Tetrahedron, 1962, Vol. 18, pp. 881 to 891. Pergamon Press Ltd. Printed in Northern Ireland

ALIPHATIC DIAZO COMPOUNDS—VII

THE REACTION OF α-DIAZO KETONES WITH DIAZOETHANE[1]

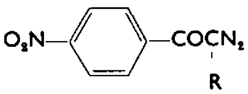
P. YATES,[2a] D. G. FARNUM[2b] and D. W. WILEY
Contribution from the Department of Chemistry, Harvard University,
Cambridge 38, Massachusetts

(*Received* 31 *January* 1962)

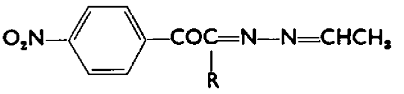
Abstract—The formation of azines in the reaction of diazoethane with α-diazo-*p*-nitroacetophenone and α-diazo-*p*-nitropropiophenone has been confirmed by the elucidation of the nature of certain of their further reaction products.

REPORTS of the reactions of α-diazo ketones with nucleophilic reagents have been limited in general to cases involving strong nucleophiles, e.g. cyanide,[3] hydroxide[4] and methoxide[4] ions. However, Baddeley *et al.*[5] have found that the weak nucleophile, diazoethane, reacts with the strongly electrophilic diazo ketones, α-diazo-*p*-nitropropiophenone (I) and α-diazo-*p*-nitroacetophenone (II). They also reported that less electrophilic diazo ketones, such as α-diazopropiophenone, react more slowly with diazoethane, while the *p*-nitrosubstituted diazo ketones I and II fail to react with the less nucleophilic diazomethane.[6]

On the basis of hydrolytic experiments, the azine structures III and IV were proposed[5] for the products from the reaction of diazoethane with I and II, respectively.[7]



I, R = CH_3
II, R = H



III, R = CH_3
IV, R = H

These reactions provide further examples of the terminal electrophilic reactivity[4] of α-diazo ketones if interpreted in the following reasonable manner:[8]

---

[1] Preliminary report, P. Yates, D. G. Farnum and D. W. Wiley, *Chem. & Ind.*, 69 (1958). Preceding paper, T. J. Clark and P. Yates, *J. Org. Chem.* **27**, 286 (1962).

[2] [a] Present address: Department of Chemistry, University of Toronto. [b] National Institutes of Health Pre-doctoral Fellow, 1957–1959.

[3] L. Wolff, *Liebigs Ann.* **325**, 148 (1902); **394**, 41 (1912).

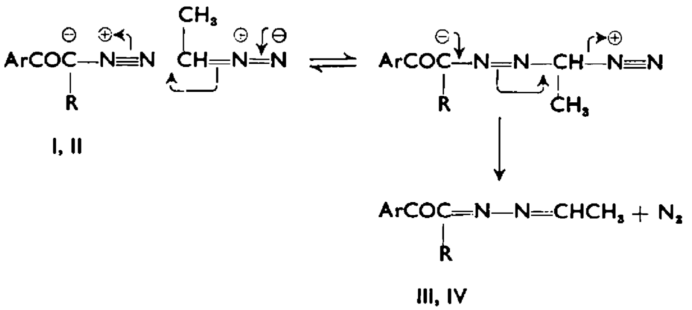
[4] P. Yates and B. L. Shapiro, *J. Amer. Chem. Soc.* **81**, 212 (1959); P. Yates and D. G. Farnum, *Tetrahedron Letters*, No. 17, 22 (1960).

[5] G. Baddeley, G. Holt and J. Kenner, *Nature, Lond.* **163**, 766 (1949).

[6] Cf. A. L. Wilds and A. L. Meader, *J. Org. Chem.* **13**, 763 (1948).

[7] It is probable that the colorless by-products obtained by Wilds and Meader[6] in their preparation of certain diazo ketones from aroyl chlorides and diazoethane are compounds of similar type.

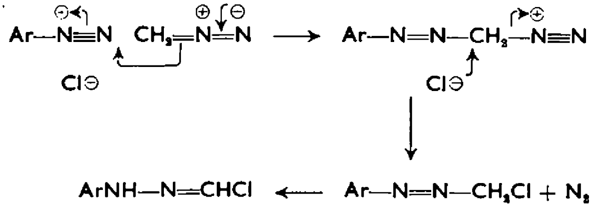
[8] Here and hereafter the *p*-nitrophenyl group is represented by the symbol Ar.



I, II

III, IV

The reactions are reminiscent of the nucleophilic addition of diazomethane to *p*-nitrobenzenediazonium chloride:[9]



In addition to these azine-forming reactions, Baddeley *et al.*[5] reported the further transformation of the azine III in boiling ethanol to a compound, $C_{11}H_9N_3O_2$, and the further reaction of the azine IV with diazoethane to give a compound, $C_{14}H_{17}N_3O_3$; no structural assignments were made for these products. In order to establish the nature of these products and, thus to obtain confirmatory evidence for the correctness of the azine formulations for the products of these unusual reactions of diazo ketones with a weak nucleophile, we have examined these reactions further.

Reaction of α-diazo-*p*-nitropropiophenone with diazoethane in ether gave a pale yellow crystalline product, $C_{11}H_{11}N_3O_3$, in moderate yield. Its spectral data were compatible with its formulation as the azine, III; thus, bands at 5·93 and 6·06 μ in its IR spectrum[10] could be assigned to C=O and C=N stretching vibrations, respectively, and its UV spectrum showed a maximum at 265 mμ (log ε 4·14) in close correspondence with that of *p*-nitroacetophenone at 266·5 mμ (log ε 4·13).[11,12]

When a solution of this compound in aqueous 70% ethanol was boiled for 15 minutes, a new substance, $C_{20}H_{20}N_6O_6$, was formed, whose melting point was very much dependent upon the rate of heating, and, apparently, the history of individual samples, but fell within the range 158–171°. This product presumably corresponds to the material, m.p. 158–159°, obtained in the same manner previously,[5] but assigned heretofore the formula, $C_{11}H_9N_3O_2$. It showed IR bands at 3·04, 6·03 (shoulder), 6·06 and 6·39 μ and UV maxima at 268 mμ (log ε 4·55), and 302–315 mμ (plateau, log ε 4·28). Attempted derivative formation with acetic anhydride or benzaldehyde led to compounds, $C_{11}H_{11}N_3O_4$ and $C_{16}H_{13}N_3O_3$, respectively. These were shown to be the

---

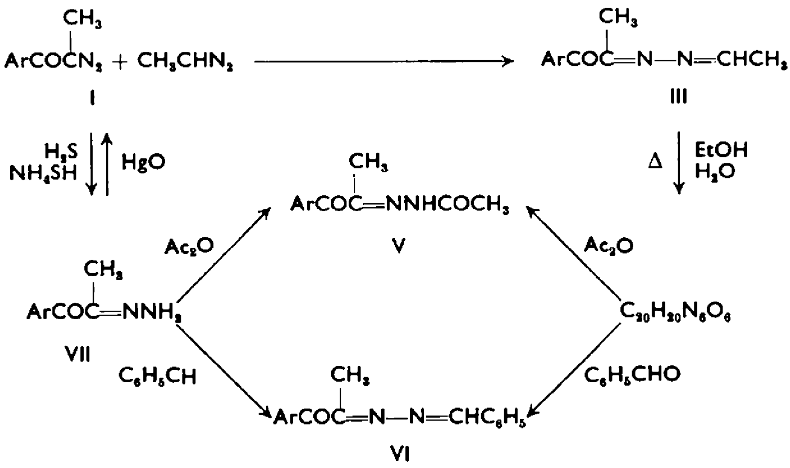
[9] K. Clusius, H. Hürzeler, R. Huisgen and H. J. Koch, *Naturwissenschaften*. **41**, 213 (1954).

[10] Bands characteristic of an aromatic nitro group were also present; such bands appear in all of the IR spectra discussed subsequently, although they are not listed.

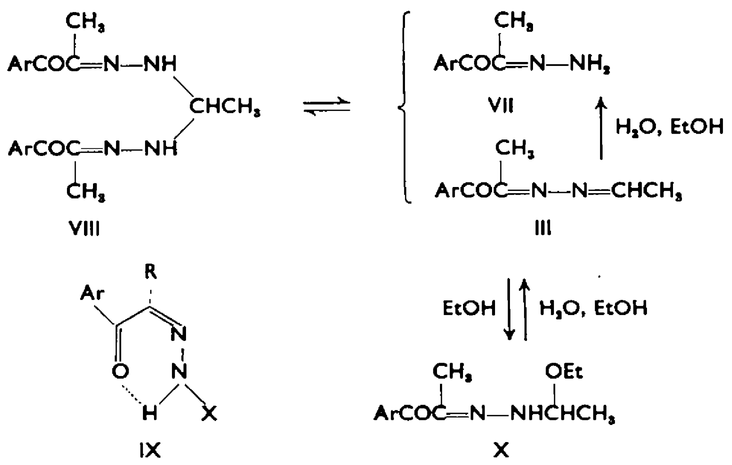
[11] H. Negoro. *Annu. Rept. Takamine Lab.* **6**, 67 (1954).

[12] These spectral data require that there be little interaction between the carbonyl group and the azine system of III.

acetyl derivative (V) and the benzylidene derivative (VI) of the hydrazone VII by comparison with authentic samples. This hydrazone was prepared by reduction of the diazo ketone I with hydrogen sulfide in the presence of a trace of ammonium hydrosulfide.[13] It was obtained in two interconvertible modifications, a yellow and a colorless form; these showed differences in their IR spectra in Nujol mulls, but gave identical solution spectra with bands at 2·95, 3·04, 3·12, 6·09, 6·16 and 6·46 μ. The hydrazone showed a maximum in its UV spectrum at 274 mμ (log ϵ 4·15). Its structure was confirmed by the demonstration that on oxidation with mercuric oxide it was reconverted to the diazo ketone I.



The formation of the hydrazone derivatives V and VI from the compound $C_{20}H_{20}N_6O_6$ suggested its formulation as VIII, which could arise by partial hydrolysis of the azine III to give the hydrazone VII, followed by reaction of the latter with unconsumed azine. The latter reaction would be expected to be readily reversible, thus accounting for the formation of derivatives of VII from VIII.



---

[13] Cf. L. Wolff, *Liebigs Ann.* 394, 23 (1912).

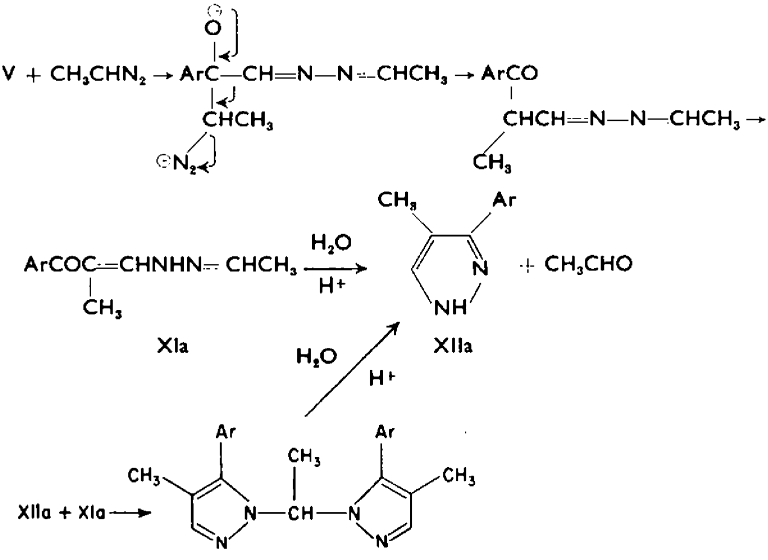
The shift of the carbonyl band in the IR spectrum of VIII to a longer wave length relative to that of the azine III may be interpreted in terms of the hydrogen-bonded array IX, which is also in accord with the position of the N—H stretching band at 3·04 μ. Similar effects may be noted in the IR spectrum of the hydrazone VII, which can possess the system IX. The long wave length band (302–315 mμ) in the UV spectrum of VIII can also be interpreted in these terms, although the fact that the UV spectrum of VII shows no maximum beyond that at 274 mμ appears at first sight to contra-indicate this. Examination of the latter band reveals that it is unsymmetrical and that high intensity absorption continues to considerably longer wave lengths, e.g: ϵ_{305} = 9300; further, when the spectrum of III is subtracted from that of the hydrazone, the resulting curve shows a maximum at 298 mμ (ϵ 7,200).

The assignment of structure VIII was confirmed by the observation that a chloroform solution of equimolar amounts of the azine III and the hydrazone VII was slowly converted to a solution of VIII, as evidenced by the change in the IR spectrum of the solution. Further, brief boiling of a solution of equimolar amounts of III and VII in *absolute* ethanol gave VIII in high yield. When the azine III was treated alone under the same conditions it was converted to a product, $C_{11}H_{12}N_3O_3(OC_2H_5)$, which readily gave VIII in boiling *aqueous* ethanol. The spectra of this product [IR bands at 3·03, 6·08 and 6·42 μ; UV maxima at 268 mμ (log ϵ 4·25) and 305 mμ (log ϵ 4·04)] were remarkably similar to those of VIII and readily permitted its formulation as X, which again can possess the system IX. Clearly, in the absence of added hydrazone, the azine is converted to VIII only in the presence of water, since this is required to form the hydrazone by hydrolysis of the azine.

Treatment of the diazo ketone II with one molar equivalent of diazoethane at 5° gave two yellow crystalline products, m.p. 69–70°d. and 121–122°d. The elemental composition of each compound indicated that they are isomers with the formula $C_{10}H_9N_3O_3$, although, because of its considerable instability, the lower-melting compound could not be obtained in a state of full analytical purity. The lower-melting isomer, with IR bands at 5·93 and 6·09 μ, on being heated at its melting point was converted to the higher-melting isomer, with IR bands at 5·99 and 6·09 μ. These products, therefore, must be two of the four possible geometrical isomers corresponding to the azine IV, the structure which Baddeley *et al.*[5] assigned to the single product which they obtained from this reaction. Reaction of diazoethane with a mixture of these azines, or, more conveniently, reaction of an excess of diazoethane with the parent diazo ketone II, led to the formation of a compound, $C_{12}H_{13}N_3O_3$, m.p. 136–136·5°. This substance gave no evidence of further reaction with diazoethane and apparently corresponds to the compound, m.p. 134–135°, previously assigned the formula $C_{14}H_{17}N_3O_3$.[5] Its IR spectrum included bands at 3·02, 6·08 and 6·16 μ and a broad, complex band at 6·31 μ; it showed maxima in its UV spectrum at 298 mμ (log ϵ 4·36) and 350 mμ (infl., log ϵ 3·95). Identification of the products from the earlier-reported[5] hydrolysis of this compound led to the elucidation of its structure.

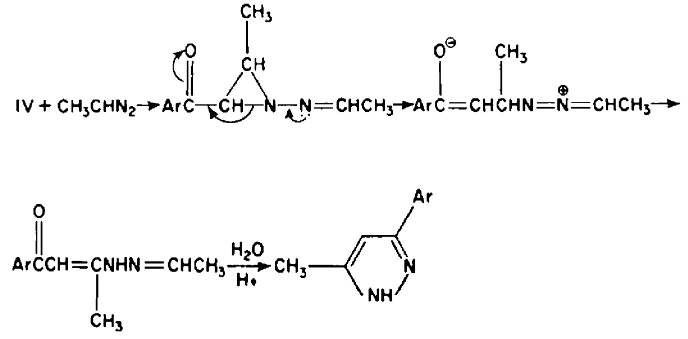
Addition of 2N hydrochloric acid to a solution of the compound in dioxane gave rise to a faintly yellow, crystalline precipitate of a compound. $C_{22}H_{20}N_6O_4$, m.p. 202–202·5°; the supernatant solution, upon dilution with water, afforded a pale yellow crystalline precipitate of a compound, m.p. 179·5–180·5°, also obtained by further hydrolysis of the higher-melting product. The IR spectrum of the latter lacked bands characteristic of NH or carbonyl groups and included bands at 6·24 and 6·44 μ;

its UV spectrum showed maxima at 231 mμ (log ε 4·35) and 318 mμ (log ε 4·34). The UV spectrum of the lower-melting hydrolysis product showed maxima in closely corresponding positions, while its IR spectrum included absorption characteristic of both unassociated (2·92 μ) and hydrogen-bonded (3·13 μ) NH groups and a band at 6·23 μ. The spectra suggested pyrazole formulations for these substances, and on this basis two series of structures could be evolved which would provide an adequate interpretation of the data. Assignment to the compound, $C_{12}H_{13}N_3O_3$, of the structure XIa, derived from the azines IV via a route analogous to a well-known type of reaction of simple ketones,[14] leads to the formulation of the hydrolysis products as 4-methyl-3-*p*-nitrophenylpyrazole (XIIa) and an ethylidenedipyrazole, XIIIa:[15]



XIIIa

Alternatively, homologation of the azine *via* ethyleneimine formation leads to the formulation XIb for the compound, $C_{12}H_{13}N_3O_3$, and XIIb and XIIIb[15] for the hydrolysis products:

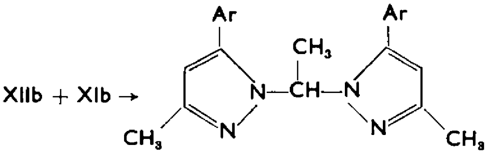


XIb XIIb

---

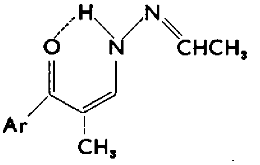
[14] C. D. Gutsche, *Org. Reactions* 8, 364 (1954). It must be noted that simple α, β-unsaturated ketones do not undergo this reaction, except in the presence of a Lewis acid: W. S. Johnson, M. Neeman and S. P. Birkeland, *Tetrahedron Letters* No. 5, 1 (1960). It is probable, however, that the strongly electron-withdrawing *p*-nitrophenyl group could facilitate such reaction in the present case.

[15] Compounds XIIIa and XIIIb may also be formulated as the corresponding ethylidene-1,2′-dipyrazole derivatives.

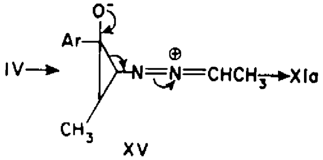


XIIIb

In order to test these views and to distinguish between the two series, the synthesis of the two pyrazoles, XIIa and XIIb was undertaken. Condensation of the known *p*-nitrobenzoylacetone[16] with hydrazine afforded 5-methyl-3-*p*-nitrophenylpyrazole (XIIb), m.p. 196–196·5°, IR bands at 2·93, 6·24 and 6·36 μ, isomeric with the lower-melting hydrolysis product. The observation that the melting point of the pyrazole XIIb corresponded with that recorded for the nitration product of 5-methyl-3-phenylpyrazole[17] suggested a simple synthesis of the isomeric compound XIIa. Treatment of the nitric acid salt of the known 4-methyl-3-phenylpyrazole[18] with concentrated sulfuric acid resulted in the formation of a nitration product XIIa, found to be identical with the lower-melting hydrolysis product. This result leads to the assignment of structure XIa to the product of the action of diazoethane on the azines IV. Further, its IR spectrum suggests its designation as one of the two geometrical isomers XIV.

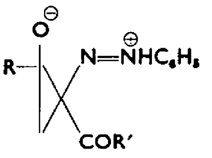


XIV

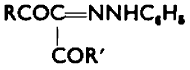


XV

Although the mechanism for the formation of XIa depicted above is that generally held to be operative in the homologation of ketones by diazohydrocarbons, the special structural features of the azines IV permit the possibility of the facilitation of the reaction in this case by formation of the intermediate XV. An intermediate of related type, XVI, could well be important in the closely analogous homologation of systems such as XVII with diazomethane.[19]



XVI



$$\underset{\substack{|\\ \mathrm{COR'}}}{\mathrm{RCOC}}{=}\mathrm{NNHC_6H_5}$$

XVII

It was of interest to find that the higher-melting geometrical isomer of the pair of azines IV reacted more rapidly with diazoethane than did the lower-melting isomer, for, when the isomer mixture was treated with excess of diazoethane at 0°, the carbonyl absorption band at 5·99 μ (characteristic of the higher-melting isomer) disappeared

---

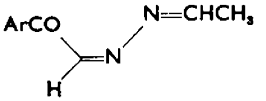
[16] C. R. Hauser, S. W. Swamer and J. T. Adams, *Org. Reactions* **8**, 132 (1954).

[17] E. Koenigs and J. Freund, *Chem. Ber.* **80**, 143 (1947).

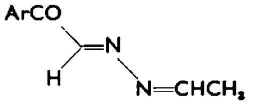
[18] C. Barat, *J. Ind. Chem. Soc.* **8**, 801 (1931).

[19] P. B. Russell, *J. Amer. Chem. Soc.* **75**, 5315 (1953).

from the IR spectrum of the reaction mixture more rapidly than that at 5·93 μ (characteristic of the lower-melting isomer). This difference in reactivity allows tentative, partial assignments of stereochemistry to be made for the two azines, on the view that the relative resistance to reaction in the case of the lower-melting isomer is steric in origin and is due to the *syn* orientation of the N—N bond relative to the *p*-nitrobenzoyl group as in XVIIIa. The higher-melting azine is then assigned the *anti* configuration as in XVIIIb (no conclusion can be reached in either case with regard to the stereochemistry at the other C═N bond).



XVIIIa



XVIIIb

The difference in the positions of the carbonyl-stretching bands in the infrared spectra of the isomeric azines can also be interpreted in terms of the stereochemical assignments XVIIIa and XVIIIb. A similar steric factor can be invoked to account for the failure of the α-methyl substituted azine III to react as rapidly with diazoethane as the azine XVIIIb.[5]

EXPERIMENTAL[20]

N-*Nitroso*-N-*methylurea* was prepared according to the method of Arndt.[21] When the operation was carried out on a scale twice that recommended, the time and attention required in the nitrosation were effectively reduced by carrying out this step in a 6-l. battery jar and stirring the reaction mixture with a polyethylene paddle driven by means of a moderate speed motor. Such stirring facilitated relatively rapid delivery of the methylurea-sodium nitrite mixture to the ice-sulfuric acid mixture with minimal foaming and temp rise, and, once the flow of the nitrite-urea solution had been suitably adjusted by means of a screw clamp attached to a syphon, the reaction could be left unattended until the addition was complete.

N-*Nitroso*-N-*ethylurea* was prepared in the same manner as that for the *N*-methyl derivative with the same molar ratio of reactants. The yield of dried product was ca. 50%.

Diazomethane was prepared by the procedure of Arndt.[22] Purification was effected by decantation and drying over solid potassium hydroxide rather than by distillation.

Diazoethane. (i) *From* N-*nitroso*-N-*ethylurea without distillation*. The preparation was carried out in the same manner as for diazomethane. The yields, however, were unpredictable, varying from 5 to 40%, as determined by the benzoic acid method.

(ii) *From* N-*nitroso*-N-*ethylurea with distillation*. In order to minimize the hazard encountered in the distillation of diazoalkanes, the following simple procedure was utilized: the reaction vessel, a suction flask of appropriate capacity, was connected by means of rubber stoppers, fire-polished glass tubing, and Tygon tubing to a receiver, also a suction flask of suitable size, containing a little ether. After the diazoethane had been prepared in the reaction flask in the usual manner by slow addition of the nitrosoethylurea to a well cooled, stirred mixture of aqueous base and ether, the receiving flask was immersed in a Dry Ice-acetone bath, the reaction mixture was stirred with a magnetic stirrer at room temp, and the system was evacuated with a water aspirator. The pressure was controlled by means of a needle valve such that the ether and diazoethane distilled at a moderate rate. The ethereal diazoethane solution could be obtained sufficiently dry for use in the present work by decantation from the thin coat of ice formed in the receiving flask. Application of this procedure to the preparation of diazomethane as a control resulted in a negligible reduction in yield as compared with the usual method. The preparation of diazoethane resulted in consistent, though moderate, yields of 20 to 30%.

---

[20] M.ps. are uncorrected. IR 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 film.

[21] F. Arndt, *Organic Syntheses* (Revised ed) Coll. Vol II p. 461. John Wiley, New York (1943).

[22] F. Arndt, *Organic Syntheses* (Revised ed.) Coll. Vol II p. 165. John Wiley, New York (1943).

*α-Diazo-*p*-nitropropiophenone* (I)

A solution of *p*-nitrobenzoyl chloride (9·2 g, 0·05 mole) in the minimal amount of ether was added slowly to a well stirred solution of diazoethane (0·105 mole) in ether maintained at −20° by immersion in acetone to which pieces of Dry Ice were added periodically. The resultant yellow slurry was stirred at −20° for an additional 15 min. Excess diazoethane was removed with water aspirator suction and the mixture was allowed to warm to room temp and concentrated at red press. The lemon yellow needles thus obtained were washed with cold ether and recrystallized from carbon tetrachloride to give long, bright yellow needles (7·6 g, 75%), m.p. 112–114° d. (lit[5] m.p. 112°).

*α-Diazo-*p*-nitroacetophenone* (II)

p-Nitrobenzoyl chloride (9·0 g, 0·048 mole) was dissolved in the minimal amount of ether and the solution was added slowly to a cold, well stirred solution of diazomethane (0·10 mole) in ether (200 ml) immersed in an ice bath. After the addition was complete, stirring was continued for a further 1 hr. The yellow slurry was concentrated to a small volume at room temp with water aspirator suction and chilled to −25°. The resulting yellow needles were collected and washed well with cold ether. The crude product (7·9 g, 86%), m.p. 117–120° d, was sufficiently pure for further reactions; recrystallization could be effected from carbon tetrachloride to give long, light yellow needles, m.p. 119–120° d (lit[23] m.p. 118°).

*Reaction of diazoethane with α-diazo-*p*-nitropropiophenone*

Formation of 1-(p*-nitrobenzoyl)-acetalazine* (III). A solution of diazoethane (4·1 mmole) in ether (15 ml) was added to a slurry of α-diazo-*p*-nitropropiophenone (700 mg, 3·9 mmole) in ether (10 ml) at 5°. The mixture was allowed to warm to room temp and stand for 16 hr with intermittent swirling. The solvent was then evaporated by gentle warming of the mixture on the steam bath at water aspirator pressure. The residue was taken up in warm methanol and the solution was chilled to 0°. The very faintly yellow, fluffy needles which deposited (270 mg, 34%), m.p. 99–100°, upon recrystallization from methanol, afforded an analytical sample, m.p. 100–100·5°. (Found: C, 56·71; H, 4·99; N, 18·15; Calc. for $C_{11}H_{11}N_3O_3$: C, 56·65; H, 4·75; N, 18·02%). $\lambda_{max}(CHCl_3)$ 5·93, 6·06 μ. $\lambda_{max}(CH_2Cl_2)$ 265 mμ (log ε 4·14).

Reaction of III *with aqueous ethanol*

Formation of VIII. A solution of III (280 mg, 1·2 mmole) in aqueous 70% ethanol (2·5 ml) was boiled for 15 min on the steam bath. The mixture of yellow needles and yellow solution was chilled to 0° and the bright yellow needles of VIII (164 mg, 61%), m.p. 166·5–169°, were recrystallized from absolute ethanol to give an analytical sample, m.p. 167–169·5°. Found: C, 54·83; H, 4·41; N, 19·16, 18·96; Calc. for $C_{20}H_{20}N_6O_6$: C, 54·54; H, 4·58; N, 19·08%). $\lambda_{max}(CHCl_3)$ 3·04, 6·03 (sh), 6·06, 6·39 μ. $\lambda_{max}(CH_2Cl_2)$ 268 mμ (log ε 4·55), 302–315 mμ (plateau, log ε 4·28).

Reaction of VIII *with acetic anhydride*

Formation of V. A solution of VIII (75 mg, 0·36 mmole) in acetic anhydride (2 ml) was boiled under reflux for 1 hr in the presence of a little sodium acetate. The solution was cooled, diluted with water, scratched, and the pale yellow solid which deposited was recrystallized from absolute ethanol. White, opaque needles of V (45 mg, 49%), m.p. 163–165°, were thus obtained. Two recrystallizations from methanol gave material, m.p. 165·5–166·5°. $\lambda_{max}(CHCl_3)$ 3·04, 5·81, 5·94, 5·99 μ. $\lambda_{max}(CH_2Cl_2)$ 245 mμ (log ε 4·08), 278 mμ (log ε 4·29). The melting point of this product was not depressed on admixture with an authentic sample of V (*vide infra*). The IR spectra of these products were identical.

Reaction of VIII *with benzaldehyde*

Formation of VI. A solution of VIII (70 mg, 0·33 mmole) in absolute ethanol (5 ml) was treated with benzaldehyde (0·5 ml) and a crystal of *p*-toluenesulfonic acid. The dark solution was boiled for 5 min on the steam bath, chilled in an ice bath, scratched, and the resultant yellow microcrystalline material (40 mg, 41%), m.p. 110–112°, was collected. Recrystallization from hexane afforded an analytical sample, m.p. 112·5–114°. (Found: N, 13·97, 14·25; Calc. for $C_{16}H_{13}N_3O_3$: N, 14·23%) $\lambda_{max}(CHCl_3)$ 5·98, 6·18 μ.

---

[23] P. Karrer and J. Schukri, *Helv. Chim. Acta.* **28**, 820 (1945).

1-(p-*Nitrophenyl*)-1,2-*propanedione* 2-*hydrazone* (VII)

A slurry of α-diazo-*p*-nitropropiophenone (500 mg, 2·4 mmoles) in 95% ethanol was chilled in an ice bath and saturated with gaseous hydrogen sulfide. A few drops of an ammonium hydrosulfide-hydrogen sulfide solution (prepared by saturation of an aqueous 20% ammonia solution with hydrogen sulfide gas) were added to the slurry. A moderate stream of hydrogen sulfide was passed through the mixture for 3 hr at 0° with intermittent swirling of the suspension. The pale yellow rods which deposited were filtered, washed with cold absolute ethanol and digested with carbon disulfide; the resulting colorless needles, m.p. 171–172.5°, were collected. The ethanolic filtrate and washings were diluted to ca. 40 ml with water, chilled, and the faintly yellow needles which deposited, m.p. 167–169° were collected (combined yield, 307 mg, 61%). Two recrystallizations from benzene–carbon disulfide and one from benzene-hexane afforded a sample for analysis as glistening, yellow leaflets, m.p. 173–173·2°, turning colorless at 125°. (Found: C, 52·01: H, 4·58; N, 20·40; Calc, for $C_9H_9N_3O_3$: C, 52·17; H, 4·38; N, 20·28%). Yellow leaflets: λ_{max}(Nujol) 2·92, 3·03, 3·13, 6·04, 6·06 (sh), 6·16, 6·36 μ; λ_{max}($CHCl_3$) 2·95, 3·04, 3·12, 6·09, 6·16, 6·46 μ; λ_{max}(CH_2Cl_2) 274 mμ (log ε 4·15). White needles: λ_{max}(Nujol) 2·94, 3·03, 3·10, 6·04, 6·12, 6·37 μ; IR spectrum in $CHCl_3$ identical with that of yellow product in $CHCl_3$.

Mercuric oxide oxidation of VII

Formation of I. A mixture of VII (109 mg, 0·53 mmole), yellow mercuric oxide (190 mg, 0·87 mmole) and anhydrous magnesium sulfate (100 mg) was ground to a powder in an agate mortar. The powder was added to cold ether (2 ml), and benzene (2 ml) and a solution of sodium methoxide in methanol (5 drops) were added. The suspended solid darkened rapidly and, after 30 min at 30°, the mixture was filtered. The black residue was washed with benzene until the washings were colorless, and the combined filtrate and washings were concentrated in a dry air stream. The yellow solution was brought to boiling, diluted with hexane to cloudiness, and chilled to 0°. The resultant yellow crystals (53 mg, 49%), m.p. 107–109° d., were identified as α-diazo-*p*-nitropropiophenone by IR spectral comparison and a mixed m.p. determination with an authentic sample.

Acetyl derivative of VII (V)

A solution of VII (150 mg, 0·72 mmole) in acetic anhydride (1·5 ml) was boiled for 5 mins, then chilled to 0°, and the faintly yellow crystals which deposited were collected and washed with several portions of cold hexane. The dense white rods thus obtained (140 mg, 78%), m.p. 165·5–166·5°, were recrystallized several times from 95% ethanol to give an analytical sample, m.p. 167·5–168·5°. (Found: C, 53·18; H, 4·51; N, 17·06; Calc. for $C_{11}H_{11}N_3O_4$: C, 53·01; H, 4·45; N, 16·86%). λ_{max}($CHCl_3$) 3·04, 5·81, 5·92, 5·99 μ.

Benzylidene derivative of VII (VI)

A solution of VII (100 mg, 0·49 mmole) in boiling 95% ethanol was treated with benzaldehyde (3 drops) and a few crystals of *p*-toluenesulfonic acid. The solution was allowed to stand for 1 hr at 30°, chilled, and the resultant yellow microcrystalline material (101 mg, 70%), m.p. 106–110°, was collected. Recrystallization from hexane afforded bright yellow, fluffy needles, m.p. 113–114°, shown to be identical with the product from the reaction of VIII with benzaldehyde (*vide supra*) by IR spectral comparison and a mixed m.p. determination.

Preparation of VIII *from* III *and* VII

A mixture of III (117 mg, 0·50 mmole) and VII (104 mg, 0·50 mmole) were ground together in an agate mortar, and 30 mg of the mixture was removed for the recording of an IR spectrum. This IR spectrum, taken immediately upon solution in chloroform, was essentially that of III superimposed upon that of VII; after standing for 6 days in a closed tube, the solution exhibited a spectrum almost identical with that of VIII except for a few bands attributable to a small amount of contamination with VII. The remaining material was dissolved in absolute ethanol (1 ml) and the solution was boiled for 15 mins. The precipitation of yellow needles was soon observed. The mixture was chilled to 0° and the bright yellow needles thus obtained (120 mg, 63%), m.p. 166–169°, were shown to be identical with VIII by means of an IR spectral comparison and a mixed m.p. determination.

Reaction of III *with absolute ethanol*

Formation of X. A solution of III (6·0 g) in absolute ethanol (10 ml) was boiled under reflux for 30 min. The mixture was cooled and the solid which separated was recrystallized 4 times from absolute ethanol to give X as almost colorless prisms, m.p. 126–127°. (Found: C, 55·92; H, 5·83; N, 15·01; OC_2H_5, 16·36; Calc. for $C_{13}H_{17}N_3O_4$: C, 55·90; H, 6·14; N, 15·05%) 1 OC_2H_5, 16·13 $\lambda_{max}(CHCl_3)$ 3·03, 6·08, 6·42 μ. λ_{max}(95% EtOH) 268 mμ (log ε 4·25), 305 mμ (log ε 4·04). When this product was treated with boiling aqueous ethanol it was rapidly converted to VIII.

*Reaction of diazoethane with α-diazo-*p*-nitroacetophenone* (II)

Formation of XVIIIa (= IV) *and* XVIIIb (= IV). A solution of diazoethane (0·054 mole) in ether (230 ml) was added at 5° to a stirred solution of α-diazo-*p*-nitropropiophenone (8·03 g, 0·042 mole) in dichloromethane (150 ml) over a period of 24 hr. A 190 ml portion of the reaction mixture was concentrated to small volume by evaporation in a stream of nitrogen; removal of the remaining solvent *in vacuo* left a dark red, viscous oil (5·28 g). This was treated with benzene (15 ml) and scratched to give a yellow crystalline product (0·72 g) shown to be XIa (*vide infra*) by IR spectral comparison. The orange mother liquor was freed of solvent by evaporation in a stream of nitrogen and the residual red oil (4·53 g) was taken up in ether (10 ml). The solution was cooled at −72° and scratched; the resulting mixture was allowed to warm to room temp and then cooled in an ice-bath for 45 min. The resulting yellow solid (0·44 g, 10%) was collected by centrifugation and washed with ice-cold ether. Recrystallization from ether in the same fashion gave XVIIIb, m.p. 121–122° d. (Found: C, 54·70; H, 4·08; N, 19·14; Calc. for $C_{10}H_9N_3O_3$: C, 54·79; H, 4·14; N, 19·17%) $\lambda_{max}(CHCl_3)$ 5·99, 6·09, 6·29 μ. The ethereal mother liquors and washings were combined and concentrated to 11–12 ml. The resulting solution was cooled at −72° for 3 days. The yellow solid (0·21 g, 5%) which was deposited was recrystallized from ether at −20° to give XVIIIa, m.p. 69–70° d; this product darkened at room temp and a subsequent attempt to recrystallize it led to extensive decomposition. (Found: C, 55·43; H, 4·78; N, 19·17; Calc for $C_{10}H_9N_3O_3$: C, 54·79; H, 4·14; N, 19·17%). $\lambda_{max}(CHCl_3)$ 5·93, 6·09, 6·22 μ.

When a sample of XVIIIa, m.p. 69–70°, was heated above its m.p. it slowly resolidified and remelted at 114°. Recrystallization of this material from ether gave a product, m.p. 119–120° d., shown to be XVIIIb by IR spectral comparison.

When the reaction between α-diazo-*p*-nitroacetophenone (9·35 g, 0·049 mole) and diazoethane (0·050 mole) was carried out at −30° to −5°, the yield of XVIIIa was considerably increased (2·8 g, 27%), but no XVIIIb was isolated; XIa was also formed.

*Reaction of excess diazoethane with α-diazo-*p*-nitroacetophenone* (II)

Formation of XIa. A cold solution of diazoethane (10 mmole) in ether was gradually added to a swirled solution of α-diazo-*p*-nitroacetophenone (1·7 g. 8·9 mmole) in dichloromethane maintained near −20° by immersion of the container in a Dry-Ice-acetone bath. The initially formed deep red color faded gradually. The container was stoppered with a drying tube containing potassium hydroxide pellets, and was maintained at ca. −20° for 24 hr. The IR spectrum ($CHCl_3$) of the viscous oil obtained upon evaporation of an aliquot of the reaction mixture included strong bands at 5·93 and 5·99 μ. The solution was allowed to warm to 0° and treated with further ethereal diazoethane (10 mmole). After 1 hr at 0°, the IR spectrum, determined as before, lacked significant absorption at 5·99 μ, but still possessed a strong band at 5·93 μ. The band at 5·93 μ, although diminishing in intensity, persisted throughout the reaction period. After 30 hr at 0°, the resultant yellow solution was evaporated to dryness in a dry air stream. The red, viscous residue, upon trituration with cold benzene, afforded yellow crystals of XIa (350 mg, 16%), m.p. 134–135·5°. Several recrystallizations from methanol afforded an analytical sample, m.p. 136–136·5°. Found: C, 58·24; H, 5·46; N, 17·04; Calc. for $C_{12}H_{13}N_3O_3$: C, 58·29; H, 5·30; N, 17·00%) $\lambda_{max}(CHCl_3)$ 3·02, 6·08, 6·16, 6·31 μ. λ_{max}(Nujol) 3·12, 3·17, 6·08, 6·12 (sh), 6·53 μ. $\lambda_{max}(CH_2Cl_2)$ 298 mμ (log ε 4·36), 344 mμ (sh, log ε 3·95). Compound XIa was also obtained when the azine XVIIIb was treated with ethereal diazoethane.

Hydrolysis of XIa

Formation of XIIa *and* XIIIa. Hydrochloric acid (2 N) was added dropwise with swirling to a solution of XIa (40 mg, 0·16 mmole) in dioxane (0·5 ml). When precipitation of a white solid began, the addition was discontinued. The solution was kept at room temp for 15 min with intermittent swirling and then chilled in the refrigerator. Colorless needles of Compound XIIIa were thus obtained (20 mg, 57%), m.p. 201·5–202·5°. A sample for analysis, m.p. 202–202·5°, was obtained by recrystallization from dichloromethane-hexane. (Found: C, 60·66, 61.15; H, 4·77, 4·81; N, 19·20; Calc. for

$C_{22}H_{20}N_6O_4$: C, 61·10; H, 4·66; N, 19·44%). $\lambda_{max}(CH_2Cl_2)$6·24, 6·44, 6·58 (sh), 6·62, 7·40, 7·45 μ. $\lambda_{max}(CH_2Cl_2)$ 231 mμ (log ε 4·35), 318 mμ (log ε 4·34).

The mother liquors from the above preparation were diluted to 5 ml with water and chilled, and the resultant white ppt (9 mg, 27%), m.p. 176·5–178°, was recrystallized from aqueous ethanol to give XIIa as colorless needles, m.p. 179·5–180·5°. $\lambda_{max}(CH_2Cl_2)$ 2·92, 3·13, 6·23, 6·61, 7·45 μ. λ_{max} (95% EtOH) 225 mμ (log ε 4·12), 317 mμ (log ε 4·13). This substance and 4-methyl-3-*p*-nitrophenylpyrazole (*vide infra*) were shown to be identical by means of infrared spectral comparison and a mixed m.p. determination.

5-*Methyl*-3-p-*nitrophenylpyrazole* (XIIb)

p-Nitrobenzoylacetone was prepared in 41% yield as faintly yellow rhombs, m.p. 114·5–115° (lit[16] m.p. 115°), by the procedure of Hauser *et al.*[16] A solution of this diketone (200 mg, 0·48 mmole) in hot absolute ethanol (ca. 1 ml) was treated with hydrazine (5 drops). After a few min, the dark solution was brought to the b.p. and diluted with water to the cloud point. The faintly yellow leaflets of XIIb (150 mg, 77%), m.p. 196·0–196·5°, which separated on cooling the solution, were recrystallized from aqueous ethanol to give a sample for analysis as faintly yellow needles, m.p. 196–196·5°. (Found: C, 58·92; H, 4·26; N, 20·37; Calc. for $C_{10}H_9N_3O_2$: C, 59·10; H, 4·46; N, 20·68%). $\lambda_{max}(CH_2Cl_2)$ 2·93, 6·24, 6·36 μ. λ_{max}(95% EtOH) 219 mμ (log ε 4·10), 319 mμ (log ε 4·19).

4-*Methyl*-3-p-*nitrophenylpyrazole* (XIIa)

A solution of 4-methyl-3-phenylpyrazole[18] (500 mg, 3·2 mmole) in acetic acid (5 ml) was treated with conc nitric acid (0·5 ml), and the mixture was warmed on a steam bath to effect solution of the immediately formed white ppt. Upon gradual cooling the solution deposited long, colorless rods (700 mg, 100%), 155–157° d, λ_{max}(Nujol) 3·8, 6·32, 6·40, 6·61, 6·70, 7·06, 7·46, 7·63 μ.

This salt (200 mg, 0·91 mmole) was treated with conc sulfuric acid (1 ml) and the yellow solution was warmed for 30 min on the steam bath, then poured into cold water. The colorless ppt was collected and stirred with aqueous 10% sodium bicarbonate on the steam bath; the pale yellow crystalline residue was recrystallized from aqueous ethanol. The faintly yellow needles of XIIa thus obtained (100 mg, 55%), m.p. 179–180°, upon recrystallization from aqueous ethanol afforded an analytical sample, m.p. 181·5–182°. (Found: C, 59·11; H, 4·61; N, 20·77; Calc. for $C_{10}H_9N_3O_2$: C, 59·10; H, 4·46; N, 20·68%). $\lambda_{max}(CH_2Cl_2)$ 2·92, 3·13, 6·23, 6·61, 7·45. λ_{max}(95% EtOH) 225 mμ (log ε 4·12), 317 mμ (log ε 4·13).