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SYNTHESIS OF AZOLOYL KETONE AND AZOLOYLACETIC ACID DERIVATIVES: REACTIONS OF 4-ARYLAZO-2-OXAZOLIN-5-ONES WITH ACTIVE METHYLENE COMPOUNDS

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Abstract - The rearrangement of 4-arylazo-2-oxazolin-5-ones (**1**) with active methylene compounds was investigated. The 1,2,4-triazolyl derivatives (**11**) could be obtained on treatment of **1** with 2-pyrazolin-5-one derivatives. The behaviour of the synthesised derivatives toward an aromatic diazonium salt was also investigated.

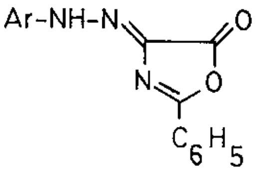
Continuing our interest in the development of new procedures for the synthesis of azoles utilising β-bifunctional reagents as starting materials[1,2] we report a new efficient procedure for the synthesis of polyfunctional 1,2,4-triazolyl ketones. 4-Arylazo-2-oxazolin-5-ones (**1**a,b) have been reported[3-8] to rearrange into 1,2,4-triazole derivatives (**2**a,b) on treatment with amines, amino acids, mercaptans and alkali. All these reactions are assumed to proceed via the attack of the reagent at the 5-oxazolone carbonyl group in **1**. It was thus thought possible to effect such rearrangement via the reaction of carbanions of the type **3** with **1**a,b. In our laboratories attempting to effect such reaction in ethanolic solutions following the procedure described for conversion of **1**a,b into **2**a,b by other reagents resulted only in the formation of ethyl 1,5-diphenyl-1,2,4-triazol-3-carboxylate and ethyl 5-phenyl-1-p-tolyl-1,2,4-triazol-3-carboxylate, respectively. However, compounds **1**a,b could be efficiently converted into the required 1,2,4-triazoles on treatment with the carbanions **3** in refluxing dioxan. Thus, **1**a,b reacted with ethyl cyanoacetate (Na salt) in refluxing dioxan for 1 h to yield colourless products of molecular formulas corresponding to the addition of the anion to **1** and elimination of water. Structure **4**a,b or tautomeric **5** were suggested for the reaction product.

The IR of the product revealed that it txists, at least in the solid state, almost completely as 5. Thus, absorption for a conjugately chelated OH extending from 3600-3300 cm^{-1} was observed. Moreover, the cyano and ester groups of the reaction products appeared at 2220 and 1660 cm^{-1} respectively. These data can only be intelegibly rationalized in terms of conjugation with a C=C as required by structure 5. (If these products were 4a,b, the absorption for both CN and ester groups at higher frequencies would be expected). The stability of the enolate 5 may be rationalized in terms of hydrogen bonding with the azole nitrogens. The possibility of existence of 5 as the Zwitter ion 6 can not be ruled out based on the available data.

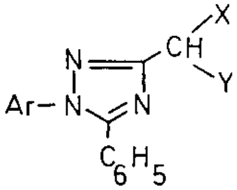
Similar to the behaviour of 1a,b toward ethyl cyanoacetate, it reacted with benzoylacetonitrile and cyanoacetanilide under the same conditions to yield the 1,2,4-triazol-3-yl derivatives 7a,b and 8a,b, respectively. The enol structure suggested for 7a,b and 8a,b was based also on IR data.

When the sodium salts of 2a,b (0.01 mol) were refluxed with the 2-pyrazolin-5-one derivatives 9a,b (0.01 mol) in dioxan (20 ml) for 2 h, the products which may be formulated as the ester 10 or the 1,2,4-triazol-5-oylpyrazolones 11a-d were obtained. Structure 11 was established for the reaction products based on IR spectra which revealed CO absorption at much lower field than that anticipated for ester derivatives. Moreover, the ^{1}H NMR of the reaction products revealed the absence of resonance in the region of 5-6 ppm for pyrazole H-4.

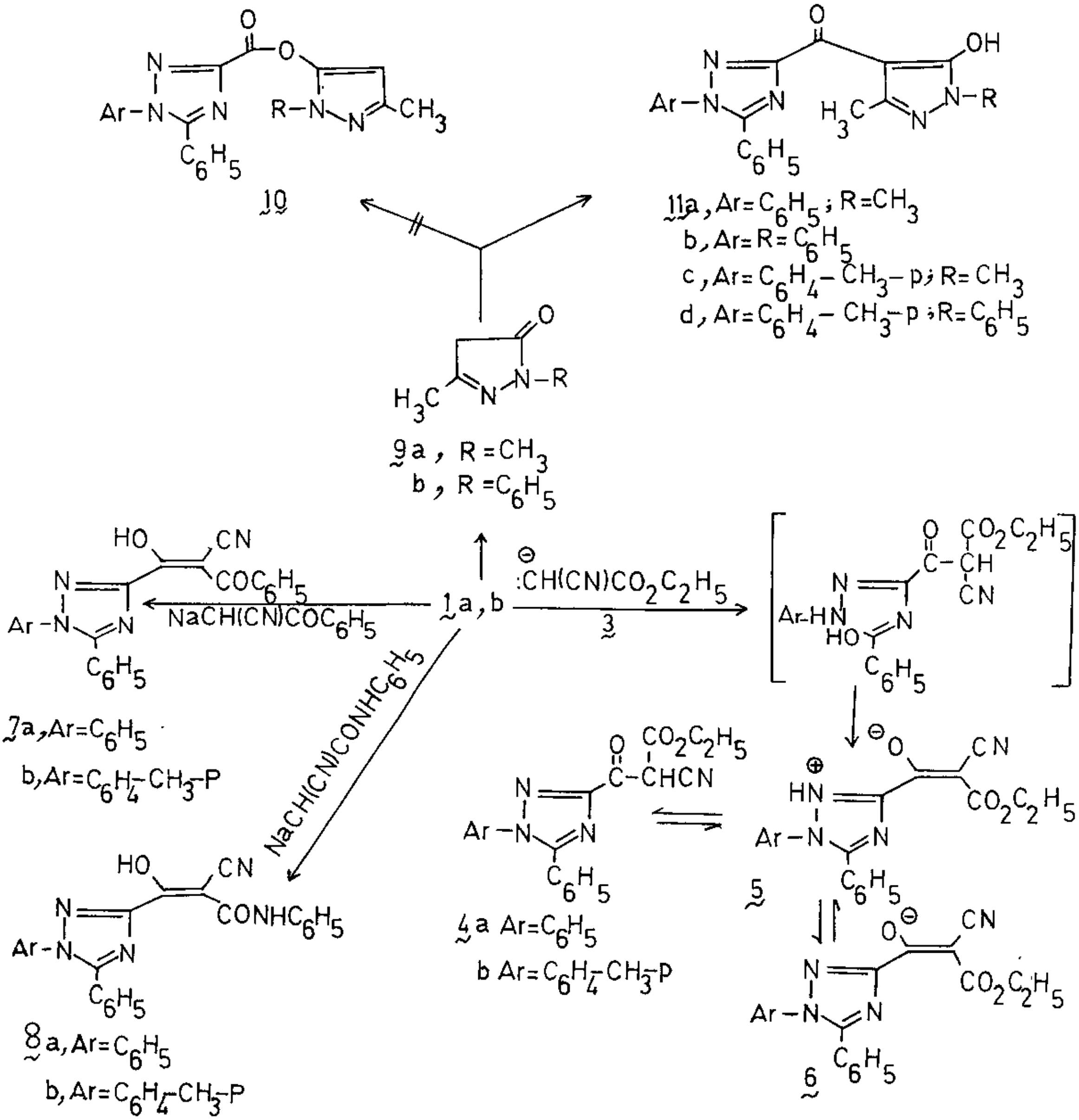
The behaviour of compounds 4b and 11d on coupling with an aromatic diazonium salt was investigated. It has been found that 4b and 11d reacted with p-chlorobenzene diazonium salt to yield the known arylhydrazono derivatives 12 and 13. This is a new example of the well known Jap-Klingmann reaction for coupling of polyfunctionally substituted methanes with aryldiazonium salt.

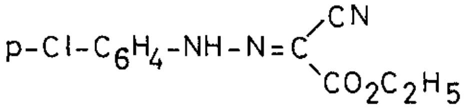


1a, Ar = C_6H_5
b, Ar = $C_6H_4-CH_3$-p



2a, Ar = C_6H_5
b, Ar = $C_6H_4-CH_3$-p





$\text{p-Cl-C}_6\text{H}_4\text{-NH-N=C}\genfrac{}{}{0pt}{}{\text{CN}}{\text{CO}_2\text{C}_2\text{H}_5}$

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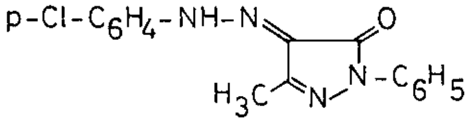

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Table 1: Characterisation data of compounds 4, 7, 8 and 11

Compound*	Solvent of crystalisation	M.P. (°C)	Yield (%)
4a	n-Propanol/DMF	214	85
4b	Ethanol	165	85
7a	Ethanol/Dioxan	213	90
7b	Ethanol	185	90
8a	Ethanol	186	80
8b	Benzene	210	80
11a	Ethanol	235	70
11b	Ethanol	215	75
11c	Ethanol	230	70
11d	Dioxan	228	75

*) Satisfactory elemental analyses for all the newly synthesised compounds were obtained.

Table 2: IR and ^{1}H NMR data of the newly synthesised compounds

Comp.	IR (KBr) , cm^{-1}	^{1}H NMR (CDCl$_3$) , ppm
4a	3600-3350(OH); 2220 (CN) and 1680(C=C)	1.33 (t, 3H, CH$_3$); 4.2 (m, 3H, CH$_2$ and OH) and 7.20-7.66 (m, 10H, 2 C$_6$H$_5$).
4b	3600-3350 (OH);2230 (CN); 1680 (CO) and 1610 (C=C).	
7a	3650-3400 (OH); 2230 (CN) and 1620 (C=C).	7.2-7.7 (m, 15H, 3 C$_6$H$_5$) and 8.2 (s,1H, OH).
7b*	3550-3350 (OH) and 2220 (CN).	
8a*	3300 (NH) and 2220 (CN).	
8b	3300 (NH); 2220 (CN)and 1640 (CO).	2.4 (s, 3H, CH$_3$); 7.2-7.7 (m. 14H,2 C$_6$H$_5$ and C$_6$H$_4$) and 9.8 (m, 2H, OH and NH).
11a*	3600-3350 (OH) and 1625 (C=C).	
11b*	3600-3350 (OH) and 1630 (C=C).	
11c	3600-3350 (OH) and 3060, 2940 (CH and CH$_3$).	2.6 (m, 9H, 3CH$_3$); 3.7 (s, 1H, OH) and 7.3-7.7 (d, 9H, C$_6$H$_5$ and C$_6$H$_4$).
11d	3570-3350 (OH) and 1630 (C=C).	2.3-2.7 (m, 6H, 2CH$_3$); 7.2-7.5 (m,14H, 2 C$_6$H$_5$ and C$_6$H$_4$) and 11.0 (s,1H,OH).

*) Compound is insoluble in all tested ^{1}H NMR solvents.

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