recrystallizations from ethanol gave blunt, white crystals, m.p. 167.4–168.8°; infrared absorption: $\nu_{\max}^{CH_2Cl_2}$ 1717 (s) (C=O), 1225 (s-m) (C—O).

Anal. Calcd. for $C_{24}H_{18}NO_2Br$: C, 66.67; H, 4.20; N, 3.24; Br, 18.49. Found: C, 65.87, 65.63, 65.97; H, 4.16, 4.34, 4.38; N, 3.34, 2.95; Br, 18.95.

B. Reaction of V with Bromine.—To a solution of 0.20 g. (0.5 mmole) of V in 3 ml. of chloroform was added 0.08 g. (0.5 mmole) of bromine. The mixture was stirred for 2 hr. and the product worked up as outlined above for the reaction with IIIb. This gave 0.15 g. of a white powder which after repeated recrystallization from ethanol melted at 161–165° (uncorr.). A mixed melting point with the sample prepared by method A was not depressed. The infrared spectrum of this material in methylene chloride was also identical with the above sample.

Methyl 2-Carboxy-1,4,5-triphenylpyrrole-3-carboxylate (V).—To a hot mixture of 6.17 g. (15 mmoles) of IIIa in 150 ml. of ethanol was added 0.84 g. (15 mmoles) of potassium hydroxide. The mixture was stirred under reflux for 16 hr., cooled to room temperature, and then poured into 800 ml. of water. After adding 45 ml. of 5% sodium bicarbonate, the aqueous mixture was extracted twice with 200 ml. of ether. The combined ether extracts were washed with water and the aqueous washings added to the above basic aqueous layer. The ethereal solution was dried with anhydrous sodium sulfate, evaporated to dryness to give 1.24 g. of starting material IIIa. The combined basic aqueous mixture from above was acidified with 15 ml. of concentrated hydrochloric acid then extracted three times with 250-ml. portions of ether. The combined ether extracts were washed with water, dried with anhydrous sodium sulfate, and evaporated to dryness on a steam bath. After filtering this gave 4.06 g. of a white solid. Two recrystallizations from a water–ethanol mixture gave fine, white needles, m.p. 169.8–170.9°[15]; infrared absorption: $\nu_{\max}^{CH_2Cl_2}$ near 2600 (m-w) (H-bonded O—H), 1724 (s) (ester C=O), 1631 (s) broad (acid C=O), 1336 (s), 1228 (s) (C—O).

Anal. Calcd. for $C_{25}H_{19}NO_4$: C, 75.55; H, 4.82; N, 3.53. Found: C, 75.43; H, 4.82; N, 3.52.

1,4,5-Triphenylpyrrole-2,3-dicarboxylic Acid (VI).—A mixture of 1.0 g. (2.4 mmoles) of IIIa and 4.0 g. of potassium hydroxide in 20 ml. of ethanol was refluxed for 35 min. The mixture was cooled then filtered, and the white solid was collected and dissolved in 160 ml. of water. The aqueous solution was extracted with ether then acidified with 5 ml. of concentrated hydrochloric acid. After extracting the acidic mixture three times with 50-ml. portions of ether, the combined ether extracts were concentrated to near dryness. On cooling this gave after filtering 0.90 g. of white powder. Two recrystallizations from ethanol gave fine, white needles, m.p. 260.4–263.4°,[15] infrared absorption: $\nu_{\max}^{KBr}$ near 3450 (m) (O—H), near 2500 (w) (H-bonded O—H), 1675 (s) (broad) (C=O), 1287 (s) and 1225 (s) (C—O).

Anal. Calcd. for $C_{24}H_{17}NO_4$: C, 75.18; H, 4.47; N, 3.66. Found: C, 75.05; H, 4.59; N, 3.65.

1,4,5-Triphenylpyrrole-3-carboxylic Acid (VII). A. Hydrolysis of IIIb Obtained from the Condensation of I and IIb.—To a hot mixture of 1.78 g. (5 mmoles) of IIIb in 75 ml. of ethanol was added 1.18 g. of potassium hydroxide. The mixture was refluxed for 19 hr., cooled, and filtered. The white solid was suspended in 1000 ml. of water, 15 ml. of 5% aqueous sodium bicarbonate was added, and the mixture was extracted with ether. The aqueous layer was acidified with 10 ml. of concentrated hydrochloric acid then extracted eight times with 100-ml. portions of ether. The combined ether layers were washed with water, dried with anhydrous sodium sulfate, then stripped of solvent until only a solid residue remained. The residue was collected in a filter funnel, washed with ether, and air-dried. This gave after recrystallization from glacial acetic acid fine, white needles, m.p. 272.5–273.5°,[15] infrared absorption: $\nu_{\max}^{KBr}$ near 2550 (w) (H-bonded O—H), 1688 (s) (with shoulder near 1650) (C=O), doublet: 1226 and 1212 (s-m) (C—O).

Anal. Calcd. for $C_{23}H_{17}NO_2$: C, 81.39; H, 5.05; N, 4.13. Found: C, 81.43; H, 5.05; N, 4.22.

B. Hydrolysis of the Product Obtained by Decarboxylation of V.—A mixture of 0.45 g. of the material and 0.38 g. of potassium hydroxide in 25 ml. of ethanol was refluxed for 16.5 hr. The product was worked up in an analogous manner as above. This gave 0.36 g. of white powder, and after repeated recrystallizations from glacial acetic gave fine, white needles, m.p. 266.8–268.4°.[15] The mixed melting point of this material with the above sample was not depressed below 269°, and the two samples were proven to be identical by their infrared examination in potassium bromide.

1,2,3-Triphenylpyrrole (VIII). Decarboxylation of VII.—A mixture of 0.2 g. of VII and 0.02 g. of copper chromite catalyst in 2 ml. of freshly distilled quinoline was heated gradually to 205–210° and maintained at this temperature for 1.5 hr. The mixture was cooled to room temperature, 25 ml. of ether was added, and the mixture filtered. The filtrate was extracted with dilute aqueous hydrochloric acid, and the organic layer separated and washed with water. Evaporation of the ethereal solution to near dryness, cooling, then filtering gave 0.14 g. of light tan needles. One recrystallization from ethanol gave fine, white needles, m.p. 179.8–180.0°, infrared absorption: $\nu_{\max}^{CH_2Cl_2}$ near 3030 (m-w) (C—H), 1596 (s-m) and 1497 (s) (C=C).

Anal. Calcd. for $C_{22}H_{17}N$: C, 89.46; H, 5.80; N, 4.74. Found: C, 89.20; H, 5.80; N, 4.75.

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[15] Compound melted with moderate to vigorous evolution of gas.

Conjugate Addition of Aryl Grignard Reagents to Unsaturated Azlactones in the Presence of Cuprous and Cobaltous Chlorides[1]

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It is well established that aryl Grignard reagents react with unsaturated azlactones to give products of 1,2-addition. Thus, for example, 2-phenyl-4-benzylidene-5(4H)-oxazolone (I) reacts with excess phenylmagnesium bromide to give 1,1-diphenyl-2-benzamidocinnamyl alcohol (II) and 2,5,5-triphenyl-4-benzylidene-2-oxazoline (III).[3–6] No products of 1,4-addition to the α,β-unsaturated moiety have been isolated under these conditions. It has also been shown that alkyl Grignard reagents give exclusive 1,4-addition with these compounds.[7] More recently, we have reported that the labile geometric isomer of I reacts with aryl

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(1) Paper VII in the series: Chemistry of Lactones; Paper VI, R. Filler and Y. S. Rao, *J. Org. Chem.*, **27**, 2403 (1962).

(2) On leave of absence from N.B.S. College, Hyderabad (India).

(3) H. Pourrat, *Bull. soc. chim. France*, 828 (1955).

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

(5) R. Filler and J. D. Wismar, *ibid.*, **22**, 853 (1957).

(6) W. I. Awad and M. S. Hafez, *ibid.*, **25**, 1180, 1183 (1960).

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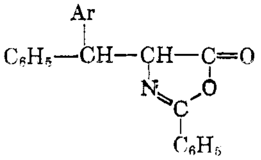
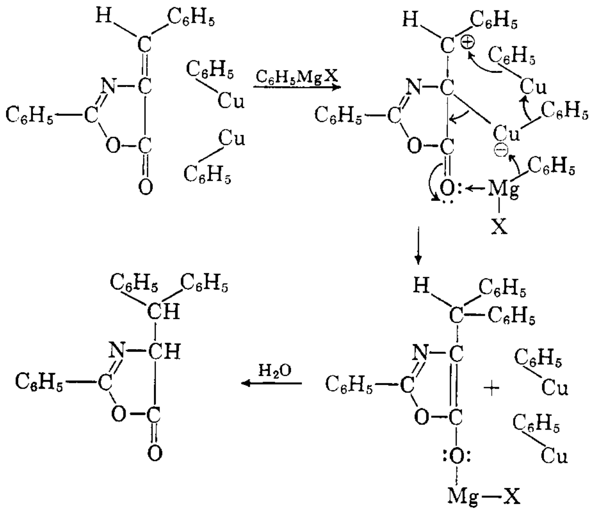
Grignard reagents to give IV, the product of 1,4-addition, as well as analogs of II and III.[8]



IV

It has now been found that the addition of cuprous chloride to the Grignard reagent in the molar ratio of 2:3, markedly alters the course of the reaction with I and its analogs and leads to the predominant formation of saturated azlactones, IV. This effect of cuprous chloride in changing the course of the reaction from 1,2- to 1,4-addition has been observed in the case of acetylene carboxylic esters,[9] which otherwise give 1,2-addition products with Grignard reagents.

In the present study, the possibility of initial isomerization of I to its labile isomer, by cuprous chloride, was examined. A blank experiment demonstrated that no isomerization occurred under the reaction conditions. The following mechanism, involving the initial formation of phenylcopper and analogous to that proposed by Munch-Petersen, *et al.*,[10] is suggested for the observed 1,4-addition.



The mechanism is supported by the following observations: (1) Phenylcopper was obtained from phenylmagnesium bromide and cuprous chloride in the absence of azlactone. (2) Two moles of phenylcopper, prepared from phenylmagnesium iodide and cuprous iodide,[11] and one mole of Grignard reagent reacted with azlactone I to give essentially the same relative yields of 1,4- and 1,2-addition products.

While the possibility of participation of phenyl radicals cannot be excluded, several lines of evidence tend to disfavor such an intermediate under the reaction conditions employed: (a) The reaction was conducted in a nitrogen atmosphere in refluxing ether. Under these conditions phenylcopper remains unchanged. Gilman[11] found that phenylcopper was stable below 80°. (b) Phenylcopper readily forms biphenyl on standing in air. No biphenyl has been isolated in any of the current experiments.

The course of the reaction was not affected by the nature of groups on the arylidene nucleus but was significantly influenced by ring substituents in the Grignard reagent, as shown in the table.

When cobaltous chloride was used instead of cuprous chloride, in the same molar ratio, the yield of 1,4-addition product from I was much lower (20%). A small amount of biphenyl and a 40% yield of 2-benzamidobenzalacetophenone (V), were also obtained. It is interesting to note that the 1,2-addition stopped at the ketone stage and V was obtained in much higher yield than reported previously.[5] In this case, it appears that a free radical mechanism is operative.

Experimental[12]

Reaction of Azlactones with Arylmagnesium Bromide in the Presence of Cuprous Chloride.—To 0.9 g. (0.0375 g.-atom) of magnesium turnings in 30 ml. of anhydrous ether in a nitrogen atmosphere was added dropwise 0.0375 mole of the aryl bromo compound dissolved in 25 ml. of ether. After the reaction had subsided, the mixture was heated under reflux for 0.5 hr. The azlactone (0.0125 mole), suspended in 125 ml. of ether, was added over a 1-hr. period together with 2.45-g. portions of cuprous chloride (0.025 mole). The mixture was heated under reflux for an additional 2 hr. and then decomposed with a saturated solution of ammonium chloride. The ether layer was removed. The residue, remaining after removal of the deep blue aqueous layer, was dissolved in dilute hydrochloric acid (1:1) and extracted with ether. The combined ether layers were washed repeatedly with water and dried over anhydrous magnesium sulfate. Ether was removed by evaporation on a water bath. The residual oil was triturated with absolute ethanol and left overnight in a refrigerator. The saturated azlactone which separated was filtered and recrystallized from absolute ethanol.

Infrared spectra: 1805–1815-cm.$^{-1}$ region (>C=O in saturated azlactones) and 1645 cm.$^{-1}$ (—C=N—).

The mother liquor was dissolved in ether and triturated with petroleum ether to give the 1,2-addition product.

Attempted Isomerization of I with Cuprous Chloride.—2-Phenyl-4-benzylidene-5(4H)-oxazolone (3.12 g.) was heated under reflux with 2.45 g. of cuprous chloride in 125 ml. of anhydrous ether for 3 hr. The reaction mixture was decomposed as described above. Starting material was recovered.

Preparation of Phenylcopper.—To a solution of phenylmagnesium bromide prepared from 7.9 ml. of bromobenzene (0.075 mole) and 1.8 g. of magnesium (0.075 g.-atom) was added 4.9 g. of cuprous chloride over a period of 1 hr.

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[8] R. Filler, K. B. Rao, and Y. S. Rao, *J. Org. Chem.*, **27**, 1110 (1962).

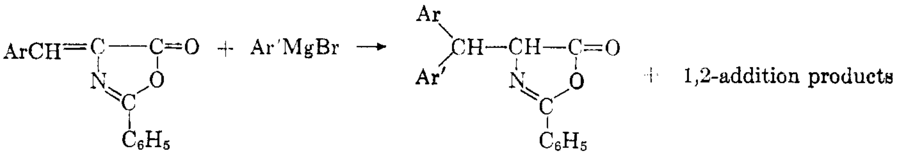
[9] C. Bretting, J. Munch-Petersen, P. M. Jørgensen, and S. Refn, *Acta Chem. Scand.*, **14**, 151 (1960).

[10] J. Munch-Petersen, C. Bretting, P. M. Jørgensen, S. Refn, and V. K. Andersen, *ibid.*, **15**, 277 (1961).

[11] H. Gilman and J. M. Straley, *Rec. trav. chim.*, **55**, 821 (1936).

[12] All melting points were determined on a Fisher-Johns block and are uncorrected.

TABLE I



Ar	Ar′	% Yield of 1,4-addition product	% Yield of 1,2-addition product	M.p.[a] of 1,4-addition product, °C.	Formula	Carbon, %		Hydrogen, %	
						Calcd.	Found	Calcd.	Found
C_6H_5	C_6H_5	65	2	...	...	...	...	...	...
C_6H_5	o-$CH_3C_6H_4$	62	3	...	...	...	...	...	...
C_6H_5	p-$CH_3C_6H_4$	25	30	...	...	...	...	...	...
C_6H_5	p-ClC_6H_4	75	1	...	...	...	...	...	...
C_6H_5	o-ClC_6H_4	50	2	...	...	...	...	...	...
C_6H_5	o-$CH_3OC_6H_4$	40	20	...	...	...	...	...	...
C_6H_5	p-$CH_3OC_6H_4$	38	40	...	...	...	...	...	...
C_6H_5	1-$C_{10}H_7$	40	19	205	...	...	...	...	...
p-$CH_3OC_6H_4$	C_6H_5	64	2	...	...	...	...	...	...
o-ClC_6H_4	C_6H_5	64	3	...	...	...	...	...	...
p-ClC_6H_4	C_6H_5	63	0	...	...	...	...	...	...
1-$C_{10}H_7$	C_6H_5	60	0	205	$C_{26}H_{19}NO_2$	82.74	82.96	5.07	5.04
2-$C_{10}H_7$	C_6H_5	62	0	105	$C_{26}H_{19}NO_2$	82.74	82.98	5.07	5.07
p-$CH_3C_6H_4$	C_6H_5	64	0	145	...	...	...	...	...
m-$CH_3C_6H_4$	C_6H_5	60	0	158	$C_{23}H_{19}NO_2$	81.15	80.93	5.63	5.43
p-$CH_3OC_6H_4$	p-$CH_3OC_6H_4$	40	10	189	$C_{24}H_{21}NO_4$	74.40	73.90	5.46	5.50
p-$CH_3OC_6H_4$	p-ClC_6H_4	60	0	170	$C_{23}H_{18}NO_3Cl$	70.65	70.30	4.63	4.52
o-ClC_6H_4	p-ClC_6H_4	60	0	149	$C_{22}H_{15}NO_2Cl_2$	66.67	67.09	3.82	4.01

[a] The compounds whose melting points and analyses have not been reported here were identical with samples reported in references 1, 4, and 6.

The reaction mixture was refluxed in a nitrogen atmosphere. A grey powder was obtained.[11] On standing in air, copper metal and biphenyl, m.p. 72°, were obtained. The copper dissolved in concentrated nitric acid to give reddish brown fumes of nitrogen dioxide and a blue solution of cupric nitrate.

Reaction of I with Phenylcopper and Phenylmagnesium Bromide.—To a suspension of phenylcopper,[11] prepared in a nitrogen atmosphere, from 0.9 g. of magnesium, 8.17 g. of iodobenzene, and 7.2 g. of cuprous iodide, was added a solution of phenylmagnesium bromide, prepared from 0.6 g. of magnesium and 2.7 ml. of bromobenzene. A suspension of I (6.25 g.) in 250 ml. of ether was added in portions over a period of 1 hr. The mixture was refluxed for an additional 2 hr. and decomposed with a saturated solution of ammonium chloride. The ether layer gave 5.3 g. of 2 phenyl-4-benzhydryl-5-oxazolone, m.p. 159°, and 0.25 g. of compound II.

Reaction of I with Phenylmagnesium Bromide in the Presence of Cobaltous Chloride.—To a solution of phenylmagnesium bromide, prepared from 0.9 g. of magnesium and 3.95 ml. of bromobenzene, was added 3.13 g. of I, suspended in ether, during a 1-hr. period. Anhydrous cobaltous chloride (2.23 g.) was added at the same time. The reaction mixture was heated under reflux for 2 hr. and decomposed with a saturated solution of ammonium chloride. The ether layer was separated, the residue dissolved in dilute hydrochloric acid (1:1), and the hydrochloric acid layer extracted with ether. The combined ether layers were washed with water and dried over anhydrous magnesium sulfate. The ethereal layer gave 0.80 g. of the saturated azlactone (20% yield), 0.5 g. of biphenyl, and 1.7 g. of α-benzamidobenzalacetophenone (V) (40%). These compounds were separated by fractional crystallization from ethanol and benzene. Compound V gave no melting point depression when mixed with an authentic sample.[5]

Spectral Measurements and Analyses.—Infrared spectra were obtained on a Perkin-Elmer 21 spectrophotometer, using chloroform or methylene chloride as solvent. Microanalyses were conducted by Micro-Tech Laboratories, Skokie, Illinois.

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A Selective Oxidation of Δ^5-3β-Hydroxy Steroids to Δ^4-3-Keto Steroids *via* 5α,6β-Dichloro Intermediates

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In connection with another project there was occasion to treat a 3β-hydroxy-5α,6β-dichloro steroid with lithium chloride in dimethylformamide. Unexpectedly, the major product was found to have properties typical of a Δ^4-3-ketone. Since dichloro alcohols[1,2] are easily prepared from Δ^5-3β-acetates

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(2) H. Ringold, G. Rosenkranz, and F. Sondheimer, *J. Am. Chem. Soc.*, **78**, 820 (1956).