COMPOUNDS RELATED TO ACRIDINE. XII.[1] REACTION OF 1-(9-ACRIDINYL)-2-BENZOYLETHYLENE AND 9-ACRIDINYLSTYRYLKETONE WITH HYDRAZINES

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The reaction of 1-(9-acridinyl)-2-benzoylethylene (1) with hydrazine hydrate (3) gave pyrazoline 4, hydrazinohydrazone 6, or pyrazole 7, depending on the reaction conditions. On the other hand, 9-acridinylstyrylketone (2) reacted with 3 under mild conditions to yield a Michael type adduct 8 as the main product, accompanied with hydrazinohydrazone 9 and 7. On heating in ethanol 8 was dissociated into starting materials. The reaction of 1 with phenylhydrazines (10) gave the expected pyrazolines 11, which on oxidation with lead tetraacetate gave pyrazoles 12, while 2 reacted with 10a to afford a Michael type adduct 13, which on heating in ethanol converted into 2 and 10a.

It is well known that the most general method for the synthesis of pyrazolines which are not only of interest as intermediates in the preparation of

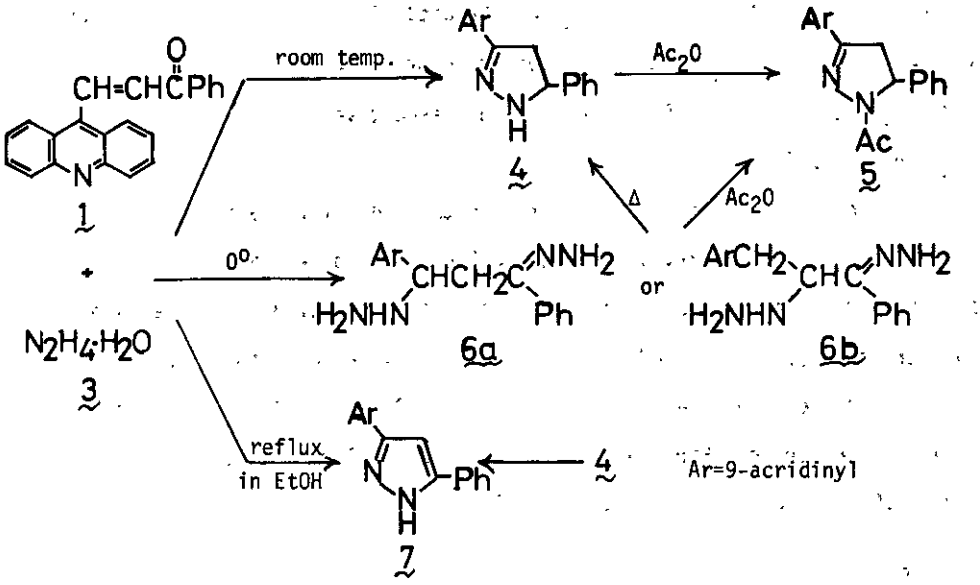
cyclopropanes, but also as effective chemical bleaching agents, and as luminescent and fluorescent substances, is the reaction of α,β-unsaturated carbonyl compounds with hydrazines.[2,3] However, little has been reported relating to the reaction of α,β-unsaturated ketones having an acridine ring with hydrazines.

In the course of preparing the pyrazolines starting with α,β-unsaturated ketones having 9-acridinyl group, we have found that the reaction of these ketones with hydrazines, especially hydrazine hydrate, revealed some unusual phenomena. In this paper we wish to report the reaction of 1-(9-acridinyl)-2-benzoylethylene (1)[4] and 9-acridinylstyrylketone (2)[4] which is an isomer of 1, with hydrazines.

The reaction of 1 with hydrazine hydrate (3) was greatly affected by reaction conditions. When 1 was treated with slight excess of 3 in ethanol containing a little acetic acid at room temperature, the expected 3(or 5)-(9-acridinyl)-5(or 3)-phenyl-Δ^2-pyrazoline (4), mp 177° dec, as yellow prisms was obtained in a 95% yield. Acetylation of 4 with acetic anhydride afforded acetyl derivative 5, mp 248°, as pale yellow prisms.

4: ν_{max} 3200 cm^{-1} (NH); δ ($CDCl_3$) 3.6 (2H, m, CH_2), 3.5 (1H, broad, NH), 6.3 (1H, m, >CH), 6.7-8.5 (13H, m, aromatic protons); m/e 323 (M^+). 5: ν_{max} 1710 cm^{-1} (C=O); δ ($CDCl_3$) 2.35 (3H, s, CH_3), 3.6 (2H, m, CH_2), 6.7 (1H, m, >CH), 7.2-8.5 (13H, m, aromatic protons); m/e 365 (M^+).

However, the reaction of 1 with excess of 3 at 0° under similar conditions gave a product 6 whose molecular formula corresponded to that of the compound derived from a 1:2 adduct of 1 and 3 with dehydration, in a 67% yield, instead of the expected hydrazone, azine, or pyrazoline 4. The structure of 6 was assumed to be either 1-(9-acridinyl)-1-hydrazino-2-benzoylethane hydrazone (6a) or its 2-hydrazino isomer (6b) on the basis of the spectal data and of chemical behavior.



Scheme 1

6: mp 168° dec, pale yellow prisms; ν_{max} 3000-3400 cm^{-1} (several bands, NH); δ ($CDCl_3$) 3.6 (2H, m, CH_2), 3.4 (5H, m, $NHNH_2$ and NH_2), 6.35 (1H, m, >CH), 7.0-8.5 (13H, m, aromatic protons); m/e 323 ($M^+ - N_2H_4$).

Brief heating of 6 in chloroform afforded pyrazoline 4 quantitatively, and on treatment with acetic anhydride 6 gave acetyl derivative 5.

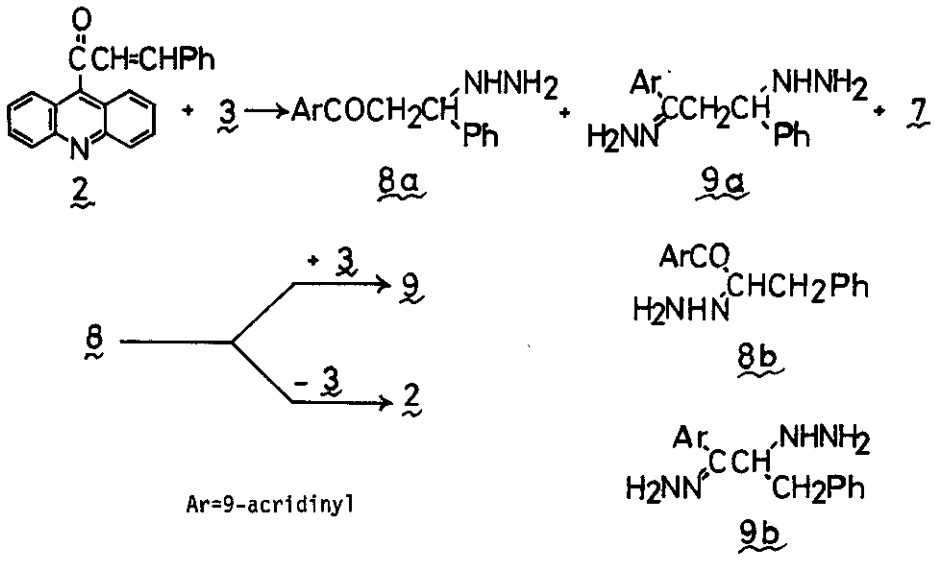
On the other hand, when 1 was allowed to react with 3 in refluxing ethanol under similar conditions, 3(or 5)-(9-acridinyl)-5(or 3)-phenylpyrazole (7) was obtained in a 64% yield. Treatment of 4 with lead tetraacetate in dichloromethane afforded pyrazole 7 (Scheme 1).

7: mp 246°, pale yellow prisms; ν_{max} 3000-3400 cm^{-1} (NH); δ ($CDCl_3$) 2.6 (1H, broad, NH), 7.3-8.8 (14H, m, aromatic protons); m/e (rel. intensity, %) 321 (M^+, 100), 293 ($M^+ - N_2$, 24), 244 (M^+ - Ph, 15), 218 (21), 217 (12).

We investigated the reaction of isomeric α,β-unsaturated ketone 2 with 3

for comparison of that of 1. When 2 was treated with 3 in ethanol under the influence of acetic acid at room temperature or 0° for 6 hr, a Michael type 1:1 adduct 8 was obtained in 59 and 68% yields respectively, accompanied with traces of 9 and pyrazole 7.

On the basis of the spectral data and the mode of formation of 8, either of two isomers, 1-(9-acridinyl)-3-hydrazino-3-phenylpropan-1-one (8a) and 2-hydrazino isomer 8b, is thought possible for the structure of 8. In connection with the structure of 9 described below, however, 8 was assumed to be 8a rather than 8b. 8: 170° dec, pale yellow crystals; ν_{max} 3180 (NH), 1730 cm^{-1} (C=O); δ ($CDCl_3$) 2.5 (3H, broad, $NHNH_2$, exchanged with D_2O), 3.0 (2H, m, CH_2), 4.4 (1H, m, CH), 6.5-7.6 (13H, m, aromatic protons).



Scheme 2

The molecular formula, $C_{22}H_{21}N_5$, of minor product 9 agreed with that of a hydrazinohydrazone compound, and the ir spectrum of 9 was quite similar to that

of 6. Although the nmr spectrum of 9 was not measured because of its insolubility, 9 was deduced to be hydrazone of 8a (9a), but not that of 8b (9b) on the basis of appearance of an ion peak at m/e 234 in the mass spectrum.

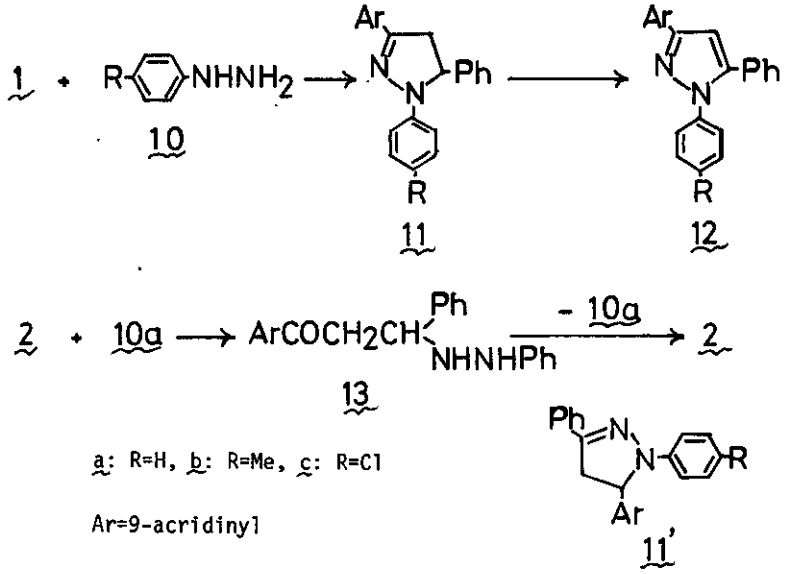
9: mp 172° dec, pale yellow crystals; ν_{max} 3000-3300 cm^{-1} (several bands, NH); m/e (rel. intensity, %) 355 (M^+, 3), 234 (M^+ - $PhCHNHNH_2$, 98), 219 (100). Treatment of 8 with 3 in ethanol containing a little acetic acid at room temperature afforded 9. Thus, this fact strongly supports that 8 is 8a, but not 8b.

Contrary to expectation, the reaction of 2 with 3 in refluxing ethanol under similar conditions gave pyrazole 7 in a low yield, and 2 was recovered in a high yield. This fact suggests that 8 formed in an initial stage was dissociated into 2 with the elimination of 3. In fact, heating of 8 in ethanol afforded 2 in a quantitative yield (Scheme 2).

The formation of 6 and 9 in the above reactions is very attractive, because no attention has been paid to the formation of hydrazinohydrazones in the reaction of α,β-unsaturated ketones with 3.

Although the reaction of 1 with phenylhydrazine (10a) did not take place under the influence of acetic acid, 1 reacted with 10a in the presence of sulfuric acid in refluxing ethanol, giving the expected pyrazoline 11a in an 83% yield. Similarly, the reaction of 1 with p-tolyl- (10b) and p-chlorophenylhydrazine (10c) afforded the corresponding pyrazolines 11b and 11c in 40 and 82% yields, respectively. On the basis of the mass spectra of all 11, another potential structure 11' was excluded (Scheme 3).

11a: mp 182°, orange prisms; m/e 399 (M^+), 205 ($Ar\text{-}CH{=}N^+$), 181 ($[Ph\text{-}CH{=}N\text{-}Ph]^+$). 11b: mp 325°, reddish orange prisms; δ ($CDCl_3$) 2.35 (3H, s, CH_3), 3.6 (2H, m, CH_2), 6.7 (1H, m, CH), 7.2-8.5 (17H, m, aromatic protons); m/e 415 (M^+), 205, 191 ($[MeC_6H_5\text{-}N{=}CH\text{-}Ph]^+$). 11c: mp 215°, reddish orange prisms, m/e 433, 435 (M^+), 215, 217 ($[ClC_6H_5\text{-}N{=}CH{=}Ph]^+$), 205.



Scheme 3

Oxidation of 11a and 11c with lead tetraacetate in dichloromethane gave the corresponding pyrazoles 12a (mp 228°) and 12c (mp 261°) in 80 and 13% yields, respectively.

On the other hand, 2 reacted with 10a under the influence of sulfuric acid in ethanol at room temperature for 2 days, giving a Michael type 1:1 adduct 13 in a 12.5% yield. On brief heating in ethanol 13 was easily converted into 2.

13: mp 150° dec, pale yellow prisms; ν_{max} 3230 (NH), 1710 cm^{-1} (C=O); δ ($CDCl_3$) 3.2 (2H, m, CH_2), 3.5, 4.3 (each 1H, m, NH, exchanged with D_2O), 4.4 (1H, m, >CH), 6.1-7.6 (18H, m, aromatic protons).

References and Notes

1 Part XI: A. Torii, H. Higashiuchi, and O. Tsuge, Heterocycles, 1974, 2, 615.
2 T. L. Jacobs, Heterocyclic Compounds eds. by R. C. Elderfield, Vol. 5, John Wiley & Sons, New York, N. Y., 1957, p. 45.
3 A. N. Kost and I. I. Grandberg, Advances in Heterocyclic Chemistry eds. by A. R. Katritzky and A. J. Boulton, Vol. 6, Academic Press, New York and London, 1966, p. 347.
4 1 (mp 211°) and 2 (mp 258°) were prepared from acridine-9-carboxaldehyde and acetophenone, and from 9-acetylacridine and benzaldehyde, respectively.

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