Tetrahedron, 1964, Vol. 20, pp. 891 to 896. Pergamon Press Ltd. Printed in Northern Ireland

STUDIES ON 2-PHENYL-4-ARYLIDENE-5-OXAZOLONES

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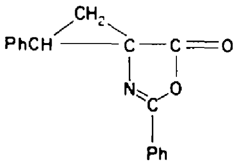
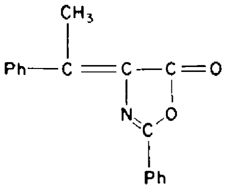
(*Received* 4 *November* 1963)

Abstract—The constitution of the product of diazoalkanes and the title compounds have been investigated by means of NMR spectra. The action of Grignard reagents and the Friedel–Crafts reaction of I has been investigated and the constitution of the products discussed. The acid cyclization of the Grignard product is described and the IR spectra of the products discussed.

2-Phenyl-4-benzylidene-5-oxazolone reacts with diazomethane, but the reported structure Ia[2] was not thoroughly investigated.

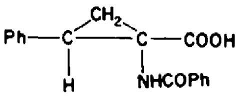


Ia



II

In the reaction an intermediate pyrazoline is probably formed as stable pyrazoline compounds have been isolated when diazomethane reacts with other ethylenic derivatives.[2,3] These pyrazolines give on pyrolysis both an unsaturated compound and a cyclopropane derivative.[2,3] By comparison the 2-phenyl-4-arylidene-5-oxazolones should react with diazomethane to give compounds of type Ia and/or II. The reaction, however, yields only one compound which has either structure Ia or II. In order to differentiate between Ia and II the NMR spectra[4] of Ia and its hydrolysis



III

product III (cf. Figs. 1 and 2 respectively) were investigated. Both spectra are in agreement with three-membered ring systems, revealing an ABX system in the region 2–3·5 ppm. The alternative structure (II) would not reveal an ABX spectrum with the observed constants. I, $J_{AB} = 5{\cdot}1$ cps., $J_{AX} = 8{\cdot}2$ cps. and $J_{BX} = 10{\cdot}1$ cps. III, $J_{AX} = J_{BX} = 9$ cps. and $J_{AB} = 6$ cps.

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[1] *The Chemistry of Penicillin* p. 737. Princeton University Press, New Jersey (1949).

[2] W. I. Awad, S. M. A. R. Omran and M. Sobhy, *J. Org. Chem.* **26**, 4126 (1961).

[3] W. I. Awad, S. M. A. R. Omran and M. Sobhy, *J. Chem. Soc. U.A.R.* in press.

[4] The NMR spectra were carried out by Attilio Melera, Research Chemist, Varian AG., Zurich 8.

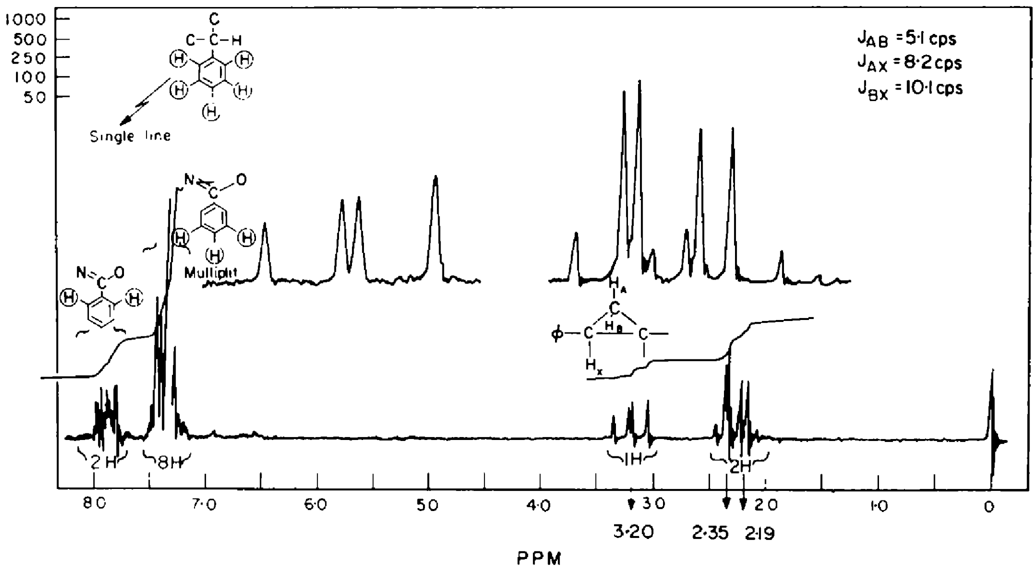

1000
500
250
100
50
J_AB = 5·1 cps
J_AX = 8·2 cps
J_BX = 10·1 cps
Single line
Multiplit
H_A
H_B
H_x
φ
2H
8H
1H
2H
8·0
7·0
6·0
5·0
4·0
3·0
2·0
1·0
0
3·20
2·35
2·19
PPM

FIG. 1

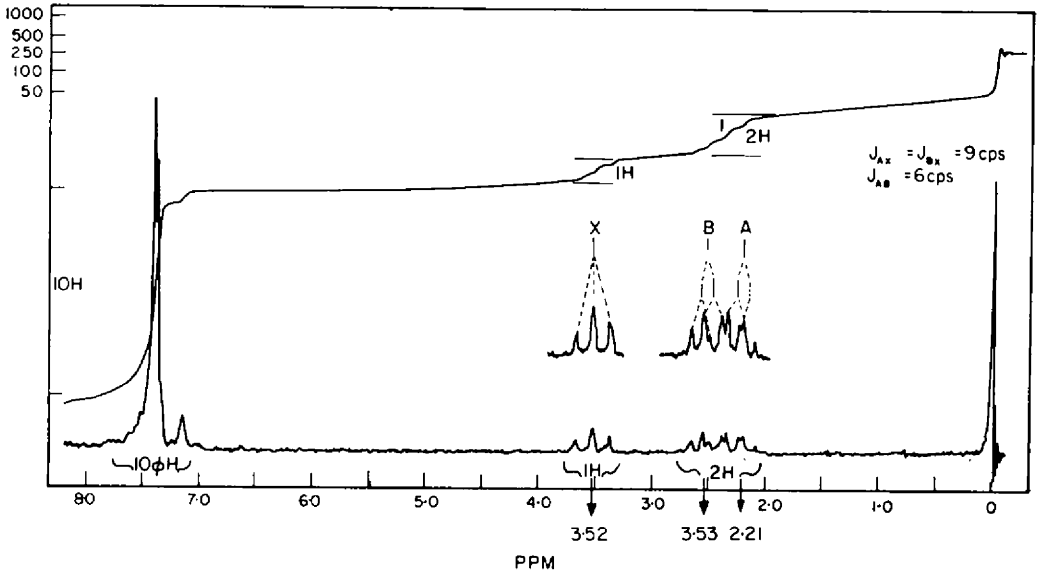
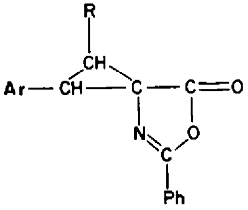

1000
500
250
100
50
10H
1H
2H
J_AX = J_BX = 9 cps
J_AB = 6 cps
X
B
A
10φH
1H
2H
8·0
7·0
6·0
5·0
4·0
3·0
2·0
1·0
0
3·52
3·53
2·21
PPM

FIG. 2

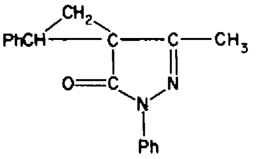
In accordance with the reaction, the following compounds (Ib–Ie) were prepared by the action of diazomethane or diazoethane on 2-phenyl-4-arylidene-5-oxazolones.



I

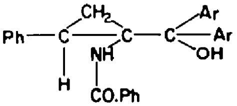
Ib, $R = CH_3$, $Ar = C_6H_5$.
Ic, $R = H$, $Ar = CH_2O_2C_6H_3$.
Id, $R = H$, $Ar = ClC_6H_4p$.
Ie, $R = H$, $Ar = CH_3O{\cdot}C_6H_4$—p.

Similarly diazomethane reacts with 2-phenyl-4-benzylidene-5-methyl-pyrazol-3-one to give IV.



IV

In agreement with the action of Grignard reagents on unsaturated azlactones,[5–8] arylmagnesium bromides react with Ia to give V.



V

Va, $Ar = C_6H_5$; Vb, $Ar = C_6H_4{\cdot}OCH_3p$

The constitution of Va was based on its IR spectrum which shows an OH stretching frequency at 2·85 μ, an NH stretching frequency at 3·05 μ and carbonyl stretching frequency at 6·1 μ.

The action of hydrochloric acid on Va yields a light yellow compound to which structures VI and VII may be assigned through the intermediate carbonium ion VIII.[8]

Structure VI was assigned to this compound from a study of its IR spectrum which shows no NH, OH or CO stretching frequency.

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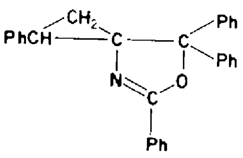
[5] H. Pourrat, *Bull. Soc. Chim. Fr.* 828 (1955).

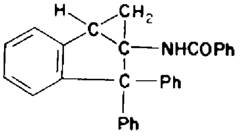
[6] A. Mustafa and A. H. E. Harhash, *J. Org. Chem.* **21**, 575 (1956).

[7] R. Filler and J. D. Wismar, *J. Org. Chem.* **22**, 853 (1957).

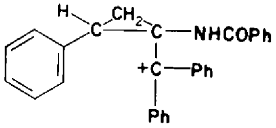
[8] W. I. Awad and M. S. Hafez, *J. Org. Chem.* **25**, 1180 and 1183 (1960).



VI

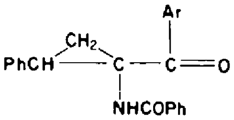


VII



VIII

When benzene, toluene, *m*-xylene or chlorobenzene are allowed to react with Ia in the presence of anhydrous aluminium chloride, a normal Friedel–Crafts reaction produces IX. No abnormal reactions were observed as in the case of 2-phenyl-4-arylidene-5-oxazolone.[9]



IX

IXa, Ar = C_6H_5; IXb, Ar = $C_6H_4CH_3$(p.); IXc, Ar = $C_6H_3(CH_3)_2$2,4-; IXd, Ar = C_6H_4Clp-. The IR spectra of IXa–d show an NH stretching frequency at 3 and two carbonyl frequencies at 5·85 and 6·1.

EXPERIMENTAL

All m.ps. are not corrected. Analyses were carried out by Alfred Bernhardt, in the Max-Plank institute, Mulheim, Germany. IR spectra were measured on a Perkin–Elmer, Infracord Model 137 spectrophotometer using KBr Wafer technique.

Action of diazoalkanes on 2-phenyl-4-arylidene-5-oxazolones. A solution of the oxazolone (2 g) in dioxane was treated with an ethereal solution of the corresponding diazoalkane (diazomethane from 12 g nitrosomethylurea in 200 ml ether; diazoethane from 15 g nitrosoethylurea in 200 ml ether at ice bath temp).

The reaction mixtures was allowed to stand overnight at room temp under anhydrous conditions. The solvent was removed *in vacuo* at room temp and left a gummy mass in the case of 2-phenyl-4-benzyliden-5-oxazolone, which was suspended in ethyl acetate to remove the gummy matter. In all other cases the oil after removal of solvent was well cooled, with separation of a colourless solid. It was triturated with pet. ether (40–60°) and filtered off. The results are given in Table 1.

Hydrolysis of Ia. Ia (1 g) was heated with 5% alcoholic NaOH (100 ml) for 1 hr. The alcohol was removed (red. press.), water was added and the mixture cooled and filtered. The filtrate was acidified with HCl and the precipitate (III) was crystallized from ethanol, yield 1 g, m.p. 242°. (Found C, 72·34; H, 5·46; N, 5·09, $C_{17}H_{15}O_2N$ requires: C, 72·58; H, 5·33; N, 5·00%.)

Action of alcoholic hydrochloric acid on III. III (1 g) was dissolved in 40 ml methanol and 10 ml HCl. The mixture was heated on a water bath 4 hr, the alcohol removed (red. press.) and the residue

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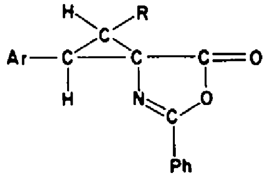
[9] W. I. Awad and M. S. Hafez, *J. Org. Chem.* **26**, 2055 (1961).

TABLE 1.



I		Diazoalkane	M.p.	Formula	Analysis							
					C		H		N		Cl	
Ar	R				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
Ia C_6H_5	H*	Diazomethane	142–143°	$C_{17}H_{13}NO_3$	77·57	77·51	4·94	4·90	5·33	5·34		
Ib C_6H_5	CH_3‡	Diazoethane	76°	$C_{18}H_{15}NO_2$	77·98	77·5	5·42	5·69	5·05	5·14		
Ic $CH_2O_2C_6H_3$	H†	Diazomethane	199°	$C_{18}H_{13}NO_4$	70·36	70·66	4·23	4·12	4·56	4·68		
Id $CClC_6H_4$p.	H‡	Diazomethane	126°	$C_{17}H_{12}NO_2Cl$	68·57	68·56	4·03	4·05	4·71	4·82	11·93	11·72
Ie $CH_3OC_6H_4$p.	H‡	Diazomethane	124°	$C_{18}H_{15}NO_3$	73·73	73·95	5·15	5·16	4·78	4·9		

* Yellow crystals recrystallized from ethyl acetate.

† Fine shiny needles recrystallized from benzene.

‡ Colourless crystals recrystallized from petroleum (60–80°).

filtered off. The ethyl ester of III was crystallized from ethanol as fine colourless crystals m.p. 163°, yield 1 g. (Found, C, 73·75; H, 6·38; N, 4·40; $C_{19}H_{19}NO_3$ requires: C, 73·78; H, 6·15; N, 4·53%).

Action of diazomethane on 2-phenyl-4-benzylidene-5-methylpyrazolone. This compound (1 g) was similarly treated with excess diazomethane to yield IV which was recrystallized from pet ether (60–80°) as colourless crystals m.p. 159°. (Found: C, 78·31; H, 5·65; N, 10·25. $C_{18}H_{16}N_2O$ requires: C, 78·26; H, 5·80; N, 10·15%).

Action of phenylmagnesium bromide on Ia. To an ethereal soln. of PhMgBr (prepared from 48 g Mg and 3·14 g bromobenzene in 20 ml ether) Ia (2·6 g in 40 ml ether) was added. The reaction mixture was refluxed for 2 hr and left overnight. It was then hydrolysed (sat NH_4Cl aq.) and extracted with ether several times. The ethereal solution (dried with Na_2SO_4) was evaporated almost to dryness. The sticky residue was crystallized form ethyl acetate to give Va as colourless crystals m.p. 206–207°. (Found: C, 83·85; H, 6·38; N, 3·25. $C_{29}H_{25}NO_2$ requires: C,83·29 H, 5·90; N, 3·34%).

Action of anisylmagnesium bromide on Ia. To a solution of anisylmagnesium bromide (prepared from 0·48 g Mg and 3·74 g *p*-bromoanisole in 20 ml anhydrous ether), Ia (2·6 g in 40 ml ether) was added. The reaction was carried out as described in the previous experiment and Vb was recrystallized from benzene as colourless crystals m.p. 160°. (Found: C, 78·48; H, 6·06. $C_{31}H_{29}NO_4$ requires: C, 77·66; H, 6·05%).

Action of hydrochloric acid on Va. To a solution of Va (1·0 g) in hot glacial acetic acid (20 ml) HCl (10 ml); sp. gr. 1·18) was added with a colour change to canary yellow. The reaction mixture was warmed on a water bath 2 min and left at room temp for 30 min. A white precipitate separated after addition of water. It was filtered off, washed with water and VI was recrystallized from benzene–pet. ether (b.p. 60–80°) as light yellow crystals m.p. 196°, yield 0·9 g. (Found: C, 86·89, H, 5·84; N, 3·94. $C_{29}H_{23}NO$ requires: C, 86·78; H, 5·73; N, 3·49%).

Friedel–Craft reaction with Ia. In a 1-l. round bottom flask fitted with a mechanical stirrer, dropping funnel and reflux condenser, a mixture of 4·0 g (3 moles) anhydrous aluminium chloride in 200 ml of the dry hydrocarbon (cf. Table 2) was cooled to 10° and stirred 1 hr.

TABLE 2

Hydrocarbon	Product	M.p.	Formula	Analysis C Calcd.	Analysis C Found	Analysis H Calcd.	Analysis H Found	Analysis N Calcd.	Analysis N Found
Benzene*	IXa	192°	$C_{23}H_{19}NO_2$	80·93	80·56	5·57	5·77	4·10	4·40
Toluene*	IXb	165°	$C_{24}H_{21}NO_2$	81·12	80·77	5·91	6·17	3·94	4·3
m-Xylene†	IXc	177°	$C_{25}H_{23}NO_2$	81·30	81·56	6·23	6·60	3·78	4·43
Chlorobenzene	IXd	203°	$C_{23}H_{18}NO_2Cl$	73·50	73·77	4·79	4·83		

* Recrystallized from Benzene.

† Recrystallized from Benzine (60–80).

To this solution was added dropwise with stirring a solution containing 2·6 g (1 mole) Ia in 80 ml of the dried hydrocarbon used in the reaction, the temp being maintained at 10–20° during the addition and the mixture being stirred for 3 hr at 10°.

The complex formed was decomposed with 250 ml dil. (1:15) HCl and two clear layers were obtained. The hydrocarbon layer was separated and the aqueous layer extracted with the same hydrocarbon and the combined extracts washed with dil. HCl and then with water until neutral to litmus. In the case of benzene, the benzene layer was dried (Na_2SO_4) and removed by evaporation. In other cases, the hydrocarbon was steam distilled and the residue extracted with ether (dried over Na_2SO_4) and distilled. The residue was recrystallized from a suitable solvent (Table 2).