[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY, THE INSTITUT DU RADIUM, FONDATION CURIE]

Synthesis of 1,4-Diacylbenzenes by Thermal Decomposition of α-(4'-Acylphenoxy)propiophenones

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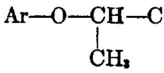
The thermal decomposition of α-(4'-acylphenoxy)propiophenones is shown to yield up to 30% of 4-acylacetophenones. 1,4-Diacetylbenzene, 4-propionyl-, and 4-benzoylacetophenones, and 2,5-diacetyl-*p*-cymene are prepared by this process.

It has been previously shown that aryloxyacetophenones (Ar—O—CH_2—CO—Ar') can undergo a thermal decomposition which yields the following compounds[1-5]:

$$\text{Ar—OH} + \text{Ar—CHO} + \text{Ar'—CHO} + \text{Ar'—COOH} + H_2O$$

Under the same conditions, α-aryloxypropiophenones



$$\text{Ar—O—}\underset{CH_3}{\underset{|}{\text{CH}}}\text{—CO—}C_6H_5$$

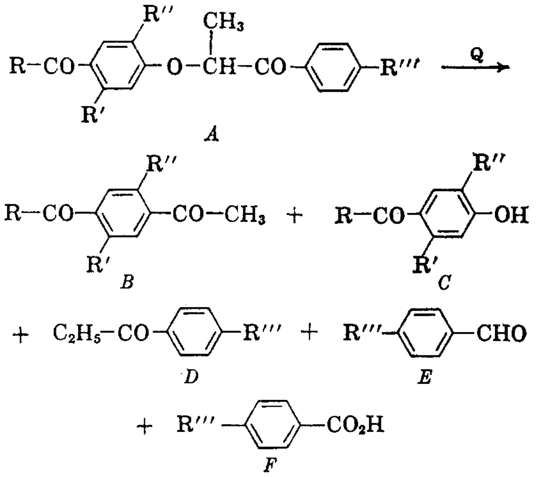
give[6]

$$\text{Ar—OH} + \text{Ar—CO—}CH_3 + C_6H_5\text{—CO}C_2H_5 + C_6H_5\text{—CHO} + C_6H_5\text{—COOH} + H_2O$$

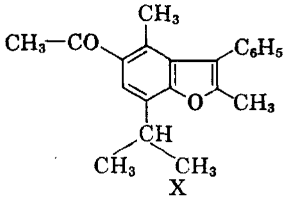
The occurrence of either aldehyde Ar—CHO or ketone Ar—CO—CH_3 corresponding to the phenolic part of the original molecule implies a rearrangement of atoms in the Ar—O—C— cracking residue, according to a hitherto unknown mechanism. This procedure provides an original way to form aldehydes or ketones from phenols, taking the corresponding aryloxyacetophenones as intermediary products.

Now the thermal decomposition of α-(4'-acylphenoxy)propiophenone (formula *A;* chart I) has been carried out, giving some 4-acylacetophenone (*B*) as the expected product besides the usual cracking material, which includes a large amount of 4-acylphenol (*C*) as well as the compounds formed at the cost of the ketonic part of the molecule: the ethyl aryl ketone (*D*) and, sometimes, some small quantities of aldehyde (*E*) and acid (*F*).

CHART I



The compounds obtained by thermal decomposition, with the corresponding yields are given in Table I. These pyrodecompositions each time gave several other products, the structures of which could not always be established, although some of them seemed to be benzofuran derivatives formed by an intramolecular cyclodehydration of the aryloxypropiophenone. For instance, starting from IV, a pure compound was obtained, showing the expected analytical composition of 2,4-dimethyl-3-phenyl-5-acetyl-7-isopropylbenzofuran (X).



X

Yields, especially those of diketones, seem to depend only slightly on the speed of the thermal decomposition, as already established in other cases.[3,4,6] However, the presence and nature of substituents on the starting aryloxypropiophenone obviously affect the relative proportion of the various products obtained and, also, the absolute quantity of diketone formed. The substitutions on the phenolic ring chiefly play a role in the diketone formation, as suggested by the comparison between the decompositions of products I, II, III, and IV. The substitution on the ring carrying the ketone group seems to be important for the pyrolytical formation of products coming from this ring, as it is shown by the increased yields of acid and aldehyde in the case of V. The important

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(1) R. Royer and E. Bisagni, *Bull. soc. chim.*, 1468 (1959).

(2) R. Royer and E. Bisagni, *Chimia*, **13**, 335 (1959).

(3) R. Royer and E. Bisagni, *Helv. Chim. Acta*, **42**, 2364 (1959).

(4) R. Royer, E. Bisagni, and A. Cheutin, *Bull. soc. chim.*, 278 (1960).

(5) R. Royer and C. Hudry, *Bull. soc. chim.*, 939 (1961).

(6) R. Royer, E. Bisagni, and C. Hudry, *Bull. soc. chim.*, 1178 (1960).

TABLE I

Starting Compounds, Formula *A*	Thermal Decomposition Rate	Diketone		Other Products							
		Formula *B*	Yield, %	*C*	%	*D*	%	*E*	%	*F*	%
I R = CH$_3$; R′ = R″ = R‴ = H	320–350° (6 min.) ↗ 445° (4 min.)	VI R = CH$_3$; R′ = R″ = H	30	R = CH$_3$; R′ = R″ = H	41	R‴ = H	15	R‴ = H	5	R‴ = H	Traces
II R = C$_2$H$_5$; R′ = R″ = R‴ = H	335–345° (16 min.) ↗ 430° (8 min.)	VII R = C$_2$H$_5$; R′ = R″ = H	28	R = C$_2$H$_5$; R′ = R″ = H	26	—	13.5	—	1.5	—	—
	340–365° (16 min.) ↗ 410° (5 min.)	—	27	—	23.5	—	14.5	—	1.5	—	—
III R = C$_6$H$_5$; R′ = R″ = R‴ = H	330–470° (19 min.)	VIII R = C$_6$H$_5$; R′ = R″ = H	13	R = C$_6$H$_5$; R′ = R″ = H	26.5	—	23.5	—	7	—	1.5
IV R = R′ = CH$_3$; R″ = C$_3$H$_7$ (iso); R‴ = H	330–430° (16 min.)	—	12.5	—	27.5	—	25	—	6	—	1.5
	310–360° (22 min.) ↗ 440° (12 min.)	IX R = R′ = CH$_3$; R″ = C$_3$H$_7$ (iso)	7	R = R′ = CH$_3$; R″ = C$_3$H$_7$ (iso)	48.5	—	24	Traces		Nothing	
V R = C$_2$H$_5$; R′ = R″ = H; R‴ = OCH$_3$	310–450° (8 min.)	—	7	—	50	—	25.5	—		—	
	345–425° (16 min.)	VII R = C$_2$H$_5$; R′ = R″ = H	22	R = C$_2$H$_5$; R′ = R″ = H	25.5	R‴ = OCH$_3$	8	R‴ = OCH$_3$	14	R‴ = OCH$_3$	3.5
	330–430° (6 min.)	—	29.5	—	30	—	19	—	7	—	4.5
	350–370° (2 min.) by 5-g. samples	—	22	—	31.5	—	19	—	7.5	—	9

fact is that the diacylbenzene yields can go up to 30%. Therefore, this method appears to be convenient for the synthesis of some compounds which would not be easy to prepare by other ways.

A few properties of the diketones obtained were studied, primarily to confirm their constitution. Among those diketones, VI, VII, and VIII were already described.[7,8] The reduction of VII, according to Huang Minlon's procedure, gives 4-(*n*-propyl)-1-ethylbenzene (XI) which had been previously prepared[9]; its permanganic oxidation gave the terephthalic acid.

In another way, VIII was reduced to 4-benzyl-1-ethylbenzene (XII), already formed by benzylation of ethylbenzene.[10] The same compound VIII was also transformed into 4-benzoyl-1-(chloroacetyl)-benzene (XIII; Chart II) by means of sulfuryl chloride in chloroform. Compound XIII had been previously obtained from 4-benzoylbenzoyl chloride.[8a] The pyridinic derivative of XIII (XIV) was degraded by sodium hydroxide into 4-benzoylbenzoic acid (XV).[11] Finally, by condensation with salicylic aldehyde in an alkaline medium, XIII was changed into 2-[(4′-benzoyl)benzoyl]benzofuran (XVI).

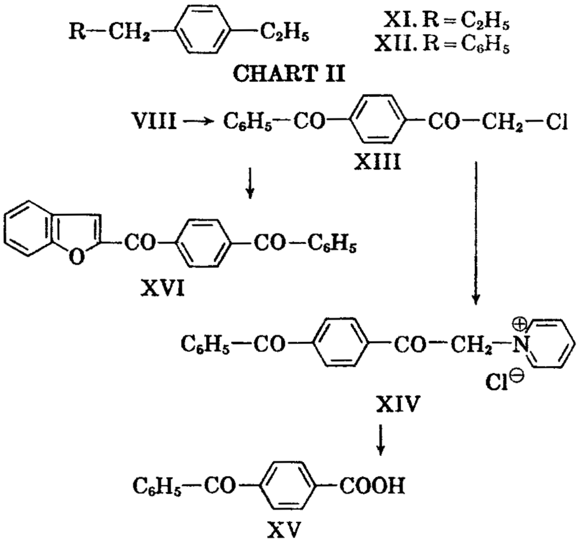

CHART II

EXPERIMENTAL[12]

Aryloxyacetophenones I to V were prepared according to the Davies and Middleton procedure[13] by condensation

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(7)(a) L. Berend and P. Herms, *J. prakt. Chem.* (2), **74,** 134 (1906); (b) H. Ingle, *Ber.,* **27,** 2527 (1894); (c) R. Mittag, German Patent, 767,385 (1952).

(8)(a) R. P. Zelinski, B. W. Turnquest, and E. C. Martin, *J. Am. Chem. Soc.,* **73,** 5521 (1951); (b) B. B. Corson, J. Dorsky, J. E. Nickels, W. M. Kutz, and H. I. Thayer, *J. Org. Chem.,* **19,** 17 (1954).

(9) P. von der Becke, *Ber.,* **23,** 3195 (1890).

(10) J. T. Walker, *Ber.,* **5,** 686 (1872).

(11) T. Zincke, *Ann.,* **161,** 98 (1872).

(12) Melting points are uncorrected; microanalyses were performed by Drs. G. Weiler and F. B. Strauss, Oxford.

(13) W. Davies and S. Middleton, *J. Chem. Soc.,* **159,** 822 (1958).

TABLE II

Compounds	B.P.	M.P.	Empirical Formula	Calcd., %		Found, %	
				C	H	C	H
I	—	76.5	$C_{17}H_{16}O_3$	76.11	5.97	76.26	6.08
II	248–253 (17 mm.)	64	$C_{18}H_{18}O_3$	76.59	6.38	76.30	6.18
III	—	95	$C_{22}H_{18}O_3$	80.00	5.45	79.73	5.43
IV	243–248 (15 mm.)	64	$C_{21}H_{24}O_3$	77.77	7.46	77.44	7.22
V	275–280 (15 mm.)	96	$C_{19}H_{20}O_4$	73.07	6.41	73.30	6.58

with the appropriate 4-acylphenol and α-chloropropiophenone or α-chloro-4-propionylanisole in the presence of potassium carbonate in acetone or dioxane. The yields averaged 80%. Aryloxyacetophenones were purified by distillation at reduced pressure—if necessary and when possible (for instance, III could not be distilled at 15 mm. without decomposition)—followed by recrystallizations in ethanol at low temperature; in this way they formed colorless needles or prisms. They are described in Table II.

Thermal decompositions and treatment of products obtained were performed as follows. The operation was carried out in a usual distilling equipment fitted not only with the column thermometer, which permitted one to follow the pattern of distillation, but also with another thermometer inside the superheated liquid. The temperature was measured every minute.

The volume of the flask used always was twice as large as that of the melted aryloxypropiophenone (50–100 g.).

After melting, the liquid aryloxypropiophenone was heated quickly to 310–320°. Heating was continued over the temperature range in which thermal decomposition occurred continuously, for the duration indicated in Table I (first parentheses). Finally, superheating was prolonged for a few minutes (second parentheses) to the maximum temperature permitting distillation. The residue after superheating was distilled at reduced pressure. The total distillate was dissolved in benzene, the benzene solution being carefully extracted with 2.5*N* sodium hydroxide solution, which yielded the following products:

1. *An alkaline extract,* which was acidified by hydrochloric acid. The precipitate thus obtained was methylated by heating for 4 hr. with methyl iodide in an alcoholic solution of potassium hydroxide. After dilution with water, it was extracted by means of benzene. The benzenic solution was washed with 2.5*N* sodium hydroxide. *Acid F* was obtained by acidification of the basic extract. The residual benzene solution contained the methyl ether of *phenol C.*

2. *A benzene solution,* which was washed with water and dried on sodium sulfate. After evaporation of the solvent, it was distilled and rectified to isolation of definite fractions. In this way the following products were successively separated:

(a) *Aldehyde E,* which was characterized by its phenylhydrazone.

(b) *Propiophenone D,* which was identified by its physical constants and its semicarbazone.

(c) *Diketone,* which was purified by recrystallizations in ethanol at low temperature.

(d) Various cyclodehydration or decomposition products, which could not be generally identified, excepted for X; colorless needles, F = 134° giving a strong yellow color with sulfuric acid.

Anal. Calcd. for $C_{21}H_{22}O_2$: C, 82.35; H, 7.18. Found: C, 82.18; H, 7.46.

Diketones characteristics and derivatives (VI). Boiling point 158–160° (15 mm.); recrystallized from a benzene and petroleum ether mixture as colorless needles, m.p. 114° (perfect agreement with lit.[7a,b]).

Dioxime, colorless microcrystals (from ethanol) m.p. 253–254° (by projection; Berend and Herms[7a] found a m.p. of 240–245°).

Anal. Calcd. for $C_{10}H_{12}O_2N_2$: C, 62.49; H, 6.24; N, 14.58. Found: C, 62.51; H, 6.30; N, 14.09.

VII, b.p. 167–168° (13 mm.); recrystallized from ethanol as colorless leaflets, m.p. 71–72° (R. Mittag[7c] gives F = 74–75°).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 75.00; H, 6.81. Found: C, 75.18; H, 6.85.

Dioxime of VII, by recrystallization from ethanol gave colorless needles, *F,* m.p. 193–194° (by projection; by progressional heating, decomposition above 180°).

Anal. Calcd. for $C_{11}H_{14}O_2N_2$: C, 64.07; H, 6.79; N, 13.59. Found: C, 63.81; H, 6.69; N, 13.75.

4-(n-Propyl)-1-ethylbenzene (XI). A mixture of 15 g. of VII and 9.5 g. of hydrazine hydrate in 75 ml. of diethylene glycol was heated for 15 min. After cooling, 10.5 g. of potassium hydroxide was added. The mixture was refluxed for 1 hr. and treated as usual. XI was a colorless liquid, b.p. 200–202° (770 mm.) (von der Becke[8] indicates a b.p. of 202–205° (765 mm.)) n_D^{22} 1.4940. Yield: 6 g. (47.5%).

Anal. Calcd. for $C_{11}H_{16}$:C, 89.18; H, 10.81. Found: C, 89.08; H, 10.75.

Oxidation of VII. Eight grams of potassium permanganate was added in small portions with occasional stirring to 2 g. of VII in a solution of 1 g. of sodium carbonate in 150 ml. of water. The mixture was heated for 1 hr., then cooled, acidified with dilute sulfuric acid, and heated again for 30 min. It was decolorized by sodium bisulfite, filtered and recrystallized in ethanol; 2 g. of colorless microcrystals was obtained, not melting under 300° but subliming as does terephthalic acid.

Anal. Calcd. for $C_8H_6O_4$: C, 57.83; H, 3.61. Found: C, 57.57; H, 3.79.

VIII, b.p. 224–226° (17 mm.). Colorless needles (from ethanol), m.p. 79° (lit., 83–84°[8a] and 85.5–86.5°[8b]).

Anal. Calcd. for $C_{15}H_{12}O_2$: C, 79.66; H, 5.26. Found: C, 80.00; H, 5.35.

Dioxime of VIII, colorless bright leaflets, m.p. 194.5°.

Anal. Calcd. for $C_{15}H_{14}O_2N_2$: C, 70.86; H, 5.51; N, 11.02. Found: C, 70.70; H, 5.33; N, 11.15.

4-Benzyl-1-ethylbenzene (XII). According to the same technique used to prepare XI, 15 g. of VIII was treated with 10 g. of hydrazine hydrate and 11 g. potassium hydroxide in 75 ml. of diethylene glycol, yielding 10 g. (77%) of XII, light yellow liquid, b.p., 157° (14 mm.); n_D^{22} 1.5619.

Anal. Calcd. for $C_{15}H_{16}$: C, 91.84; H, 8.16. Found: C, 91.40; H, 8.48.

4-Benzoyl-1-(chloroacetyl)benzene (XIII). A mixture of 22 g. of VIII and 15 g. of sulfuryl chloride in 250 ml. of chloroform was heated for 2 hr. After evaporation of solvent, a crystallized substance was obtained (22 g., 91.5%) which yielded, in ethanol, some colorless leaflets, m.p. 80° (lit.: 86.5–88°[8a]).

Anal. Calcd. for $C_{15}H_{11}O_2Cl$: C, 69.63; H, 4.25; Cl, 13.73. Found: C, 69.21; H, 4.19; Cl, 13.92.

4-Benzoyl-1-(chloropyridinium acetyl)benzene (XIV). Ten grams of XIII and 10 g. of pyridine were heated for a few minutes. The reaction material was triturated in acetone and recrystallized from an acetone (80%) and ethanol (20%) mixture giving little yellow needles, m.p. 225° (by projection; by progressional heating, decomposition began at 160–165°), yield, 7.5 g. (58%).

Anal. Calcd. for $C_{20}H_{16}O_2NCl$: C, 71.11; H, 4.74; N, 4.14; Cl, 10.51. Found: C, 70.50; H, 4.97; N, 3.81; Cl, 10.35.

4-Benzoylbenzoic acid (XV). Five grams of XIII was heated for 1 hr. in a solution of 1.8 g. of sodium hydroxide in 40 ml. of water. The acidification with hydrochloric acid gave 3 g. (91%) of XV which formed in ethanol gray leaflets, m.p. 191.5–192°. (Zincke[9] indicates the same melting point.)

Anal. Calcd. for $C_{14}H_{10}O_3$: C, 74.33; H, 4.42. Found: C, 73.96; H, 4.27.

2-[(4'-Benzoyl)benzoyl)benzofuran (XVI). A mixture of 4 g. of XIII, 2 g. of salicylaldehyde, and 2.2 g. of potassium carbonate in 50 ml. of acetone was refluxed with stirring for 10 hr. The mixture was poured into 250 ml. of water. The crystallized material was filtered off and recrystallized in an ethanol and dioxane (10%) mixture. Thus, 4.2 g. (84%) of XVI was obtained, yielding in pure dioxane creamy microcrystals, m.p. 162°. In sulfuric acid, this compound formed an orange yellow halochromic coloration.

Anal. Calcd. for $C_{22}H_{14}O_3$: C, 80.98; H, 4.17. Found: C, 80.98; H, 4.27.

IX formed bright colorless needles (from petroleum ether at low temperature) m.p. 58°.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.06; H, 8.25. Found: C, 76.84; H, 8.00.

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PARIS, FRANCE

[CONTRIBUTION FROM THE AGRICULTURAL RESEARCH LABORATORY, ORGANIC CHEMICALS DIVISION, MONSANTO CHEMICAL CO.]

Pyranylation of Amides

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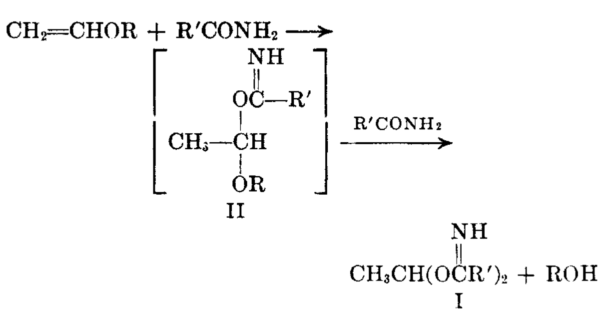
It has been found that 2,3-dihydropyran, in the presence of catalytic amounts of hydrogen chloride, forms 1:1 adducts with amides. The products of this reaction have been formulated as *N*-(2-tetrahydropyranyl)amides. Amides that undergo pyranylation include aromatic and aliphatic amides, ureas, sulfonamides, and imides.

Glacet[1,2] found that strongly basic amines (amylamine) do not add to 2,3-dihydropyran whereas aromatic amines (aniline, *N*-methylaniline) do.[3] After the completion of our work Robins and Lewis[4] reported the addition of purines to 2,3-dihydropyran and 2,3-dihydrofuran in the presence of an acid catalyst. This paper deals with the addition of amides, which are only very slightly basic, to 2,3-dihydropyran, a cyclic vinyl ether.

Addition of amides to vinyl ethers has been reported by Voronkov.[5] The products were reported to be ethylidene-*O*-acylamides (I). The mono-*O*-acylamide derivatives (II) were supposedly intermediates in this reaction.



$$CH_2{=}CHOR + R'CONH_2 \longrightarrow \left[\begin{array}{c} NH \\ \| \\ OC{-}R' \\ | \\ CH_3{-}CH \\ | \\ OR \end{array}\right] \xrightarrow{R'CONH_2} CH_3CH(O\overset{NH}{\overset{\|}{C}}R')_2 + ROH$$

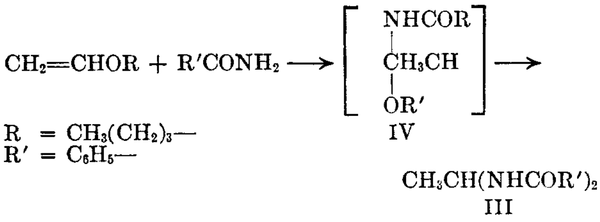
II

I

$R = CH_3{-}, CH_3CH_2{-}, CH_3(CH_2)_3{-}$

$R' = CH_3{-}, C_6H_5{-}, C_6H_5CH_2{-}$

Furukawa and co-workers[6] reported the addition of benzamide to phenyl vinyl ether and *n*-butyl vinyl ether. Ethylidenedibenzamide (III), the *N*-alkylated product, was obtained from these reactions. α-Butoxyethylbenzamide (IV) was suggested as the intermediate.



$$CH_2{=}CHOR + R'CONH_2 \longrightarrow \left[\begin{array}{c} NHCOR \\ | \\ CH_3CH \\ | \\ OR' \end{array}\right] \longrightarrow CH_3CH(NHCOR')_2$$

$R = CH_3(CH_2)_3{-}$

$R' = C_6H_5{-}$

IV

III

p-Toluenesulfonamide also gave the corresponding ethylidene di-*p*-toluenesulfonamide presumably *via* the α-amido ether intermediate. However, *N*-methyl-*p*-toluenesulfonamide reacted with *n*-butyl vinyl ether to give *N*-methyl-*N*-α-butoxyethyl-*p*-toluenesulfonamide. In this case the second molecule of amide did not replace the alkoxy group.

The reactions of vinyl ethers with acidic imino compounds such as dicarboxylic acid imides have been investigated.[6] These compounds added to vinyl ethers to give α-imido ethers (V). The products were shown to be *N*-alkylated by removal of alcohol from the α-imido ether to form known *N*-vinylimides (VI).

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(1) C. Glacet, *Bull. soc. chim.*, 575 (1954).

(2) C. Glacet and G. Bonnemaison, *Compt. rend.*, **247**, 305 (1958).

(3) The reaction of 2,3-dihydropyran with alcohols, acids, and mercaptans is well known; W. E. Parham and D. M. Delaitsch, *J. Am. Chem. Soc.*, **70**, 4187 (1948); W. E. Parham and E. L. Anderson, *J. Am. Chem. Soc.*, **76**, 4962 (1954). H. D. Finch, E. A. Peterson, and S. A. Ballard, *J. Am. Chem. Soc.*, **74**, 2018 (1952).

(4) R. K. Robins and L. R. Lewis, 138th ACS National Meeting, Sept. 11–16, 1960, New York, N. Y.

(5) M. G. Voronkov, *J. Gen. Chem.* (*U.S.S.R.*), **21**, 1494 (1951).

(6) J. Furukawa, A. Onishi, and T. Tsuruta, *J. Org. Chem.*, **23**, 672 (1958).