[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI]

Preparation of 1-Indanones from α-Bromoaralkyl Ketones[1]

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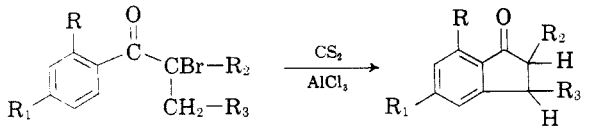
α-Bromoaralkyl ketones are shown to be useful as starting materials for the synthesis of 1-indanones. Ketones in which a bromine atom is attached to a tertiary carbon atom require treatment with aluminum chloride in refluxing carbon disulfide, whereas ketones with the bromine atom attached to a secondary carbon require the more severe reaction conditions of treatment with aluminum chloride as a dry mixture at a temperature of 150°. The effects of substituents on the aryl portion of the ketone on the ease of ring closure are analogous to their effects in Friedel and Crafts alkylation reactions. The effects of substituents on the alkyl portion of the ketone are summarized in Table I.

1-Indanones have commonly been prepared from β-aryl acids,[2] β-aryl acyl halides,[3] α,β-unsaturated ketones,[4] and from β-haloaralkyl ketones[4] by ring closure effected with acids such as sulfuric acid or aluminum chloride. The only reference to the cyclization of an α-bromoaralkyl ketone by this method is in the work of Kishner[5] who found that α-bromoisobutyrophenone yielded 2-methyl-1-indanone when cyclized in the presence of aluminum chloride. Since α-bromoaralkyl ketones are readily available, the general usefulness of α-bromo ketones in synthesizing 1-indanones has been investigated.

α-Bromoaralkyl ketones, I-A through I-E, were treated with aluminum chloride in refluxing carbon disulfide.



A R = R_1 = R_2 = CH_3; R_3 = H
B R = R_1 = R_3 = CH_3; R_2 = C_2H_5
C R = R_1 = H; R_2 + R_3 = —$CH_2CH_2CH_2$—
D R = R_1 = CH_3; R_2 = R_3 = H
E R = R_1 = R_3 = CH_3; R_2 = H

Compounds I-A through I-C were found to give, respectively, the substituted 1-indanones, II-A through II-C. Compounds I-D and I-E were recovered unchanged. From a consideration of these results it can be seen that α-bromo ketones with a bromine atom on a tertiary carbon atom undergo ring closure, whereas those in which the bromine is on a secondary carbon do not. The difference in reactivities of these compounds is attributed to the relative ease of ionization of the bromine atom. A bromine atom attached to a tertiary carbon will ionize more readily than one attached to a secondary carbon. To cyclize the α-*sec*-bromo compounds to 1-indanones, conditions were necessary which would increase the ease of ionization of the bromine atom attached to a secondary carbon. Since a powerful catalyst was already being used, higher reaction temperatures seemed necessary. α-Bromopropiophenone, when treated with aluminum chloride in refluxing ligroin at 125°, surprisingly gave propiophenone in 60% yield. The same treatment of α-bromobutyrophenone gave a 64% yield of butyrophenone. These reactions are essentially other examples of the Bartlett-Condon-Schneider reaction.[6] The over-all result of these reactions was the replacement of a bromine atom by a hydrogen rather than the desired cyclization. To avoid any further reactions with solvents α-bromopropiophenone was treated with aluminum chloride as a dry mixture at a temperature of 140 to 160°. 1-Indanone was formed in 60% yield. To be assured that the same reaction occurs with other α-*sec*-bromoketones, compound I-E was reacted in the same manner. 3,5,7-Trimethyl-1-indanone (II-E) was obtained in 64% yield.

Effects of substituents on ring closure. The cyclization reaction has been considered to proceed through an α,β-unsaturated ketone intermediate.[5] Thus the effects of substituents on both the aryl and alkyl portion of the α-bromoaralkyl ketone would be expected to be analogous to those of the corresponding α,β-unsaturated ketone.

The effect of nuclear substituents would be expected to be similar to their effects in a Friedel and Crafts alkylation reaction. Unfortunately, exceptions to this hypothesis are found in the literature. von Auwers[7] related the ease of ring closure in methyl-substituted benzalacetophenones to the position of the methyl group, relative to the site of ring closure, to be:

ortho-methyl > *para*-methyl > no methyl > *meta*-methyl

This finding surprisingly indicated that a *meta*-

(1) This paper was abstracted from the Ph.D. thesis of Robert W. Layer, University of Cincinnati, 1955. (a) Ernst D. Twitchell fellow, 1954–1955.

(2) J. von Braun and K. Heider, *Ber.*, **49**, 1268, 1274 (1916).

(3) J. Kenner and E. Witham, *J. Chem. Soc.*, **119**, 1452 (1921).

(4) F. Mayer and P. Muller, *Ber.*, **60**, 2278 (1927).

(5) N. Kishner, *J. Russ. Phys.-Chem. Soc.*, **46**, 1411 (1914).

(6) P. D. Bartlett, F. E. Condon, and A. Schneider, *J. Am. Chem. Soc.*, **66**, 1531 (1944).

(7) K. von Auwers and E. Risse, *Ann.*, **502**, 282 (1933).

methyl group would hinder ring closure. To clarify the effects of nuclear substituents on the ease of ring closure the following compounds were prepared and treated with aluminum chloride in refluxing carbon disulfide.

I-A	α-bromoisobutyrophenone
III	α-bromo-4-methylisobutyrophenone
IV	α-bromo-2,4-dimethylisobutyrophenone
V	α-bromo-2,5-dimethylisobutyrophenone
VI	α-bromo-4-chloroisobutyrophenone
VII	α-bromo-2-chloro-4-methylisobutyrophenone
VIII	α-bromo-3-nitroisobutyrophenone

Compounds, I-A through VII, were found to yield the corresponding 1-indanones. Compound VIII, when treated in this manner, was found to give a large amount of polymer along with some unreacted α-bromo ketone. From these results it can be seen that von Auwers' findings are misleading. α,β-Unsaturated ketones and α-bromo ketones will ring close or can be made to ring close no matter what the position of the nuclear methyl group. Also, *ortho* and *para* directing groups, even deactivating ones, will allow ring closures. The effect of every group, or combination of groups, could not be studied, but from the limited data it appears that the effect of a nuclear substituent on the ease of ring closure is similar to its effect in a typical Friedel and Crafts alkylation.

Work of both Mayer[4] and von Auwers[7] indicated that the effects of alkyl side chain substituents on the ease of ring closure were of as much importance as the effects of nuclear substituents. For example, Mayer found that, when he refluxed 2-methyl-4-chloroacrylophenone with aluminum chloride in carbon disulfide, he obtained 5-chloro-7-methyl-1-indanone. Similar treatment of 2-methyl-4-chloro-α-butenophenone gave no reaction. Similarly, von Auwers found that treatment of 2,4-dimethyl-α-butenophenone in the same manner gave only a small amount of the 1-indanone. These results indicated that a β-methyl group on the side chain inhibited ring closure. To verify this hypothesis, 2,4-dimethyl-α-butenophenone was prepared and treated with aluminum chloride in refluxing carbon disulfide. It was found that only a small amount of the ketone was converted to the 1-indanone. This was in full agreement with Mayer's and von Auwers' findings, and it was concluded that a β-methyl group on the side chain does inhibit ring closure.

Since α-bromo-2,4-dimethylbutyrophenone (I-E) was found to cyclize when heated as a dry mixture with aluminum chloride at 150°, it appeared that the retarding effect of the β-alkyl group was overcome by such treatment. To be certain that the ring closure was not due to the fact that an α-bromo ketone was used as a starting material rather than the α,β-unsaturated ketone, 2,4-dimethyl-α-butenophenone was treated in the same manner. The 1-indanone formed in 64% yield and no unsaturation could be detected. Compounds with β-alkyl substituents which remain unreacted on treatment with aluminum chloride in refluxing carbon disulfide can be cyclized by carrying out the reaction at 150° with no solvent present.

At the outset it had been found that α-bromo-α-ethyl-2,4-dimethylbutyrophenone and 1-bromocyclohexyl phenyl ketone both gave the corresponding 1-indanone without the isolation of any unsaturated compound. Interestingly, both of these compounds have β-alkyl groups, yet they easily cyclized. From this it appeared that compounds with an α-alkyl group overcame the deactivating effect of the β-alkyl group. Again to be certain that ring closure was not due to the fact that an α-bromo ketone was used as a starting material rather than the α,β-unsaturated intermediate, *m*-xylene was reacted with α-ethyl-α-butenyl chloride. The product was the same 1-indanone (II-B) as that formed from the α-bromo ketone (I-B). It was concluded that the ring closure is facilitated by the presence of the α-alkyl group. Treatment of α-bromo-α-phenyl-2,4-dimethylbutyrophenone under either conditions (with carbon disulfide or as a dry mixture) yielded tarry products from which we could isolate no 1-indanone. α-Phenyl compounds apparently polymerize too easily to undergo ring closure under either set of conditions.

From these observations of the effects of side chain substituents we can draw some useful conclusions which can serve as a guide in predicting their effect on the ease of ring closure. These effects are summarized in Table I.

TABLE I

EFFECT OF GROUPS ON EASE OF RING CLOSURE TO 1-INDANONES

Group	Ring Closure at 45°		Ring Closure at 100°	
	Yes	No	Yes	No
β-Alkyl		+	+	
α-Alkyl	+		+	
α- and β-Alkyl	+		+	
α-Phenyl		+		+
β-Phenyl[7]		+	+	

EXPERIMENTAL[8]

Preparation of aralkyl ketones. To a mixture of 0.2 mole of the aromatic compound and 33.0 g. (0.25 mole) of finely powdered aluminum chloride in 200 ml. of carbon disulfide was slowly added with stirring 0.2 mole of the acyl halide. The reaction mixture was refluxed at 45° for one hour and then was allowed to cool. The contents of the flask then were hydrolyzed with dilute hydrochloric acid and extracted with ether. The ether extract was dried over sodium sulfate and the ether was removed by distillation. The residue then was distilled through a short Vigreux column. New ketones prepared are listed in Table II.

(8) Temperatures are uncorrected.

TABLE II

ARALKYL KETONES

Compd. No.	Name	Yield, %	B.p., °C. /1 mm.	n_D^{25}	Empirical Formula	Carbon Calc'd	Carbon Found	Hydrogen Calc'd	Hydrogen Found	Halogen Calc'd	Halogen Found
1	α-Ethyl-2,4-dimethylbutyrophenone	80	112–114	1.5100	$C_{14}H_{20}O$	82.12	82.30	9.89	9.72		
2	α-Phenyl-2,4-dimethylbutyrophenone	78	164–166	1.5635	$C_{18}H_{20}O$	86.40	85.33	8.06	8.02		
3	4-Chloroisobutyrophenone[a]	71	100–104	1.539	$C_{10}H_{11}ClO$					19.40	18.99
4	2-Chloro-4-methylisobutyrophenone[b]	76	107–108	1.5235	$C_{11}H_{13}ClO$					18.23	18.07

[a] The position of acylation was determined by oxidation with alkaline potassium permanganate, yielding 4-chlorobenzoic acid, m.p. 236°.[9] [b] The position of acylation was determined by oxidation with alkaline potassium permanganate, yielding 2-chloroterephthalic acid, m.p. 300°.[10]

TABLE III

DERIVATIVES OF ARALKYL KETONES

Derivative	Compd. No.	M.p., °C.	Empirical Formula	Carbon Calc'd	Carbon Found	Hydrogen Calc'd	Hydrogen Found	Nitrogen Calc'd	Nitrogen Found
2,4-Dinitrophenylhydrazone	2	94–95[a]	$C_{24}H_{22}N_4O_4$	66.95	66.75	5.15	5.67	13.02	13.26
2,4-Dinitrophenylhydrazone	3	132–133[b]	$C_{16}H_{15}ClN_4O_4$	52.97	52.47	4.17	4.30		
2,4-Dinitrophenylhydrazone	4	126–127[c]	$C_{17}H_{17}ClN_4O_4$	54.19	54.29	4.95	4.51	14.87	14.84

[a] Recrystallized from chloroform-ethanol. [b] Recrystallized from carbon tetrachloride. [c] Recrystallized from ethanol.

Preparation of α-bromoaralkyl ketones. To 0.1 mole of the aralkyl ketone in 100 ml. of chloroform was added slowly with stirring 16.0 g. (0.1 mole) of bromine. The reaction mixture was allowed to stand for two hours. It was washed with a 5% sodium bisulfite solution, followed by a washing with water. The chloroform layer was dried with sodium sulfate before the solvent was removed by distillation. The residue was distilled through a short Vigreux column at reduced pressures. The compounds prepared in this way are reported in Table IV. All of these α-bromo ketones became dark on standing in sealed ampules.

1-Indanones. I. Refluxing carbon disulfide method. To a refluxing mixture (45°) of 200 ml. of carbon disulfide and 15.0 g. (0.11 mole) of aluminum chloride was added 0.05 mole of the α-bromo ketone. It then was heated for one hour, cooled to room temperature, and the contents of the flask were hydrolyzed with dilute hydrochloric acid. The organic layer was extracted with ether, dried with sodium sulfate and the ether was removed by distillation. The residue was distilled under a vacuum through a short Vigreux column. New 1-indanones prepared in this way are listed in Table V.

1-Indanones. II. Dry mixture method. A mixture of 65.0 g. (0.5 mole) of aluminum chloride and 0.15 mole of the α-bromoaralkyl ketone or the α,β-unsaturated ketone was placed in a 250-ml. flask and with stirring was heated in an oil-bath, held at a temperature of 140–160°, for four hours and then was cooled. Pieces of ice were cautiously added

TABLE IV

α-BROMOARALKYL KETONES

Compound	Yield, %	B.p., °C.	Mm.	n_D^{25}	Empirical Formula	Halogen Calc'd	Halogen Found
α-Bromo-2,4-dimethylisobutyrophenone	82	121–122	1	1.5390	$C_{12}H_{15}BrO$	31.32	31.06
α-Bromo-α-ethyl-2,4-dimethylbutyrophenone	83	146–147	1	1.5410	$C_{14}H_{19}BrO$	28.22	27.98
1-Bromocyclohexyl phenyl ketone	54	156	2	1.5733	$C_{13}H_{15}BrO$	29.92	29.49
α-Bromo-2,4-dimethylpropiophenone	85	124–125	2	1.5603	$C_{11}H_{13}BrO$	33.12	32.82
α-Bromo-2,4-dimethylbutyrophenone	82	115–118	1	1.5513	$C_{12}H_{15}BrO$	31.32	31.34
α-Bromo-4-methylisobutyrophenone	82	133	2	1.5529	$C_{11}H_{13}BrO$	33.15	32.58
α-Bromo-3-nitroisobutyrophenone	79	156–159	2[a]	1.5680	$C_{10}H_{10}BrNO_3$	29.37	29.76
α-Bromo-2,5-dimethylisobutyrophenone	79	111	1	1.5365	$C_{12}H_{15}BrO$	31.33	31.24
α-Bromo-4-chloroisobutyrophenone	81	117–119	1	1.565	$C_{10}H_{10}BrClO$	44.12	43.72
α-Bromo-2-chloro-4-methylisobutyrophenone	81	137–139	2	1.5500	$C_{11}H_{12}BrClO$	41.88	41.62

[a] M.p. 85–86°.

(9) S. Fels, *Z. Kryst. Mineral.*, **32**, 389 (1871).

(10) M. Fileti and F. Crosa, *Gazz. chim. ital.*, **18**, 298 (1888).

TABLE V

1-INDANONES

Compd. No.	Name	Yield, %	B.p., °C.	Mm.	n_D^{25}	Empirical Formula	Carbon Calc'd	Carbon Found	Hydrogen Calc'd	Hydrogen Found	Halogen Calc'd	Halogen Found
5	2,5,7-Trimethyl-1-indanone	71	118–119	2	1.5493	$C_{12}H_{14}O$	82.73	82.76	8.10	8.28		
6	2,4,7-Trimethyl-1-indanone	50	115	2	1.5497	$C_{12}H_{14}O$	82.73	82.91	8.10	8.31		
7	2-Ethyl-3,5,7-trimethyl-1-indanone	72	132–134	1	1.5362	$C_{14}H_{18}O$	83.14	83.33	8.95	8.80		
8	7-Chloro-2,5-dimethyl-1-indanone	66	131–137	2	1.5665	$C_{11}H_{11}ClO$					18.21	18.18
9	5-Chloro-2-methyl-1-indanone	59	136–138	4	1.5691	$C_{10}H_9ClO$					19.63	19.73

TABLE VI

DERIVATIVES OF 1-INDANONES

Derivative	Compd. No.	M.p., °C.	Empirical Formula	Carbon Calc'd	Carbon Found	Hydrogen Calc'd	Hydrogen Found	Nitrogen Calc'd	Nitrogen Found
Oxime	5	144–145[a]	$C_{12}H_{15}NO$	76.15	75.44	7.99	8.16	7.40	7.42
2,4-Dinitrophenylhydrazone	6	218–220[a]	$C_{18}H_{18}N_4O_4$					15.72	15.51
2,4-Dinitrophenylhydrazone	7	191–192[a]	$C_{20}H_{20}N_4O_4$	62.81	62.92	5.81	5.84		
2,4-Dinitrophenylhydrazone	9	222–223[a]	$C_{16}H_{13}ClN_4O_8$					15.53	15.38

[a] Recrystallized from ethanol.

until the violent hydrolysis was completed. The solution was extracted with ether and the ether layer was dried with sodium sulfate. The ether was removed by distillation and the crude product was vacuum-distilled. 1-Indanone was obtained in 60% yield from α-bromopropiophenone. 3,5,7-Trimethyl-1-indanone was obtained in 64% yield from the α-bromo ketone.

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