[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF NEW HAMPSHIRE AND OBERLIN COLLEGE]

Acid Catalyzed Condensations. I. 1,3,5-Triarylbenzenes[1]

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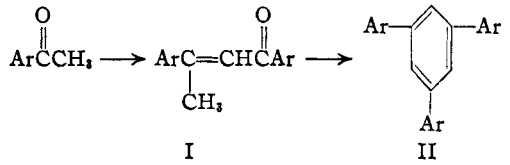
The preparation of a series of 1,3,5-triarylbenzenes from substituted acetophenones is described. The effect of solvent and concentration on the yield of product and the course of reaction is noted.

The condensation of acetophenone to 1,3,5-triphenylbenzene has been studied extensively; however, the preparation of only isolated examples of 1,3,5-triarylbenzenes (II) from substituted acetophenones by this type of reaction has been mentioned.[2-7] The reported methods of inducing condensation involve primarily one of three catalysts: sulfuric acid and sodium pyrosulfate mixture,[2] hydrogen chloride or hydrochloric acid,[3] or aniline and aniline hydrochloride.[4] In isolated cases other catalysts were used, such as beryllium chloride,[5] sodium ethoxide,[6] and sulfoacetic acid.[7] It will be noted that the most satisfactory results were obtained using an acidic catalyst.

Only one instance is reported in which an attempt was made to prepare a series of substituted acetophenones.[1a] This was inadequate since only one alkyl acetophenone, *p*-methylacetophenone, could be caused to condense and condensation was attempted with only one halo-acetophenone, *p*-chloroacetophenone. Since the 1,3,5-triarylbenzenes (II) would be a rather interesting series of compounds and their preparation could give some indication of the effect of substituents on acid catalyzed condensations, a study of the reactions of substituted acetophenones in alcoholic hydrogen chloride was initiated. A consideration of the yields, length of reaction time and purity of products for the reactions reported in the literature led to this choice of solvent and catalyst.

Both methanol and ethanol were considered as solvents for the reactions. Ethanol consistently gave higher yields than methanol, and both of these solvents were more efficient than methanol and dioxane mixtures (see Table I). As would be expected, the greater the concentration with respect to the substituted acetophenone the more rapid the reaction. The concentration of the reaction mixture used was limited, however, by the fact that the dypnones (I) formed from the nitro- and *p*-haloacetophenones were insoluble in the alcohols and, on precipitating from the reaction mixture, stopped the condensation before the 1,3,5-triarylbenzenes (II) were formed (see Table I). Conditions which were successful for the synthesis of 1,3,5-tri-nitrophenylbenzenes could not be found due to the great insolubility of the intermediate dypnones. The *p*-haloacetophenones were all successfully converted to the corresponding II by using very dilute reaction mixtures.



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Although better yields of many of the 1,3,5-triarylbenzenes (II) could be obtained by other conditions (see Table I), the methanol–dioxane reaction medium described in Procedure A was found to be the most convenient for comparative purposes. From the variations in yields given in Table I, Procedure A, it can be seen that the mechanism of the reaction is complex and a definite statement as to the effect of the substituents would not be in order. In general, however, it is evident that substituents which increase the negativity of the acetyl group by resonance or inductive effects retard the formation of II. Thus poor yields of II were obtained from *p*-methyl, *p*-ethyl and *p*-fluoroacetophenones.

Substituted acetophenones having a strongly electron releasing group were not studied extensively, for these basic substituents undoubtedly formed salts in the reaction media, thus complicating the reaction. *p*-Aminoacetophenone precipitated immediately as the hydrochloride salt and thus underwent no further reaction. *p*-Dimethylaminoacetophenone gave no precipitate after a long period of standing, and only a highly colored solid, probably largely a pyrylium salt, could be isolated from the reaction mixture. The product recovered from the condensation reaction of *p*-methoxyacetophenone contained some 2,4,6-tri-*p*-methoxyphenylpyrylium chloride, as well as the corresponding II.

The literature is somewhat confusing with respect to the melting point of 1,3,5-tri-*p*-methoxyphenylbenzene, for Schneider[7a] reported a value of 142° but Hariharan,[7b] who repeated their work, found the melting point to be 157 or 169°. Adkins[8] more recently agreed with the value of

(1) This work was abstracted from the B.S. theses, Oberlin College, of Nancy M. Nichols and Wallace Cleland and the M.S. thesis, University of New Hampshire, of Elmer J. DeWitt.

(2) (a) K. Bernhauer, *et al.*, *J. prakt. Chem.*, **145**, 301 (1936); (b) A. F. Odell and C. W. Hines, THIS JOURNAL, **35**, 81 (1913); (c) R. J. W. Le Feave, *J. Chem. Soc.*, 1467 (1938); (d) J. R. Sampey, THIS JOURNAL, **62**, 1953 (1940); (e) T. Davis and C. Armstrong, *ibid.*, **57**, 1583 (1935).

(3) (a) C. Engler, *et al.*, *Ber.*, **7**, 1123 (1874); **26**, 1444 (1893); (b) A. Claus, *J. prakt. Chem.*, [2] **41**, 405 (1890); (c) B. N. Dolgov and Y. N. Yol'nov, *J. Gen. Chem. (USSR)*, **1**, 340 (1931); (*C. A.*, **26**, 2186 (1932)); (d) E. P. Kohler, *Am. Chem. J.*, **31**, 642 (1904); (e) Z. Skrowaczewska and E. Sucharda, *Roczniki Chem.*, **16**, 151 (1936), (*C. A.*, **31**, 2196 (1937)).

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(5) H. Bredereck, *et al.*, *Ber.*, **72B**, 1414 (1939).

(6) C. Gastaldi and F. Cerchi, *Gazz. chim. ital.*, **45**, II, 251 (1915), (*C. A.*, **10**, 1637 (1916)).

(7) (a) W. Schneider and F. Seeback, *Ber.*, **54B**, 2298 (1921); **69B**, 2543 (1936); (b) K. V. Hariharan and J. J. Sudborough, *J. Indian Inst. Sci.*, **8A**, 189 (1925), (*C. A.*, **19**, 3263 (1925)).

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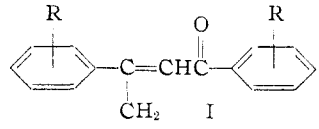
TABLE I

THE REACTION OF ACETOPHENONES IN METHANOLIC AND ETHANOLIC HYDROGEN CHLORIDE



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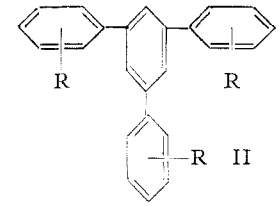

II

Acetophenone	Procedure	Product	Yield, %	M.p.,[a] °C.	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
Unsubstituted	A	II, R = H	26	172[b]					
	B	II, R = H	49						
p-Methyl-	A	II, R = *p*-CH_3	5	178[c]					
	B	II, R = *p*-CH_3	33						
	D	II, R = *p*-CH_3	12						
p-Ethyl-	A	II, R = *p*-C_2H_5	8	114	$C_{30}H_{30}$	92.26	7.74	91.77	7.80
	B	II, R = *p*-C_2H_5	20						
	D	II, R = *p*-C_2H_5	23						
p-Isopropyl-	A	II, R = *p*-$CH(CH_3)_2$	19	166	$C_{33}H_{36}$	91.16	8.39	91.19	8.50
	B	II, R = *p*-$CH(CH_3)_2$	43						
p-*t*-Butyl-	A	II, R = *p*-$C(CH_3)_3$	21	296	$C_{36}H_{42}$	91.08	8.92	90.68	9.01
	B	II, R = *p*-$C(CH_3)_3$	74						
p-Fluoro-	A	II, R = *p*-F	9	238	$C_{24}H_{15}F_3$	79.99	4.20	79.52	4.27
	C	II, R = *p*-F	7						
	D	II, R = *p*-F	19						
p-Chloro-	A	II, R = *p*-Cl	14	246[d]					
	B	II, R = *p*-Cl	49						
	C	II, R = *p*-Cl	10						
	D	II, R = *p*-Cl	18						
p-Bromo-	A	II, R = *p*-Br	15	262	$C_{24}H_{15}Br_3$	53.06	2.78	53.32	3.19
	B	II, R = *p*-Br	52						
	C	II, R = *p*-Br	11						
	D	II, R = *p*-Br	5						
		I, R = 4-Br	46	104	$C_{16}H_{12}Br_2O$	50.56	3.18	50.27	3.46
p-Iodo-	A	I, R = 4-I	45	136	$C_{16}H_{12}I_2O$	40.53	2.55	40.72	2.80
	B	I, R = 4-I	85						
	C	II, R = *p*-I	17	265	$C_{24}H_{15}I_3$	42.13	2.21	42.09	2.02
p-Nitro-	A	I, R = 4-NO_2	73	153	$C_{16}H_{12}N_2O_5$	61.54	3.88	61.44	4.17
p-Methoxy-	B	II, R = *p*-OCH_3	54	143[e]					
m-Fluoro[f]	A	II, R = *m*-F	8	173	$C_{24}H_{15}F_3$	79.99	4.20	80.17	4.44
m-Chloro[g]	A	II, R = *m*-Cl	9	171	$C_{24}H_{15}Cl_3$	70.35	3.69	70.28	4.00
m-Iodo-	A	II, R = *m*-I	14	164	$C_{24}H_{15}I_3$	42.13	2.21	42.34	2.48
m-Nitro-	A	I, R = 3-NO_2	57	120	$C_{16}H_{12}N_2O_5$	61.54	3.88	61.42	4.10
		II, R = *m*-NO_2	Trace	310[h]	$C_{24}H_{15}N_3O_6$	65.32	3.43	64.81	3.63
o-Nitro-	A	No reaction							

[a] All solids were recrystallized from dioxane diluted with ethanol except where otherwise noted. The range of all melting points was less than one degree. [b] Lit.[2b] m.p. 172°. [c] Lit.[2a] m.p. 170°. [d] Lit.[2a] m.p. 238°. [e] Recrystallized from acetic acid; lit.[7a] m.p. 142°. [f] 2,4-Dinitrophenylhydrazone, m.p. 238° after recrystallization from ethanol. *Anal.* Calcd. for $C_{14}H_{11}FN_4O_4$: C, 52.83; H, 3.48. Found: C, 52.56; H, 3.65. [g] 2,4-Dinitrophenylhydrazone, m.p. 208° after recrystallization from ethanol. *Anal.* Calcd. for $C_{14}H_{11}ClN_4O_4$: C, 50.23; H, 3.31. Found: C, 49.92; H, 3.45. [h] Lit.[2a] m.p. 299°.

Schneider. This value of 142° is consistent with the melting point of the product of the condensation of *p*-methoxyacetophenone using procedure B.

A comparison of the melting points of the 1,3,5-triarylbenzenes (II) (see Table I) presents a rather interesting illustration of the effect of symmetry of the molecule on this physical property. The 1,3,5-tris-*p*-halophenylbenzenes show an increase in melting point in changing the group from fluoro- to chloro- to bromo- to iodo-. On the other hand, however, the less symmetrical 1,3,5-tris-*m*-halophenylbenzenes have decreasing values for melting points in the above order, fluoro- greater than chloro- greater than iodo-; for, as the weight and bulk of the halogen substituent increases, the overall symmetry of the molecule decreases. The 1,3,5-tris-*p*-alkyl-phenylbenzenes also have an unusual order of melting point. 1,3,5-Tris-*p*-methylphenylbenzene, which is symmetrical, has a higher value for the melting point than either of the less symmetrical compounds, 1,3,5-tris-*p*-ethyl- or 1,3,5-tris-*p*-isopropylphenylbenzene. The melting point of the highly symmetrical 1,3,5-tris-*p*-*t*-butylphenylbenzene is more than 100° higher than any of the other 1,3,5-tris-*p*-alkylphenylbenzenes.

A further study of the properties of the 1,3,5-triarylbenzenes (II) is in progress.

Experimental

The Condensation of Substituted Acetophenones in Alcoholic Hydrogen Chloride. Procedure A.—A solution of 3.0 g. of the acetophenone in 15 ml. of a 50% methanol–dioxane mixture was placed in a 50-ml. erlenmeyer flask and was saturated, with cooling, with dry hydrogen chloride. After constant weight was reached, a gain in weight of about 10 g., the flask was closed except for a small capillary outlet which allowed the escape of hydrogen chloride expelled from the solution on warming to room temperature.

After 10 days, any solid which had precipitated was removed by filtration, and the solution again saturated with hydrogen chloride. After standing a total of 18 days, the solution was filtered and the residue combined with the solid from the original filtration. The filtrate was poured into about 200 ml. of water, and the mixture was extracted with petroleum ether. Any solid remaining undissolved was filtered off and added to that above. From the petroleum ether solution could be recovered unreacted acetophenone, small amounts of dypnone, and polymers.

The yields listed in Table I, with the exception of 1,3,5-tris-*m*-chlorophenylbenzene, were based on the weight of unrecrystallized solid recovered from the reaction. These yields do not include consideration of recovered starting material.

Procedure B.—To 50 ml. of absolute ethanol saturated with hydrogen chloride was added 10 g. of the substituted acetophenone. After standing for 30 days, the reaction mixtures were filtered, and the solid residue was washed with cold alcohol giving pure 1,3,5-triarylbenzene or dypnone. A small amount of product was obtained by pouring the above filtrate into water and filtering the mixture. The crude product from this operation was oily and required washing with alcohol before it could be considered as yield.

p-Methoxyacetophenone was allowed to stand for four months before being treated as above. (The yield at the end of 34 days was 2%.) The solid residue was extracted with ether and on evaporation of the ether solution 1,3,5-tri-*p*-methoxyphenylbenzene was obtained. The small amount of ether insoluble residue was identified as 2,4,6-tri-*p*-methoxyphenylpyrylium chloride, m.p. 197–204° (dec.), for it could be converted to the known 2,4,6-tri-*p*-methoxyphenylpyrylium picrate, m.p. 276–283° (dec.) (lit.[2e] m.p. 283–284°).

Procedure C.—A solution of 1 g. of the acetophenone in 15 ml. of 60% absolute methanol–40% dioxane mixture was saturated with hydrogen chloride and treated as in Procedure B.

Procedure D.—A solution of 3 g. of the acetophenone in 7 ml. of absolute methanol was treated as in Procedure A.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF FORDHAM UNIVERSITY]

The Pinacol Rearrangement in the Heterocyclic Series. II. Thiophene and Furan Analogs of Benzopinacol

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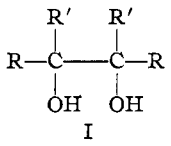
Symmetrical analogs of benzopinacol containing two phenyl groups with either two 2-thienyl groups, two 2,5-dimethyl-3-thienyl groups or two 2-furyl groups have been synthesized and rearranged. The structures of the products of rearrangement have been determined by characterization of their degradation products.

In a previous report,[1] the authors have described their extension to the pyridine series of the studies of earlier workers on the migratory aptitudes of aromatic groups. These migratory aptitudes were determined by rearranging pinacols of the type shown in I, where R and R′ are aryl, and determining the structures of the resulting pinacolones by degradation. It was found in this way that the



I

migratory aptitudes of the 2-pyridyl and 3-pyridyl groups were very small compared to that of the phenyl group. An explanation of this fact was offered.

Turning next to the five-membered heterocycles, we have examined the 2-thienyl, the 2,5-dimethyl-3-thienyl and the 2-furyl groups in a similar manner.

The magnesium–magnesium iodide reducing reagent of Gomberg and Bachmann,[2] which is ordinarily very effective in converting diaryl ketones into the corresponding pinacols, furnished only an insoluble complex when applied to phenyl 2-thienyl ketone. (This had also been found to be the case with the ketones of the pyridine series.) Hydrolysis of this complex resulted in recovery of the original ketone. Treatment of 2,2′-thenil with phenylmagnesium bromide produced a tarry mass. The reaction of 2-thienylmagnesium iodide with benzil, on the other hand, did give rise to the desired pinacol although in very small yield. The same pinacol was eventually found to be produced in excellent yield by reducing phenyl 2-thienyl ketone with zinc and acetic acid.

When this pinacol was rearranged and the resulting pinacolone cleaved, there were only two products of degradation, *i.e.*, benzoic acid and phenyldi-(2-thienyl)-methane. The latter substance was identified by comparison with an authentic sample. Since no 2-thenoic acid was produced, the 2-thienyl group had migrated to the exclusion of the migration of the phenyl group.

In order to determine whether the pronounced tendency for the thienyl group to migrate would be overcome by the influence of substituents in the ortho position, which are notoriously detrimental to migration in the pinacol rearrangement, a symmetrical pinacol containing two phenyl groups and two 2,5-dimethyl-3-thienyl groups was synthesized. This was accomplished by the action of 2,5-dimethyl-3-thienylmagnesium iodide on benzil. The results of the rearrangement of this pinacol exactly paralleled those obtained with the 2-thienyl analog. Thus, the 2,5-dimethyl-3-thienyl group also migrates to the exclusion of migration of the phenyl group. The di-(2,5-dimethyl-3-thienyl)-phenylmethane was characterized by independent synthesis.

(1) M. R. Kegelman and E. V. Brown, THIS JOURNAL, **75**, 4649 (1953).

(2) M. Gomberg and W. E. Bachmann, *ibid.*, **49**, 236 (1927).