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ISOLATION OF BENZALACETOPHENONE, β-MORPHOLINOBENZYLACETOPHENONE AND β-MORPHOLINOBENZALACETOPHENONE AMONG THE INTERMEDIATES OF THE REACTION OF ω-PHENYLPROPIOPHENONE WITH SULPHUR AND MORPHOLINE

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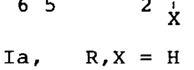
Preceding research[1] on the Willgerodt-Kindler (W-K) reaction has shown, among other things, that the vinyl group of the unsaturated ketones, supposed intermediates of the process,[2,3] in fact reacts with sulphur and sec. amines,[1,4,5] contrary to what had been previously reported.[6]

The present work was undertaken with the purpose of verifying the formation, in the course of the W-K reaction, of unsaturated ketones and other possible intermediates, such as β-aminoketones.[3]

Since the unsaturated ketone which should be formed in the reaction of propiophenone (Ia), i.e. phenyl vinyl ketone (IIa), rapidly reacts with sec. amines even at room temperature to give the Mannich base IIIa, isolation of the unsaturated ketone was attempted working with α,ω-bisarylsubstituted ketones (I, R=Ar) considering the lesser reactivity of the chalcones (II, R=Ar) towards the nucleophilic species. Some preliminary data relative to the unsubstituted compound Ib are reported here.

As expected, when ketone Ib was made to react with sulphur and morpholine (OC_4H_8NH) in various experimental conditions it was possible to isolate the cor-

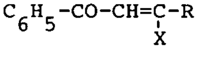

$C_6H_5\text{-CO-CH}_2\text{-}\underset{X}{\text{CH}}\text{-R}$

Ia, R,X = H

Ib, R = C_6H_5-; X = H

IIIa, R = H; X = OC_4H_8N-

IIIb, R = C_6H_5-; X = OC_4H_8N-


$C_6H_5\text{-CO-CH=}\underset{X}{\text{C}}\text{-R}$

IIa, R,X = H

IIb, R = C_6H_5-; X = H

IVb, R = H; X = OC_4H_8N-

IVb, R = C_6H_5-; X = OC_4H_8N-

$C_6H_5\text{-CH}_2\text{-CO-CH}_2\text{-R}$

Va, R = H ; Vb, R = C_6H_5-

responding unsaturated ketone IIb as well as β-aminoketone IIIb and enaminoketone IVb.Compounds of such types had never been previously identified as products of the W-K reaction.[x] Moreover,dibenzylketone (Vb) is formed by an isomerization process[xx] and compounds VI-XI are produced by hydrolysis and fragmentation processes (Scheme 1).

In any case the starting ketone Ib is present in the reaction mixture even prolonging the reaction time for many hours (Tab.1).

Even when one of the compounds IIb-IVb is made to react with sulphur and morpholine a mixture is obtained that contains all the compounds Ib-IVb (Tab.2).

The behaviour of α,ω-bisarylsubstituted compounds in the W-K reaction is due to the fact that lack of a terminal methyl group does not allow the irreversible formation of a thioamide group;[8] from this follows the determining of cyclical processes whose isolable components are,in fact,compounds Ib-IVb.

Compounds Ib and IIIb,as CH acids,undergo the electrophilic attack of the sulphur-containing species (which can be represented as R_2NS_xH[9])[xxx] with the formation of chalcone IIb and enaminoketone IVb,respectively (Scheme 1).(The process may take place through thiolation of the acid CH α to the carbonyl group[11] followed by removal of a sulphurated species).[12]

On the contrary,compounds IIb and IVb react with the nucleophilic species (amine,sulphur-containing species,water) present in the reaction mixture.

In this way,from the chalcone IIb,β-aminoketone IIIb is formed through the action of the amine;through the action of the sulphur-containing nucleophilic species (which can be represented as H_2S) ketone Ib is formed.[12]

Enaminoketone IVb also reacts with the sulphur-containing nucleophilic species to give,in the conditions of the W-K reaction,the saturated ketone Ib and the β-aminoketone IIIb (Scheme 1).

Accordingly,when the reaction of compounds Ib-IIIb with sulphur and morpholine is carried out in the presence of H_2S trapper (PbO,C_6H_5CN,etc.) an increase in the yield of IVb is observed (Tab.2).

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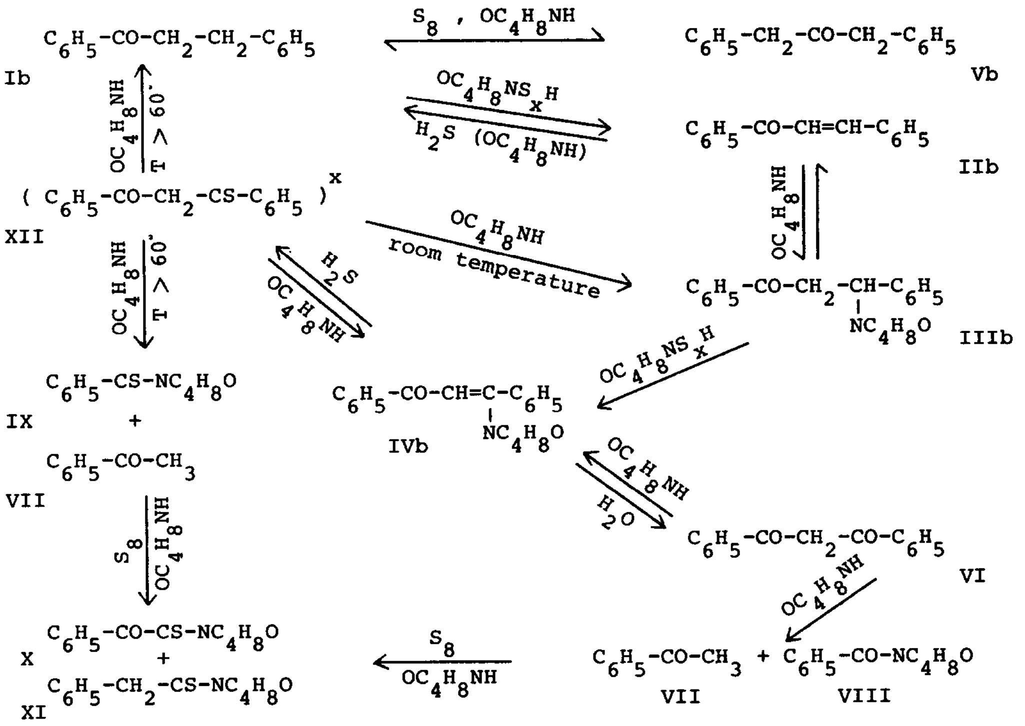
[x] In previous research of this type[4] small quantities of a Mannich base IIIb, p-chlorosubstituted,and of the compound IVb had been isolated,by chance,by reaction of corresponding chalcones with sulphur and morpholine.

[xx] Isomerizations in the course of the W-K reaction have been already reported.[3,4,7]

[xxx] A compound of this type,$C_5H_{10}NS_3H$,was obtained by reaction of sulphur with piperidine.[10]

Scheme 1



The reaction of IIb and IVb with the sulphur-containing nucleophilic species (verified by making them react with hydrogen sulphide in the presence of morpholine)[xx] explains both the formation of the compound Ib observed when these compounds react with sulphur and morpholine (Tab.2) and the fact that when the reaction of the compound Ib is carried out at a higher temperature (and for long enough periods of time) compound Ib is the main component since (in these conditions) the increased availability of the sulphur-containing nucleophilic species promote its formation from IIb-IVb[3] (Scheme 1 and Tab.1).

In drastic conditions, particularly when non-anhydrous reagents are used, the hydrolysis and fragmentation processes leading to the formation of the β-diketone VI and to the compounds VII-XI become prevailing (Scheme 1 and Tab.1).

In the Scheme 1 the observed reactions are summarized. A more detailed discussion will be repprted in the near future.

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[x] Some reactions of XII with morpholine and with sulphur and morpholine have already been reported.[13]

[xx] The experimental details will be given in a later report.

Table 1. Reaction of Ib with sulphur and morpholine (ratio 1:3:2)[x]

reaction temp. °C	reaction time, hr.	yield of (%) Ib	IIb	IIIb	IVb	Vb	VI	VII	VIII	IX	X	XI
24	12	72	1	4	15							
24	48	78	/	5	12							
55	6	68	3	1.5	18	3						
55	44	43	4	0.7	30	4		2				
75	3	74	2	1.5	9	7						
75	6	55	3	0.5	12	7		2				
75	285	9	3	/	9	3	26		12.5	5	11	14
135	1/4	65	9	0.3	13	3			5			
135	1/2	30	7	2.5	23	8	1		13.5	3	1	4
135	4	15	/	/	/	1			17	14		5

Table 2.

Comp.	ratio (comp.:S:Amine)	reaction temp. °C	reaction time, hr.	yield of (%) Ib	IIb	IIIb	IVb
IIb	1:3:2	55	2	3	43	24	9
IIb	1:3:2	55	4	19	14	12	41
IIb	1:1.5:1.5	80	12	31	5	/	48
IIb	1:1.5:1.5 (with PbO)	80	12	14	3	/	67
IIIb	1:3:2	55	4	4	2	/	71

[x] Compounds Ib-XI were isolated by column chromatography and tlc and identified by comparison with authentic samples (u.v. and i.r. spectra). The amounts of the individual compounds were estimated by glc. During the gas-chromatographic analysis the Mannich base IIIb decomposes completely to give morpholine and the chalcone IIb; the determination of the latter was therefore carried out on an aliquot of a solution in benzene of the reaction products previously saturated with HCl in order to remove compounds IIIb and IVb. Blank tests carried out on IIb, IIIb and mixture of IIb and IIIb gave values in good agreement with the theoretical ones.

References

1. G.Purrello, Gazz.Chim.Ital., 97, 557 (1967).
2. W.G.Dauben and J.B.Rogan, J.Am.Chem.Soc., 78, 4135 (1956).
3. A.Compagnini and G.Purrello, Gazz.Chim.Ital., 95, 676 (1965).
4. A.Compagnini and G.Purrello, ibid., 95, 686 (1965).
5. F.Bottino and G.Purrello, ibid., 95, 693 (1965); G.Purrello, ibid., 97, 549 (1967); G.Purrello, M.Piattelli and A.Lo Vullo, Boll.Sedute Accad.Gioenia sci.nat., Catania (IV), 10, 33 (1967).
6. D.Nightingale and R.A.Carpenter, J.Am.Chem.Soc., 71, 3560 (1949).
7. R.H.Bible, ibid., 79, 3924 (1957); G.A.Berchtold and M.Carmack, Dissertation Abstr. 20, 1162 (1959); F.Asinger, H.Offermanns and H.D.Köhler, Tetrahedron Letters, 631 (1967).
8. Cf. W.A.Pryor, Mechanisms of Sulfur Reactions, McGraw-Hill, New York 1962.
9. G.Purrello, Gazz.Chim.Ital., 95, 1089 (1965); 97, 539 (1967).
10. G.K.Stergiu, N.V.Vasil'eva, Ya.V.Nadol'skii, G.K.Kostyushko and A.G.Andreev, Dokl. Akad.Nauk Uz.SSR 20 (7), 29 (1963); Chem.Abstr., 60, 7989a (1964).
11. F.Asinger, Angew.Chem., 68, 413 (1956).
12. G.Purrello and A.Lo Vullo, this Journal, following paper.
13. G.Purrello, Gazz.Chim.Ital., 95, 1072 (1965).