chilling the mixture to −10° afforded colorless needles of XIX (4.35 g., 93%), m.p. 89–90° (lit.[20] 90.5–91°); λ_{max} (CH_2Cl_2) 2.97, 6.22, 6.30, 6.40 μ.

A much reduced yield of the same product was obtained by the method of Bülow and Grotowsky.[20]

3-Benzoyl-5-phenylpyrazole (XVIII).—3-Benzyl-5-phenylpyrazole (0.47 g., 2.0 mmoles) was dissolved in a few ml. of acetic acid, and chromium trioxide (0.30 g., 3.0 mmoles) in a little water was added. Concentrated sulfuric acid (0.3 ml.) was then added dropwise with ice-bath cooling. After the initial vigorous reaction had moderated, the ice-bath was removed, and the reaction was allowed to proceed at room temperature for 1 hour. The mixture was then poured into water, the green chromium salts were brought into solution by stirring, and the light yellow precipitate was extracted with dichloromethane. The organic extracts were filtered through sodium sulfate and evaporated to dryness on the steam-bath, and the residue was crystallized from a small volume of 95% ethanol. The light buff flakes thus obtained (0.35 g., 70%), m.p. 169.5–170.5°, afforded an analytical sample as colorless leaflets, m.p. 170.5–171°, upon recrystallization from 95% ethanol; λ_{max} (CH_2Cl_2) 2.98, 6.07, 10.50, 11.20 μ; λ_{max}(CH_2Cl_2) 258 mμ (log ϵ 4.55).

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.33, 77.26; H, 5.10, 5.03; N, 11.43.

Attempted Hydrolysis of XIII.—A sample of XIII (100 mg.), m.p. 147.5–1.48.5°, was dissolved in warm, 50% aqueous sulfuric acid, and the faintly yellow solution was boiled under reflux for 30 minutes. The color of the solution appeared to intensify slightly, but no gas evolution was noted. The solution was poured into dilute, aqueous sodium bicarbonate, and the resulting yellow, crystalline precipitate (90 mg., 90%), m.p. 146.5–148°, was shown to be identical with the starting material by means of an infrared spectral comparison and a mixture melting point determination.

Photolysis of XIII in Aqueous Acetone. Formation of 3-Benzoyl-4-hydroxy-5-phenylpyrazole (XX).—The diazopyrazole (270 mg., 1 mmole) was dissolved in aqueous 75% acetone, and the solution was irradiated overnight in a Pyrex flask with a G.E. 275 watt sun lamp. The pale yellow solution was poured into water and the pale yellow solid which separated was collected, dried, and dissolved in hot chloroform–methanol. The solution was boiled until crystallization began, chilled to 0°, and the pale yellow needles were collected. The product thus obtained (170 mg., 65%), m.p. 209–210°, was shown to be identical with the compound, $C_{16}H_{12}N_2O_2$, m.p. 210–210.5°, obtained by the action of sodium methoxide on α-diazoacetophenone,[17] by a comparison of infrared spectra and a mixture melting point determination.

Photolysis of XIII in Acetic Acid. Formation of 4-Acetoxy-3-benzoyl-5-phenylpyrazole (XXI).—A sample of XIII (270 mg., 1.0 mmole) was dissolved in acetic acid (*ca.* 10 ml.) to which a little acetic anhydride had been added. The yellow solution was irradiated in a Pyrex flask stoppered with a calcium chloride drying tube for 12 hours with a G.E. 275 watt sun lamp. The solution was poured into aqueous 5% potassium carbonate, and the precipitate was extracted into dichloromethane. The organic extracts were filtered through sodium sulfate and evaporated to dryness on the steam-bath. The residue was crystallized from benzene. The buff crystals (250 mg., 83%), m.p. 160–165°, thus obtained were recrystallized from aqueous ethanol with the use of Norit to give long, colorless needles (185 mg., 60%), m.p. 165–166°. Recrystallization from aqueous ethanol afforded a sample for analysis, m.p. 165–166°; λ_{max}(CH_2Cl_2) 2.95, 3.10(w), 5.75, 6.12, 8.45, 11.00 μ.

Anal. Calcd. for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.74; H, 4.52; N, 8.87.

Photolysis of XIII in Benzene. Formation of 3-Benzoyl-4,5-diphenylpyrazole (XXII).—A sample of XIII (270 mg., 1.0 mmole) was dissolved in dry benzene (*ca.* 75 ml.) and the resultant yellow solution was irradiated in a Pyrex flask stoppered with a soda-lime drying tube for 12 hours with a G.E. 275 watt sun lamp. The pale yellow solution was then concentrated to a small volume on the hot-plate and diluted with hexane to the cloud point. Crystallization was induced by scratching, and the mixture was cooled slowly to 0°. The colorless crystalline solid (320 mg., 100%), m.p. 176–176.5°, which deposited, upon recrystallization from 95% ethanol, afforded a sample for analysis, m.p. 177–177.5°; λ_{max}(CH_2Cl_2) 2.90, 3.10(br, w), 6.08, 11.05 μ; λ_{max}(95% EtOH) 256 mμ (log ϵ 4.45).

Anal. Calcd. for $C_{22}H_{16}N_2O$: C, 81.46; H, 4.97; N, 8.64. Found: C, 81.66; H, 5.21; N, 8.29, 8.70.

2,4-Diphenyl-3-ketobutyronitrile (XXIV).—Methyl phenylacetate (15 g., 0.10 mole) and benzyl cyanide (23.4 g., 0.20 mole) were dissolved in anhydrous ether (300 ml.). The solution was added to a stirred slurry of sodium hydride (10 g. of a 52% dispersion in mineral oil, 0.22 mole) in anhydrous ether (250 ml.), a few drops of *t*-butyl alcohol was added, and the mixture was stirred under reflux overnight. The slurry was poured into ice-water, the basic layer was separated, and the organic layer was extracted with aqueous 2% sodium hydroxide. The combined basic extracts were acidified with concentrated hydrochloric acid and extracted with several portions of ether. The organic extracts were dried over sodium sulfate and concentrated on the steam-bath. The hot concentrate was diluted with petroleum ether, scratched, digested on the steam-bath and cooled to 0°. Filtration afforded a colorless crystalline solid (17.3 g., 75%), m.p. 80–82° (lit.[34] 85–86°); $\lambda_{max}(CH_2Cl_2)$ 2.85, 4.45, 4.52, 5.80, 6.2(br), 6.70 μ.

3-Amino-5-benzyl-4-phenylpyrazole (XXV).—The ketonitrile XXIV (12 g., 0.051 mole) was dissolved in acetic acid (*ca.* 50 ml.), and 95% hydrazine (4 ml.) was added gradually with swirling. The solution was left overnight at room temperature, then poured into dilute aqueous potassium carbonate and the gummy precipitate was extracted with dichloromethane. The organic extracts were dried over sodium sulfate, concentrated on the steam-bath, diluted with hexane until crystallization began in the hot solution and chilled to 0°. The gelatinous mass was drained thoroughly by suction filtration, pressed, washed with hexane, and dried. The product was thus obtained as colorless, fluffy needles (11.2 g., 89%), m.p. 110–112°.

Several recrystallizations from aqueous ethanol afforded a sample for analysis, m.p. 110.5–112°; λ_{max} (CH_2Cl_2) 2.90, 2.95, 6.26 μ.

Anal. Calcd. for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.86. Found: C, 77.04; H, 6.01; N, 17.11.

3-Benzoyl-5-diazo-4-phenylpyrazole (XXIII).—The aminopyrazole XXV (2.5 g., 0.010 mole) was dissolved in acetic acid (*ca.* 20 ml.). The solution was chilled in an ice-bath, and a solution of sodium nitrite (0.8 g., 0.012 mole) in a little water was added with swirling. After 5 minutes, a solution of chromium trioxide (5 g., 0.050 mole) in a little water was added, followed by concentrated sulfuric acid (5 ml.) with ice-bath cooling. A small portion of the deep red solution was withdrawn and heated strongly on the steam-bath until the precipitation of green chromic sulfate was evident, then returned to the main reaction mixture. The reaction was allowed to proceed for 2 days at room temperature, poured into cold water (*ca.* 400 ml.), and the resulting bright yellow solid was taken up in dichloromethane. The aqueous layer was extracted with two further portions of dichloromethane, and the combined organic extracts were washed exhaustively with saturated aqueous sodium bicarbonate, dried over sodium sulfate, and evaporated to dryness with gentle warming at water aspirator pressure. The residual glass, $\lambda_{max}(CH_2Cl_2)$ 4.68, 6.06, 11.05 μ, was taken up in warm benzene, and the deep yellow solution was diluted with hexane to the cloud point, filtered through Norit, and cooled to −10°. Vigorous scratching induced the separation of deep yellow rhombs of XXIII (1.0 g., 37%), dec. *ca.* 100°. Several recrystallizations in this manner afforded a sample for analysis, dec. 104°; $\lambda_{max}(CH_2Cl_2)$ 4.68, 6.06, 11.05 μ; λ_{max} (Et_2O) 225 mμ (log ϵ 4.24), 272 mμ (log ϵ 4.35), *ca.* 370 mμ (shoulder, log ϵ 3.52).

Anal. Calcd. for $C_{16}H_{10}N_4O$: C, 70.06; H, 3.68; N, 20.43. Found: C, 70.37; H, 3.82; N, 20.27.

Reduction of XXIII with Methanolic Potassium Carbonate. Formation of 3-Benzoyl-4-phenylpyrazole (XXVII).—Concentrated aqueous potassium carbonate (3 drops) was added to a solution of XXIII (100 mg. 0.36 mmole) in methanol (*ca.* 1 ml.). Immediate, vigorous gas evolution began, and ceased within a few minutes. The solution was poured into water and the light yellow solid which precipitated was filtered and recrystallized from chloroform. The product thus obtained (80 mg., 88%), m.p. 193–194°, was shown to be 3-benzoyl-4-phenylpyrazole by comparison with an authentic sample.[35]

Hydrolysis of XXIII.—A sample of XXIII (100 mg., 0.36 mmole) was dissolved in hot, 50% aqueous sulfuric acid. Immediate gas evolution was evident. The yellow solution was boiled briefly, diluted with ice-water and the pale yellow precipitate which deposited (90 mg.) was collected. This substance decomposed over a broad temperature range beginning at *ca.* 240°. The infrared spectrum (Nujol) included bands at 3.3–4 (broad), 6.10, 6.25, 6.32, 6.44, 10.95 and 11.15 μ, and was different from that of 3-benzoyl-5-hydroxy-4-phenylpyrazole.[17] The substance was insoluble in cold, dilute aqueous sodium hydroxide, but dissolved in dilute alcoholic sodium hydroxide.

Photolysis of XXIII in Aqueous Acetone. Formation of 3-Benzoyl-4-phenylpyrazole (XXVII).—A solution of XXIII (100 mg., 0.36 mmole) in 50% aqueous acetone was irradiated for 12 hours in a Pyrex flask with a G.E. 275 watt sun lamp. The resultant, cloudy solution was poured into cold water, and the precipitated solid was collected and recrystallized from chloroform. Faintly yellow needles of 3-benzoyl-4-phenylpyrazole (80 mg., 88%), m.p. 193–194°, identical with an authentic specimen,[35] were thus obtained.

Photolysis of XXIII in Benzene. Formation of 3-Benzoyl-4,5-diphenylpyrazole (XXII).—A solution of XXIII (50 mg., 0.18 mmole) in dry benzene was irradiated in a Pyrex flask stoppered with a calcium chloride drying tube for 12 hours with a G.E. 275 watt sun lamp. The resultant faintly yellow solution was concentrated to a very small volume and chilled in the refrigerator. Colorless crystals of XXII (45 mg., 78%), m.p. 176–177°, were thus obtained. The infrared spectrum of this product was identical with that of the product obtained by photolysis of XIII in benzene. The melting point of a mixture of these two substances was undepressed.

3-Benzyl-5-diazo-4-phenylpyrazole (XXIX).—The aminopyrazole XXV (1.0 g., 4.0 mmoles) was dissolved in acetic acid (*ca.* 10 ml.), the solution was cooled in an ice-bath, and a solution of sodium nitrite (0.3 g.) in a little water was added dropwise while the reaction mixture was swirled. After 15 minutes, the solution was poured into cold dilute aqueous sodium bicarbonate, and the gummy yellow precipitate was extracted into dichloromethane. The organic extracts were filtered through sodium sulfate and evaporated to dryness at reduced pressure with gentle warming. The yellow, crystalline residue was taken up in a little dichloromethane, and the resultant solution was diluted with hexane to the cloud point, filtered through Norit and chilled to −25°. Deep yellow rhombs of XXIX (380 mg., 38%), λ_{max} (CH_2Cl_2) 4.72, 6.26, 9.10μ, were thus obtained. This product was too unstable to permit the preparation of an analytical sample.

3-Phenyl-5-pyrazolone.—Ethyl α-benzoylacetate (38 g., 0.20 mole) was dissolved in 95% ethanol (*ca.* 100 ml.), and 95% hydrazine (10 ml.) and acetic acid (*ca.* 1 ml.) were added. The solution was maintained at room temperature overnight, and the colorless crystals which deposited (30 g., 95%), m.p. 239–240° (lit.[36] 236°), λ_{max}(Nujol) 3.8(br), 6.15, 6.25, 6.45 μ, were collected.

3-Phenyl-4-phenylazo-5-pyrazolone.—The pyrazolone obtained above (16 g., 0.10 mole) was slurried in a solution of excess sodium acetate in water. Dilute aqueous sodium hydroxide was slowly added to the mixture with stirring until a clear yellow solution was obtained. A freshly prepared slurry of benzenediazonium chloride in dilute hydrochloric acid was then added slowly with vigorous stirring of the pyrazolone solution. After 30 minutes at room temperature, the deep red precipitate which formed was collected. Recrystallization of this crude product from 95% ethanol afforded deep red needles (21 g., 80%), m.p. 209–210° (lit.[26] 207.5°), λ_{max}(Nujol) 3.10, 6.00, 6.44, 8.0, 10.55 μ.

4-Amino-3-phenyl-5-pyrazolone (XXXII).—The azo compound obtained above (13 g., 0.050 mole) was slurried in boiling aqueous 80% ethanol (*ca.* 100 ml.). Sodium hydrosulfite was added to the boiling solution in small portions until a clear, faintly yellow solution was obtained. Ethanol and aniline were distilled by boiling the solution, and ammonium chloride was added to near saturation. Boiling was then continued until crystallization was observed. The mixture was chilled to 0°, and the colorless, glistening leaflets (7.4 g., 84%), dec. *ca.* 100°, were collected, washed well with cold water, and dried *in vacuo*. The substance turned

(34) E. F. J. Atkinson and J. F. Thorpe, *J. Chem. Soc.*, **89**, 1906 (1906).

(35) P. Yates and B. L. Shapiro, *J. Am. Chem. Soc.*, **81**, 212 (1959).

(36) T. Curtius, *J. prakt. Chem.*, [2] **50**, 515 (1894).

purple in air within a few days, while, under nitrogen, it remained almost colorless for prolonged periods (*cf.* ref. 26).

Attempted recrystallization from organic solvents or aqueous solvent mixtures resulted in rapid and extensive decomposition with the formation of intensely red or purple products. However, recrystallization could be effected satisfactorily from aqueous methanol containing a little sodium bisulfite. Several recrystallizations in this fashion afforded a sample for analysis as colorless, glistening leaflets, dec. *ca.* 100°; λ_{max}(Nujol) 2.95, 3.70(br), 6.25(br) μ.

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.70; H, 5.19; N, 23.89.

4-Diazo-3-phenyl-5-pyrazolone (XXXIII).—Compound XXXII (1.75 g., 0.010 mole) was dissolved in a mixture of ice and concentrated sulfuric acid, and a solution of sodium nitrite (1.0 g., 0.014 mole) in a little water was added slowly to the stirred mixture. The deep yellow slurry was poured into dilute aqueous sodium bicarbonate. The deep yellow, crystalline deposit upon recrystallization from benzene afforded yellow-orange, glistening leaflets (1.3 g., 70%), m.p. 180–181° dec. Several recrystallizations from benzene afforded a sample, m.p. 182–183°, for analysis; λ_{max}(CH_2Cl_2) 2.95, 4.78, 5.93 μ.

Anal. Calcd. for $C_9H_6N_4O$: C, 58.06, H, 3.25; N, 30.10. Found: C, 58.29; H, 3.41; N, 30.04.

This product dissolved in dilute aqueous sodium hydroxide to give yellow solutions from which it was reprecipitated upon acidification.

Sodium Hydrosulfite Reduction of XXXIII. Formation of 4-Amino-3-phenyl-5-pyrazolone (XXXII).—Compound XXXIII (190 mg., 1.0 mmole) was dissolved in boiling 80% aqueous ethanol, and powdered sodium hydrosulfite was added in small portions. Immediate, vigorous gas evolution was evident, and the mixture turned red. Deep yellow-orange leaflets slowly deposited, then went back into solution with the further addition of sodium hydrosulfite to the boiling mixture. A colorless solution eventually resulted. The solution was concentrated to a small volume, saturated with ammonium chloride, cooled and scratched. The colorless crystals which deposited (100 mg., 57%), dec. *ca.* 100°, had an infrared spectrum identical with that of 4-amino-3-phenyl-5-pyrazolone (XXXII).

Attempted Decomposition of XXXIII in Methanolic Sodium Hydroxide.—Compound XXXIII (190 mg., 1.0 mmole) was dissolved in warm methanol (*ca.* 5 ml.) and the yellow-orange solution was treated with several drops of aqueous 40% potassium hydroxide. No gas evolution was evident. The solution was boiled under reflux for 30 minutes, neutralized with acetic acid, diluted to the cloud point with water and chilled to −10°. The yellow-orange needles thus formed (180 mg., 95%), m.p. 180–181°, were shown to be identical with the starting material by infrared spectral comparison and a mixture melting point determination.

Attempted Thermal Decomposition of XXXIII.—Compound XXXIII (0.50 g., 2.7 mmoles) was dissolved in hot xylene (*ca.* 20 ml.), and the yellow-orange solution was boiled under reflux for 12 hours. Upon slow cooling to 5°, deep yellow-orange, glistening leaflets deposited. This substance (0.45 g., 90%), m.p. 180–181° dec., was shown to be identical with the starting material by infrared spectral comparison and a mixture melting point determination.

Pyrolysis of XXXIII in Benzyl Alcohol. Formation of 4-Benzyl-3-phenylpyrazolone (XXXIV).—Compound XXXIII (380 mg., 2.0 mmoles) was dissolved in hot benzyl alcohol (*ca.* 25 ml.) and the deep yellow-orange solution was gradually brought to the boiling point. Slow gas evolution began at *ca.* 160°. The solution was boiled under reflux for 4 hours, during which time it turned deep red, then finally became pale yellow. The reaction mixture was poured into water, and benzyl alcohol was steam distilled from the mixture. The mixture was cooled and the light yellow solid was extracted with ethyl acetate. The organic extracts were dried over sodium sulfate and evaporated to dryness on the steam-bath; the residue was crystallized from benzene. The colorless crystals thus obtained (180 mg., 51%), m.p. 179.5–181.5°, upon recrystallization from benzene afforded an analytical sample, m.p. 185–186°; λ_{max} (Nujol) 2.98, 3.9 (br), 6.65 μ.

Anal. Calcd. for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 77.04; H, 5.29; N, 10.92, 11.67.

The substance was soluble in dilute aqueous sodium hydroxide to give a colorless solution from which it was recovered unchanged upon acidification, and gave an intense red color with ferric chloride in ethanol.

4-Benzyl-3-phenyl-5-pyrazolone (XXXIV).—3-Phenyl-5-pyrazolone[36] (1.6 g., 10 mmoles) was dissolved in hot benzyl alcohol, and benzaldehyde (5 drops) was added. The resultant solution was boiled under reflux for 4 hours, cooled and poured into water. Benzyl alcohol was then steam distilled from the resultant mixture. Upon cooling, the remaining insoluble oil solidified and was collected. Recrystallization from benzene, after filtration of the hot, benzene solution from some insoluble material, afforded colorless needles of XXXIV (1.0 g., 40%), m.p. 184–185° (lit.[28] 186°). The melting point of this substance was undepressed on admixture with the product obtained from pyrolysis of XXXIII in benzyl alcohol. The infrared spectra of these compounds were identical.

[CONTRIBUTION OF DEPARTMENTS OF BIOCHEMISTRY AND UROLOGY, COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK 32, N. Y.]

Cytidine 5′-Sulfate and Related Nucleotide Analogs

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Synthesis of pentose-sulfated analogs of cytidine ribonucleotides has been achieved by 3 methods: (i) reaction of chlorosulfonic acid with cytidine, yielding 7 different cytidine sulfates, (ii) reaction of chlorosulfonic acid with 2′,3′-*O*-isopropylidene followed by mild acid hydrolysis, yielding cytidine 5′-sulfate only and (iii) reaction of sulfuric acid with cytidine at 60°, yielding the same cytidine derivatives as Method i. Procedures for separation of products are presented. Paper chromatographic, electrophoretic, ion exchange, spectrophotometric, radiochemical and acid degradation studies were applied to characterize products and investigate their properties. All evidence indicates that the products are cytidine 2′-sulfate, cytidine 3′-sulfate, cytidine 5′-sulfate, cytidine 2′,3′-disulfate, cytidine 2′,5′-disulfate, cytidine 3′,5′-disulfate and cytidine 2′,3′,5′-trisulfate.

Egami and Takahashi[2] have synthesized adenosine sulfates (adenosine sulfuric acids) by reaction of chlorosulfonic acid with adenosine in pyridine solution. Ion exchange chromatography resolved the product mixture into three fractions characterized as adenosine mono-, di- and tri-sulfates. The adenosine monosulfate product competes with the natural nucleotides, diphosphopyridine nucleotide,[3] flavin adenine dinucleotide[4] and adenosine 5′-monophosphate[5] in certain of their enzyme-

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