reaction of 2-phenyl-4-(*p*-anisylidene)-5(4*H*)-oxazolone with benzene.

(d) **With Toluene.**—The reaction was run as described in (c). The product obtained (4.8 g.), m.p. 117° (lit.,[4] m.p. 118°), was ω-benzamido-*p*-methylacetophenone.

(e) **With Benzene at 80°.**—The experiment was carried out as described in (a), except that after the addition of the azlactone solution, the reaction mixture was heated under reflux at 80° for 1 hr. The mixture was decomposed with dilute hydrochloric acid. The benzene layer was removed, washed with water, and left overnight. The product which separated was filtered and dissolved in sodium carbonate solution. The alkaline solution was decolorized with charcoal and acidified to give 1 g. of a white compound, m.p. 221°, mol. wt., calcd.: 249, found (neut. equiv.):248. Anal. calcd for $C_{16}H_{11}NO_2$: C, 77.11, H, 4.42. Found: C, 76.50, H, 4.59.

The benzene layer gave ω-benzamidoacetophenone, m.p. 124°, after removal of benzene and treatment of the residual oil with ether and petroleum ether.

Decarboxylation of 1-Phenylisoquinoline 3-Carboxylic Acid.[17]—The acid (0.8 g.) was mixed with 4 g. of benzophenone and the mixture was heated for 24 hr. at 155°–165° in a nitrogen atmosphere in a round-bottomed flask, provided with a condenser. The flask was cooled, its contents extracted with ether, and the ether-insoluble portion was removed by filtration. The ether soluble portion was extracted three times with 1:15 hydrochloric acid and the hydrochloric acid extract, saturated with sodium carbonate. The sodium carbonate layer was then extracted with ether. The ether layer was saturated with dry hydrogen chloride gas to give solid 1-phenylisoquinoline hydrochloride, m.p. 234°, lit.[18] (a) m.p. 235–36°; (b) m.p. 237–39°.

Preparation of 1-Phenylisoquinoline.[19]—To a solution of phenylmagnesium bromide, prepared from 0.9 g. of magnesium metal and 5.9 g. of bromobenzene, was added 10 g. of isoquinoline. The reaction mixture was heated under reflux for 2 hr. and decomposed with a saturated solution of ammonium chloride. The ethereal extract, on evaporation, gave 1-phenylisoquinoline. Its hydrochloride melted at 235°.

Debenzoylation of ω-Benzamidoacetophenone.—III (2 g.) was heated under reflux with 50 ml. of a 2:1 mixture of glacial acetic acid–48% hydrobromic acid for 6 hr. The excess of acid mixture was distilled under reduced pressure. The residue was dissolved in water and extracted with ether. The ethereal extract gave benzoic acid on evaporation. The aqueous layer gave, when concentrated, phenacylamine hydrobromide, m.p. 217°, lit.[20] m.p. 217°–218°.

Preparation of ω-Benzamidoacetophenone.—Phenacylamine hydrochloride (1 g.) (Aldrich Chemical Co.) was benzoylated by the Schotten-Baumann method and the benzoyl derivative was recrystallized from ethanol, m.p. 124°.

All the cleavage products obtained from the various azlactones proved to be identical with this sample (m.p. and mixed m.p.).

Reaction in Tetrachloroethane Medium.—Compound I reacted with aluminum chloride in the molar quantities given in (a) in 100 ml. of tetrachloroethane at 60°, following Awad and Hafez's[4] procedure. 2-Benzamidoindenone, m.p. 140°, and 1-phenylisoquinoline-3-carboxylic acid were obtained.

5-Methoxy-1-phenylisoquinoline-3-carboxylic acid, m.p. 213°.

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; Found: C, 72.90, H, 4.58) and 7-methyl-1-phenylisoquinoline 3-carboxylic acid, m.p. 227°.

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.98; H, 4.99; Found: C, 77.29; H, 5.10), were prepared from 2-phenyl 4-(*o*-methoxybenzylidene)-5(4*H*)-oxazolone and 2-phenyl-4-(*p*-tolylidene)-5(4*H*)-oxazolone, respectively.

Spectral Measurements and Analyses.—Infrared spectra were obtained on a Perkin-Elmer Infracord. The samples were examined in chloroform or methylene chloride. Microanalyses were conducted by Micro-Tech Laboratories, Skokie, Illinois.

(17) T. L. Jacobs, S. Winstein, R. B. Henderson, and E. C. Spaeth, *J. Am. Chem. Soc.*, **68**, 1310 (1946).

(18) (a) E. Bergmann, O. Bergmann, and A. Christiani, *Ann.*, **483**, 80 (1930); (b) M. Whaley and W. Hartung, *J. Org. Chem.*, **14**, 650 (1949).

(19) E. Bergmann and W. Rosenthal, *J. prakt. Chem.*, **135**, 267 (1932).

(20) I. M. Heilbron: Dictionary of Organic Compounds, Vol. 3, Oxford University Press, New York, 1938, p. 361.

Action of Grignard Reagents. XXIII. Action of Organomagnesium Compounds on Saturated and Unsaturated Azlactones. Addition Reactions of Mercaptans and Piperidine with Unsaturated Azlactones

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The reaction between alkyl- and aralkylmagnesium halides on unsaturated azlactones (I) was studied, and was found to give compounds having structure IV, while the reaction between the same reagents and ethyl 2-benzamidocinnamate gave compounds having structure II, which were converted to the corresponding oxazolines (III) by the action of alcoholic potassium hydroxide. The reaction between arylmagnesium halides and 2-benzamidobenzalacetophenone (VII), unsaturated azlactones (I), and saturated azlactones (VIII) was also studied. The Friedel-Crafts reaction on unsaturated azlactones (I) was also discussed. The behavior of unsaturated azlactones toward arylmercaptans was investigated, and products having structure X were obtained. Ie reacted with piperidine to give the ring-opened piperidide.

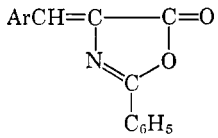
It had been shown that the oxazolone ring in 2-phenyl-4-methyl-5(4*H*)-oxazolone,[1] and 2-phenyl-4-arylidene-5(4*H*)-oxazolone (I)[2] was readily cleaved by the action of arylmagnesium halides to give

(1) E. Mohr and F. Stroschein, *Ber.*, **42**, 2521 (1909); H. T. Clarke, J. R. Johnson, and R. Robinson, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 738.

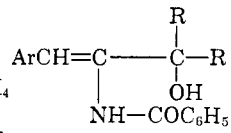
(2) (a) A. Mustafa and A. H. E. Harhash, *J. Org. Chem.*, **21**, 575 (1956); (b) H. Pouratt, *Bull. soc. chim. France*, 828 (1955); (c) R. Filler and J. D. Wismar, *J. Org. Chem.*, **22**, 853 (1957).

1,1-diaryl-2-benzamido-1-propanol and 1,1-diaryl-2-benzamidocinnamyl alcohol (II) together with 2-phenyl-5,5-diaryl-4-arylidene-2-oxazoline (III), respectively.

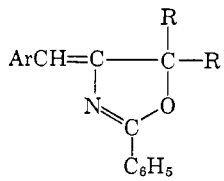
Action of Alkyl- and Aralkylmagnesium Halides on: (a) 2-Phenyl-4-arylidene-5(4*H*)-oxazolones (I).—Recently, Horner and Schwahn[3] explained the reaction of I with alkyl- and aralkylmagnesium halides on the basis of 1,4-addition to the α,β-unsaturated carbonyl system. On the other hand, Mustafa and Harhash[2a] had shown that excess of methylmagnesium iodide effected the opening of the oxazolone ring.



Ia. Ar = C_6H_5
b. Ar = p-$CH_3C_6H_4$
c. Ar = o-$CH_3OC_6H_4$
d. Ar = p-$CH_3OC_6H_4$
e. Ar = 1-$C_{10}H_7$
f. Ar = 3-C_5H_5(pyridyl)
g. Ar = 4-C_5H_5N(pyridyl)



IIa. Ar = R = C_6H_5
b. Ar = C_6H_5; R = CH_3
c. Ar = C_6H_5; R = C_2H_5
d. Ar = C_6H_5; R = $CH_2C_6H_5$
e. Ar = C_6H_5; R = p-$CH_3OC_6H_4$
f. Ar = p-$CH_3C_6H_4$; R = CH_3
g. Ar = o-$CH_3OC_6H_4$; R = C_6H_5
h. Ar = p-$CH_3OC_6H_4$; R = C_6H_5
i. Ar = 1-$C_{10}H_7$; R = C_6H_5



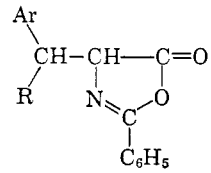
IIIa. Ar = R = C_6H_5
b. Ar = C_6H_5; R = CH_3
c. Ar = C_6H_5; R = C_2H_5
d. Ar = C_6H_5; R = $CH_2C_6H_5$
e. Ar = C_6H_5; R = p-$CH_3OC_6H_4$
f. Ar = p-$CH_3C_6H_4$; R = CH_3
g. Ar = o-$CH_3OC_6H_4$; R = C_6H_5
h. Ar = p-$CH_3OC_6H_4$; R = C_6H_5
i. Ar = 1-$C_{10}H_7$; R = C_6H_5

A similar behavior was observed when Ib was treated with excess of methylmagnesium iodide, whereby IIf was obtained, which was readily converted to IIIf by the action of hot alcoholic potassium hydroxide.

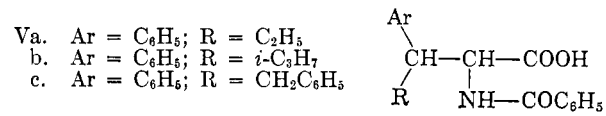
The infrared spectrum of compound IIf exhibited absorption bands at 1650 cm.$^{-1}$ and 1532 cm.$^{-1}$ (amide I and II bands), 3440 cm.$^{-1}$ (—NH stretching), and 3500 cm.$^{-1}$ (—OH stretching).

The suggested structure for IIIf was given support by the presence of a medium intensity band at 1600 cm.$^{-1}$ (probably due to >C=N stretching)[4] and the absence of —OH, —NH—, and amide absorptions.

We studied the behavior of Ia toward the action of excess of ethyl-, isopropyl-, and of benzylmagnesium halides to effect the isolation of a number of saturated azlactones. When an ethereal suspension of Ia was added to an ethereal solution of ethylmagnesium iodide (5 moles) at room temperature, followed by decomposition, IVa together with an oily product was obtained. Both, upon treatment with normal aqueous sodium hydroxide solution, gave *N*-benzoyl-3-ethyl-3-phenylalanine (Va). Similarly, IVb and IVc were obtained upon treatment of Ia with excess of isopropyl- and benzylmagnesium halides, respectively. Treatment of IVb and, IVc with sodium hydroxide, as mentioned above gave *N*-benzoyl-3-isopropyl-3-phenylalanine (Vb) and *N*-benzoyl-3-benzyl-3-phenylalanine (Vc). The isolation of IVa–d favored the assumption of Horner and Schwahn.[3]

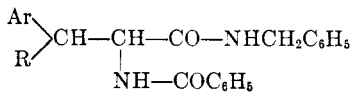


IVa. Ar = C_6H_5; R = C_2H_5
b. Ar = C_6H_5; R = i-C_3H_7
c. Ar = C_6H_5; R = $CH_2C_6H_5$
d. Ar = p-$CH_3C_6H_4$; R = C_2H_5



Va. Ar = C_6H_5; R = C_2H_5
b. Ar = C_6H_5; R = i-C_3H_7
c. Ar = C_6H_5; R = $CH_2C_6H_5$

The assigned structures for the adducts IVa–d were confirmed from the fact that IVa and IVc reacted readily with benzylamine to form the corresponding 2-benzamidobenzylamides (VIa) and (VIb), respectively.[5] The formation of an amide had at times been the sole evidence of the presence of an oxazolone, and benzylamine was used for determining the proportion of oxazoline in a mixture "azlactone equivalent."[6]



VIa. Ar = C_6H_5; R = C_2H_5
b. Ar = C_6H_5; R = $CH_2C_6H_5$

(b) Ethyl 2-Benzamidocinnamate.—When ethyl-2-benzamidocinnamate was treated with excess of methyl-, ethyl-, and benzylmagnesium halides, 1,2-addition took place leading to the formation of 1,1-dimethyl (IIb), 1,1-diethyl- (IIc), and 1,1-dibenzyl-2-benzamidocinnamyl alcohol (IId), respectively, contrary to the behavior of the exocyclic

(3) L. Horner and H. Schwahn, *Ann.*, **591**, 99 (1955).

(4) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," J. Wiley & Sons, Inc., New York, N. Y., 1954, p. 226.

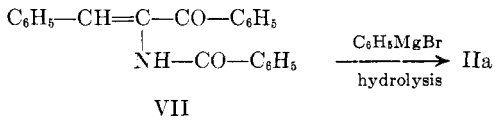
(5) Saturated azlactones are generally very susceptible to aminolysis [H. E. Carter, *Org. Reactions*, 215 (1946); E. Baltazzi, *Quart. Rev.* (London), IX, No. 2, 160 (1955)].

(6) J. W. Cornforth, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949, p. 735.

double bond in Ia toward the action of the same reagents. The structure proposed for IIc, taken as an example, was supported by its infrared spectrum.

The previous finding by Mustafa and Harhash[2a] that the opening of the oxazolone ring in Ia could be effected by the action of excess of methylmagnesium iodide was confirmed. The resulting 1,1-dimethyl-2-benzamidocinnamyl alcohol (IIb) was found to be identical with the product obtained by the action of methylmagnesium iodide on ethyl 2-benzamidocinnamate, and was successfully transformed into 2-phenyl-5,5-dimethyl-4-benzylidene oxazoline (IIIb) by the action of hot alcoholic potassium hydroxide.

Action of Arylmagnesium Halides on: (a) 2-Benzamidobenzalacetophenone (VII).—We found that 1,1 - diphenyl - 2 - benzamidocinnamyl alcohol (IIa) was obtained when VII was allowed to react with excess of phenylmagnesium bromide.

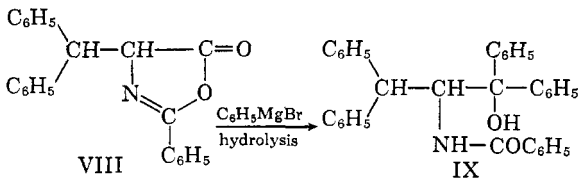


VII

(b) **Unsaturated Azlactones (Ia,c–e).**—In extension of the previous work by Mustafa and Harhash,[2a] we investigated the behavior of Ia and Ic–e toward the action of arylmagnesium halides. Thus, whereas IIh was isolated upon treatment of Id with excess of phenylmagnesium bromide,[2a] the yellow IIIe and not the expected carbinol IIe was isolated upon treatment of Ia with *p*-methoxyphenylmagnesium bromide. IIIe was also obtained without isolation of IIe when ethyl 2-benzamidocinnamate was treated with the same reagent. Ic and Ie behaved as Ia when allowed to react with excess of phenylmagnesium bromide yielding IIg and IIi, respectively.

It was found that alcoholic potassium hydroxide solution could effect the conversion of the carbinols IIa–d and IIf–i into the corresponding oxazoline derivatives IIa–d and IIf–i, in an almost quantitative yield.

(c) **Saturated Azlactones (VIII).**—We found that 2-phenyl-4-benzhydryl-5(4*H*)-oxazolone (VIII)[7] reacted with excess of phenylmagnesium bromide by ring opening followed by 1,2-addition to give the tertiary alcohol (IX).



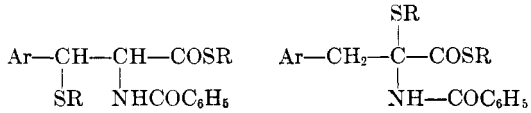
VIII IX

The structure proposed for IX was supported by its infrared spectrum which exhibited absorption band at 1630 cm.$^{-1}$ and 1520 cm.$^{-1}$ (amide I and II bands) and 3332 cm.$^{-1}$ (—NH stretching), and by its identity with the product obtained by the action of phenylmagnesium bromide on ethyl 2-benzamido-3,3-diphenylpropionate. The latter compound was obtained by the opening of the oxazolone ring in VIII with ethyl alcohol in presence of sulfuric acid.[8]

While preparing this manuscript for publication, the Friedel-Crafts reaction on unsaturated azlactones described by Filler and Hebron[7] was questioned.[9a,b] We would like to report that in our hands VII was readily obtained as the main product after the procedure reported by Filler and Hebron[7] (*cf.*, the Experimental). The ready opening of the oxazolone ring in VIII by the action of: (a) alcoholic potassium hydroxide solution, (b) ethyl alcohol in presence of concentrated sulfuric acid, and (c) phenylmagnesium bromide, to give *N*-benzoyl-3,3-diphenylalanine, ethyl 2-benzamido-3,3-diphenylpropionate, and IX (see above), respectively, was in favor of the structure proposed by Filler and Hebron for VIII.[7]

Using aged anhydrous aluminum chloride, benzylidene cleavage and acylation took place with the formation of ω-benzamidoacetophenone as the main product (*cf.*, the Experimental).

Action of Arylmercaptans on Ie–g.—In conjunction with the study of pharmacological action of sulfur-containing compounds against Bilharziasis snails,[10] we extended the study[11] of the addition of mercaptans to the exocyclic double bond of type I, a reaction which had been extensively studied in connection with the synthesis of penicillamine, probably followed cleavage of the hetero ring.[12]



Xa. Ar = R = C_6H_5
b. Ar = 1-$C_{10}H_7$; R = C_6H_5
c. Ar = 3-C_5H_5N(pyridyl); R = C_6H_5
d. Ar = 3-C_5H_5N(pyridyl); R = *p*-$CH_3C_6H_4$
e. Ar = 4-C_5H_5N(pyridyl); R = C_6H_5
f. Ar = 4-C_5H_5N(pyridyl); R = *o*-$CH_3C_6H_4$
g. Ar = 4-C_5H_5N(pyridyl); R = *p*-$CH_3C_6H_4$

XI

Treatment of Ie with thiophenol effected opening of the hetero ring and addition to the double bond to give Xb which was decomposed readily by

(7) R. Filler and L. M. Hebron, *J. Org. Chem.* **23**, 1815 (1958).

(8) H. Erlenmeyer, *Ann.*, **275**, 11 (1893).

(9) (a) W. I. Awad and M. S. Hafez, *J. Org. Chem.*, **26**, 2055 (1961). (b) R. Filler, H. Leipold, and Y. Shyamsundar Rao, Abstracts of Papers Presented by Division of Organic Chemistry of the American Chemical Society, at Chicago, Illinois, September 3–8, 1961, p. 5Q, reported that azlactones react by 1,4-addition to α,β-unsaturated carbonyl system to give saturated azlactones which may then be readily converted to 3,3-diaryl-2-amino acids. ω-Benzamidoacetophenone was found as by-product due to benzylidene cleavage and acylation. At 80°, the azlactones also form small amounts of 1-phenylisoquinoline carboxylic acids by intramolecular alkylation.

(10) M. O. Nolan, H. W. Bond, and E. R. Mann, *Am. J. Trop. Med. Hyg.*, II (4), 716 (1953).

(11) A. Mustafa, A. H. E. Harhash, and M. Kamel, *J. Am. Chem. Soc.*, **77**, 3860 (1955).

(12) H. T. Clarke, J. R. Johnson, and R. Robinson, "The Chemistry of Penicillin," Princeton University Press, Princeton, N. J., 1949 p. 737.

TABLE I

GRIGNARD PRODUCTS (IV) FROM 2-PHENYL-4-ARYLIDENE-5(4*H*)-OXAZOLONES (I)

Grignard product	Solvent[a] of crystallization	M.p.,[b] °C.	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
IVa	A	109–110 dec.	80	$C_{18}H_{17}O_2N$	77.42	77.77	6.09	6.07	5.01	5.01
IVb	B	210–211 dec.	79	$C_{19}H_{19}O_2N$	77.81	77.18	6.47	6.64	4.71	5.03
IVc	B	152 dec.	76	$C_{23}H_{19}O_2N$	80.94	80.61	5.57	5.75	4.10	4.20
IVd	B	184	78	$C_{19}H_{19}O_2N$	76.86	77.05	6.76	6.80	4.98	4.71

[a] A = petroleum ether (b.p. 70–80°); B = benzene–petroleum ether (b.p. 30–50°). [b] Melting points were not corrected.

TABLE II

GRIGNARD PRODUCTS II FROM 2-PHENYL-4-ARYLIDENE-5(4*H*)-OXAZOLONES (I) AND FROM ETHYL 2-BENZAMIDOCINNAMATE

Grignard product	Solvent[a] of crystallization	M.p.,[b] °C.	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
IIc	C	111–112	84	$C_{20}H_{23}O_2N$	77.67	77.62	7.44	7.39	4.53	4.67
IId	D	128	77	$C_{30}H_{27}O_2N$	83.14	63.18	6.24	6.63	3.23	3.19
IIf	B	122	80	$C_{19}H_{21}O_3N$	77.28	77.29	7.11	7.04	4.74	4.99
IIg	B	147	88	$C_{29}H_{25}O_3N$	80.00	79.69	5.74	5.76	3.22	3.25
IIi	A	113–114	89	$C_{32}H_{25}O_2N$	84.39	84.25	5.49	5.20	3.07	2.97

[a] A = ethyl alcohol; B = benzene; C = benzene–petroleum ether (b.p. 40–60°); D = petroleum ether (b.p. 70–80°). Melting points were not corrected.

alcoholic potassium hydroxide solution to give 2-benzamido-3-(1-naphthyl)acrylic acid and thiophenol. The acid was transformed readily to the oxazolone (Ie) with acetic anhydride.

Action of Piperidine on Ie.—When the reaction of Ie and arylmercaptans was carried out in presence of piperidine, the same substance was obtained, believed to be the ring-opened piperidide. The same product was obtained when Ie was heated with piperidine, whereby the oxazolone ring was opened.

Treatment of the piperidide with hot alcoholic potassium hydroxide solution, followed by acidification effected the formation of 2-benzamido-3-(1-naphthyl)acrylic acid.

Preparation of Ig.—Ig was prepared by the same procedure described by Wibaut[13] for the preparation of If.

Experimental

Action of Alkyl- and Aralkylmagnesium Halides on 2-Phenyl-4-arylidene-5(4*H*)-oxazolones (Ia–b).—The following illustrates the procedure: To a Grignard solution (prepared from 1.0 g. of magnesium and the appropriate quantity of the alkyl halide in 150 ml. of dry ether) was added a suspension of 2.5 g. of each of Ia–b in dry ether. The reaction mixture was left overnight at room temperature, then decomposed by about 100 ml. of saturated aqueous ammonium chloride solution to which 3 ml. of concentrated hydrochloric acid was added. The etheral layer was separated and the aqueous layer was extracted with two 25-ml. portions of ether. The combined ethereal solution was evaporated on a warm water bath, and the residue thus obtained was washed several times with petroleum ether (b.p. 40–60°). The residue was crystallized from the appropriate solvent (*cf.*, Table I).

The Grignard products (IVa–d) listed in Table I were all colorless, soluble in aqueous sodium hydroxide (10%), gave no color with alcoholic ferric chloride solution, and were generally soluble in alcohol and benzene, but were sparingly soluble in petroleum ether.

Treatment of 2.0 g. of each of IVa and IVc with benzylamine under the same conditions described by Filler and Hebron,[7] gave colorless crystals of VIa, m.p. 176, and VIb, m.p. 186–187°. Both VIa and VIb were soluble in alcohol but were difficultly soluble in cold benzene and petroleum ether (b.p. 40–60°) and gave no color with concentrated sulfuric acid.

Anal. Calcd. for $C_{25}H_{26}O_2N_2$: C, 77.72; H, 6.74; N, 7.25. Found: C, 77.96; H, 6.47; N, 6.98. *Anal.* Calcd. for $C_{30}H_{28}O_2N_2$, VIb: C, 80.35; H, 6.25; N, 6.25. Found: C, 79.90; H, 6.27; N, 6.07.

Action of Methylmagnesium Iodide on Ia–b.—IIb and IIf, listed in Table II were obtained upon treatment of 1.0 g. of each of Ia and Ib, respectively, with methylmagnesium iodide (prepared from 6.0 g. of methyl iodide in 100 ml. of dry ether). The reaction mixture was refluxed for 1 hr., cooled, decomposed, and worked up as described in the case of IVa–c. IIb and IIf were colorless and were generally soluble in benzene and hot alcohol, but were difficultly soluble in petroleum ether.

Action of Grignard Reagents on Ethyl 2-Benzamidocinnamate.—The Grignard products IIb–d (*cf.* Table II) were similarly obtained, as described above, as colorless crystals. They were soluble in hot benzene and alcohol, but were sparingly soluble in petroleum ether.

The infrared spectrum of IIc showed a medium intensity band at 1650 cm.$^{-1}$ and 1350 cm.$^{-1}$ (amide I and II bands), 3332 cm.$^{-1}$ (—NH stretching), 3600 cm.$^{-1}$ (=OH stretching).[14]

Action of Phenylmagnesium Bromide on Ic and Ie.—In a similar manner, IIg and IIi (listed in Table II) were obtained as colorless crystals. They were soluble in hot benzene and alcohol, but were sparingly soluble in petroleum ether.

Action of Phenylmagnesium Bromide on 2-Benzamidobenzalacetophenone (VII).[2c]—The Grignard product that was obtained in an almost quantitative yield was crystallized from benzene as colorless crystals, m.p. 165°, identified as III by melting point and mixed melting point.

Action of Alcoholic Potassium Hydroxide on IIa–d and IIf–i.—Refluxing a mixture of 1.0 g. of each of the above mentioned Grignard products and 10 ml. of alcoholic potassium hydroxide solution (10%) for *ca.* 30 min., followed by cooling the reaction mixture, effected the separation of the corresponding oxazoline derivatives (IIIb–d and IIIf–i (*cf.*, Table III) as yellow crystals. They were soluble in

(13) J. P. Wibaut, H. P. Wallingford, H. J. Rang, and D. A. Kettenes, *Rec. trav. chim.*, **74**, 1049 (1955).

(14) The infrared spectra were produced on a Perkin-Elmer Infracord Model 137 B in Nujol solution.

TABLE III

2-PHENYL-5,5-DI(ALKYL OR ARYL)-4-ARYLIDENE-2-OXAZOLINES (III)

Grignard product	Solvent[a] of crystallization	M.p.,[b] °C.	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
IIIb	A	119	91	$C_{18}H_{16}ON$	82.44	82.47	6.10	6.86	5.34	5.26
IIIc	A	104	88	$C_{20}H_{21}ON$	82.48	83.12	7.22	7.38	4.81	4.82
IIId	A	107	85	$C_{30}H_{25}ON$	86.74	86.40	6.03	6.27	3.37	3.21
IIIf	A	108–109	90	$C_{19}H_{19}ON$	82.31	82.77	6.86	6.84	5.05	4.85
IIIg	B	163	86	$C_{29}H_{23}O_2N$	83.45	83.07	5.51	5.66	3.35	3.64
IIIh	B	150	92	$C_{29}H_{23}O_2N$	83.45	83.12	5.51	5.53	3.35	3.45
III	B	171	84	$C_{32}H_{23}ON$	87.87	87.59	5.26	5.45	3.20	3.28

[a] A = ethyl alcohol; B = benzene–ethyl alcohol. [b] Melting points were not corrected.

TABLE IV

ADDUCTS (X) OF MERCAPTANS 2-PHENYL-4-ARYLIDENE-5(4*H*)-OXAZOLENES (I)

Grignard product	Solvent[a] of crystallization	M.p.,[b] °C.	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Sulphur, % Calcd.	Sulphur, % Found
Xb	A	176	71	$C_{32}H_{25}O_2NS_2$	73.98	74.04	4.82	5.08	2.69	2.86	12.33	12.09
Xc	A	139	82	$C_{27}H_{22}O_2N_2S_2$	68.93	68.26	4.68	4.73	5.95	5.84	13.62	13.85
Xd	A	165	83	$C_{29}H_{26}O_2N_2S_2$	69.87	69.27	5.22	5.29	5.62	5.45	12.85	12.96
Xe	B	163	76	$C_{27}H_{22}O_2N_2S_2$	68.93	58.61	4.68	4.28	5.95	5.59	13.62	13.18
Xf	A	149	78	$C_{29}H_{26}O_2N_2S_2$	69.87	70.03	5.22	5.44	5.62	5.58	12.85	12.63
Xg	B	146	72	$C_{29}H_{26}O_2N_2S_2$	69.87	69.58	5.22	5.40	5.62	5.38	12.85	12.59

[a] A = benzene; B = benzene–petroleum ether (b.p. 40–60°). [b] Melting points were not corrected.

benzene and petroleum ether (b.p. 70–80°), but were difficultly soluble in alcohol.

The infrared spectrum of IIIg showed a medium intensity band at 1610 cm.$^{-1}$ (probably due to >C=N stretching), and the absence of —OH, —NH—, and amide absorption.

Reaction of Ia with Benzene in Presence of Aluminum Chloride.—(a). To a cooled mixture of 9.5 g. of anhydrous aluminum chloride (sublimed, powered, aluminum chloride, VEB LABORCHEMIE APOLDA) and 125 ml. of dry thiophene-free benzene which was stirred for 1 hr. at 10° was added dropwise a suspension of 6.0 g. of Ia in 150 ml. of dry benzene. The temperature of the reaction mixture was maintained at 10–20° during the addition. Stirring was continued for an additional 3 hr. at room temperature. The complex was decomposed with 250 ml. of dilute (1:15) hydrochloric acid. The benzene layer was separated and the aqueous layer was extracted with benzene. The combined benzene extracts were washed thoroughly with dilute hydrochloric acid, then with water until neutral to litmus. Benzene was evaporated and the yellow oily residue was dissolved in ether and precipitated with petroleum ether (b.p. 40–60°). The pale yellow precipitate was collected and crystallized from benzene as colorless crystals (*ca.* 4.8 g.), m.p. 155–157°; identified as VIII by melting point and mixed melting point with an authentic specimen.[15]

(b). On repeating the previous experiment using aged anhydrous aluminum chloride (May and Baker), the main product obtained was ω-benzamidoacetophenone, m.p. 123°.[9]

Action of Aqueous Sodium Hydroxide on VIII.—One gram of VIII and 10 ml. of aqueous sodium hydroxide solution (10%) were refluxed for 15 min. The reaction mixture solution was cooled, poured onto crushed ice, and acidified with dilute hydrochloric acid. The product so obtained was crystallized from dilute alcohol (50%) as colorless crystals (*ca.* 0.9 g.), identified as *N*-benzoyl-3,3-diphenylalanine by melting point and mixed melting point.

Action of Phenylmagnesium Bromide on 2-Phenyl-4-benzhydryl-5(4*H*)-oxazolone (VIII).—IX, so obtained, was crystallized from benzene as colorless crystals, m.p. 244°. It was soluble in hot benzene, chloroform, and alcohol, but was difficultly soluble in petroleum ether and gave a yellow color with sulfuric acid.

Anal. Calcd. for $C_{34}H_{39}O_2N$: C, 84.47; H, 6.00; N, 2.91. Found: C, 84.51; H, 5.66; N, 3.11.

Action of Phenylmagnesium Bromide on Ethyl 2-benzamido-3,3-diphenylpropionate.—The ester needed for this investigation was prepared by treating VIII with absolute ethyl alcohol in presence of concentrated sulfuric acid after the procedure described for the preparation of ethyl 2-benzamidocinnamate.[8] It was crystallized from alcohol as colorless crystals, m.p. 177°. Yield was *ca.* 82%.

Anal. Calcd. for $C_{24}H_{22}N$; C, 77.42; H, 5.91; N, 3.60. Found: C, 77.21; H, 5.84; N, 3.58.

Treatment of the ester with phenylmagnesium bromide according to the general procedure gave colorless crystals from benzene, m.p. 244°; yield was *ca.* 75% identified as IX by melting point and mixed melting point.

Action of Arylmercaptans on Ie–g.—A 0.5-g. sample of the azlactone (Ie–g) and 0.5 g. of the mercaptan were heated on a boiling water bath for about 2 hr. The reaction mixture was cooled and triturated with petroleum ether (b.p. 40–60°), whereby it solidified, filtered, and crystallized from the appropriate solvents (*cf.* Table IV).

The addition products listed in Table IV were all colorless, soluble in hot benzene and alcohol, but were difficultly soluble in petroleum ether.

Action of Alcoholic Potassium Hydroxide on Xb.—The thiol adduct (1.0 g.) was refluxed with 100 ml. of alcoholic potassium hydroxide solution (5%) for 4 hr. The cooled reaction mixture was poured onto ice-cold water, acidified with dilute hydrochloric acid, and the product that was precipitated was filtered off, washed with water several times and crystallized from dilute alcohol as colorless crystals m.p. 221°. It was identified as 2-benzamido-3-(1-naphthyl)acrylic acid (melting point and mixed melting point).

The mother liquor was extracted several times with ether. The ethereal solution gave, on shaking with lead acetate solution, yellow crystals (ca 0.2 g.) of the lead salt of thiophenol (melting point and mixed melting point).[11]

Action of Piperidine on Ie.—One gram of Ie and 0.5 g. of piperidine in a 100-ml. round bottom flask were heated in an oil bath at 120–125° for 1 hr., the reaction mixture was cooled, triturated with petroleum ether (b.p. 40–60°), and

(15) A. Mustafa and M. M. M. Sallam, *J. Org. Chem.*, **26**, 1782 (1961).

the residue thus obtained was crystallized from benzene as colorless crystals, m.p. 199–200°.

Anal. Calcd. for $C_{25}H_{24}O_2N_2$: C, 78.12; H, 6.25; N, 7.29. Found: C, 77.86; H, 6.18; N, 7.37.

The ring-opened piperidide was soluble in hot benzene, but sparingly soluble in petroleum ether.

The infrared spectrum of the piperidide showed absorption at 1600 cm.$^{-1}$, 3332 cm.$^{-1}$ (—NH stretching), and 1640 cm.$^{-1}$ and 1525 cm.$^{-1}$ (amide I and II bands).

Preparation of Ig.—A 1.0-g. sample of pyridine-4-carboxaldehyde, 1.8 g. of hippuric acid, 2.7 g. of acetic anhydride, and 0.6 g. of freshly fused sodium acetate were heated on a boiling water bath for 0.5 hr. The reaction mixture was poured onto about 10 ml. water. After cooling, the product that was precipitated was filtered off, washed with a little ethyl alcohol, and crystallized from benzene as dirty green crystals, m.p. 167°.

Anal. Calcd for $C_{15}H_{10}O_2N_2$: C, 72.00; H, 4.00; N, 11.20. Found: C, 71.58; H, 4.14; N, 11.22.

Ig was soluble in hot benzene and hot acetic acid, but was sparingly soluble in ethyl alcohol and petroleum ether and gave no color with concentrated sulfuric acid.

The infrared spectrum of Ig showed a strong absorption at 1810 cm.$^{-1}$ which might be attributed to a conjugated carbonyl group, and a medium intensity band at 1660 cm.$^{-1}$ (>C=H stretching).[4]

Direct Synthesis of Organotin Compounds. III. Reaction of α-Substituted Benzyl Halides with Metallic Tin

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Wurtz condensation products, instead of organotin compounds, were obtained in the reaction of metallic tin powder with diphenylmethyl chloride, α-phenylethyl chloride, anethole hydrobromide, and benzal chloride, respectively, in boiling toluene as a solvent. When the reaction was carried out in water suspension, hydrolysis occurred along with the condensation. Bis(diphenylmethyl)tin dichloride was prepared from diphenylbis(diphenylmethyl)tin by the preferential cleavage of phenyl groups, and the reaction of diphenylmethylpotassium or -magnesium bromide with stannic chloride was examined.

A previous paper[1] from this laboratory recorded the reaction of metallic tin powder with benzyl chloride and its ring-substituted derivatives. Whereas dibenzyltin dihalides were obtained in toluene solution, tribenzyltin halides were the products in water-suspension reaction. The present paper comprises an examination of the reaction of metallic tin with α-substituted benzyl halides in these media. No detectable amounts of organotin compounds were formed, but the Wurtz type products have been obtained in fair to excellent yields.

Upon treatment with metallic tin powder suspended in boiling toluene, diphenylmethyl chloride afforded *sym*-tetraphenylethane in an 85% yield. Similar reaction of α-phenylethyl chloride gave a mixture of *meso*- and *dl*-2,3-diphenylbutane in an 82% yield. Remarkably high yields of these hydrocarbons prompted the authors to examine the reaction of anethole hydrobromide under similar conditions in view of the interests in the preparation of hexestrol derivatives.[2] The reaction, however, afforded less satisfactory yields (12–15%) of *meso*-3,4-bis(*p*-methoxyphenyl)hexane, which can satisfactorily be explained by the thermal instability of anethole hydrobromide at the boiling point of toluene.

When benzal chloride was heated with metallic tin suspended in toluene under refluxing for three hours, α-stilbene dichloride and *trans*-stilbene were obtained in 12% and 67% yields, respectively. A shorter period of refluxing (30 min.) changed the product ratio in favor of α-stilbene dichloride (50%) over *trans*-stilbene (27%).[3]

Attempted condensation of α-methoxybenzyl chloride by means of tin powder under similar conditions afforded a resinous mixture, from which nothing identifiable could be isolated.

Replacement of toluene with water in these reactions resulted in lowering of the yields of Wurtz type condensates, concurrent hydrolysis of the halides being observed. With water as a reaction medium, diphenylmethyl chloride gave a 74% yield of *sym*-tetraphenylethane besides benzhydrol and bisbenzhydryl ether, while α-phenylethyl chloride afforded a 33% yield of *meso*-2,3-diphenylbutane along with α-phenylethyl alcohol, bis-α-phenylethyl ether, and styrene.[4] The reaction of benzal chloride with tin powder suspended in water afforded *trans*-stilbene and benzaldehyde in 23% and 43% yields, respectively, no stilbene dichloride being isolated. Similar treatment of α-methoxybenzyl chloride gave mainly benzaldehyde besides a small amount of tar.

(1) K. Sisido, Y. Takeda, and Z. Kinugawa, *J. Am. Chem. Soc.*, **83**, 538 (1961). *Cf.* K. Sisido and Y. Takeda, *J. Org. Chem.*, **26**, 2301 (1961).

(2) (a) K. Sisido and H. Nozaki, *J. Am. Chem. Soc.*, **70**, 778 (1948). (b) K. Sisido, H. Nozaki, and H. Kuyama, *J. Org. Chem.*, **14**, 1124 (1949). (c) K. Sisido, Y. Udô, and H. Nozaki, *J. Org. Chem.*, **26**, 1227 (1961).

(3) Ogata and Nakamura have previously recorded a similar stepwise dechlorination condensation of benzal chloride by the action of reduced iron suspended in water. See Y. Ogata and H. Nakamura, *J. Org. Chem.*, **21**, 1170 (1956).

(4) The hydrolysis of diphenylmethyl chloride and α-phenylethyl chloride in water was recorded by A. M. Ward, *J. Chem. Soc.*, 445, 2285 (1927).