Addition And Cycloaddition Reactions With Pyrazole Blue

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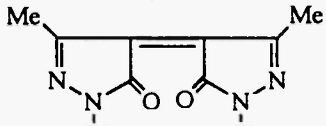
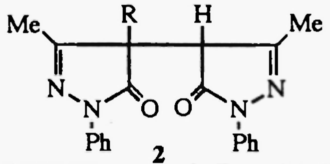
Abstract: Pyrazole blue **1** readily reacts with primary aromatic amines to give the corresponding adducts **2a-c**,with N,N-disubstituted aromatic amines yielding **2d-e**, with dimethyl amine gives **3** and with benzyl amine to afford rubazonic acid **4**. α-Amino acids and thioglycolic acid readily reduces **1** to give **2i**. It behaves as a diene to give **6** and as a dienophile yielding **8a,b** and **10a-c** in Diels- Alder cycloaddition.

Westoo[1-3] and others[4-6] reported that **1** reacts smoothly with active methylenes and Grignard reagents through a 1,4-addition process across one of the carbonyl groups. Pyrazole blue **1** was prepared according to our modified procedure[7]. The aim of our work was to study the scope and limitation of the reactions of **1** with other reagents such as amines, phenols, thiophenols, water, amino acids and thioglycolic acid. Thus, boiling an equimolar mixture of primary aromatic amines and **1** in dry benzene gave the corresponding adducts **2a-c** in moderate to excellent yields (50-96%). However, **1** reacted with 10 fold excess of N,N-disubstituted aromatic amines in ethanol at room temperature to afford **2d,e** in a fairly good yield (56%) together with unidentified decomposition products. The structures of **2a-e** was assigned on the basis of spectral and analytical data. It is believed that compounds **2a-e** are obtained via a 1,4-addition process across one of the carbonyl groups. On the other hand, stirring of **1** with 10 fold excess of dimethyl amine in absolute ethanol for 5 days at ambient temperature gave 77% yield of **3**. The structure of **3** was established on the basis of its spectral and analytical data. There is further supporting evidence, thus **3** was authentically prepared by the reaction of the diketone **5** and dimethyl amine[7]. Interestingly, stirring a mixture of **1** (1 mmol) and benzyl amine (10 mmol) in ethanol at room temperature for 30 minutes afforded rubazonic acid **4**[8] in a good yield (72%). We believe that the diketone **5** is obtained in situ as an intermediate (Scheme), which in turn reacts with benzyl amine to give **4**. We reported recently that **5** reacts readily with α-amino acids and amines to give **4**[9]. Similarly, **1** reacted with phenol and thiophenol yielding **2f** and **2g** in 48% and 51% yields respectively. However, boiling **1** with aqueous ethanol gave **2h** in a 77% yield. Surprisingly, boiling an equimolar mixture of **1** and α-amino acid, e.g., glycine, alanine, serine, valine, threonine and phenylglycine in glacial acetic acid for 1 hour gave **2i** in 72%, 68%, 65%, 61%, 63% and 69% yields respectively. On the other hand, refluxing **1** with 2 fold excess of thioglycolic acid in dry benzene for 5 hours yielded 52% of **2i**. The structure of **2i** was established on the basis of its spectral and analytical data. It was also confirmed by the preparation of an authentic sample of **2i** via a different route.[10]

It also attracted our attention to study the reactivity of **1** in both normal and inverse electron demand Diels- Alder cycloaddition reactions. Thus heating under reflux pyrazole blue **1** with an excess of ethyl vinyl ether for 0.5h afforded a reasnable good yield (67%) of the corresponding cycloadduct **6**. The sructure of **6** was established on the basis of its spectral and analytical data. In contrast, compound **1** reacted with homo- and heterodienes as a dieneophile.Thus, boiling an equimolar mixture of **1** and dienes **7a,b** in acetonitrile for 0.5h gave **8a,b** in 58 and 66% yields respectively. Analogously, **1** reacted with

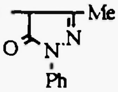


1

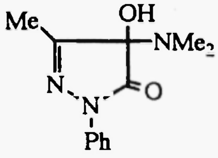


2

a, R = C6H5NH
b, R = *p* MeC6H4NH
c, R = *p* MeOC6H4NH
d, R = *p* Me2NC6H4NH
e, R = *p* Et2NC6H4NH
f, R = C6H5O
g, R = C6H5S
h, R =



i, R = H



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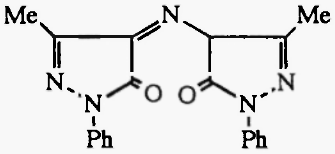

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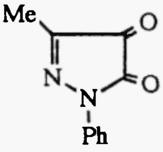

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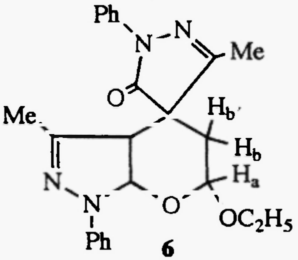

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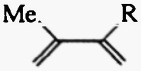
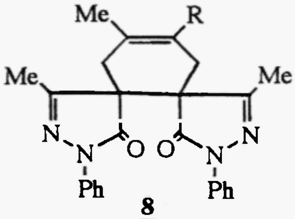


7 a, R = H
b, R = Me



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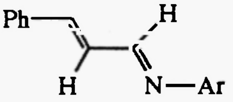
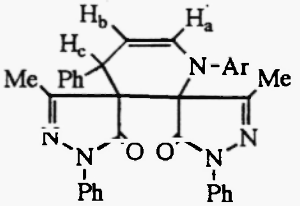
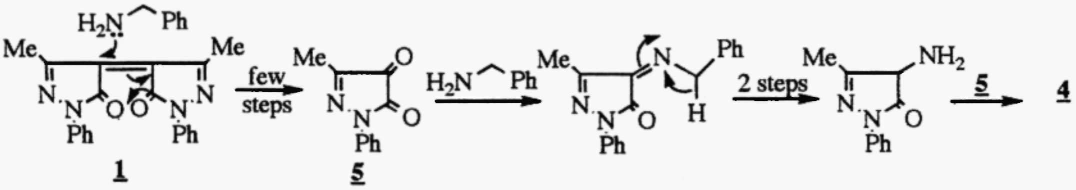


9 a, Ar = C6H5
b, Ar = *p* MeOC6H4
c, Ar = *p* MeC6H5



10 a, Ar = C_6H_5
b, Ar = *p* $MeOC_6H_4$
c, Ar = *p* MeC_6H_4



Scheme

Table:

Compd.	mp.°C	Yield%	Molecular formula#	IR υ cm⁻¹	^{1}H-NMR (CDCl$_3$, δ: ppm)
2a	95-98	96	$C_{26}H_{23}N_5O_2$ (437)	3500,330,1720	2.0 (s, 6H, 2CH$_3$), 6.5 (s, 1H, CH) and 7.4 (m, 15H, Ar).
2b	118-120	58	$C_{27}H_{25}N_5O_2$ (451)	3500,320,1750	2.0 (s, 6H, 2CH$_3$), 2.1 (s, 3H, CH$_3$), 6.5 (s, 1H, CH) and 7.4 (m, 14H, Ar).
2c	123-125	71	$C_{27}H_{25}N_5O_3$ (467)	3450,330,1715	2.1 (s, 6H, 2CH$_3$), 3.7 (s, 3H, CH$_3$), 6.7 (s, 1H, CH) and 7.6 (m, 14H, Ar).
2d*	159-161	56	$C_{28}H_{27}N_5O_2$ (465)	.1715	1.8 (s, 3H, CH$_3$), 2.1 (s, 3H, CH$_3$), 2.85 (s, 6H, 2CH$_3$) and 7.3 (m, 14H, Ar).
2e*	207	57	$C_{30}H_{31}N_5O_2$ (493)	1720	1.1 (t, 6H, 2CH$_3$), 1.8 (s, 3H, CH$_3$), 2.15 (s, 3H, CH$_3$), 3.35 (q, 4H,2CH$_2$)and7.5 (m,14, Ar).
2f	112-113	48	$C_{26}H_{22}N_4O_3$ (438)	3300,1700	2.05 (s, 3H, CH$_3$), 2.15 (s, 3H, CH$_3$), 3.3 (s, 1H, OH) and 7.3 (m, 14H, Ar).
2g*	208-212	51	$C_{26}H_{22}N_4O_2S$ (454)	1720	2.25 (s, 3H, CH$_3$), 2.5 (s, 3H, CH$_3$) and 7.4(m, 14H, Ar).
2h*	199	77	$C_{30}H_{26}N_6O_3$ (518)	3400, 1720	2.1 (s, 9H, 3CH$_3$), 7.5 (m, 15, Ar).
2i*	>300	61-72	$C_{20}H_{18}N_4O_2$ (346)	3100	2.1 (s, 6H, 2CH$_3$), 7.4 (m, 10h, Ar).
3*	203	77	$C_{12}H_{15}N_3O_2$ (233)	3450,1670	2.0 (s, 3H, CH$_3$), 2.95 (s, 3H, CH$_3$), 3.1 (s, 3H, CH$_3$), 7.1 (m, 5H, Ar) and 9.1 (s, 1H, OH).
6	116	67	$C_{24}H_{24}N_4O_3$ (416)	1710,1210	1.4 (t, 3H, CH$_3$), 2.5 (s, 3H, CH$_3$), 2.15 (s, 3H, CH$_3$), 2.5 (m, 2H, H$_6$, H$_6$), 3.75 (q, 2H, CH$_2$), 5.4 (d, 1H, H$_a$) and 7.45 (m, 10H, Ar).
8a	151-152	58	$C_{25}H_{24}N_4O_2$ (412)	1715	1.7 (s, 3H, CH$_3$), 2.15 (s, 6H,2 CH$_3$), 2.5 (m, 4H, 2CH$_2$), 5.6 (t, 1H, CH)and7.5 (m, 10H, Ar).
8b	162	66	$C_{26}H_{26}N_4O_2$ (426)	1720	1.7 (s, 6H, 2CH$_3$), 2.15 (s, 6H,2 CH$_3$), 2.4 (s, 4H, 2CH$_2$) and 7.5 (m, 10H, Ar).
10a	204	58	$C_{35}H_{29}N_5O_2$ (551)	1715	1.9 (s, 6H, 2CH$_3$), 4.3 (t, 1H, H$_c$), 5.15 (d, 1H, H$_b$), 6.95 (m, 1H, H$_a$) and 7.4 (m, 20H, Ar).
10b	217	71	$C_{36}H_{31}N_5O_3$ (581)	1710	1.8 (s, 6H, 2CH$_3$), 3.8 (s, 3H, OCH$_3$), 4.26 (t, 1H, H$_c$), 5.1 (d, 1H, H$_b$), 6.85 (d, 1H, H$_a$) and 7.4 (m, 19H, Ar).
10c	223	78	$C_{36}H_{31}N_5O_2$ (565)	1710	1.8 (s, 6H, 2CH$_3$), 2.38 (s, 3H, CH$_3$), 4.28 (t, 1H, H$_c$), 5.15 (d, 1H, H$_b$), 6.85 (d, 1H, H$_a$) and 7.4 (m, 19H, Ar).

Satisfactory elemental analyses for all the synthesised compounds were obtained.

* ^{1}H-NMR solvent: ducterated DMSO.

9a-c to give **10a-c** in fairly good yield (58-78%). The sructure of compounds **8a,b** and **10a-c** was assigned on the basis of their spectral and analytical data.

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