

**Effect of Solvent on the Product Formation
in the Reaction of Hydrazines with
 β -Aroyl- α -[4(1,3-Disubstituted-2-Pyrazolin-5-One)]
Propionic Acids**

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ABSTRACT. The reaction of β -aroyl- α -[4(1,3-disubstituted-2-pyrazolin-5-one)] propionic acids **1** with hydrazines in acetic acid afforded the unexpected 6-aryl-pyridazin-3-ones **3** instead of the expected 4-pyrazolinonyl pyridazinones through the fission of the 1,3-disubstituted-2-pyrazolin-5-one. A probable mechanism has been proposed. Reactions of 6-aryl-pyridazin-3-ones with dimethylsulfate, diethylsulfate, ethyl bromoacetate, phosphorus oxychloride and phosphorus pentasulfide have also been described.

It was stated (Sayed *et al.* 1984) that the reaction of equimolar amounts of β -aroyl- α -[4(1,3-disubstituted-2-pyrazolin-5-one)] propionic acids with hydrazines hydrate in ethanol gave the 4-pyrazolinonyl pyridazinone derivatives. The object of the present work is to replace ethanol as a solvent, with acetic acid, in order to study the influence of the solvent on the type of reaction products.

Thus, the reaction of **1a** and **1b** with hydrazine hydrate in acetic acid gave the 6-aryl-pyridazin-3-ones **3a** and **3b** respectively (Scheme 1), instead of the expected 4-pyrazolinonyl pyridazinones **2** (Scheme 2). The 6-aryl-pyridazin-3-ones **3** were produced presumably according to the following mechanism (Scheme 2). The structures of compounds **3** were supported by the following facts:

1. By similarity of melting points with the same compounds prepared alternatively by the reaction of the corresponding β -aroylacrylic acids **5a,b**

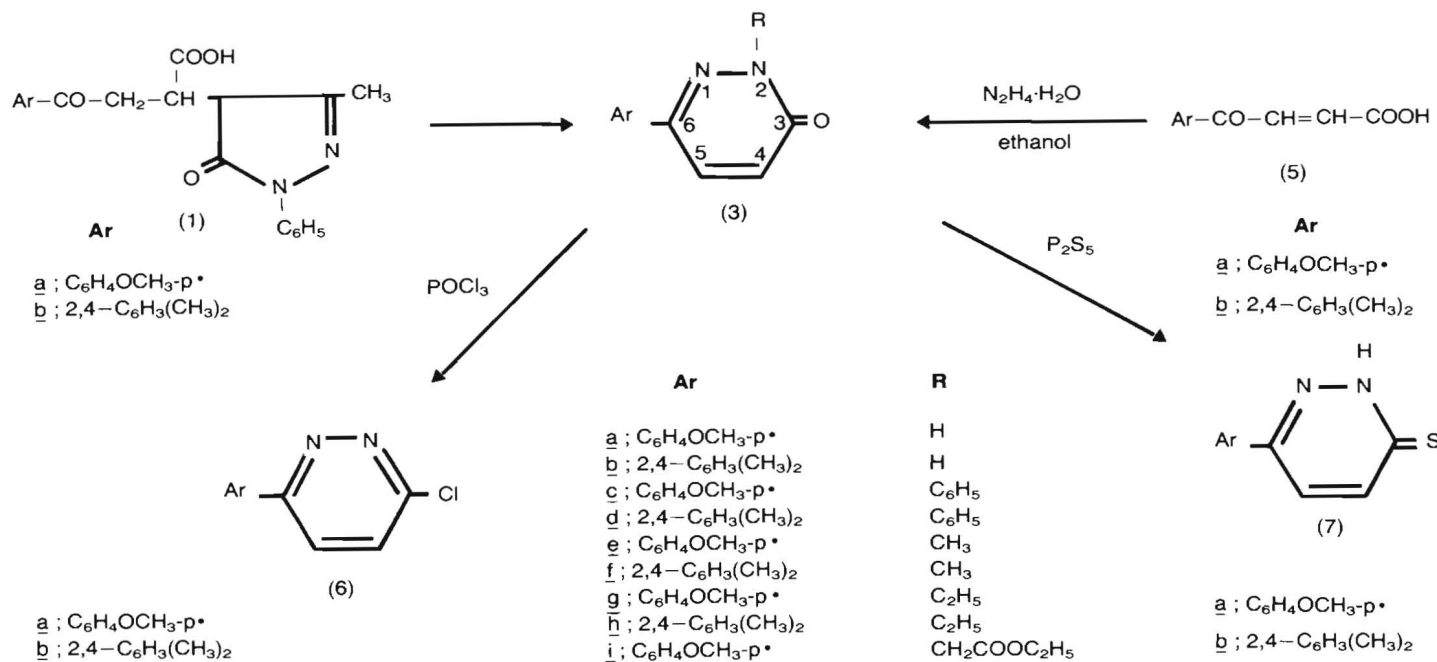
with hydrazine hydrate in ethanol (Baddar *et al.* 1965 and Rupert *et al.* 1976a and b).

- The PMR (acetone- d_6) spectrum of **3a** showed signals at 12.1 (1H, s broad, NH), 7.9-6.8 (6H, m, Ar-H + -CH=CH-) and 3.84, s, Ar-OCH₃), and that of **3b** showed signals at 12.4 (1H, s, NH), 7.6-6.3 (5H, m, Ar-H + -CH=CH-) and at 2.3 (6H, s, 2CH₃).
- The mass spectrum of **3a** showed a molecular ion peak at $m/e = 202$ (100%). Pyridazone **3a** fragments initially by loss of carbon monoxide followed by loss of N₂, H[•], then CH₂, to give charged ions at $m/e = 174$ (5.3%), 146 (4%), 145 (30.6%) and 131 (8.6%), whilst the loss of 15 mass units from the parent ion corresponds to the loss of CH₃ with subsequent formation of the charged ion at $m/e = 187$ (5.3%) (Scheme 3). The mass spectrum of **3b** showed a molecular ion peak at $m/e = 200$ (100%), then followed the same pathway of fragmentation (loss of CO, N₂, H[•] and CH₃) to give the corresponding charged ions at $m/e = 172$ (22%), 144 (4%), 143 (17.3%), 128 (24.6%), 185 (8%).
- The IR spectra (ν_{\max} cm⁻¹) of **3** showed $\nu_{C=O}$ at 1630-1620, $\nu_{C=N}$ at 1585-1570 and ν_{NH} at 3380-3200.

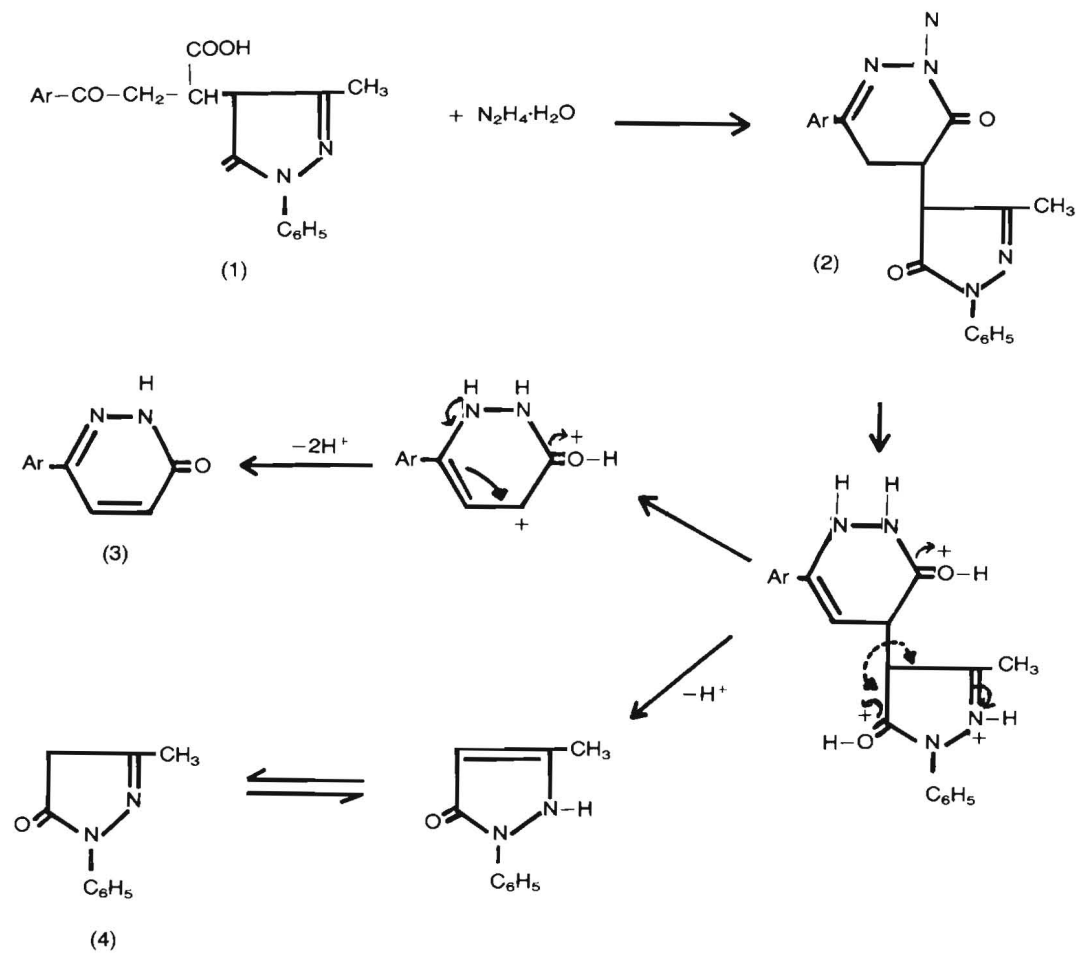
When the reaction of **1a** and **1b** was carried out with phenylhydrazine under the same conditions **3c** and **3d** respectively, were obtained, according to the same above mentioned mechanism. The IR spectra of **3c** and **3d** showed $\nu_{C=O}$ at 1635-1630 and $\nu_{C=N}$ at 1590-1585.

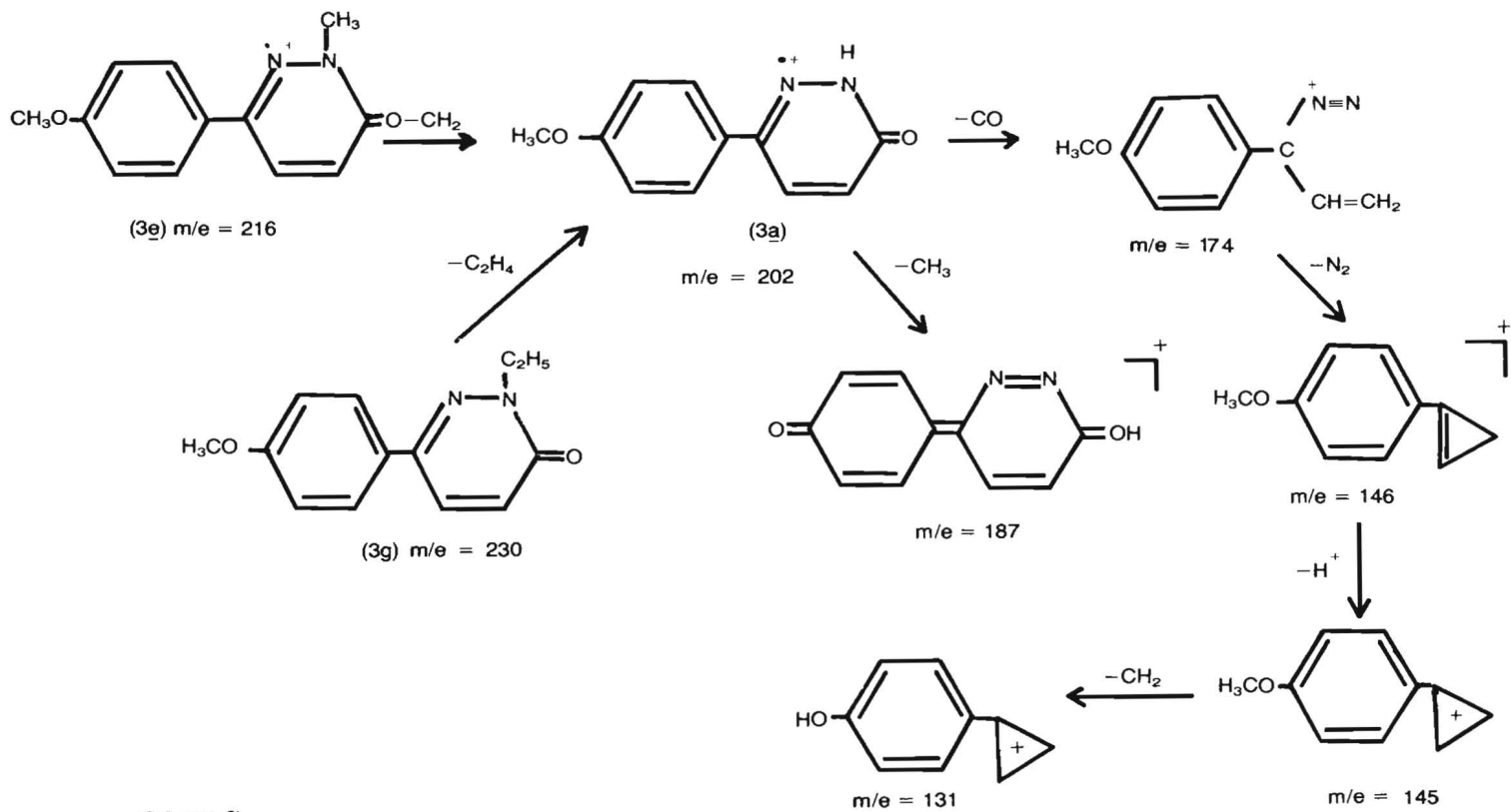
Compounds **3a** and **3b** were subjected to further studies. Thus, reaction with dimethylsulfate, diethylsulfate or ethyl bromoacetate gave the N-substituted products **3e-i**. The IR spectra of **3e-i** showed $\nu_{C=O}$ at 1665-1630 and $\nu_{C=N}$ at 1605-1585; an additional band at 1720 for **3i** being attributable to $\nu_{C=O}$ (carboxylic ester). The PMR (acetone- d_6) of **3g** showed signals at 7.9-6.8 (6H, m, Ar-H + -CH=CH-), 4.1 (2H, q, CH₃CH₂), 3.8 (3H, s, Ar-OCH₃) and 1.3 (3H, t, CH₃CH₂). The mass spectrum of **3e** showed a molecular ion peak at $m/e = 216$ (15.8%); the parent ion lost CH₂ to give the charged ion with mass 202 (100%) which followed the same pathway of fragmentation as **3a** to give the same charged ions at $m/e = 187$ (5.3%), 174 (5.3%), 146 (5.3%), 145 (30.6%), 131 (8.0%) (Scheme 3). Similarly, the mass spectrum of **3g** showed a peak at $m/e = 230$ (100%), of the molecular ion which lost C₂H₄ to give again the charged ion of $m/e = 202$ (64.6) with the typical fragment pattern of $m/e = 187$ (7.3%), 174 (3.3%), 146 (6.0%), 145 (42.6%) and 131 (3.3%).

Treatment of **3a** and **3b** with POCl₃ gave the chloro derivatives **6a** and **6b**, respectively. The IR spectra of **6** were devoid of $\nu_{C=O}$ and showed $\nu_{C=N}$ at 1610-1590.



(Scheme 1)





(Scheme 3)

Furthermore reaction of **3a** and **3b** with phosphorus pentasulfide in dry xylene gave the corresponding thiones **7a** and **7b**. The IR spectra of **7** showed $\nu\text{N}=\text{C}=\text{S}$ at 1480–1475, $\nu\text{C}=\text{S}$ at 1390, $\nu\text{C}=\text{N}$ at 1600–1580 and νNH at 3430–3410. The PMR (acetone- d_6) of **7a** revealed signals at 12.1 (1H,s (broad),NH), 7.9-6.8 (6H,m,Ar-H + -CH=CH) and 3.86 (3H,s,Ar-OCH₃). The mass spectrum of **7a** showed a molecular ion peak at $m/e = 218(14.6\%)$.

Experimental

All melting points are uncorrected, IR spectra (KBr discs) were recorded on a Unicam SP 1200 spectrophotometer, PMR spectra on a Jeol FX 100 Fourier transform instrument using tetramethyl silane as internal standard. Mass spectra were obtained with an AEI MS 902 mass spectrometer operated at 70 eV electron energy, 6 KV accelerating voltage and ion source temperature of 120-150°C using the direct insertion probe.

Reaction of 1a and 1b with hydrazines; formation of 3a-d

A solution of **1a** and **1b** (0.01 mol) and hydrazine hydrate or phenylhydrazine (0.015 mol) in acetic acid (30 ml) was refluxed for 5 hrs, concentrated and cooled. The separated solid was filtered and fractionally crystallized from benzene to give **3a-d**, and the residue was crystallized from ethanol to give **4**, which is identified by m.p. determination.

Reaction of 5a and 5b with hydrazines; formation of 3a and 3d

A solution of **5a** or **5b** (0.01 mol) and hydrazine hydrate (0.015 mol) in ethanol (20 ml) was refluxed for 5 h, concentrated, cooled, and the solid separated was filtered and crystallized from benzene to give **3a** and **3b**, respectively.

Reaction of 3a and 3b with dimethylsulfate, diethylsulfate and ethyl bromoacetate; formation of 3e-i

A mixture of **3a** or **3b** (0.01 mol), anhydrous potassium carbonate (0.03 mol), dimethylsulfate, diethylsulfate or ethyl bromoacetate (0.03 mol) and dry acetone (50 ml) was refluxed for 20 h. After removing of the excess of the solvent, the products were crystallized from the proper solvent to give compounds **3e-i** (Table 1).

Reaction of 3a and 3b with POCl₃; formation of 6a and 6b

A mixture of **3a** and **3b** (0.01 mol) and POCl₃ (10 ml) was gently refluxed for 30 min, cooled, treated with crushed ice, and the precipitated solid filtered and crystallized from a suitable solvent to give **6a** and **6b** respectively.

Table 1. Physical Data of various compounds prepared

Compd.	M.p.°C	Solvent yield %	Mol. formula (M.Wt.)	Analysis % Found/Calcd.		
				C	H	N
3 _a	187	benzene 35	C ₁₁ H ₁₀ N ₂ O ₂ (202)	65.40 65.34	5.00 4.99	13.70 13.86
3 _b	141	benzene 33	C ₁₂ H ₁₂ N ₂ O (200)	72.20 71.98	6.10 6.00	14.10 14.00
3 _c	129	benzene 29	C ₁₇ H ₁₄ N ₂ O ₂ (278)	73.50 73.36	5.10 5.07	10.20 10.07
3 _d	130	benzene 30	C ₁₈ H ₁₆ N ₂ O (276)	78.30 78.23	5.80 5.84	10.30 10.14
3 _e	100	(Pet. ether 80-100) 20	C ₁₂ H ₁₂ N ₂ O ₂ (216)	66.80 66.66	5.60 5.57	13.10 12.96
3 _f	67	n-hexane 37	C ₁₃ H ₁₄ N ₂ O (214)	72.80 72.87	6.40 6.59	13.20 13.08
3 _g	73	(Pet. ether 40-60) 29	C ₁₃ H ₁₄ N ₂ O ₂ (230)	67.90 67.82	6.20 6.13	12.20 12.17
3 _h	122	(Pet. ether 80-100) 25	C ₁₄ H ₁₆ N ₂ O (228)	73.60 73.65	7.20 7.06	12.30 12.28
3 _i	104	(Pet. ether 40-60) 30	C ₁₅ H ₁₆ N ₂ O ₄ (288)	62.60 62.50	5.60 5.55	9.80 9.72
6 _a	168	benzene 60	C ₁₁ H ₉ ClN ₂ O (220.5)	59.80 59.86	4.10 4.11	12.80 12.69
6 _b	135	(Pet. ether 40-60+benz.) 63	C ₁₂ H ₁₁ ClN ₂ (218.5)	66.10 65.90	5.20 5.03	12.60 12.81
7 _a	189	ethanol 39	C ₁₁ H ₁₀ N ₂ OS (218)	60.40 60.55	4.70 4.62	12.70 12.84
7 _b	162	ethanol 35	C ₁₂ H ₁₂ N ₂ S (216)	66.60 66.66	5.70 5.59	12.80 12.96

Action of P₂S₅ on 3_a and 3_b; formation of 7_a and 7_b

A solution of 3_a or 3_b (0.01 mol), P₂S₅ (0.02 mol) and dry xylene (50 ml) was boiled under reflux for 6 h. The reaction mixture was filtered while hot and then concentrated. The product which separated on cooling, was crystallized from a suitable solvent to give the thione derivative 7_a and 7_b, respectively.

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تأثير المذيب على ناتج تفاعل الهيدرازينات مع أحماض بيتا ارويل الفا [٤ (١ ، ٣ ثنائي أحلال البيرازولين - ٥ - اون)] أحماض البروبيونيك

مدحت المبيض^١ و جلال حسني سيد^٢ و علي الشكيل^٣ و عصام عبدالغني^١

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تم في هذا البحث دراسة تفاعل بيتا - ارويل - α - [٤ - (١ - فينيل
- ٣ - ميثيل - ٢ - بيرازولين - ٥ - اون)] أحماض البروبيونيك مع هيدرات
الهيدرازين و فينيل الهيدرازين في وجود حمض الخليك ليعطي ٦ - اريل
- بيريدازين - ٣ - اون وتم شرح ميكانيكية التفاعل الذي تم بتكاثف الحمض
مع هيدرات الهيدرازين أو فينيل الهيدرازين ثم انفصال حلقة البيرازولون لتعطي
٦ - اريل - بيريدازين - ٣ - اون .

كما تمت مقارنة درجات انصهار المركبات الناتجة بالمركبات المحضرة بالطريق
التبادلي بين حمض بيتا ارويل اكريليك وهيدرات الهيدرازين في الكحول الايثيلي،
ودراسة طيف الاشعة تحت الحمراء وطيف الرنين النووي المغناطيسي وطيف
الكتلة وأوضح الاخير ان عملية الكسر تبدأ بفقد المركب أول أكسيد الكربون
يتلو ذلك فقد النيتروجين ثم مجموعة الميثيلين كما اتضح ظهور مركب وزنه ينقص
١٥ وحدة عن المركب الأصلي نتيجة فقد مجموعة ميثيل .

كما درس تفاعل ٦ - اريل - بيريدازين - ٣ - اون مع كبريتات ثنائي الميثيل

ليعطى مشتق ن - ميثيل وتفاعله مع كبريتات ثنائي الايثيل ليعطى مشتق ن - ايثيل وكذلك التفاعل مع ايثيل برومو الخلات .

وتمت كذلك دراسة تفاعل ٦ - اريل - بيريدازين - ٣ - اون مع أوكسي كلوريد الفوسفور ليعطى مشتق الكلورو .

تم درس تفاعل ٦ - اريل - بيريدازين - ٣ - اون مع خامس كبريتيد الفوسفور ليعطي الثيون المقابل .

وأخيراً تمت دراسة تركيب المركبات الناتجة باستخدام طيف الأشعة تحت الحمراء وفوق البنفسجية وطيف الرنين النووي المغناطيسي وطيف الكتلة .