Studies on 3,5-pyrazolidinediones. IV. Addition of 4-Arylazo-3,5-pyrazolidinediones to Ethyl Acrylate

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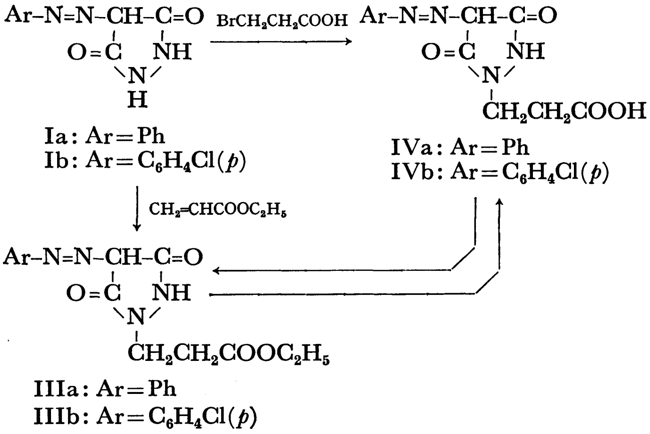
(Received December 22, 1972)

4-Arylazo-3,5-pyrazolidinediones (I) react with ethyl acrylate to yield the corresponding 1-β-ethoxycarbonylethyl derivatives (III), which were readily hydrolyzed into the acids IV. Compounds III and IV were found to react with acrylonitrile to yield the corresponding 1-substituted 2-β-cyanoethyl derivatives V and VI respectively. Whereas III and IV were recovered unchanged upon treatment with aniline or piperidine, the arylazomalonic acid dihydrazide (IX) were formed upon treatment of III or IV with hydrazine hydrate. 2-*p*-Chlorophenylazotetrahydropyrazolo[1,2-*a*]pyrazole-1,3,7-trione (XI) has been prepared by the action of phosphorus oxychloride on IVb. 3-Amino-4-phenylazo-2-pyrazolin-5-one (II) react with ethyl acrylate to yield the pyrazolo[1,5-*a*]pyrimidine derivative XII.

In a previous paper¹⁾ it has been shown that 4-arylazo-3,5-pyrazolidinediones (I) react with acrylonitrile to yield either the 1-β-cyanoethyl or the 1,2-di(β-cyanoethyl) derivatives depending on the reaction conditions. It has also been shown that 3-amino-4-phenylazo-2-pyrazolin-5-one (II) react with the same reagent to yield a pyrazolopyrimidine derivative. As an extention of this work, it was thought worthwhile to investigate the behavior of compounds I and II toward other systems containing activated double bond. In the present paper, the behavior of I and II toward ethyl acrylate is reported.

Upon treatment of I with ethyl acrylate in molecular proportions the 1-β-ethoxycarbonylethyl derivatives (III) were formed.²⁾ The structure of these derivatives was established from their IR spectra and from identity with authentic specimens prepared by the action of ethanol and concentrated sulfuric acid on 4-arylazo-1-β-carboxyethyl-3,5-pyrazolidinediones (IV),²⁾ now obtained by the action of β-bromopropionic acid on I. Furthermore, compounds IV were formed upon treatment of III with acetic acid-hydrochloric acid mixture.

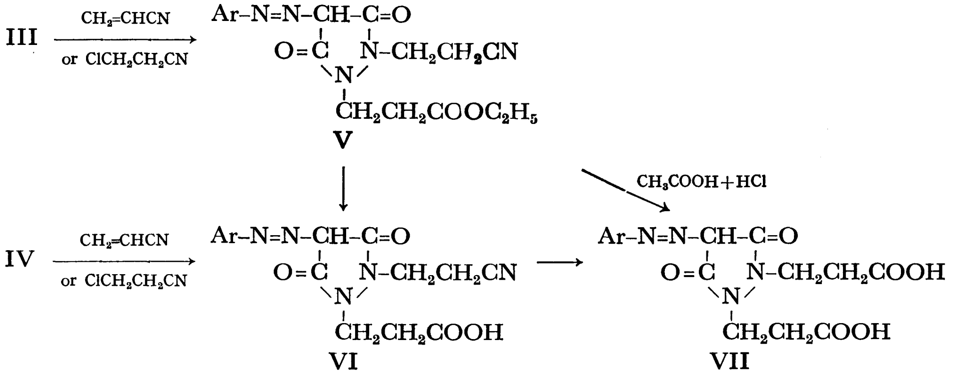
In contrast to the reported unreactivity of 4-arylazo-1-phenyl-3,5-pyrazolidinediones toward the action of acrylonitrile,¹⁾ compounds III and IV were found to add readily to acrylonitrile to yield the 1,2-disubstituted 3,5-pyrazolidinedione derivatives, V and VI respectively. Compounds V and VI were also obtained upon treatment of III and IV with β-chloropropiononitrile respectively.



Ia: Ar=Ph
Ib: Ar=$C_6H_4Cl(p)$

IVa: Ar=Ph
IVb: Ar=$C_6H_4Cl(p)$

IIIa: Ar=Ph
IIIb: Ar=$C_6H_4Cl(p)$

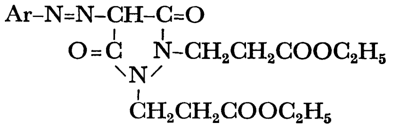


V

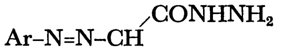
VI

VII

V, VI and VII a: Ar=Ph
b: Ar=$C_6H_4Cl(p)$



VIIIa: Ar=Ph
b: Ar=$C_6H_4Cl(p)$



IXa: Ar=Ph
b: Ar=$C_6H_4Cl(p)$

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1) M. H. Elnagdi, N. A. L. Kassab, S. M. Fahmy, and F. A. El-All, *J. Prakt. Chem.*, in press.

2) For the sake of convenience, all compounds described in this paper are referred to as arylazo-3,5-pyrazolidinediones derivatives, irrespective of their actual structure.

Compounds V were readily hydrolyzed with aqueous sodium hydroxide to the corresponding VI. On the other hand, treatment of V and VI with acetic acid–hydrochloric acid mixture results in the formation of the known[1] 4-arylazo-1,2-di(β-carboxyethyl)-3,5-pyrazolidinedione derivatives (VII).

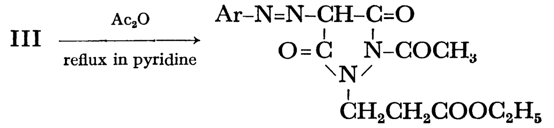
Compounds III react also with ethyl acrylate to yield the corresponding 4-arylazo-1,2-di(β-ethoxycarbonylethyl)-3,5-pyrazolidinediones (VIII). Compounds VIII are readily converted into VII by the action of acetic acid–hydrochloric acid mixture.

Whereas the compounds III and IV were recovered unchanged upon treatment with aniline or piperidine, the arylazomalonic acid dihydrazides (IX) were formed upon treatment of III with hydrazine hydrate. The stability of the pyrazolidinedione ring in III and IV toward the action of piperidine is in contrast to the reported[3,4] hetero-ring opening of 4-arylazo-1-phenyl- and 1,2-diphenyl-3,5-pyrazolidinediones by the action of the same reagent.

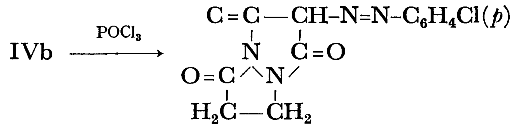
In a trial to effect cyclization of III into a pyrazolo[1,2-*a*]pyrazole derivative by the action of acetic anhydride, the acetyl derivatives (X) were obtained. Although compounds III have three sites for acylation to occur,[5] compounds X were assigned the *N*-acetyl structure based on their stability toward the action of acetic acid[6] and from a study of their spectral data. The IR spectra of compound Xb, taken as an example, reveals the presence of four carbonyl sretching absorption bands at 1740, 1730, 1690, and 1675 cm^{-1}. The former two were considered to be due to the acetyl and ester carbonyl groups and the latter due to the ring carbonyl groups. Compounds X were converted readily into III on reflux with pyridine.

2-*p*-Chlorophenylazotetrahydropyrazolo[1,2-*a*]pyrazole-1,3,7-trione (XI) has now been prepared through cyclization of the acid (IVb) by the action of phosphorus oxychloride. The structure XI, presented here, finds support from analytical and spectral (IR) data. Thus, the IR spectrum was characterized by the presence of three carbonyl bands at 1770, 1710, and 1680 cm^{-1} and revealed the absence of absorption in the region of 2500—3000 cm^{-1} present in the spectrum of the starting acid (IVb).

The behavior of 3-amino-4-phenylazo-2-pyrazoline-5-one (II) toward ethyl acrylate shows that II did not add to ethyl acrylate in aqueous pyridine solution, while it react with the same reagent in the presence of catalytic amount of potassium hydroxide to yield the pyrazolo[1,5-*a*]pyrimidine derivative (XII). This is in analogy with the recently reported behavior of 3-phenyl-5-aminopyrazole toward methyl phenylpropiolate.[7] The structure proposed for compound XII finds support from analytical data, IR spectrum, and its conversion into IVa through the action of acetic acid–hydrochloric acid mixture.



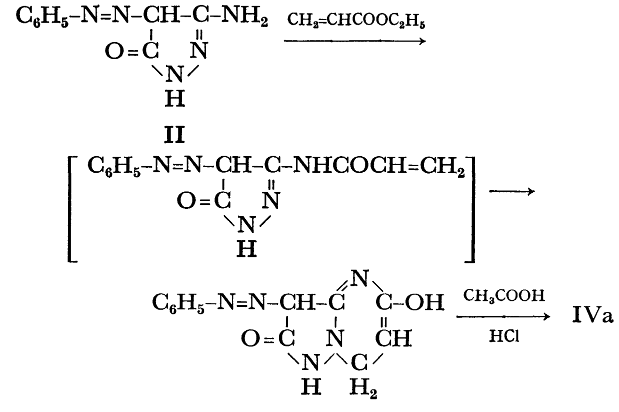
Xa: Ar=Ph
b: Ar=$C_6H_4Cl(p)$



XI

The IR spectrum of compound XII does not show free hydroxyl absorption around 3600 cm^{-1} and shows a broad band (2430—2800 cm^{-1}) similar to the OH group absorption of fatty acid dimers. Similar behavior has been reported for β-keto-enols and was attributed to intramolecular conjugate chelation.[8] However, in compound XII steric considerations will prevent a direct intramolecular hydrogen bond. This may lead to the conclusion that XII, at least in solid state, exists in a highly stable dimeric structure capable of similar resonance stabilization. Similar system in which such conjugate chelation could arise from intermolecular hydrogen bond has been reported in case of 5,5-dimethyl-1,3-cyclohexanedione.[9]

In part III of this series[1] it has been shown that position 1 in compound II is the most reactive position for cyanoethylation. That this position is not involved in the reaction of II with ethyl acrylate may lead to the assumption that in case of ethyl acrylate the first step in the reaction is acylation of the amino group followed by cyclization to yield XII.



II

XII

Experimental

All melting points were determined on a micro hot stage and are uncorrected. The infrared spectra were recorded

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3) M. H. Elnagdi and S. M. Fahmy, *Indian J. Chem.*, **10**, 461 (1972).

4) M. H. Elnagdi, A. S. A. Shawali, and M. R. Elaukby, *ibid.*, in press.

5) *Cf.* the behavior of 3,5-pyrazolidinediones on acylation, R. H. Wiely and P. Wily, "Pyrazolones, Pyrazolidionones and Derivatives" John Wiley & Sons, New York (1964), p. 126 and 130.

6) *Cf.* the ready rearrangement of 5-acetoxy-3-phenylpyrazole into the 1-acetyl derivative by the action of acetic acid, A. Weissberger and H. D. Porter, *J. Amer. Chem. Soc.*, **65**, 1495 (1943).

7) V. Sprio and S. Plescia, *J. Heterocycl. Chem.*, **9**, 951 (1972).

8) J. L. Bellamy "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc. New York (1958), p. 104.

9) R. S. Rasmussen, D. D. Tunnicliff, and R. R. Brattain, *J. Amer. Chem. Soc.*, **71**, 1068 (1949).

with Hitachi Grating Infrared Spectrometer Model EPI-G3. Ultraviolet spectra were measured in ethanol with Hitachi 124 Spectrophotometer.

4-Arylazo-1-β-ethoxycarbonylethyl-3,5-pyrazolidinediones (IIIa and IIIb). *From I and Ethyl Acrylate*: Ten mmol of I was added to a solution of ethyl acrylate (0.01 mol) in pyridine (50 ml) and water (10 ml). The reaction mixture was refluxed for 6 hr and evaporated *in vacuo* to leave a residue which was purified by recrystallization from ethanol.

IIIa. Yellow crystals, yield 80%, mp 115 °C. IR: 3150 (NH), 1725 (ester CO), 1690 and 1660 cm^{-1} (ring CO). Found: C, 55.50; H, 5.37; N, 18.69%. Calcd for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41%.

IIIb. Orange crystals, yield 85%, mp 164 °C. IR: 3120 (NH), 1730 (ester CO), 1690 and 1660 cm^{-1} (ring CO). Found: C, 49.60; H, 4.50; N, 16.55%. Calcd for $C_{14}H_{15}N_4O_4Cl$: C, 49.63; H, 4.46; N, 16.54%.

From IV by Esterification: A suspension of IV (see below) in ethanol (30 ml) containing sulfuric acid (1.5 ml; 98%) was refluxed for 16 hr, cooled and poured into ice water. The solid product, so formed, was purified by recrystallization and identified (mp and mixed mp) as IIIa or IIIb. Yields, 60 and 67% respectively.

4-Arylazo-1-β-carboxyethyl-3,5-pyrazolidinediones (IVa and IVb). *From I and β-Bromopropionic Acid*: Ten mmol of I was added to a solution of β-bromopropionic acid (0.01 mol) in 100 ml of aqueous ethanol (1 : 1) containing 2.0 g of sodium carbonate and refluxed for 3 hr. Evaporation of the solvent *in vacuo* afforded a solid product which was dissolved in water (100 ml), washed with ether, and then acidified with concentrated hydrochloric acid to give crude IV.

IVa. Yellow crystals (from ethanol), yield 82%, mp 230 °C (decomp.). IR: 3000—2600 (OH), 1752 (carboxyl CO), 1690 and 1660 cm^{-1} (ring CO). Found: C, 51.94; H, 4.09; N, 19.95%. Calcd for $C_{12}H_{12}N_4O_4$: C, 52.17; H, 4.38; N, 20.28%.

IVb. Yellow needles (from acetic acid), yield 87%, mp 248 °C (decomp.). IR: 3030—2600 (OH), 1758 (CO), and 1690, 1660 cm^{-1} (CO). Found: C, 46.54; H, 3.54; N, 18.08%. Calcd for $C_{12}H_{11}N_4Cl$: C, 46.38; H, 3.56; N, 18.03%.

From III by Hydrolysis: A solution of III (2.0 g) in acetic acid (20 ml) containing concentrated hydrochloric acid (5.0 ml) was refluxed for 3 hr, allowed to cool and poured into ice-water. The solid product, so formed, was collected, crystallized and identified (mp and mixed mp) as IVa or IVb. Yields, 90 and 93% respectively.

4-Arylazo-1-β-cyanoethyl-2-β-ethoxycarbonylethyl-3,5-pyrazolidinediones (Va and Vb). *From III and Acrylonitrile*: Ten mmol of III was added to a solution of pyridine (50 ml) and water (10 ml) containing acrylonitrile (3 ml) and the reaction mixture was refluxed for 12 hr, left overnight at room temperature, and then evaporated *in vacuo*. The resulting oily product was triturated with petrolum ether and crystallized from ethanol.

Va. Yellow crystals, yield 75%, mp 58 °C. IR: 3154 (NH), 2230 (CN), 1730 (ester CO), 1710 and 1670 cm^{-1} (ring CO). Found: C, 57.23; H, 5.30; N, 19.26%. Calcd for $C_{17}H_{19}N_5O_4$: C, 57.13; H, 5.36; N, 19.60%.

Vb. Yield 90%, mp 100 °C. IR: 3150 (NH), 2230 (CN), 1730 (CO), 1715 and 1675 cm^{-1} (CO). Found: C, 52.03; H, 4.57; N, 17.58%. Calcd for $C_{17}H_{18}N_5O_4Cl$: C, 52.11; H, 4.63; N, 17.63%.

From III and β-Chloropropiononitrile: A mixture of III (0.01 mol), β-chloropropiononitrile (0.01 mol), sodium acetate (2.0 g) and ethanol (30 ml) was refluxed for 5 hr. The solvent was removed *in vacuo* and the remaining solid was washed with dilute hydrochloric acid and then water. The crude product was purified by recrystallization from ethanol and identified (mp and mixed mp) as Va or Vb. Yields, 70 and 72% respectively.

4-Arylazo-1-β-carboxyethyl-2-β-cyanoethyl-3,5-pyrazolidinedione (VIa and VIb). *From IV and Acrylonitrile*: To a solution of pyridine (50 ml) and water (10 ml) containing acrylonitrile (3 ml) 2.0 g of IV was added and refluxed for 3 hr and then evaporated *in vacuo*. The resulting crystalline mass was purified by recrystallization.

VIa. Yellow crystals (from ethanol), yield 72%, mp 195 °C. IR: 3150 (NH), 2400—2900 (OH), 2238 (CN), 1732 (carboxyl CO), 1670 and 1660 cm^{-1} (ring CO). Found: C, 54.41; H, 4.49; N, 21.14%. Calcd for $C_{15}H_{15}N_5O_4$: C, 54.71; H, 4.59; N, 21.27%.

VIb. Yellow crystals (from acetic acid), yield 75%, mp 205 °C. IR: 3125 (NH), 2400—2900 (OH), 2240 (CN), 1735 (carboxyl CO), 1660 and 1670 cm^{-1} (ring CO). Found: C, 49.16; H, 3.82; N, 19.44%. Calcd for $C_{15}H_{14}O_4N_5Cl$: C, 49.52; H, 3.87; N, 19.25%.

From V by Hydrolysis: A solution of V (2.0 g) in ethanolic aqueous sodium hydroxide (30 ml of 50% ethanol containing 1.0 g of NaOH) was refluxed for 45 min. The reaction mixture was allowed to cool and then acidified with concentrated hydrochloric acid to produce a solid product which was purified and identified as VIa or VIb.

From IV and β-Chloropropiononitrile: A mixture of IV (0.01 mol), β-chloropropiononitrile (0.01 mol), sodium carbonate (2.0 g) and ethanol (30 ml, 75%) was refluxed for 6 hr and then evaporated *in vacuo*. The remaining solid was dissolved in water and acidified with concentrated hydrochloric acid. The precipitates were purified by recrystallization and identified as V. Yields, 60 and 62% respectively.

4-Arylazo-1,2-di(β-carboxyethyl)-3,5-pyrazolidinedione (VIIa and VIIb). *From V by Hydrolysis*: A suspension of V (1.0 g) in acetic acid (20 ml) and hydrochloric acid (5 ml, 35%) was refluxed for 4 hr and then the solvent was removed under vacuum. The resulting crude product was treated with water, filtered and identified as VIIa or VIIb[1] after crystallization. Yields are 62 and 68% respectively.

From VI by Hydrolysis: In a similar manner as described above, hydrolysis of VI afforded VIIa or VIIb. Yields are 72 and 75% respectively.

From VIII by Hydrolysis: The procedure described above was used and the product proved to be VIIa of VIIb by mp and mixed mp.

4-Arylazo-1,2-di(β-ethoxycarbonylethyl)-3,5-pyrazolidinediones (VIIIa and VIIIb). Ten mmol of III was added to a solution of pyridine (50 ml) containing ethyl acrylate (0.02 mol) and was refluxed for 16 hr. The reaction mixture was left for two days at room temperature and then evaporated *in vacuo*. The resulting oily residue was dissolved in hot ethanol. After cooling, a small amount of unchanged material was removed by filtration. Evaporation of the filtrate afforded a crude product which was purified and identified as VIII.

VIIIa. Yellow crystals (from benzene–petroleum ether), yield 60%, mp 55 °C. Found: C, 56.69; H, 5.85; N, 13.70%. Calcd for $C_{19}H_{24}N_4O_6$: C, 56.43; H, 5.98; N, 13.86%.

VIIIb. Yellow crystals (from benzene–petroleum ether), yield 64%, mp 95 °C. IR: 1740, 1730 (ester CO), 1700 and 1680 cm^{-1} (ring CO). Found: C, 52.07; H, 5.10; N, 12.59%. Calcd for $C_{19}H_{23}N_4O_6Cl$: C, 51.99; H, 5.28; N, 12.76%.

Reaction of III or IV with Hydrazine Hydrate. Two grams of III or IV was added to a solution of ethanol (30 ml) containing hydrazine hydrate (2.0 ml) and refluxed for 3 hr. After cooling, the product was collected, recrystallized from dioxane and proved to be arylazomalonic acid dihydrazide by mixed mp determination with an authentic sample.[3]

4-Arylazo-1-β-ethoxycarbonylethyl-2-acetyl-3,5-pyrazolidinedione (X). A mixture of III (2.0 g) and acetic anhydride (30 ml) was refluxed for 3 hr. After cooling, the reaction mixture was poured into water and stirred to decompose the excess acetic anhydride. The product, which separated out, was collected and recrystallized from ethanol.

Xa. Yellow crystals, mp 95 °C. IR: 3155 (NH), 1742 (acetyl CO), 1718 (ester CO), 1690 and 1665 cm^{-1} (ring CO). Found: C, 55.81; H, 5.26; N, 16.61%. Calcd for $C_{16}H_{18}N_4O_5$: C, 55.48; H, 5.24; N, 16.18%.

Xb. Yellow needles, mp 127 °C. IR: 3150 (NH), 1740 (acetyl CO), 1730 (ester CO), 1690 and 1675 cm^{-1} (ring CO). Found: C, 50.46; H, 4.50; N, 14.59%. Calcd for $C_{16}H_{17}N_4O_5Cl$: C, 50.46; H, 4.47; N, 14.71%.

*2-*p*-Chlorophenylazotetrahydropyrazolo[1,2-*a*]pyrazole-1,3,7-trione (XI).* A suspension of IVb (2.0 g) in phosphorus oxychloride (20 ml) was heated on a water bath for 3 hr. The resulting solution was then poured into ice-water and the resulting solid product was crystallized from ethanol. Yield was 50%. Yellow crystals, mp 275 °C. IR: 1770, 1710, and 1680 cm^{-1} (ring CO). Found: C, 49.09; H, 3.33; N, 18.77%. Calcd for $C_{12}H_9N_4O_3Cl$: C, 49.23; H, 3.09; N, 19.14%.

*1, 2-Dihydro-5-hydroxy-3-phenylazopyrazolo[1, 5-*a*]pyrimidine-2-one (XII).* Two grams of II was added to a solution of pyridine (50 ml) and water (10 ml) containing 1 ml of ethyl acrylate and then one drop of potassium hydroxide solution was added. The mixture was refluxed for 14 hr and then left overnight at room temperature. Removal of the solvent *in vacuo* afforded an oily residue which was dissolved in ethanol and acidified with concentrated hydrochloric acid. The crystals, which separated out, were collected and recrystallized from dimethylformamide to give 1.2 g (60%) of XII. Mp 301 °C. IR: 1690 (CO), 2430—2900 cm^{-1} (OH). Found: C, 55.62; H, 4.39; N, 27.30%. Calcd for $C_{12}H_{11}N_5O_2$: C, 56.02; H, 4.31; N, 27.23%.

Compound XII produces a red color with ferric chloride solution and is soluble in sodium carbonate solution. In the absence of potassium hydroxide, compound II was recovered unchanged after being refluxed with ethyl acrylate for 36 hr.