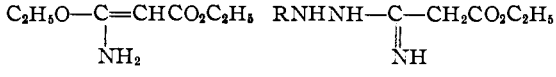
[COMMUNICATION NO. 1198 FROM THE KODAK RESEARCH LABORATORIES]

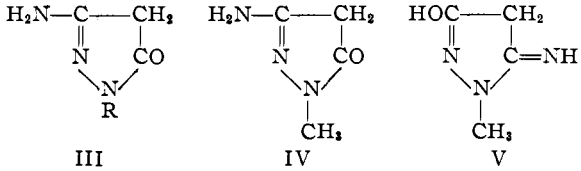
Investigation of Pyrazole Compounds. VIII.[1] Synthesis and Acylation of Pyrazolones Derived from Hydrazine and Methylhydrazine

BY BRUCE GRAHAM, H. D. PORTER AND A. WEISSBERGER

Aromatic hydrazines and ethyl β-amino-β-ethoxyacrylate, I,[2] form the respective ethyl β-imino-β-(β-R-hydrazino)-propionates, II,[2] and/or 1-R-3-amino-5-pyrazolones, III.[3] The isolation of the intermediate, II, in high yields (80–90%) proves (1) that the $=C(NH_2)OC_2H_5$ group of I reacts in preference to the $-CO_2C_2H_5$ group, and (2) that the β-nitrogen atom of the aromatic hydrazines is much more reactive (basic) than the α-nitrogen atom. The latter observation agrees with the fact that aromatic hydrazines are acylated in the β-position exclusively.[4] However, aliphatic hydrazines are acylated[5] primarily at the more basic[6] α-nitrogen atom, although some acylation takes place in the β-position.[7] In a similar twofold reaction, *methylhydrazine* reacted with I to give two isomers: a compound melting at 180–182° in a yield of 47%, and another compound melting at 192–194° in a 6% yield. Both isomers analyze for the cyclized products, IV or V, and form soluble dyes in the oxidation film-strip test[8] and by condensation with *p*-nitrosodimethylaniline.[9] The formation of dye with both isomers in this latter test is unusual, because 1-aryl or 1-heterocyclic substituted 3-hydroxy-5-pyrazolone imides, *i. e.*, the isomers corresponding to V, give no dye in this test.[9] The fact that the higher-melting isomer obtained from methylhydrazine gives more dye with nitrosodimethylaniline than the lower-melting isomer, suggests[9] the structure *1-methyl-3-amino-5-pyrazolone*, IV, for the compound melting at 192–194°, and the structure *1-methyl-3-hydroxy-5-pyrazolone imide*, V, for the compound melting at 180–182°.



I II



III IV V

An attempt was made to prove the structure of the higher-melting compound to be IV by an unequivocal synthesis similar to that described in the first paper of this series.[10] 1-Methyl-3-carbethoxy-5-pyrazolone, VI, was prepared from methylhydrazine and ethyl oxalacetate. No intermediate methylhydrazone could be isolated in the reaction. However, the product couples in the film-strip test[8] which proves it to be VI and excludes the remotely possible structure, VII. Next, VI was converted to the hydrazide, VIII, and many attempts were made to obtain the azide, IX, from the latter. However, at best only a trace of the azide was isolated because nitrous acid reacted at the 4-position of the pyrazolone ring under the conditions of the experiments. Kufferath[11] got similar results when he treated 5-pyrazolone-3-acethydrazide with nitrous acid. The difference in reactivity between VIII and 1-phenyl-5-pyrazolone-3-carboxhydrazide[10] toward nitrous acid is noteworthy, since the 4-position of the latter is unaffected during the formation of the azide. Excess nitrous acid produced X in good yield. The compound gave uninviting products when subjected to the Curtius degradation.

In order to avoid nitrosation at the 4-position, VI was treated with *p*-methoxybenzenediazonium chloride to give XI. This was converted to the hydrazide, XII, which readily formed the azide, XIII. This azide was subjected to the Curtius degradation, producing 1-methyl-3-amino-4-(*p*-methoxyphenylazo)-5-pyrazolone. XVI, by way of the intermediates, XIV and XV XVI is a red dye, melting at 172–174°.

The two products from the reaction of methylhydrazine with I were treated with *p*-methoxybenzenediazonium chloride to produce dyes for comparison with XVI. The higher-melting (192–194°) compound formed a red dye, melting at 172–174°, identical in every respect with XVI. The parent compound is, therefore, 1-methyl-3-amino-5-pyrazolone, IV. The lower-melting (180–182°) product formed a bright yellow dye, melting at 240–242°, XVII.

Upon benzoylation with two moles of benzoyl chloride in pyridine, IV and V yielded the dibenzoyl derivatives, XVIII, melting at 146–148°,

(1) Weissberger, Porter and Gregory, VII, THIS JOURNAL, **66**, 1851 (1944).

(2) This compound, previously[1] formulated as ethyl malonate monoimidoester, $C_2H_5OCCH_2CO_2C_2H_5$ (NH), was shown by Glickman and Cope [*ibid.*, **67**, 1017 (1945)] to be the tautomer, I. We continue to formulate the *hydrazine* derivative, II, as an imino compound without wishing to imply that this structure is more probable than other tautomeric forms.

(3) All derivatives of pyrazole, which, by prototropic shifts, could form pyrazolones are named pyrazolones [see Weissberger and Porter, *ibid.*, **64**, 2133 (1942)].

(4) Fischer, *Ann.*, **190**, 125 (1878).

(5) Michaelis and Hadanek, *Ber.*, **41**, 3286 (1909).

(6) Sidgwick, "The Organic Chemistry of Nitrogen," 2nd ed., Oxford Press, New York, N. Y., 1937, p. 378.

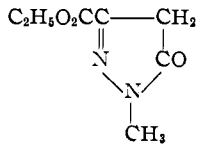
(7) Folpmers, *Rec. trav. chim.*, **34**, 34 (1915).

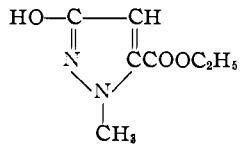
(8) Weissberger and Porter, THIS JOURNAL, **65**, 1495 (1943).

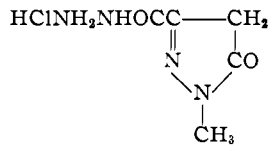
(9) Weissberger and Porter, *ibid.*, **65**, 732 (1943); **66**, 1849 (1944).

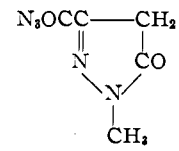
(10) Weissberger and Porter, *ibid.*, **65**, 1495 (1943).

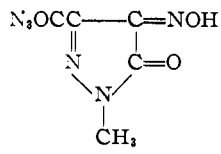
(11) Kufferath, *J. prakt. Chem.*, **65**, 336 (1901).

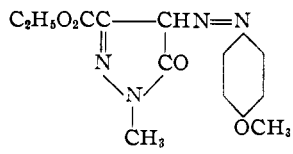

VI

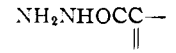

VII


VIII

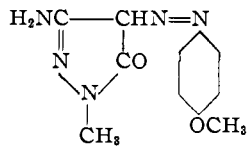

IX

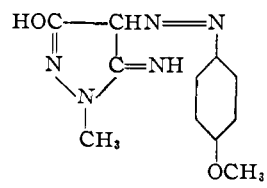

X

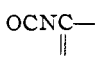

XI

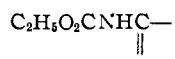

XII


XIII

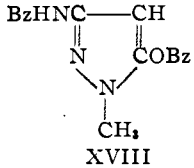

XVI

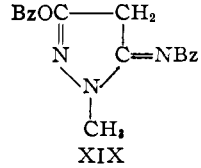

XVII

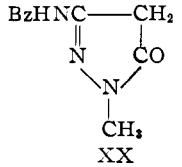

XIV

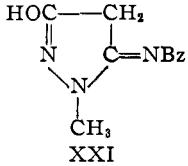

XV

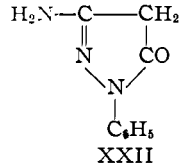
and XIX, melting at 150–153°, respectively. Both are insoluble in dilute sodium carbonate solution, but with alcoholic potassium hydroxide at room temperature, one benzoyl group was hydrolyzed from each of these compounds. The monobenzoyl derivative, XX, of IV formed in the film-strip test a magenta dye typical of 1-aryl-3-benzamido-5-pyrazolones. The corresponding derivative, XXI, of V formed no dye on the film strip but did form a very soluble blue dye in the test solution. It is noteworthy that the difference in the color test, which is pronounced[9] with the 1-phenyl derivatives, XXII and XXIII, and which is smaller with the 1-methyl derivatives, IV and V, becomes strong again if the 1-methyl pyrazolones bear a phenyl group on the 3-amino, XXIV, or the 5-imino nitrogen, XXV.[9] The relative yields of IV and V are those to be expected if the $=C(NH_2)OC_2H_5$ group of I reacts first and predominantly with that nitrogen which is more reactive in common acylations.[5,7]

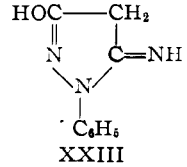

XVIII

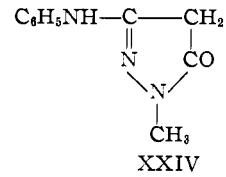

XIX

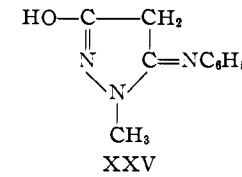

XX


XXI


XXII


XXIII


XXIV


XXV

Two isomers were also formed in the condensation of α-carbethoxyacetothioacetanilide with methylhydrazine,[9] *viz.*, 1-methyl-3-anilino-5-pyrazolone, XXIV, in 11% yield and 1-methyl-3-hydroxy-5-pyrazolone anil, XXV,[9] in 2% yield. If, as we assumed,[1] the $-CO_2C_2H_5$ group reacts first in this case, the relative yields agree with the higher reactivity of the α-nitrogen in methylhydrazine because XXIV is the result of primary reaction with the α-nitrogen atom, while XXV is the result of primary reaction at the β-nitrogen. However, the low total yield renders these observations rather inconclusive.

Methylhydrazine reacts with ethyl cyanoacetate under very mild conditions and *without alkali* to produce a mixture of IV and V. The yields are 29 and 26%, respectively. The high yield of *cyclized* products is rather surprising in view of the results obtained with hydrazine and with phenylhydrazine. When reacted with ethyl cyanoacetate *in the absence of alkali, hydrazine* produces only cyanoacethydrazide (quantitative),[12] and *phenylhydrazine* produces only cyanoacetphenylhydrazide[13] (10%, see Experimental). The cyanoacethydrazide and the cyanoacetphenylhydrazide can be cyclized in the presence of alkali to 3-amino-5-pyrazolone, XXVI,[14] and 1-phenyl-3-hydroxy-5-pyrazolone imide, XXIII,[13] respectively.

The same three hydrazines reacted with ethyl cyanoacetate *in the presence of two moles of sodium*

(12) Darapsky and Hillers, *J. prakt. Chem.*, **92**, 297 (1915).
(13) Weissberger and Porter, THIS JOURNAL, **65**, 52 (1943).
(14) Hepner and Fajersztejn, *Bull. soc. chim.*, **4**, 854 (1937).

methylate. Methylhydrazine and *hydrazine* gave no color-forming products so this reaction was not explored further. Phenylhydrazine formed 1-phenyl-3-amino-5-pyrazolone, XXII,[3] in 43% yield.

The different behavior of the three hydrazines in the absence of caustic alkali can be explained by the high basicity of the methylhydrazine. It appears that the latter takes over the role which, in the reaction of phenylhydrazine, is played by sodium methylate, and that methylhydrazine acts as its own condensing and cyclizing agent. The nitrile group probably reacts with the more reactive α-nitrogen of methylhydrazine to produce the intermediate, $CH_3N(NH_2)C(NH)CH_2COOC_2H_5$, which immediately cyclizes, forming V. IV is probably produced by an initial reaction of the carbethoxy group at the α-nitrogen of the methylhydrazine to form the intermediate, $CH_3N(NH_2)COCH_2CN$, which cyclizes to IV.

The formation of the two isomers, IV and V, might also be explained by a primary reaction of the nitrile group at the β-nitrogen and at the α-nitrogen of the methylhydrazine, respectively. However, we are inclined to believe that the relative yields would then probably show a larger difference and would be in the opposite direction.

Hepner and Fajersztejn[14] prepared several acyl derivatives of 3-amino-5-pyrazolone. Acetylation with boiling acetic anhydride gave two isomeric triacetyl derivatives, melting at 190° and 130°. They considered them to be 1,4,4-triacetyl-3-imino-5-ketopyrazolidine, XXVII (R = CH_3), and 2,4,4-triacetyl-3-imino-5-ketopyrazolidine, XXVIII (R = CH_3), respectively, because neither compound reacted with nitrous acid, and boiling water hydrolyzed both to the parent compound. The same authors obtained a tribenzoyl derivative, melting at 183°, by a Schotten–Baumann reaction of XXVI with benzoyl chloride. They formulate this, by analogy, as 1,4,4-tribenzoyl-3-imino-5-ketopyrazolidine, XXVII (R = C_6H_5).

In our work, by using sodium methylate for the cyclization of cyanoacethydrazide we raised the melting point of XXVI by 10°. XXVI was also obtained by the reaction of I with hydrazine. On heating with acetic anhydride on the steam-bath and fractional crystallization, XXVI gave two triacetyl derivatives, melting at 202° and 130°. Not only the latter but probably also the higher-melting compound are identical with the products obtained by Hepner and Fajersztejn.

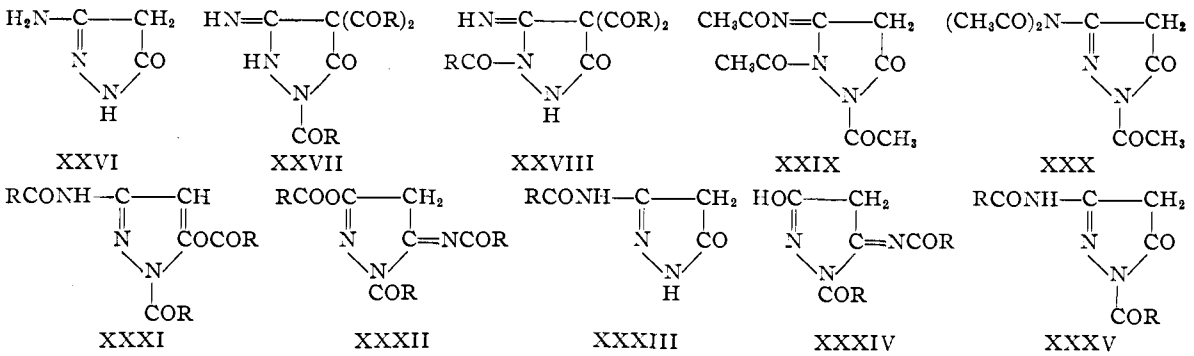
Both *triacetyl compounds* are insoluble in dilute sodium carbonate and do not couple with *p*-nitrosodimethylaniline.[9] On mild hydrolysis with dilute sodium hydroxide, both give the same *monoacetyl derivative*, melting at 227°, which is soluble in 3% sodium carbonate and couples with *p*-nitrosodimethylaniline. When the high-melting triacetyl compound is treated with one equivalent of piperidine, a *diacetyl* derivative, melting at 195°, is formed, which is soluble in 3% sodium carbonate and couples with *p*-nitrosodimethylaniline.[9] The lower-melting isomer gave the *monoacetyl* derivative, m. p. 227°, even under very mild conditions, *e. g.*, when the piperidine was added slowly at room temperature. Similar difficulties in selective deacylations have been noted before.[8]

The structures, XXVII and XXVIII (R = CH_3), which were given by Hepner and Fajersztejn to the triacetyl derivatives, are untenable because the ready hydrolysis of *all three acetyl* groups[14] excludes any 4-acetyl groups.[8] Moreover, the coupling action of the monoacetyl derivative, m. p. 227°, and the diacetyl derivative, m. p. 195°, excludes a 4-acetyl group in either of these compounds.[15] The structures, XXIX and XXX, are excluded because these compounds should be soluble in dilute carbonate and couple with *p*-nitrosodimethylaniline. This leaves for the two isomeric triacetyl compounds only structures XXXI and XXXII (R = CH_3). Inasmuch as both isomers hydrolyze to the same monoacetyl derivative, the latter compound, melting at 227°, is assigned the structure *3-acetamido-5-pyrazolone*, XXXIII (R = CH_3), because the other acetyl group which is common in XXXI and XXXII would be hydrolyzed[8,15] under the conditions for the preparation of XXXIII. The diacetyl compound, melting at 195°, is considered to be *1-acetyl-3-acetamido-5-pyrazolone*, XXXV (R = CH_3), because the isomeric compound, XXXIV, would not couple in the *p*-nitrosodimethylaniline test.[16] The triacetyl compound, melting at 202°, is therefore *1-acetyl-3-acetamido-5-acetoxypyrazole*, XXXI (R = CH_3), which leaves for the triacetyl compound, melting at 130°, the structure of *1-acetyl-3-acetoxy-5-pyrazolone acetylimide*, XXXII (R = CH_3).

By analogy with the determination of the structures of the acetyl derivatives, the structure of the tribenzoyl derivative (m. p. 185°), prepared as given in the literature was readily determined. It gives, on hydrolysis in dilute sodium hydroxide, a monobenzoyl derivative, melting at 205°. This is carbonate-soluble and couples in the *p*-nitrosodimethylaniline test and is, therefore, assigned the structure of *3-benzamido-5-pyrazolone*, XXXIII (R = C_6H_5). Reaction of the tribenzoyl compound with one equivalent of piperidine gives a dibenzoyl derivative, melting at 175°. Since this is soluble in carbonate and does not couple to form a dye even in the film-strip test,[15] it is assigned the structure *1-benzoyl-3-hydroxy-5-pyrazolone benzoylimide*, XXXIV (R = C_6H_5). This leaves only the structure *1-benzoyl-3-benzoyloxy-5-pyrazolone benzoylimide*, XXXII (R = C_6H_5), for the tribenzoyl compound (m. p. 185°) because of its insolubility in alkali.

If 3-amino-5-pyrazolone is benzoylated in pyridine solution, a different tribenzoyl derivative,

(15) Weissberger and Porter, THIS JOURNAL, **65**, 2180 (1943).
(16) *Cf.* XVII in ref. 8.



XXVI XXVII XXVIII XXIX XXX

XXXI XXXII XXXIII XXXIV XXXV

melting at 161°, is obtained. On hydrolysis with dilute sodium hydroxide, this also gives 3-benzamido-5-pyrazolone, XXXIII (R = C_6H_5). When the tribenzoyl derivative (m. p. 161°) is treated with one equivalent of piperidine, a dibenzoyl derivative, melting at 171°, is obtained. Since this is soluble in carbonate and couples in the film-strip test,[8] it is assigned the structure *1-benzoyl-3-benzamido-5-pyrazolone*, XXXV (R = C_6H_5). It follows that the tribenzoyl compound, melting at 161°, is *1-benzoyl-3-benzamido-5-benzoyloxypyrazole*, XXXI (R = C_6H_5).

Experimental

1-Methyl-3-amino-5-pyrazolone, IV, and 1-Methyl-3-hydroxy-5-pyrazolone Imide. V.—(a) A solution of 21 g. (0.46 mole) of methylhydrazine in 75 ml. of absolute alcohol was added to a solution of 72.5 g. (0.46 mole) of ethyl β-amino-β-ethoxyacrylate I, in 75 ml. of absolute alcohol. The mixture warmed spontaneously to 60°. The solution was allowed to stand for twenty hours. Two easily distinguishable types of crystals separated. The crystals were large enough to be separated mechanically.

There were 24.3 g. (47%) of large prisms, 3.1 g. (6%) of needles, and 5 g. (10%) of mixed material. These fractions were carefully recrystallized to produce 14 g. of prisms, melting at 180–182°, and 1 g. of needles, melting at 192–194° in a sealed tube (190° if heated very slowly in an open tube). The needles were proved (by compound XVI) to be 1-methyl-3-amino-5-pyrazolone while the prisms were the 1-methyl-3-hydroxy-5-pyrazolone imide.

(b) Methylhydrazine (5 g., 0.11 mole) was dissolved in 10 ml. of water and the resulting solution was cooled. To this was added 12.3 g. (0.11 mole) of ethyl cyanoacetate. After a few minutes the ester dissolved, and the solution was placed in a vacuum desiccator for three days. Large prisms (some an inch long) formed but no needles were present. The prisms were collected and washed with 50 ml. of absolute alcohol; 3.2 g. (26%) melting at 180°. The mother liquor and washings were evaporated on a steam-bath. The residue was dissolved in 25 ml. of boiling absolute alcohol and cooled slowly. The needles were collected and washed with alcohol; 3.5 g. (29%), m. p. 190°. Recrystallization raised the melting point to 192–194° (in a sealed tube).

Anal. Calcd. for $C_4H_7N_3O$: C, 42.5; H, 6.2; N, 37.1. Found, for isomer melting at 180–182°: C, 42.4; H, 6.2; N, 36.9. Found, for isomer melting at 192–194°: C, 42.3; H, 6.2; N, 37.1.

1-Methyl-3-carbethoxy-5-pyrazolone, VI.—Freshly prepared methylhydrazine (2.3 g.) in 20 ml. of dry benzene was added to a solution of freshly prepared ethyl oxalacetate (9.4 g.) in 80 ml. of dry benzene. The temperature of the solution rose from 28° to 41°. After standing one hour at room temperature, the solution was refluxed for five minutes and cooled. The precipitate of sirupy crystals was collected and recrystallized from 50 ml. of water. The resulting white needles weighed 3.5 g. (41%) and melted at 148–150°.

The compound can also be prepared from the salts of the two starting materials. A solution of 14.4 g. of methylhydrazine sulfate in 20 ml. of water was diluted with 300 ml. of hot ethanol. To this was added a hot solution of 21.0 g. of sodium ethyl oxalacetate in 700 ml. of ethanol. Sufficient alcoholic potassium hydroxide was added to neutralize the solution. The inorganic salts were removed by filtration, and the alcoholic solution was concentrated under reduced pressure to near dryness. The residue was recrystallized from 200 ml. of water. The yield using this procedure was 11.5 g. (68%), m. p. 148–150°.

Anal. Calcd for $C_7H_{10}N_2O_3$: N, 16.5. Found: N, 16.6.

1-Methyl-5-pyrazolone-3-carboxyhydrazide Hydrochloride, VIII.—1-Methyl-3-carbethoxy-5-pyrazolone, VI, (6.9 g.) was suspended in 18 ml. of 42% hydrazine hydrate solution. After sixteen hours, the solution was acidified with 14 ml. of concentrated hydrochloric acid under cooling. The product was collected and washed with 30 ml. of water in three portions. It was recrystallized from 25 ml. of water. The product weighed 3.6 g. (46%) and melted at 253–255°.

Anal. Calcd. for $C_5H_8N_4O_2 \cdot HCl$: C, 31.3; H, 4.5; N, 28.3. Found: C, 31.2; H, 4.7; N, 29.1.

1-Methyl-5-pyrazolone-3-carbazide, IX.—1-Methyl-5-pyrazolone-3-carboxyhydrazide hydrochloride, VIII (0.90 g.) was suspended in 10 ml. of water. The slurry was layered with 20 ml. of ether and cooled to 0°. To this was added a solution of 0.33 g. of sodium nitrite in 5 ml. of water. The mixture was strongly agitated for ten minutes before the ether layer was removed. This ether layer yielded 0.05 g. of light yellow crystals after standing at 0° for one hour. The compound deflagrates at 113°.

Anal. Calcd. for $C_5H_5N_5O_2$: C, 35.9; H, 3.0. Found: C, 36.5; H, 2.9.

1-Methyl-4-isonitroso-5-pyrazolone-3-carbazide, X.—1-Methyl-5-pyrazolone-3-carboxyhydrazide hydrochloride, VIII (4.0 g., 0.021 mole), was suspended in 50 ml. of water, and the mixture was cooled in a salt–ice-bath.

A solution of 1.47 g. (0.021 mole) of sodium nitrite in 10 ml. of water was added to the slurry at such a rate that the temperature did not exceed 0°. The mixture was stirred for one hour. The yellow precipitate was collected, washed with water, and dried at room temperature. The yield was 2.1 g. The material explodes at 112° (slightly higher if heated rapidly).

Anal. Calcd. for $C_5H_4N_6O_3$: C, 30.6; H, 2.1; N, 42.6. Found: C, 30.1; H, 2.3; N, 42.6.

1-Methyl-3-carbethoxy-4-(*p*-methoxyphenylazo)-5-pyrazolone, XI.—1-Methyl-3-carbethoxy-5-pyrazolone, VI (5.0 g., 0.029 mole), was dissolved in 50 ml. of pyridine. The solution was cooled to 0° and treated with a cold solution of 0.029 mole of *p*-methoxybenzenediazonium chloride in 60 ml. of water. After ten minutes, 50 ml. of water was added to the mixture. The dye was

collected, washed with water, and recrystallized from 100 ml. of ethanol. There resulted 6.8 g. of orange dye, melting at 125–127°.

Anal. Calcd. for $C_{14}H_{18}N_4O_4$: C, 55.3; H, 5.3; N, 18.4. Found: C, 55.7; H, 5.6; N, 18.7.

1-Methyl-4-(*p*-methoxyphenylazo)-5-pyrazolone-3-carboxyhydrazide, XII.—1-Methyl-3-carbethoxy-4-(*p*-methoxyphenylazo)-5-pyrazolone, XI (6.5 g.), was stirred into 80 ml. of 42% hydrazine hydrate solution. The stirring was continued for four hours. All the dye changed from orange to yellow. Water (100 ml.) was added, and the solution was filtered to remove a small amount of insoluble material. The clear solution was acidified with 50 ml. of acetic acid. The red dye was collected and washed with 100 ml. of boiling alcohol. The material weighed 3.8 g. (60%) and melted at 212–214°.

Anal. Calcd. for $C_{12}H_{14}N_6O_3$: C, 49.7; H, 4.9; N, 29.0. Found: C, 50.1, 49.9; H, 4.8, 4.9; N, 29.6.

1-Methyl-4-(*p*-methoxyphenylazo)-5-pyrazolone-3-carbazide, XIII.—1-Methyl-4-(*p*-methoxyphenylazo)-5-pyrazolone-3-carboxyhydrazide, XII (2.9 g.), was dissolved in a solution of 100 ml. of water, 100 ml. of dioxane, and 5 ml. of concentrated hydrochloric acid. The solution was cooled to 0°, and 0.70 g. of sodium nitrite in 30 ml. of water was added. The azide precipitated immediately. It was washed with water and ethanol. This process yielded 2.5 g. of the azide which explodes at 120°.

Anal. Calcd. for $C_{12}H_{11}N_7O_3$: N, 33.2. Found: N, 32.6.

1-Methyl-4-(*p*-methoxyphenylazo)-5-pyrazolone-3-isocyanate, XIV.—A suspension of 2.5 g. of 1-methyl-4-(*p*-methoxyphenylazo)-5-pyrazolone-3-carbazide, XIII, in 150 ml. of absolute alcohol was refluxed on a steam-bath for two hours. When all evolution of nitrogen had ceased, the insoluble product was collected and washed with ethanol. The product, 1.5 g., melted at 245–249°. A sample recrystallized from dioxane melted at 253–255°. Analysis proved it to be the isocyanate rather than the expected urethan.

Anal. Calcd. for $C_{12}H_{11}N_5O_3$: C, 52.8; H, 4.2; N, 25.7. Found: C, 52.5; H, 4.2; N, 24.9.

1-Methyl-3-carbethoxyamino-4-(*p*-methoxyphenylazo)-5-pyrazolone, XV.—A suspension of 0.35 g. of 1-methyl-4-(*p*-methoxyphenylazo)-5-pyrazolone-3-isocyanate, XIV, in 50 ml. of absolute alcohol was refluxed for twenty hours. The resulting solution was filtered and cooled. The precipitate was collected, washed with alcohol, and recrystallized from alcohol. The product was 0.20 g. of bright orange dye, melting at 181–182°.

Anal. Calcd. for $C_{14}H_{17}N_5O_4$: C, 52.7; H, 5.4; N, 21.9. Found: C, 52.4; H, 5.4; N, 22.1.

1-Methyl-3-amino-4-(*p*-methoxyphenylazo)-5-pyrazolone, XVI.—(a) A solution of 0.10 g. of 1-methyl-3-carbethoxyamino-4-(*p*-methoxyphenylazo)-5-pyrazolone, XV, in 4 ml. of 10% sodium hydroxide was warmed for two hours on a steam-bath. The solution was filtered, and acidified with 0.60 ml. of acetic acid. The precipitate was recrystallized from ethanol. It was a dull red dye, melting at 172–174°.

(b) A solution of 1.13 g. (0.01 mole) 1-methyl-3-amino-5-pyrazolone, IV, in 20 ml. of 5% sodium hydroxide solution at 0° was treated with (0.01 mole) of benzene diazonium chloride in 20 ml. of cold water. After fifteen minutes, the solution was acidified with acetic acid, and the dye was collected. It was washed with water and recrystallized from 20 ml. of ethanol. This procedure produced 1.0 g. of dull red dye, melting at 172–174°. The mixed melting point of (a) and (b) was 172–174°.

Anal. Calcd. for $C_{11}H_{13}N_5O_2$: C, 53.5; H, 5.3; N, 28.4. Found: C, 53.4; H, 5.2; N, 28.3.

1-Methyl-3-hydroxy-4-(*p*-methoxyphenylazo)-5-pyrazolone Imide, XVII.—A solution of 1.13 g. (0.01 mole) of 1-methyl-3-hydroxy-5-pyrazolone imide, V, in 25 ml. of pyridine and 5 ml. of water was cooled to 0° and treated with a cold solution of 0.01 mole of benzenediazonium chloride in 15 ml. of water. After a few minutes, a yellow dye separated. It was collected, washed with water, and recrystallized from 50 ml. of ethanol. There resulted 0.9 g. of bright yellow dye, melting at 240–242°. A mixture of this material with XXIa melted at 167°.

Anal. Calcd. for $C_{11}H_{13}N_5O_2$: C, 53.5; H, 5.3; N, 28.4. Found: C, 53.5; H, 5.7; N, 27.9.

1-Methyl-3-benzamido-5-benzoyloxypyrazole, XVIII.—Benzoyl chloride (3 g., 0.021 mole) was added dropwise to a solution of 1-methyl-3-amino-5-pyrazolone, IV (1.13 g., 0.010 mole) in 20 ml. of pyridine at room temperature. The mixture was warmed for one-half hour on a steam-bath, cooled, and drowned out with 20 ml. of water. The solid was collected, washed, dried, and recrystallized from 25 ml. of ethanol. This process yielded 1.9 g. (60%) of white powder, m. p. 146–148°.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.5, H, 4.9; N, 13.1. Found: C, 67.4; H, 4.6; N, 13.3.

1-Methyl-3-benzoyloxy-5-pyrazolone Benzoylimide. XIX.—1-Methyl-3-hydroxy-5-pyrazolone imide, V, was acylated, and the product was purified by the same procedure used in making XVIII. The yield was 1.9 g. (60%) of white powder, m. p. 150–153°. A mixture of XVIII and XIX melted above 130°.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.5; H, 4.9; N, 13.1. Found: C, 67.0; H, 4.8; N, 12.6.

1-Methyl-3-benzamido-5-pyrazolone, XX.—To a solution of 5 ml. of alcohol and 10 ml. of 5% sodium hydroxide was added 1.6 g. of 1-methyl-3-benzamido-5-benzoyloxypyrazole, XVIII. The solution was stirred for one hour, filtered, and acidified with acetic acid. The precipitate was collected, washed with alcohol, dried, and recrystallized from 40 ml. of ethanol; 0.7 g. (65%) of white crystals, which slowly melted, with decomposition, at 215°.

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.9; H, 5.1; N, 19.3. Found: C, 61.1; H, 5.1; N, 19.7.

1-Methyl-3-hydroxy-5-pyrazolone Benzoylimide, XXI.—1-Methyl-3-benzoyloxy-5-pyrazolone benzoylimide, XIX (3.2 g.) was added to a solution of 10 ml. of ethanol and 20 ml. of 5% sodium hydroxide. The solution was stirred for one hour, filtered, and acidified with acetic acid; 2.1 g. (96%), m. p. 243–249°. The material melted over the same range after recrystallization from ethanol.

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.9; H, 5.1; N, 19.3. Found: C, 60.5; H, 4.6; N, 19.2.

Reaction of Phenylhydrazine with Methyl Cyanoacetate.—A mixture of 10.8 g. of phenylhydrazine and 9.9 g. of methyl cyanoacetate in 20 ml. of dioxane was heated on the steam-bath for eighteen hours, cooled, drowned out with 100 ml. of water, and the solution decanted from the precipitated oil. The latter was triturated with ether, cooled, filtered, and the gummy product extracted with 100 ml. of benzene in four portions. The combined extracts, on cooling, gave 1.8 g. (10%)[17] of β-cyanoacetphenylhydrazide.

3-Amino-5-pyrazolone, XXVI.—Cyanoacethydrazide[8] (10 g.), in sodium methylate solution (4.6 g. of sodium in 50 ml. of methanol) was refluxed for one hour, cooled, and the sodium salt filtered off. The latter was dissolved in 35 ml. of water, acidified with 6 ml. of acetic acid, and the precipitated product was recrystallized from water; 7 g. (71%) of short, ivory needles, m. p. 214–215° dec. The compound deteriorates considerably on standing for more than a week at room temperature.

Ethyl β-amino-β-ethoxyacrylate, I (15.9 g.), and 5.9 g. of hydrazine hydrate (85%) in 25 ml. of absolute ethanol were brought to boiling on the steam-bath and the heat supply removed. Heat was evolved and crystals sepa-

(17) The low yield in the case of the phenylhydrazine is in agreement with low yields in the reaction of phenylhydrazine with other esters because of numerous side reactions. *Cf.* Baidowski and Slepak, *Chem. Zentr.*, **74**, I, 829 (1903).

rated. After standing at room temperature for one hour, the product was collected and washed with alcohol and ether; 7.0 g. (71%), m. p. 213–215° dec. When recrystallized from water, it formed short, ivory needles, m. p. 214–215° dec.

Anal. Calcd. for $C_5H_5N_3O$: C, 36.36; H, 5.09; N, 42.41. Found: C, 36.50; H, 5.12; N, 42.39.

1-Acetyl-3-acetamido-5-acetoxypyrazole, XXXI (R = CH_3).—A mixture of 2.3 g. of 3-amino-5-pyrazolone, XXVI, and 11 ml. of acetic anhydride was stirred on the steam-bath for twenty minutes. The resulting solution was cooled under the tap and filtered; 1.8 g. (36%), m. p. 192–196°. The product was recrystallized twice from *n*-propanol; it gave white, pearly flakes; m. p. 202–203°.

Anal. Calcd. for $C_9H_{11}N_3O_4$: C, 48.01; H, 4.92; N, 18.66. Found: C, 47.99; H, 5.02; N, 18.76.

Under the conditions for the hydrolysis of XXXII (R = CH_3) to XXXIII (R = CH_3), XXXI (R = CH_3) also gave XXXIII (R = CH_3) (60%) identified by melting point and mixed melting point. There was no evidence of rearrangement of XXXI into XXXII on heating in glacial acetic acid.

1-Acetyl-3-acetoxy-5-pyrazolone Acetylimide, XXXII (R = CH_3).—The filtrate from XXXI (above) was cooled in an ice-salt-bath, the mixture (m. p. 125–135°) which crystallized was filtered out, and the filtrate stirred with ice water and filtered; 0.45 g. (9%), m. p. 130–132°. Recrystallization from a 1:1 mixture of benzene and cyclohexane produced white needles, m. p. 131–132°.

Anal. Calcd. for $C_9H_{11}N_3O_4$: C, 48.01; H, 4.92; N, 18.66. Found: C, 48.25; H, 5.02; N, 18.64.

Under the conditions for the preparation of XXXV, XXXII gave XXXIII (81%).

3-Acetamido-5-pyrazolone, XXXIII (R = CH_3).—To a suspension of 1.8 g. of 1-acetyl-3-acetoxy-5-pyrazolone acetylimide, XXXII (R = CH_3), in 9 ml. of water was added dropwise 1.7 ml. of 40% sodium hydroxide diluted with 3 ml. of water, while stirring vigorously in an ice-bath. Ten minutes after addition was complete (five minutes), the solution was filtered from a slight insoluble portion, acidified with glacial acetic acid, and filtered; 0.85 g. (75%); m. p. 225–227°. Recrystallization from methanol produced short, white needles, m. p. 227–228° dec.

Anal. Calcd. for $C_5H_7N_3O_2$: C, 42.55; H, 5.00; N, 29.79. Found: C, 42.64; H, 5.15; N, 29.58.

1-Acetyl-3-acetamido-5-pyrazolone, XXXV (R = CH_3).—To a solution of 0.7 g. of 1-acetyl-3-acetamido-5-acetoxypyrazole, XXXI (R = CH_3), in 25 ml. of 1-1 isopropyl alcohol–dioxane was added 0.3 ml. of piperidine in 5 ml. of isopropyl alcohol dropwise (twenty-five minutes) while stirring at room temperature. The solution was allowed to evaporate to dryness, the residue was triturated with *n*-propanol, and filtered; 0.5 g. (86%), m. p. 193–195°. Recrystallization from dioxane produced fine, white granules, m. p. 195–196°.

Anal. Calcd. for $C_7H_9N_3O_3$: C, 45.90; H, 4.95, N, 22.93. Found: C, 46.02; H, 5.13; N, 22.57.

1-Benzoyl-3-benzoyloxy-5-pyrazolone Benzoylimide, XXXII (R = C_6H_5).—The directions in the literature[14] were followed, and the product was recrystallized from isopropyl alcohol. The yield was 25% of fine, white needles, m. p. 185–186°.

Hydrolysis of XXXII (R = C_6H_5) as of XXXI (R = C_6H_5) gave XXXIII (R = C_6H_5).

1-Benzoyl-3-hydroxy-5-pyrazolone Benzoylimide, XXXIV (R = C_6H_5).—To a solution of 0.6 g. of 1-benzoyl-3-benzoyloxy-5-pyrazolone benzoylimide XXXII (R = C_6H_5) in 6 ml. of dioxane, heated on the steam-bath, was added dropwise, with stirring, a solution of 0.15 ml. of piperidine in 1 ml. of dioxane. After heating for fifteen minutes, the solution was cooled to room temperature, diluted with 5 ml. water, cooled under the tap, and filtered; 0.3 g. (65%), sinters at 170°, m. p. 172–175°. Recrystallization from *n*-propanol gave fine, white, feathery crystals, m. p. 175–176°.

Anal. Calcd. for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.23; N, 13.68. Found: C, 66.39; H, 4.44; N, 13.81.

1-Benzoyl-3-benzamido-5-benzoyloxypyrazole, XXXI (R = C_6H_5).—To a mixture of 2.5 g. of 3-amino-5-pyrazolone, XXVI (3 ml.), in 25 ml. of pyridine was added 10.5 g. of benzoyl chloride. The solution was heated one-half hour on the steam-bath. When cool, it was diluted with 5 ml. of water, cooled under the tap, filtered, rinsed with 50% ethanol, and recrystallized from 150 ml. of isopropyl alcohol; 5.9 g. (57%) of fine, white crystals, m. p. 161–163°.

Anal. Calcd. for $C_{24}H_{17}N_3O_4$: N, 10.21. Found: N, 9.92.

3-Benzamido-5-pyrazolone, XXXIII (R = C_6H_5).—A mixture of 3 g. of 1-benzoyl-3-benzamido-5-benzoyloxypyrazole, XXXI (R = C_6H_5), in 50 ml. of 2% sodium hydroxide and 20 ml. of 95% ethanol was stirred for one and one-half hours, filtered from a small amount of insoluble material, acidified with acetic acid, and concentrated *in vacuo* until the solution clouded. It was cooled and filtered. The product was digested with 8 ml. of methanol, cooled, and filtered; 1.2 g. (80%), m. p. 203–205°. Recrystallization from methanol gave a white powder, m. p. 205–206°.

Anal. Calcd. for $C_{10}H_9N_3O_2$: N, 20.68. Found: N, 20.84.

1-Benzoyl-3-benzamido-5-pyrazolone, XXXV (R = C_6H_5).—To a solution of 0.6 g. of 1-benzoyl-3-benzamido-5-benzoyloxypyrazole, XXXI (R = C_6H_5), in 12 ml. of boiling isopropyl alcohol was added dropwise 0.15 ml. of piperidine in 1 ml. of isopropyl alcohol. The solution was refluxed fifteen minutes, cooled, filtered, and the product was recrystallized from 95% ethanol; 0.2 g. (43%), white microcrystals, m. p. 171–172°.

Anal. Calcd. for $C_{17}H_{13}N_3O_3$: N, 13.68. Found: N, 13.26.

1-Methyl-5-pyrazolone-3-carboxamide.—1-Methyl-3-carbethoxy-5-pyrazolone, VI (10 g.), was dissolved in 100 ml. of 28% ammonium hydroxide. After three days, the solution was neutralized with acetic acid, the precipitate was collected, washed with water, and recrystallized from water. The yield was 5 g. of fine, white needles that sinter above 230°.

Anal. Calcd. for $C_5H_7N_3O_2$: C, 42.5; H, 5.0. Found: C, 42.7; H, 5.1.

This compound brominates readily so that no attempts were made to use it in a Hofmann degradation.

Summary

1. Methylhydrazine, when reacting with either ethyl cyanoacetate or ethyl β-amino-β-ethoxyacrylate, yields two pyrazolones, namely, 1-methyl-3-hydroxy-5-pyrazolone imide and 1-methyl-3-amino-5-pyrazolone. The structure of the latter was proved unequivocally.

2. Acetylation of 3-amino-5-pyrazolone with boiling acetic anhydride produces 1-acetyl-3-acetamido-5-acetoxypyrazole and 1-acetyl-3-acetoxy-5-pyrazolone acetylimide rather than 1,4,4-triacetyl-3-imino-5-ketopyrazolidine and 2,4,4-triacetyl-3-imino-5-ketopyrazolidine suggested by Hepner and Fajersztejn.[12]

3. 1-Benzoyl-3-benzoyloxy-5-pyrazolone benzoylimide was obtained using benzoyl chloride in a Schotten–Baumann reaction on 3-amino-5-pyrazolone. 1-Benzoyl-3-benzamido-5-benzoyloxypyrazole was produced when the benzoylation was done in pyridine.

ROCHESTER 4, N. Y. RECEIVED MAY 15, 1948