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Synthesis of Arylhydrazono-tetrazolopyrimidones, -thiazolopyrimidones, -pyrazolopyridones and -benzimidazolopyrimidines. Part-4†

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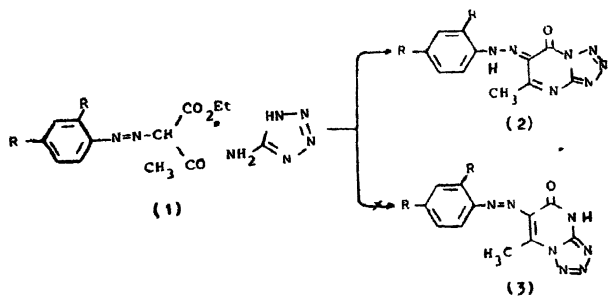
Ethyl α-arylazo-β-oxobutyrates (1a–e) undergoes condensation with 5-amino-tetrazole, 2-amino-4-carboethoxythiazole and 3-amino-1-phenyl-2-pyrazolin-5-one to give the linearly fused condensation products (2, 4 and 5). While the condensation of α-arylhydrazonoacetylacetone with 2-aminobenzimidazole gives the arylazobenzimida-zolopyrimidines (7). The structures of the compounds were established by analytical and spectral methods.

As a part of our studies directed towards the development of new arylhydrazono derivatives of pharmaceutical interest containing a bridgehead nitrogen atom[2,3], considerable attention has been drawn to the synthesis of several condensed heterocyclic systems, especially derived from tetrazole, thiazole, pyrazole and benzimidazole.

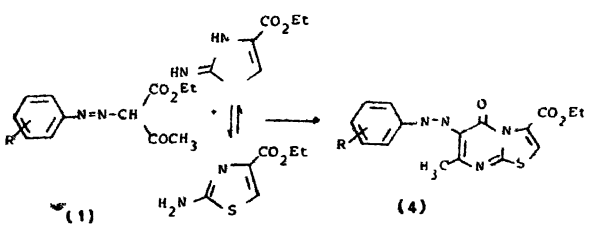
The condensation of 5-aminotetrazole with ethyl α-arylazo-β-oxobutylate (1) gave two possible structures 2 or 3. The ir spectrum shows only one carbonyl absorption and NH, and no absorption due to a CONH group of cyclic structure 3. The assignment of structure 2 is consistent with (i) the observations made in our previous publications[2], (ii) that in β-keto ester, the amino group attacks the methyl ketone first, then the ester group, to give the arylhydrazonotetrazolopyrimidones (2a–e), (iii) ^{1}H nmr spectrum (2c) displayed signals at δ 2.5 (3H, s, CH_3), 8.3 (1H, s, NH) and 6.8–7.8 (4H, m, ArH) and (iv) ir spectrum (2c) showed the CO absorption at 1 690 cm^{-1}.

The reaction of 1 with 2-amino-4-carboethoxy-thiazole afforded the arylazothiazolopyrimidones (4) in good yield. The ir spectra showed absorption bands at 1 600–1 610 (C=N), 1 640–1 665 (C=O), 1 680–1 710 (CO ester) and no (NH). The ^{1}H nmr spectrum of 4a displayed signals at δ 1.35 (3H, t, CH_3 of ester), 2 6 (3H, s, CH_3), 4.4 (2H, q, CH_2 of ester), 5.4 (1H, s, CH olefinic) and 7.35–7.5 (5H, m, ArH). The mass spectrum of 4e gave an M^+ at 387 which fitted exactly with the calculated molecular weight.

Condensation of 1 with 3-amino-1-phenyl-2-pyrazolin-5-one gave two possible structures 5 or 6.



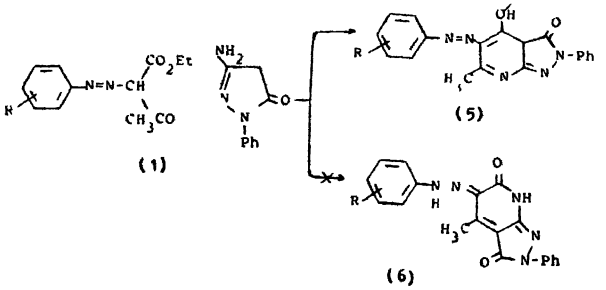
a ; R=H, R′=H
b ; R=CH_3, R′=H
c ; R=Cl, R′=H
d ; R=Br, R′=H
e ; R=OC_2H_5, R′=NO_2



a ; R=H
b ; R=4-Cl
c ; R=4-Br
d ; R=4-CH_3
e ; R=3-NO_2

† For Part 3, see Ref. 1.

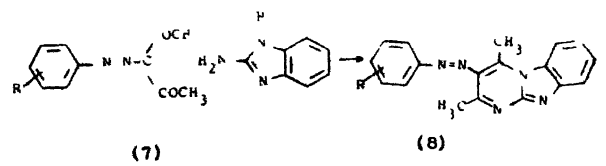
Based on the ir spectral data and our previous findings we favour structure **5** rather than **6**. The ir spectra showed absorptions at 3 500–3 400 (OH), 1 680–1 700 (C=O of pyrazolone), 1 610–1 635 (C=N) and 1 595–1 600 cm^{-1} (N=N). The ^1H nmr spectra of **5b** displayed signals at δ 2.1 (3H, s, CH_3), 2.5 (3H, s, CH_3), 14.1 (1H, s, OH) and 7.1–7.5 (9H, m, ArH).



(1) (5) (6)

a; R=4-Cl
b; R=4-CH_3

In connection with the above successful reaction, it seemed of interest to react α-arylhydrazonoacetylacetone (**7**) with 2-aminobenzimidazole in 5% sodium hydroxide solution to give the arylazobenzimidazolopyrimidines (**8a–b**) in good yield, as inferred from the absence of any absorption due to carbonyl or NH. The ^1H nmr spectra of **2a** displayed signals at δ 2.1 (6H, s, $2CH_3$) and 7.15–7.4 (9H, m, ArH).



(7) (8)

a; R=H
b; R=2-CH_3

Experimental

All melting points are unconnected. Infrared spectra (KBr) were recorded on a Pye-Unicam SP 2000 spectrophotometer, and ^1H nmr spectra on a Jeol Fx90 Q FT spectrometer.

6-Arylhydrazono-5-methyl[1,2,3,5]tetrazolo[5,1-a]pyrimid-7-one (**2a–e**). *Method-A :* A mixture of ethyl α-arylazo-β-oxobutyrate (**1**; 0.01 mol) and 5-aminotetrazole (0.01 mol) in xylene was refluxed for 24 h in presence of catalytic amount of piperidine. After cooling, the resulting precipitate was filtered, washed well with petroleum ether (b.p. 60–80°), dried and crystallised from the appropriate solvent to give compounds **2a–e** (Table 1).

Method-B : A mixture of ethyl α-arylazo-β-oxobutyrate (**1**; 0.01 mol) and 5-aminotetrazole (0.01 mol) in ethanol was refluxed for 16 h in presence of catalytic amount of piperidine. After cooling, the resulting precipitate was filtered, wahsed with petroleum ether, dried and crystallised from the appropriate solvent to give compounds **2a–e**.

TABLE 1—PHYSICAL DATA OF COMPOUNDS 2, 4, 5 AND 8*

Compd. no.	Yield %	M.p.** °C	Mol. formula (Mol. wt.)
2a	70	96[a]	$C_{11}H_9N_7O$ (255.24)
2b	65	190[a]	$C_{12}H_{11}N_7O$ (269.268)
2c	65	>260[a]	$C_{11}H_8N_7OCl$ (289.689)
2d	70	160[a]	$C_{11}H_8N_7OBr$ (334.48)
2e	80	175[b]	$C_{13}H_{12}N_8O_4$ (344.3)
4a	65	155[a]	$C_{16}H_{14}N_4SO_3$ (342.366)
4b	70	95[a]	$C_{16}H_{13}N_4SO_3Cl$ (376.813)
4c	70	148[a]	$C_{16}H_{13}N_4SO_3Br$ (421.272)
4d	60	65[b]	$C_{17}H_{16}N_4SO_3$ (356.396)
4e	75	222[b]	$C_{16}H_{13}N_5SO$ (387.366)
5a	70	120[b]	$C_{19}H_{14}N_5O_2Cl$ (379.797)
5b	60	95[b]	$C_{20}H_{17}N_5O_2$ (359.38)
8a	55	172[b]	$C_{18}H_{15}N_5$ (301.34)
8b	75	167[b]	$C_{19}H_{17}N_5$ (315.37)

*All compounds showed satisfactory C, H, N and S analysis.
**Solvent for crystallisation : [a]ethanol, [b]dilute ethanol.

6-Arylazo-4-ethoxycarbonyl-7-methylthiazolo[3,2-a]pyrimid-5-one (**4a–e**) *:* The experimental conditions previously used to effect condensation of **1** with 5-aminotetrazole were adopted for the preparation of **4a–e** via condensation of **1** with 2-amino-4-carboethoxythiazole (Table 1).

5-Arylazo-4-hydroxy-6-methy-3-oxo-2-phenylpyrazolo[5-4a]pyridine (**5a, b**) *:* The above experimental procedures were adopted for preparation of **5a,b** using **1** and 3-amino-1-phenyl-2-pyrazolin-5-one (Table 1).

3-Arylazo-2,4-dimethylpyrimido[1,2-a]benzimidazole (**8a, b**) *:* The compounds were prepared by adopting the general procedure of treating **1** with 2-aminobenzimidazole using xylene–piperidine or ethanol–piperidine (Table 1).

References

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