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Reactions with Heterocyclic Arylazo Compounds: Synthesis of New 1-Azoloylimidazolones

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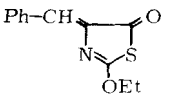
Several new carboxamide derivatives of 1-azoloylimidazolones and 1-aryl-1,2,4-triazolones were synthesised by reaction of 2-alkoxy-4-benzylidene-2-thiazolin-5-ones and 2-alkoxy-4-phenylhydrazone-2-thiazolin-5-ones with heterocyclic amines.

Reaktionen mit heterocyclischen Arylazoverbindungen: Synthese neuer 1-Azoloylimidazolone

Einige neue Carboxamid-Derivate von 1-Azoloylimidazolonen und 1-Aryl-1,2,4-triazolonen wurden durch Umsetzung von 4-Benzyliden-2-ethoxy-2-thiazolin-5-on und 2-Ethoxy-4-phenylhydrazono-2-thiazolin-5-on mit Aminoheterocyclen synthetisiert.

Schistosomiasis is one of the most difficult descisies to treat[1]. As a part of our program directed for development of new antischistosomiasis agents we report here the synthesis of several new 1-azoloylimidazole derivatives utilising 2-ethoxycarbonyl-4-benzylidene-2-thiazolin-5-one **(1)** and 2-ethoxy-4-phenylazo-2-thiazolin-5-one **(2)** as starting materials. Compound **1** has been previously reported by one of us to react with aromatic and aliphatic amines to yield thiohydantoin derivatives[2]. On the other hand **2** was reported to yield 1,2,4-triazole derivatives on treatment with the same reagents[3]. The nature of the reaction products of **1** and **2** with amines has been shown however to be dependent on the reaction conditions and on the nature of the amines. It has been found that **1** reacts with 5-amino-3-phenylpyrazole **(3)** to yield the hydantoin derivative **4a**. The structure of **4a** was inferred from analytical and spectral data. The formation of **4a** from reaction of **1** and **3** is assumed to proceed via ring opening to yield the cinnamic acid amide derivative **5** which undergoes simultaneous cyclisation into the final product **4a** via loss of ethyl mercaptan.

Similar to the behaviour of **1** and **3**, compound **1** reacted with **6–9** to yield the hydantoin derivatives **4b–e**, resp..



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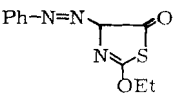

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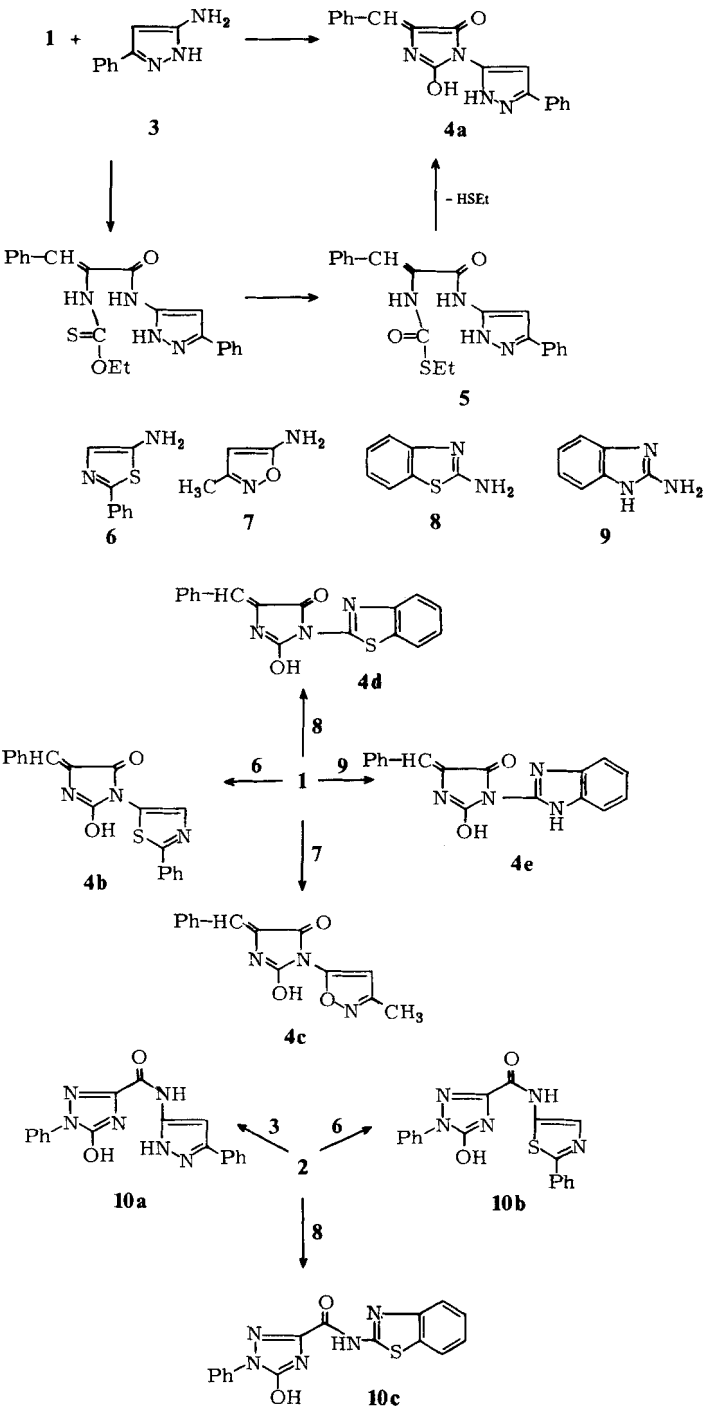
1 +
3
4a
- HSEt
5
6
7
8
9
4d
4b
4e
4c
10a
10b
10c
2
3
6
8
9
7

Similar to the reaction of **1**, compound **2** reacted with **3, 6** and **8** to yield the 1-phenyl-3-azoloyl-$\triangle^2$-1,2,4-triazole derivatives **10a–c**. The structures of **10a–c** are assumed to be formed according to the sequence shown in chart 2 based on analytical and spectral data.

Attempts to utilise **4a** for the synthesis of imidazopyrazolo[1,5-a]pyrimidine derivatives which might be considered as analogues to *Robins* new Schistosomiasis[4] agents were unsuccessfull.

Now we are investigating the reaction of **1** and **2** with other heterocyclic amines. The results of this work together with full data on the Schistosomiasis activity of the so far prepared compounds will be published soon. Preliminary results revealed that **4a** has pronounced activity.

Experimental Part

MP: uncorr. *IR spectra*: Pye Unicam SP-1000 spectrophotometer (KBr). *^{1}H-NMR spectra*: EM-390 90 MHZ in DMSO-d_6, TMS as int. stand., chemical shifts as δ (ppm). *Analytical data*: Analytical Data Unit at Cairo University.

Table 1: *Compounds* **4a–e** *and* **10a–c**

Compound (Colour)	Solvent of Cryst.	Yield (%)	M.p (°C)	Mol. formula (Mol. weight)	Found analysis Required C	H	N
4a (Yellow)	Dioxan	70	280	$C_{19}H_{14}N_4O_2$ (330)	69.0 69.1	4.0 4.2	17.2 17.0
4b (Yellow)	Dioxan	65	250	$C_{19}H_{13}N_3O_2S$ (347)	66.0 65.7	4.0 3.7	12.4 12.1
4c (Colourless)	EtOH	75	179	$C_{14}H_{11}N_3O_3$ (269)	62.1 62.5	3.8 4.1	15.2 15.6
4d (Yellow)	Dioxan	60	92	$C_{17}H_{11}N_3O_2S$ (321)	63.2 63.5	3.7 3.4	13.3 13.1
4e (Yellow)	Dioxan	70	>300	$C_{17}H_{12}N_4O_2$ (304)	67.5 67.1	4.4 4.0	18.2 18.4
10a (Colourless)	DMF/EtOH	65	270	$C_{18}H_{14}N_6O_2$ (346)	61.9 62.4	4.2 4.1	24.0 24.3
10b (Colourless)	Dioxan	75	>300	$C_{18}H_{13}N_5O_2S$ (363)	59.2 59.5	4.0 3.6	16.9 17.2
10c (Yellow)	DMF	70	>300	$C_{16}H_{11}N_5O_2S$ (337)	56.6 57.0	3.1 3.3	20.5 20.8

Reactions of **1** *and* **2** *with amino-substituted azoles* **3** *and* **6–9**, *General Procedure*

A suspension of equimolecular amounts (0.01 mol) of **1** or **2** and the appropriate amino substituted azoles **3** or **6–9** was refluxed in 5 ml triethylamine for 3 h, then evaporated i.vac. The remaining product was washed with petroleum ether, triturated with ethanol and the resulting solid product was crystallised from the proper solvent (cf. Table 1 and 2).

Table 2: *IR and* ^{1}*H-NMR spectra of the compounds* **4a–e** *and* **10a–c**

Compound	IR cm^{-1} (selected bands)	^{1}H-NMR δ (ppm) =
4a	3300 (NH); 1760, 1730 (CO) and 1650 (C=N),	Insoluble in commonly used NMR solvents.
4b	3350 (NH); 1730, 1680 (CO) and 1630 (C=N).	6.6 (s, 1H, benzylidene CH), 7.3–8.1 (m, 11H, 2 C_6H_5 and thiazole CH) and 11.2 (s, br, 1H, NH).
4c	3320–3200 (NH), 17,30, 1680 (CO) and 1620 (C=N).	2.5 (s, 3H, CH_3), 6.65 (benzylidene CH), 7.1–8.1 (m, 6H, C_6H_5 and CH) and 11.2 (s, br, 1H, NH).
4d	3300 (NH), 1730, 1670 (C)) and 1620 (C=N).	6.8 (s, 1H, benzylidene CH), 7.4–8.2 (m, 10H, C_6H_5, C_6H_4 and NH).
4e	3400, 3300 (NH), 1730, 1670 (CO) and 1620 (C=N).	Insoluble in commonly used NMR solvents.
10a	3300 (NH), 1750, 1700 (CO) and 1610 (C=N).	Insoluble in commonly used NMR solvents.
10b	3300–3200 (NH), 1750, 1720 (CO) and 1650 (C=N).	7.0–8.2 (m, 12H, 2C_6H_5, thiazole CH, NH) and 12.9 (s, br, 1H, NH).
10c	3400–3200 (NH), 1740, 1710 (CO) and 1640 (C=N).	Insoluble in commonly used NMR solvents.

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[Ph 654]