tillation. The aqueous solution was washed with several portions of ether and then cautiously acidified by the addition of cold 50% sulfuric acid. Isolation of the product was effected by ether extraction followed by crystallization from benzene–petroleum ether or from 95% ethanol. There was obtained 3.2 g. (16%) of the acid (XX), m.p. 144–147°. Further purification from ethanol raised the m.p. to 154–155°.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 70.08: H, 5.72.

3-Methoxy-4-methylxanthone (XVI). A mixture of 1.5 g. of 2-carboxy-2′-methyl-3′-methoxydiphenyl ether (XX) and 15 g. of polyphosphoric acid was stirred and heated on a steam cone. Stirring was continued until it became homogeneous and the flask was then stoppered and heated, with occasional swirling, for an additional 30 min. Isolation of the product in the usual manner and recrystallization from 95% ethanol gave 1.0 g. (72%) of the xanthone (XVI) as colorless fibrous solid, m.p. 177–178°.

Anal. Calcd. for $C_{15}H_{12}O_3$: C, 74.98; H, 5.04. Found: C, 75.22; H, 5.15.

This substance exhibits carbonyl absorption in the infrared at 6.04 μ. Its ultraviolet spectrum is shown in Fig. 1.

When preparations of 2-methylresorcinol methyl ether used in this sequence were not carefully fractionated, substantial quantities of 2-methylresorcinol persisted as a contaminant. Utilization of such material in the two-step process described above, without isolation of the intermediate acid, gave varying quantities of a high-melting by-product. Purification by recrystallization from ethanol gave a pure sample as pale yellow needles, m.p. 377–380°. Analytical data, spectral data, and its high melting point suggested it to be a bis condensation product, 12*H*,14*H*-6-methyl[1]benzopyrono[3,2-*b*]xanthone (XXI).

Anal. Calcd. for $C_{21}H_{12}O_4$: C, 76.82; H, 3.69. Found: C, 76.50; H, 3.80.

Lithium aluminum hydride reduction of this substance exactly as described in the general method of Mustafa and Hilmy[13] gave a virtually quantitative yield of 12*H*,14*H*-6-methyl[1]benzopyrono[3,2-*b*]xanthene (XXII). Several recrystallizations from petroleum ether gave very pale yellow needles, m.p. 177–178°.

Anal. Calcd. for $C_{21}H_{14}O_2$: C, 83.97; H, 5.37. Found: C, 84.08; H, 5.42.

Acknowledgment. The authors are indebted to the Robert A. Welch Foundation for the financial support of this study and to M. J. O'Neal and his colleagues at the Houston laboratory of Shell Oil Company for mass spectral data and its interpretation.

AUSTIN 12, TEX.

[CONTRIBUTION NO. 1116 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

Some Reactions of 2-Furyllithium[1]

VISVANATHAN RAMANATHAN AND ROBERT LEVINE

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The reactivity of 2-furyllithium toward carbon dioxide, aldehydes, ketones, esters, nitriles, and alkyl halides has been studied. Carbinols and ketones containing 2-furyl groups as well as 2-*n*-butylfuran and 2-furoic acid have been prepared in high yields.

Very little has been published in the literature about the carbanions of furan and its derivatives. Metallic derivatives of furan were first prepared by Gilman and Breuer.[2] Furan was metalated by reaction with sodium, diethylmercury, diphenylmercury, and dibenzylmercury. Dibenzylmercury gave the best results as shown by the formation of 2-furoic acid in 58% yield on subsequent carbonation. Carbonation of the reaction product(s) of furan, sodium sand, and *n*-amyl chloride gave furan-2,5-dicarboxylic acid (6.5%) in addition to 2-furoic acid (27%), indicating that the furan had probably been converted to its dianion to a small extent.[3] Earlier a 40% yield of 2-furoic acid was obtained by the metalation of furan with phenyllithium while only 7.5% of the acid was obtained with methyllithium as the metalating agent.[4]

Derivatives containing germanium and silicon have been prepared by the reaction between 2-furyllithium and germanium tetrabromide[5] and trimethylchlorosilane, respectively.[6] Sulfur dioxide was absorbed by 2-furyllithium leading to lithium 2-furylsulfinate.[7,8] Carbinols have been obtained by treating 2-furyllithium with 1-alkyl-4-piperidones.[9]

The present work deals with a study of the reactivity of 2-furyllithium toward several different types of compounds including carbon dioxide, alkyl halides, nitriles, aldehydes, ketones, and esters.

Furan (one equivalent) was metalated in high yield by reaction with *n*-butyllithium (one equivalent) in refluxing ether for four hours as evidenced by the fact that carbonation gave 2-furoic acid in

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[1] This study was supported by a grant from Lithium Corporation of America.

[2] H. Gilman and F. Breuer, *J. Am. Chem. Soc.*, **56**, 1123 (1934).

[3] A. H. Morton and G. H. Patterson, *J. Am. Chem. Soc.*, **65**, 1346 (1943).

[4] H. Gilman and R. L. Bebb, *J. Am. Chem. Soc.*, **61**, 109 (1939).

[5] H. Gilman and R. W. Leeper, *J. Org. Chem.*, **16**, 474 (1951).

[6] R. A. Benkeser and R. B. Currie, *J. Am. Chem. Soc.*, **70**, 1780 (1948).

[7] W. E. Truce and E. Wellisch, *J. Am. Chem. Soc.*, **76**, 5177 (1952).

[8] J. F. Scully and E. V. Brown, *J. Org. Chem.*, **19**, 894 (1954).

[9] L. Berger, A. Zierling, and J. Lee, *J. Org. Chem.*, **12**, 904 (1947).

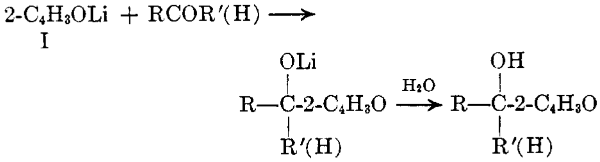
TABLE I

2-FURYLCARBINOLS OF THE TYPE $2\text{-}C_4H_3OCR(OH)R'$ FROM 2-FURYLLITHIUM AND CARBONYL COMPOUNDS

Reactant	Product R	Product R′	Carbinol, Yield, %	M.P. or B.P.	Mm.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Benzophenone	C_6H_5	C_6H_5	98.2	92[a]					
Benzaldehyde	C_6H_5	H	98.3	110[b]	1				
Acetophenone	C_6H_5	CH_3	96.0	94	0.6	76.60	76.62	6.38	6.59
Methyl ethyl ketone	CH_3	C_2H_5	88.1	79–80[c]	20				
Isobutyraldehyde	$i\text{-}C_3H_7$	H	93.3	83–84[b]	12				
Cyclohexanone	Cyclohexyl		94.7	38					
				74	0.8	72.26	71.92	8.49	8.52
Ethyl acetate	$2\text{-}C_4H_3O$[d]	CH_3	94.4	74–75	0.8	67.39	67.61	5.67	5.86
Ethyl benzoate	$2\text{-}C_4H_3O$[d]	C_6H_5	44.4	152–155	0.8[e]				
				122	0.1				

[a] W. J. Hale, W. D. McNally, and C. J. Peter, *Am. Chem. J.*, **35**, 68 (1906). [b] F. N. Peters and R. Fischer, *J. Am. Chem. Soc.*, **52**, 2079 (1930). [c] H. Gilman and N. O. Calloway, *J. Am. Chem. Soc.*, **55**, 4197 (1933). [d] $2\text{-}C_5H_4O$ = 2-furyl radical. [e] Polymerized before it could be analyzed.

76.8% yield. 2-Furyllithium also added across the carbonyl groups of several aldehydes and ketones to give the corresponding secondary and tertiary alcohols in yields of 88–98%. The results of these reactions, which can be represented by the following scheme, are summarized in Table I.



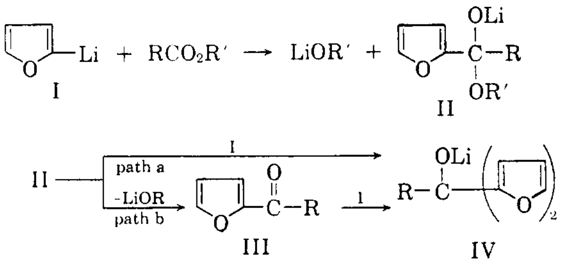
$$\underset{\text{I}}{2\text{-}C_4H_3OLi} + RCOR'(H) \longrightarrow R\text{—}\overset{OLi}{\underset{R'(H)}{C}}\text{-}2\text{-}C_4H_3O \xrightarrow{H_2O} R\text{—}\overset{OH}{\underset{R'(H)}{C}}\text{-}2\text{-}C_4H_3O$$

R = 2-furyl radical

That the yield (88%) of carbinol which was obtained from the reaction of 2-furyllithium (I) with methyl ethyl ketone is considerably lower than the yields which were isolated from the reaction of I with the other aldehydes and ketones may be due to the possibility that methyl ethyl ketone self-condensed to some extent during the reaction.

The secondary alcohols, $RC(H)(OH)(2\text{-}C_4H_3O)$, were obtained earlier by the reactions of furfural with Grignard reagents while the tertiary alcohols were prepared from the interaction of 2-furoic esters or 2-acylfurans with Grignard reagents.[10] However, compounds such as 1-(2-furyl)cyclohexanol, which cannot be made by the procedures just described, became accessible in high yield (94.7%) by reaction of I with cyclohexanone.

From the reaction of I with esters only the corresponding tertiary alcohols were isolated in spite of the fact that equivalents of I and ester were used, a situation which might favor ketone formation. It appears that the initially formed adducts (II), between I and the esters, are sufficiently unstable or reactive that as soon as they are formed they (1) either react with more I (path a) or (2) they decompose to the free ketones III, which then react with more of I to give the lithium salts of the carbinols, IV (path b).



The tertiary alcohols (IV, where Li is replaced by H) are colorless viscous liquids or white solids when pure. The presence of the two 2-furyl groups make the alcohols quite sensitive to oxygen and when exposed to air they become oxidized to black resins. Difurylphenylcarbinol was an extreme case and had to be distilled at the low pressure of 0.1 mm. Even then, it changed through all the colors of the visible spectrum and polymerized before an elemental analysis could be performed. Gomberg[11] had included this compound as one to be studied during his work on the triphenylmethyl radical.

The possibility of preparing ketones by the use of nitriles was also investigated. Benzonitrile gave, on hydrolysis of the intermediate ketimine, 2-benzoylfuran in 88.6% yield. The reaction with acetonitrile failed. The presence of hydrogen atoms on its α-carbon atom may have led to side reactions and to the formation of products which could not be identified.

Alkyl- and arylfurans, with a few exceptions, have been obtained only by indirect means. Friedel-Crafts catalysts for direct alkylation also catalyze resinification. Furan was successfully alkylated with trimethylethylene under the influence of boron trifluoride to give a mixture of 2-*t*-amyl- and 2,5-di-*t*-amylfuran.[12] It appeared that the direct alkylation of 2-furyllithium by alkyl

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(10) A. D. Dunlop and F. N. Peters, "The Furans," Reinhold Publishing Corp., New York, 1953, pp. 253–260.

(11) M. Gomberg and R. L. Jickling, *J. Am. Chem. Soc.*, **35**, 446 (1913).

(12) H. Pines and J. A. Vesely to Universal Oil Products Co., U. S. Patent **2,532,515** (1950).

TABLE II

OTHER REACTIONS OF 2-FURYLLITHIUM USING DIETHYL ETHER AS THE REACTION SOLVENT

Reactant	Product	% Yield,	M.P. or B.P.	Mm.
Carbon dioxide	2-Furoic acid	76.8	132	
Benzonitrile	2-Benzoylfuran	88.6	102–103[a] 285	0.7 759
n-Butyl bromide	2-*n*-Butylfuran	2.4	137[b]	759
n-Butyl bromide	2-*n*-Butylfuran	77.4[c]	137[b]	759
Benzyl chloride	2-Benzylfuran	10.8[d]	92	8
Benzyl chloride	Dibenzyl	45.0[c]	52[e]	

[a] Oxime, m.p. 134° [P. Marquis, *Ann. Chim. Phys.* [8], **4**, 276 (1905)]. [b] See footnote *c* to Table I. [c] Tetrahydrofuran was used as the solvent. [d] T. Kariyone, *J. Pharm. Soc. Japan*, **428**, 891 (1917). [e] G. Wittig and H. Witt, *Ber.*, **74**, 1474 (1941).

halides might be a route to this class of compounds. 2-Furyllithium in ether was treated with *n*-butyl bromide but only a 2.4% yield of 2-*n*-butylfuran could be isolated. The more reactive benzyl chloride gave 10.8% of 2-benzylfuran. Recently tetrahydrofuran has been used as a solvent for a number of reactions involving organometallic reagents.[13] Since these reactions either do not proceed in diethyl ether or proceed at a very slow rate and in considerably lower yields, tetrahydrofuran was tried as a solvent for the alkylation reactions. By this modification, the yield of 2-*n*-butylfuran was raised to 77%. This procedure might well be applicable to the synthesis of a variety of 2-*n*-alkylfurans. Benzyl chloride, however, failed to alkylate 2-furyllithium and only dibenzyl (45%) and resins were produced. Dibenzyl could conceivably arise by the halogen exchange between benzyl chloride and furyllithium to give benzyllithium followed by coupling with more benzyl chloride.

EXPERIMENTAL

The reactions were carried out under an atmosphere of dry, oxygen-free nitrogen with mechanical stirring. The solvents and other chemicals used were commercial products and were dried and distilled. Tetrahydrofuran was freed from peroxides and moisture before use by refluxing over sodium for 2 hr. followed by distillation. Lithium ribbon was supplied through the courtesy of Lithium Corporation of America.

2-Furyllithium. *n*-Butyllithium (0.1 mole) in ether was prepared according to the method of Gilman.[14] Furan (0.1 mole) was added at about −20°, and the mixture was warmed to room temperature and refluxed 4 hr. It was then poured onto a slurry of Dry Ice and ether. After the disappearance of the Dry Ice, enough water was added to dissolve the solids. The ether layer was separated and washed with water. The washings were added to the aqueous layer. The combined aqueous phases were cooled in an ice bath and acidified with hydrochloric acid. The precipitate was filtered. The filtrate was extracted with ether to give more of the acid. The combined yield of 2-furoic acid was 8.6 g. (76.8%), m.p. 132° alone and when mixed with an authentic sample.

When the metalation was carried out for 2 hr. at room temperature, the yield of 2-furoic acid was only 66.1%.

Reactions of 2-furyllithium with carbonyl compounds. 2-Furyllithium was prepared as described above using 0.3 mole of the reactants. The carbonyl compound (0.3 mole) was diluted with an equal volume of dry ether and added slowly to 2-furyllithium at about −20°. Then, the cooling bath was removed, and the mixture was refluxed for 16 hr. In most of the reactions a precipitate had formed by this time. The slurry was poured onto crushed ice. The ether layer was separated, washed with water, dried, and fractionated.

A reaction time of 3 hr. in refluxing ether in the case of benzophenone reduced the yield only from 98.2% to 90.4%. Therefore, it appears that the reactions are nearly complete after 3 hr.

When an ester (0.3 mole) was used for the condensation, nearly half of it was recovered after the reaction and carbinol was the only product.

The carbinols, when pure, were colorless, viscous liquids or colorless solids. They were susceptible to air oxidation and had to be stored in a refrigerator, under an atmosphere of nitrogen. In the case of difurylphenylcarbinol, the distillation apparatus was flushed with dry nitrogen before distillation, and then it was distilled under a low pressure of 0.1 mm. This was necessary to keep the temperature below 150° which appeared to be a critical temperature for rapid polymerization; at this temperature it passed through all the colors of the visible spectrum. Even when the sample was sealed under those conditions, it polymerized before an elemental analysis could be performed.

Reaction with nitriles. 2-Furyllithium (0.2 mole) was prepared and the nitrile (0.2 mole), diluted with an equal volume of dry ether, was added at −20°. A solid, the ketimine salt, separated, and made stirring difficult. The reaction mixture was allowed to stand overnight. It was poured over crushed ice and made acidic with hydrochloric acid. The liquids were shaken up in a separatory funnel and the ether layer was separated. The aqueous layer was warmed to and maintained at 60° for 2 hr. to hydrolyze the ketimine hydrochloride. An oil had separated at this point. The reaction was cooled, extracted with ether, and the extract added to the other ether layer. The combined ether solutions were washed with water, dried, and fractionated.

From the reaction with acetonitrile no identifiable product could be isolated. Much resin formation took place.

Alkylation of furan (A). In ether. 2-Furyllithium (0.3 mole) was prepared and the halide (0.3 mole), diluted with an equal volume of dry ether, was added at −20°. The cooling bath was removed and the mixture was refluxed for 16 hr. The mixture was poured over crushed ice. The ether layer was separated, washed with water, dried, and fractionated.

B. *In tetrahydrofuran*[15] Tetrahydrofuran (90 ml.) was placed in a three-necked, round bottom flask fitted with a slip-sealed stirrer, a condenser, and a jacketed addition funnel. The air was swept out of the flask with dry nitrogen and a steady flow of the gas was maintained throughout the reaction. Lithium metal, finely cut (3.0 g., 0.43 g.-atom) was introduced. The suspension was cooled to −25°. *n*-Butyl chloride (18.5 g., 0.2 mole), diluted with tetrahydrofuran (90 ml.), was placed in the addition funnel. It was cooled and a few milliliters were added to the stirred suspension of lithium to start the reaction. When the reaction had started as indicated by the appearance of cloudiness, the rest of the chloride solution was added in the course of 1 hr. while the cooling bath was maintained at −30° to −35°. After the addition of the halide, the mixture was stirred for 1 hr.

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(13) H. Gilman and B. J. Gaj, *J. Org. Chem.*, **22**, 447 (1957).

(14) H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. F. Dunn, and L. S. Miller, *J. Am. Chem. Soc.*, **71**, 1499 (1949).

(15) H. Gilman and B. J. Gaj, *J. Org. Chem.*, **22**, 1165 (1957).

with the cooling bath at −25°. Furan (13.6 g., 0.2 mole) was added dropwise at −25° and stirring was continued for 4 hr. at −15°. The halide (0.2 mole), diluted with an equal volume of tetrahydrofuran, was added. Stirring was continued for 1 hr. at −15° and then the cooling bath was removed. The mixture was allowed to stand overnight. It was poured over crushed ice and the two layers were separated. The aqueous layer was extracted with ether, and the ether extract was added to the tetrahydrofuran layer. The combined organic layers were dried and fractionated. In this way 19.2 g. (77.4%) of 2-n-butylfuran, b.p. 137° at 759 mm., was obtained.

Pittsburgh 13, Pa.

[Contribution from the Noyes Chemical Laboratory, University of Illinois]

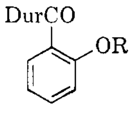
p-Benzylation of Duryl o-Methoxyphenyl Ketone with the Grignard Reagent[1]

REYNOLD C. FUSON and COLIN R. McARTHUR

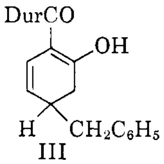
Received October 26, 1961

Duryl o-methoxyphenyl ketone and duryl o-phenoxyphenyl ketone were found to react with benzylmagnesium chloride to give duryl 2-hydroxy-4-benzyl-3,4-dihydrophenyl ketone. Aromatization of this ketone gave duryl 2-hydroxy-4-benzylphenyl ketone, the structure of which was established by its conversion into duryl 2-phenyl-4-benzylphenyl ketone, which was synthesized by an independent method.

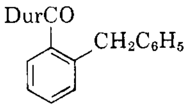
p-Alkylation of hindered ketones takes place with a number of Grignard reagents including the t-butyl and benzyl reagents.[2,3] In particular, t-butylmagnesium chloride has been found to convert duryl o-methoxyphenyl ketone (I) into duryl 2-methoxy-4-t-butylphenyl ketone.[3] In the present work, the action of benzylmagnesium chloride has been studied; with the methoxy ketone I, however, it gave an unexpected product which proved to be duryl 2-hydroxy-4-benzyl-3,4-dihydrophenyl ketone (III). The same product III was obtained by treatment of duryl o-phenoxyphenyl ketone (II) with benzylmagnesium chloride. In either case, ether group displacement occurred to a small extent to give o-benzylphenyl duryl ketone (IV).



I. R = CH_3
II. R = C_6H_5



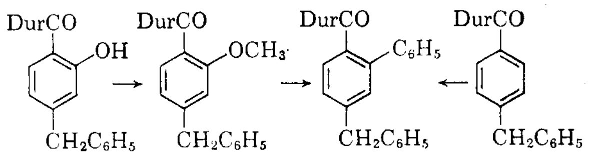
III



IV

The dihydro compound III underwent dehydrogenation when heated with a palladium-on-charcoal catalyst to give duryl 2-hydroxy-4-benzylphenyl ketone (V). The infrared spectra of hydroxy ketones III and V both have an absorption band at 1630 cm.$^{-1}$ assignable to a conjugated, hindered, hydrogen-bonded ketone. Methylation of compound V gave duryl 2-methoxy-4-benzylphenyl ketone (VI) in which the carbonyl group absorption band is raised to 1670 cm.$^{-1}$, assignable to a conjugated and hindered, but not hydrogen-bonded, ketone.

The structure of the ketone V was established by treating the methylation product VI with phenylmagnesium bromide, which gave duryl 2-phenyl-4-benzylphenyl ketone (VII). This ketone was prepared by an independent synthesis which consisted in conjugate addition of phenyllithium to the known[2] p-benzylphenyl duryl ketone (VIII).



V VI VII VIII

Treatment of 2-duroylphenol with t-butylmagnesium chloride is known to give duryl 2-hydroxy-4-t-butyldihydrophenyl ketone, presumably the 3,4-dihydro derivative.[4] The assigned positions of the double bonds in the dihydro compound III also have not been unequivocally established but are consistent with the nuclear magnetic resonance spectrum of this ketone. A doublet appears at 4.44 τ assignable to the vinyl proton at the 6-position, the absorption line of which would be expected to be split into a doublet by the vinyl proton at the 5-position. A doublet appears in the region of 4.63 τ assignable to a vinyl proton at the 5-position, the absorption line of which would be expected to be split by the vinyl proton at the 6-position. Each half of this doublet is split further; this effect would be expected to be caused by the tertiary proton at the 4-position.

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(1) This investigation was supported in part by a grant from the Office of Ordnance Research, U. S. Army (Contract No. DA-11-022-ORD-874).

(2) R. C. Fuson and B. C. McKusick, *J. Am. Chem. Soc.*, **65**, 60 (1943).

(3) R. C. Fuson and B. Vittimberga, *J. Am. Chem. Soc.*, **79**, 6030 (1957).

(4) R. C. Fuson and F. T. Fang, *J. Am. Chem. Soc.*, **77**, 3781 (1955).