[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, VANDERBILT UNIVERSITY]

The Swamping Catalyst Effect. II. Nuclear Halogenation of Aromatic Aldehydes and Ketones[1,2]

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Sufficient aluminum chloride to complex with aromatic carbonyl compounds completely has been found to deactivate the aliphatic side chain toward substitution and to permit nuclear substitution. In this manner, good yields of 3-bromo-, 3-bromo-4-methyl-, 3,4-dibromo-, 3-bromo-4-*tert*-butyl-, 3-bromo-4-ethyl-, and 3,5-dibromo-4-methylacetophenones and of 3-bromobenzaldehyde, 3-bromo-4-tolualdehyde, 3-bromopropiophenone, and 3,3'-dibromobenzophenone have been obtained. Good yields of chloroaldehydes and ketones, including tetrachloroacetophenones, and fair yields of iodoketones have also been obtained by this method using the reagents chlorine and iodine monochloride, respectively. No other catalyst has been found to function in the same manner as aluminum chloride or bromide.

The preparation of phenacyl bromide from acetophenone and bromine in the presence of catalytic amounts of aluminum chloride is a well known procedure.[5] We have found that, if sufficient catalyst is used to complex completely the carbonyl compound without solvent and to activate the halogen, side-chain halogenation is suppressed completely and nuclear halogenation takes place. The result brought about by the large excess of catalyst used, of necessity one equivalent to complex the carbonyl compound and of desirability an extra equivalent to complex the halogen and accelerate the rate of reaction, has been called the swamping catalyst effect. The swamping catalyst effect with acetophenone and bromine yielded 60% (now raised to 70%) of *m*-bromoacetophenone with no trace whatever of phenacyl bromide as communicated previously. A small amount of tar, dibrominated ketone, and starting material accompanied the bromoketone. The purpose of this paper is to report the scope of the swamping catalyst effect.

A brief history of halogenation of aromatic carbonyl compounds is pertinent. Emmerling and Engler[6] in 1871 mixed equimolecular quantities of bromine and acetophenone at room temperature and claimed that the lachrymatory, crystalline and oily portions obtained from the mixture could be oxidized in part to a bromobenzoic acid. No one has ever been able to substantiate this claim. Hunnius[7] showed that the product was actually phenacyl bromide, later confirmed by other workers.[8,9] Previous to this work Graebe had shown that only phenacyl chloride was obtained by introducing chlorine into boiling acetophenone.[10] Even benzophenone, which has no aliphatic side-chain to be substituted, does not seem to lend itself well to halogenation.[11-13] No other nuclear halogenations of simple aromatic ketones, containing groups of less activating power than hydroxyl or amino groups, have been found in the literature. Of course, the latter groups do activate sufficiently to permit nuclear substitution. Buu-Hoï,[14,15] for example, found that side-chain bromination of 2- and 4-hydroxyacetophenones took place with bromine in glacial acetic acid and nuclear bromination in aqueous acetic acid.

The nuclear halogenation of aromatic aldehydes is more common, although here again side-chain halogenation leading to benzoyl chlorides can take place if no catalyst is used.[16-18] For example nuclear chlorination of benzaldehyde, yielding a mixture of chlorinated benzaldehydes, occurred in the presence of antimony chloride and iodine.[19] Also, 3-iodobenzaldehyde was made in 30% yield by bringing together benzaldehyde, iodine, and silver sulfate in 80 percent aqueous sulfuric acid.[20] In this concentration of sulfuric acid benzaldehyde is no doubt protonated since it is probably more basic than acetophenone,[21] and the silver ion and iodine mixture is no doubt a source of strong electrophilic reagent,[22]

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(1) Paper I: D. E. Pearson and H. W. Pope, *J. Org. Chem.*, **21**, 381 (1956).

(2) Patents applied for.

(3) Taken in part from the Ph.D. thesis of H. W. P., University Microfilms, Publ. 22,020, Ann Arbor, Mich. Present address: Chemstrand Corp., Decatur, Ala.

(4) Taken in part from pending Ph.D. theses.

(5) R. M. Cowper and L. H. Davidson, *Org. Syntheses*, **Coll. Vol. II**, 480 (1944).

(6) A. Emmerling and C. Engler, *Ber.*, **4**, 148 (1871).

(7) H. Hunnius, *Ber.*, **10**, 2006 (1877).

(8) R. Mohlau, *Ber.*, **15**, 2465 (1882).

(9) W. Staedel and F. Kleinschmidt, *Ber.*, **13**, 837 (1880).

(10) C. Graebe, *Ber.*, **4**, 35 (1871).

(11) W. Kottenhahn, *Ann.*, **264**, 170 (1891).

(12) R. Demuth and M. Dittrich, *Ber.*, **23**, 3614 (1890).

(13) J. Szper, *Bull. soc. chim.*, **51**, 655 (1932).

(14) N. P. Buu-Hoi, N. D. Xuong, and D. Lavit, *J. Chem. Soc.*, 1034 (1954); N. P. Buu-Hoi and D. Lavit, *J. Chem. Soc.*, 18 (1955).

(15) For possible explanation: D. H. Derbyshire and W. A. Waters, *J. Chem. Soc.*, 564 (1950).

(16) F. Wöhler and J. Liebig, *Ann.*, **3**, 262 (1832).

(17) H. T. Clarke and E. R. Taylor, *Org. Syntheses*, **Coll. Vol. I**, 155 (1944).

(18) W. Herz and H. Dick, *Ber.*, **41**, 2645 (1908).

(19) R. Gnehm and E. Banziger, *Ber.*, **29**, 875 (1896).

(20) I. R. L. Barker and W. A. Waters, *J. Chem. Soc.*, 150 (1952).

(21) L. A. Flexser, L. P. Hammett, and A. Dingwall *J. Am. Chem. Soc.*, **57**, 2103 (1935).

(22) For example see J. H. Gorvin, *Chem. and Ind.*, (*London*), 910 (1951).

the reaction thus serving as an example of the swamping catalyst effect. In summary, no examples of aromatic substitution of ketones of the simple acetophenone type have been found. Several examples of aromatic substitution of benzaldehyde have been found, using silver sulfate as a catalyst in cases where yields were satisfactory. The need for a reagent of general applicability to bring about nuclear substitution of carbonyl compounds becomes apparent when it is noted in the next section that so many rather simple compounds, like 3-iodo-4-methylacetophenone, have been made for the first time.

The best conditions for the swamping catalyst effect were developed in the preparation of 3-bromoacetophenone. The success of the preparation depended upon three important factors: (1) the ketone must be complexed rapidly and completely with aluminum chloride before the addition of bromine; (2) no solvent is used; (3) the complex must be molten enough to be stirred during the addition of bromine. In addition, sufficient aluminum chloride to complex the bromine was found to accelerate the rate of reaction considerably. Thus, most of the other reactions were investigated under conditions where one equivalent of carbonyl compound was added to 2.5 equivalents of aluminum chloride and where 1.1 equivalents of bromine were added to the molten complex maintained at temperatures between 25–100°. The scope is discussed under the headings bromination, chlorination, iodination, and search for other catalysts.

Bromination. The yields in the bromination experiments are given in Table I.

TABLE I

PREPARATIONS OF BROMO CARBONYL COMPOUNDS

Substituted Acetophenone	Yield, %	Compound	Yield, %
3-Bromo-	71[a]	3-Bromobenzaldehyde	52
3-Bromo-	73[a]		
3-Bromo-4-methyl-	60	3-Bromo-4-tolualdehyde	44[c]
3,4-Dibromo-	55[b]		
3-Bromo-4-*tert*-butyl-	42[c]	3-Bromopropiophenone	60
3-Bromo-4-ethyl-	59[c]	3,3′-Dibromobenzophenone	35
2,5-Dibromo-	6[d,e]		
3,5-Dibromo-4-methyl-	57[c,e]		

[a] First run at 25°, second at 80–85°. [b] From 4-bromoacetophenone. [c] New compound. [d] Other isomers present which were difficult to separate. [e] Dibromination of corresponding ketone.

The poor yield in dibromination of acetophenone was caused by difficulty of separation of other bromoketones present. On the other hand, the yield of 3,5-dibromo-4-methylacetophenone from dibromination of 4-methylacetophenone was good. These facts suggested that the orientation of the second bromine atom entering acetophenone was not well controlled. The presence of a 4-methyl group was sufficient to alter a mixed orientation to one where the second bromine atom entered *meta* to the ketone group. We shall see a similar behavior in chlorination.

The bromination of benzaldehyde was undertaken with some trepidation since several papers suggested that aluminum chloride brought about decarbonylation or other profound changes at temperatures as low as 60°.[23,24] The complex of benzaldehyde and aluminum chloride indeed was harder to make: it seemed higher melting than that of acetophenone, and it gave very poor yields if the temperature was higher than about 100°. Within the limitations of temperature imposed by fluidity and decomposition, however, the preparations of haloaldehydes were extremely satisfactory considering our initial pessimism.

The preparation of 3,3′-dibromobenzophenone in 35% yield may seem unsatisfactory, but it is the best yield by direct halogenation recorded in the literature.[11,12] The difficulty was the separation of other brominated ketones. Our work suggested that the preparation of 3-bromobenzophenone was not satisfactory and perhaps not even feasible by this method.

Chlorination. Two main differences exist between chlorination and bromination in swamping catalyst experiments. First, chlorine, being a gas, must be fed into the system over a longer period of time to avoid its loss with the effluent gases. Second, the reactivity of chlorine is much greater, thus giving less product control but also permitting the introduction of up to four chlorine atoms. The experiments with acetophenone were run with such quantities of chlorine as to give mono-, di-, tri-, and polychlorination. The products from each of these runs are listed in Table II.

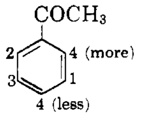
TABLE II

PER CENT YIELD OF ACETOPHENONES OBTAINED BY CHLORINATION

Chlorination Process	3-Chloro	2,5-Dichloro-	2,3,5-Trichloro-[a]	2,3,5,6-Tetrachloro-[a]	2,3,4,5-Tetrachloro-[a]
Mono-	60				
Di-	Some	43	Some		
Tri-		17	38	22	5
Exhaustive				54	13

[a] New compound.

The results in Table II suggest that the chlorine atoms enter in the following sequence:



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(23) D. H. Hey, *J. Chem. Soc.*, 72 (1935).

(24) With boron trichloride: M. S. Frazer, W. Gerrard, and M. F. Lappert, *J. Chem. Soc.*, 741 (1957).

In addition to the above chlorinations the following preparations were made. (1) 3,5-Dichloro-4-methylacetophenone, 15% yield, a new compound. The yield was not maximum and could perhaps be improved by taking more care to keep the complex molten. Trace amounts of hexachlorobenzene were also found which is not unusual in chlorination processes.[25]

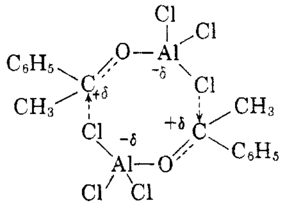
(2) 2,3,5,6-Tetrachloro-4-methylacetophenone, 67% yield, a new compound.

(3) 3-Chlorobenzaldehyde, 43% conversion, 59% yield.

Iodination. Although iodine cannot be made to substitute in swamping catalyst experiments, iodine monochloride was found to give halogenated products with acetophenone. Unfortunately, both 3-iodoacetophenone (15%) and 3-chloroacetophenone (47%) were formed simultaneously. We suspected that aluminum chloride brought about isomerization of iodine monochloride to unreactive iodine and to chlorine. The following facts more or less confirmed this suspicion: iodine monochloride pre-equilibrated with aluminum chloride gave only 6% of 3-iodoacetophenone and 32% of 3-chloroacetophenone, and the more reactive 4-methylacetophenone gave a higher yield of 3-iodoketone, 36%, and a lower yield of 3-chloroketone, 25%. Despite the fact that mixtures of iodo- and chloroketones are obtained, the swamping catalyst method with iodine monochloride is so simple and the separation of the ketones is so easy that this process is the method of choice for synthesis of *m*-iodo ketones.

Search for other catalysts. The most surprising aspect of the swamping catalyst experiments is that aluminum chloride (or bromide) is the only catalyst which seems to be effective in bromination of aldehydes and ketones.[26a] Sulfuric acid either alone or mixed with aluminum chloride gave lachrymatory products. Chlorosulfonic acid gave a sulfonated ketone. Boron trifluoride proved very difficult to handle and impossible to keep in excess, as is necessary for successful bromination.[26b] Boron trichloride gave a solid complex with acetophenone which could be stirred readily in excess boron trichloride. Nevertheless, only lachrymatory substances were isolated after bromination. Benzaldehyde, the stannic chloride complex of which was suspended in excess stannic chloride, gave no chlorinated product after chlorination.[27]

From the negative results of these experiments we are almost forced to believe that the action of aluminum chloride (or antimony pentachloride) is specific. In any specific catalytic effect of this nature, a cyclic electron shift mechanism is to be suspected, and one can be visualized in which both bromine and the ketone are complexed in the aluminum chloride dimer in such a way as to bring the bromine atom over the face of the benzene ring and in the vicinity of the π-electron cloud. We have rejected this possibility, however, since the swamping catalyst effect takes place with an aluminum chloride-ketone ratio of 1, not the ratio 2 to be expected for the dimer of aluminum chloride. Furthermore, the orientation, predominantly *meta* but occasionally *ortho*, or *para*, is not truly specific. We are more inclined to believe tentatively that the main function of the aluminum chloride is to block side-chain halogenation by forming a *very stable* hybrid complex of a dimeric, cyclic nature:[28,29]



This structure explains the stoichiometry of the reaction, the deactivation of the methyl group toward side-chain substitution[30] through preferential coordination of the carbonyl carbon with the chlorine atom in the catalyst, the weakening of the carbonyl double-bonded structure,[31] the molecular weight found for the complex between acetophenone and aluminum bromide,[32,33] and inability of protonic acids to catalyze this reaction. Perhaps this structure also explains why boron trihalides are ineffective catalysts because the small size of the boron atom precludes its inclusion in an eight-membered ring complex. With side-chain bromination suppressed in the aluminum chloride complex, nuclear bromination can now take place. The nucleus of

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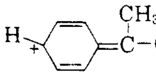
[25] From toluene: F. Fichter and L. Glantzstein, *Ber.*, 49, 2473 (1916).

[26] (a) In later experiments, antimony pentachloride has been found to yield 3-chloroacetophenone upon chlorination of acetophenone. The yield, however, is lower than with aluminum chloride. (b) Liquid hydrogen fluoride, either by itself or mixed with boron trifluoride, was unsuccessful as a catalyst in the chlorination of acetophenone.

[27] In all of these negative experiments, a few per cent, but no more, of nuclear-halogenated carbonyl compounds may have escaped detection.

[28] C. A. Thomas, *Anhydrous Aluminum Chloride in Organic Chemistry*, Reinhold Publishing Corp., New York, N. Y. (1941).

[29] The nucleus in the complex also may be more susceptible to substitution than the nucleus in the free ketone because of the loss of contribution of canonical forms such as  to the resonance hybrid representing the free ketone. These forms deactivate the hybrid of the free ketone toward aromatic substitution.

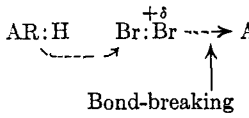
[30] For theory of side-chain substitution including enolization see W. D. Emmons and M. F. Hawthorne, *J. Am. Chem. Soc.*, **78**, 5593 (1956).

[31] From infrared studies in which the absorption peak for the carbonyl group shifts from 1675 cm.$^{-1}$ in the ketone to 1555 cm.$^{-1}$ in either the aluminum chloride or bromide complex: B. P. Susz and I. Cooke, *Helv. Chim. Acta*, **37**, 1273 (1954); from ultraviolet studies: N. N. Lebedev, *J. Gen. Chem., U.S.S.R.*, **21**, 1788 (1951).

[32] E. P. Kohler, *Am. Chem. J.*, **24**, 385 (1900).

[33] M. G. Perrier, *Compt. rend.*, **116**, 1140, 1298 (1893).

acetophenone must be suceptible to substitution for we know that it is easily nitrated to yield 3-nitroacetophenone.[34] Thus, our tentative theory requires complete and perhaps specific complex formation between ketone and Lewis acid, presently found only with the catalysts, anhydrous aluminum chloride or bromide and antimony pentachloride.[19,26a] The theory also suggests that an extra mole of catalyst is desirable to increase the activity of the attacking reagent. A mixture of halogen and aluminum chloride should by all means give rise to a transition complex in which the bond-breaking process of bromine is well advanced:



$$\mathrm{AR{:}H\quad \overset{+\delta}{Br}{:}Br \dashrightarrow \overset{-\delta}{AlCl_3}}$$

thus making bromine a more active substituting agent as is noted in the acceleration of the rate of bromination when larger excesses of catalyst are used. All the experimental evidence obtained to date supports the tentative theory. It remains to be seen whether future evidence shows it to be the right theory. A reaction of such relatively narrow scope perhaps does not seem worthy of labelling with a new name, the swamping catalyst effect. We have reason to believe that the scope is in reality much greater than described here. For example, we have been able to obtain good yields of 3-bromo- and 2,5-dibromobenzonitrile by bromination of benzonitrile. We have also under study the effect of substituting agents other than halogens. These experiments will be described in a later paper.

EXPERIMENTAL

All melting points are corrected and boiling points uncorrected. Analyses were by Galbraith Laboratories, Knoxville, Tenn. Greater detail of experimental work is to be found in the thesis of H. W. Pope[3] and the forthcoming theses of W. W. Hargrove and W. E. Stamper. Hexane refers to petroleum ether, b.p. 69–70°, and pentane to petroleum ether b.p. 35–60°. Oximes[35] and 2,4-dinitrophenylhydrazones[36] were made by published methods.

General procedure exemplified by preparation of 3-bromoacetophenone. The apparatus was usually a 1-l., three necked, standard tapered, round bottomed flask equipped with condenser, dropping funnel, and glass stirrer terminating in a stiff, crescent a-shaped Teflon paddle. Occasionally a Tru-Bore stirrer and a pressure-equalizer dropping funnel were used. The hydrogen bromide gas evolved through the condenser was led to the sink by means of rubber tubing. A motor with good torque (Sargent Cone Drive or Waco) was used to provide stirring. The assembled apparatus, protected from moisture by means of drying tubes in the condenser and funnel, was pre-dried by passing a slow stream of air through entire apparatus while each section was warmed with a soft flame. The condenser jacket was not filled with water until the drying process was complete.

The catalyst was dispensed very conveniently by adding rapidly the entire contents of a 4-oz. bottle of Baker and Adamson Anhydrous Aluminum Chloride, Resublimed. About 110 g. (0.825 mole) to 112 g. (0.84 mole) was delivered to the flask in this manner. The catalyst was quite free-flowing and could be stirred. Acetophenone (40.4 g., 0.336 mole) was added in a slow stream from the dropping funnel to the stirred solid over a period of 10–15 min. Considerable heat was evolved and, if the drops of ketone were not dispersed, darkening or charring occurred. At about the half-way point of addition the solid became a viscous, ball-like mass which was difficult to stir. It was necessary on occasion to turn the stirrer by hand at this point. More rapid addition of ketone also aided stirring but not so rapid as to produce an unduly high temperature. Near the end of the addition, the mass became molten and could be stirred easily. No heat or cooling was applied. At the end of a successful addition the mixture was molten, quite warm but below 100°, and tan to clear brown in color. In the event that the complex was higher melting than that of aluminum chloride–acetophenone, the aluminum chloride was heated before the addition of the ketone, and a minimum temperature maintained to keep the complex molten. A molten mixture was essential to the success of all halogenation reactions. Some of the remarks above are matters of convenience rather than of necessity.

Bromine (64.4 g., 0.403 mole) was added dropwise to the stirred, molten mass over a period of about 20 min. The rate of addition was regulated by the rate of evolution of hydrogen bromide. About one hour after the completion of the addition of bromine, the stirred mass solidified. The solid complex was then (or the next day) carefully dropped portionwise into a 2-l. beaker containing cracked ice and 100 ml. of concentrated hydrochloric acid while the ice was hand stirred vigorously. The acid was found to be quite necessary, for if it were omitted, separation of ether-water layers became difficult because of the effect of small amounts of insoluble aluminum salts. The dark colored oil at the bottom of the beaker was extracted with ether; the ether solution was washed consecutively with water and with sodium bicarbonate solution and dried with anhydrous sodium sulfate. After removal of the ether, the oil was stripped from a few grams of heavy residue by distillation from a short necked flask at 1 mm. pressure. The distillate was separated by fractionation in a 200 × 15 mm. column filled with carborundum or Helipak filling. The combined middle fractions were 3-bromoacetophenone: 47 g., 71%, b.p. 75–76° at 0.5 mm., n_D^{25} 1.5740, m.p. 7–8°; oxime m.p. 100–101°; reported[37] n_D^{20} 1.5755; reported[38] m.p. 7–8°.

Further comments about the bromination of acetophenone. When the reaction mixtue was maintained at 80–85° during addition of bromine rather than at room temperature or slightly higher, the yield of 3-bromoacetophenone was 73.5% rather than 71%. This experiment suggested that the temperature of reaction for *this* preparation was not critical.

Three runs were made under the same conditions (except those mentioned) to test the effect of mole ratio of catalyst. The results were as follows:

Run	$AlCl_3$	C_6H_5-$COCH_3$	Br_2	Time, Min.	Yield, %
1	3	1	1	69	60
2	2.5	1	1.2	65	59
3	1.2	1	1	180	63

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(34) B. B. Corson and R. K. Hazen, *Org. Syntheses*, **Coll. Vol. II**, 434 (1944).

(35) D. E. Pearson and J. D. Bruton, *J. Org. Chem.*, **19**, 957 (1954).

(36) D. E. Pearson and Frances Greer, *J. Am. Chem. Soc.*, **77**, 1294 (1955).

(37) C. S. Marvel, R. E. Allen, and C. B. Overberger, *J. Am. Chem. Soc.*, **68**, 1089 (1946).

(38) L. A. Elson, C. S. Gibson, and J. D. A. Johnson, *J. Chem. Soc.*, 1128 (1930).

Although the third run appeared to be superior, the rate of substitution was perceptibly slower. On the basis of these experiments, the mole ratio $AlCl_3$ 2.5, ketone 1.0, and bromine 1.1 was used for most other experiments unless otherwise specified.

General procedure for preparation of 3-chloroacetophenone. In place of the separatory funnel in the apparatus just described, an inlet tube for chlorine was inserted in the three necked flask so that the gas could be introduced under the surface of the molten complex. The complex of acetophenone and aluminum chloride was made in the same quantities as described above. In the meantime 19.5 ml. of chlorine was condensed in a trap cooled with Dry Ice and acetone. The weight of this volume of chlorine was assumed to be 30 g., 0.42 mole. The gas was bubbled through concentrated sulfuric acid into the stirred complex, the rate being controlled by gradually lowering the Dry Ice container surrounding the liquid chlorine trap. Evolution of hydrogen chloride was noticeable; the internal temperature of reaction mixture rose to about 45°; the color changed from light brown to deep red-brown. The addition of chlorine was complete in 5 hr. and the stirring continued for at least another hour. The reaction mixture was handled from here in the same manner just described, and the separation by fractionation yielded 5.2 g. of acetophenone and 38.8 g., 60% of 3-chloroacetophenone: b.p. 61–63° at 0.5 mm., $n_{\rm D}^{25}$ 1.5480, oxime m.p. 87.5–88.5°, reported[39] 88°.

3-Bromopropiophenone. The yield was 60% of white, small plates, once recrystallized from hexane: m.p. 40–41°, semicarbazone m.p. 181.5–182°; reported[40] m.p. of ketone 37.5–40° and of semicarbazone 182–183°.

3-Bromo-4-methylacetophenone. The yield was 56% of white plates, once recrystallized from petroleum ether, m.p. 42–43°, reported[41] m.p. 43°; oxime m.p. 94–95°; reported[42] m.p. the same.

3,4-Dibromoacetophenone. This compound was made from *p*-bromoacetophenone. The bromination rate was considerably slower than that of acetophenone. The complex in contact with bromine was allowed to stir for 24 hr. at room temperature. A higher temperature may have improved the yield. The yield was 55% of white, thick needles, once recrystallized from hexane: m.p. 89–90°, erroneously reported[43] m.p. 31–32°; oxime m.p. 116–117°. 3,4-Dibromobenzoic acid made from the ketone by hypobromite oxidation had a m.p. 235–236°, reported[44] m.p. 232°, and 3,4-dibromoacetanilide made by Beckmann rearrangement of the oxime had a m.p. 126.5–127.5°, reported[45] m.p. 128°.

3-Bromo-4-tert-butylacetophenone. The yield was 42% of an oil: b.p. 112–113° at 1 mm., d_{25}^{25} 1.325, $n_{\rm D}^{25}$ 1.5589–1.5595 which was not chemically pure according to refractive indices of consecutive fractions and according to analysis.

Anal. Calcd. for $C_{12}H_{15}BrO$: Br, 31.33. Found: Br, 32.32.

Oximation apparently gave an *oxime* of good quality, m.p. 94.5–95.5°.

Anal. Calcd. for $C_{12}H_{16}BrON$: Br, 29.58. Found: Br, 29.65.

Hydrolysis of the oxime with aqueous hydrochloric acid gave the pure ketone, b.p. 92° at 0.1 mm., $n_{\rm D}^{25}$ 1.5582.

The Beckmann rearrangement of the oxime in concentrated sulfuric acid gave an impure anilide with the odor of polyisobutylene. The rearrangement in polyphosphoric acid at 120° for 10 min. gave presumably 3-bromo-4-*tert*-butylacetanilide, m.p. 141–142°, reported[46] m.p. 142–143°.

3-Bromo-4-ethylacetophenone. The yield of colorless oil (turning yellow on standing) was 59%: b.p. 105–106° at 2 mm., $n_{\rm D}^{25}$ 1.5668; *2,4-dinitrophenylhydrazone* m.p. 193–194°; *oxime* m.p. 70–71°.

Anal. Calcd. for $C_{10}H_{12}BrNO$: Br, 33.0. Found: Br, 33.0.

3-Bromobenzaldehyde. This preparation was somewhat more difficult than those of bromoketones. More heat was evolved in forming the complex between benzaldehyde and aluminum chloride. The complex was more difficult to stir, at least until over half the aldehyde was added, and seemed less stable at temperature over 100°. The aldehyde was added within 7 min. and the bromine in 13 min. and the mixture was stirred for an additional 4 hr. at which time it solidified. No heat nor cooling was applied at any time. Care was taken to minimize contact of the bromoaldehyde with air during the purification process. The yield of 3-bromobenzaldehyde was 52%, b.p. 68° at 0.5 mm., $n_{\rm D}^{25}$ 1.5920, *oxime* m.p. 72–73°, reported[47] m.p. 71.5°.

3-Bromo-4-tolualdehyde. The crude solid, b.p. 79–86° at 0.5 mm., was recrystallized from hexane: 44% yield of white crystals, m.p. 48–49°.

Anal. Calcd. for C_8H_7BrO: Br, 40.16. Found: Br, 39.95.

3-Bromo-4-toluic acid, made from the aldehyde by oxidation in 72% yield, had m.p. of 205–206°, reported[48] m.p. 204°.

Attempted dibromination of acetophenone. The mole ratio was ketone 1, bromine 2.1, and aluminum chloride 3.1. The temperature of the mixture was maintained at 80–85° during the addition of bromine. From 0.27 mole of acetophenone, 57.6 g. of a crude oil was obtained which by fractionation yielded 0.07 mole of 3-bromoacetophenone and a mixture of dibromoacetophenones, b.p. 82–89° at 0.5 mm., $n_{\rm D}^{25}$ 1.5877–1.6147 from which 4.6 g., 0.017 mole of 2,5-dibromoacetophenone, m.p. 40–41°, was isolated by further fractionation and by freezing. This ketone was oxidized to 2,5-dibromobenzoic acid, m.p. 156–157°, reported[49] m.p. 156°. Attempts to dibromate acetophenone at room temperature led to complexes which could not be stirred and subsequently to mixtures of 3-bromo- and 2,5-dibromoacetophenones and some lachrymatory material assumed to be phenacyl bromide.

Attempted monobromination of 3-methylacetophenone. A mixture of brominated ketones was obtained, b.p. 94–117° at 2 mm., $n_{\rm D}^{25}$ 1.5632–1.5731 which could not be separated in the Helipak column used for other separations.

3,5-Dibromo-4-methylacetophenone. The ratio of reagents was ketone 1, bromine 2.3, and aluminum chloride 3. The crude solid, obtained from this reaction, b.p. 109–140° at 0.5 mm., was recrystallized from hexane: white needles, 57%, m.p. 102.5–103.5°.

Anal. Calcd. for $C_9H_8Br_2O$: Br, 54.73. Found: Br, 54.65.

The ketone was converted to 3,5-dibromo-4-toluic acid by hypobromite oxidation, m.p. 239.5–240.5°, reported[50] m.p. 235–236°.

3,3'-Dibromobenzophenone.[51] The molar quantities were benzophenone 0.05 mole, aluminum chloride 0.11 mole, and bromine 0.11 mole. Bromine was added dropwise to the yellow-green fluid complex over a period of 0.5–2 hr. while the temperature was maintained near 25° by intermittent

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(51) We are indebted to Mr. James W. Utley for the work on this ketone.

cooling. At the completion of the addition of bromine the mixture was warmed by means of a water-bath to 70° and held there for an hour or two. The mixture became a thick orange to brown colored paste on cooling to room temperature. The paste was poured into ice and water, an equal volume of concentrated hydrochloric acid added, and the mixture digested by refluxing for a hour. On being cooled, the crude solid was removed by filtration, thoroughly washed with water and aqueous sodium bicarbonate, and recrystallized from ethanol. The yield was 5-6 g., 30-35% of white plates, m.p. 137-140°. Further recrystallization gave small glistening plates m.p. 138-140°, reported m.p. 140°[52] and 141°.[11] Attempts to prepare 3-bromobenzophenone in good yield were unsuccessful. Bromination at higher temperatures than those reported above led to resinous products. The above preparation of 3,3'-dibromobenzophenone is evidently superior to any other method of direct bromination[11,12] although the preparation of 3-chlorobenzophenone by electrochemical generation of chlorine has been reported.[13] The product, however, was not well characterized.

3-Chlorobenzaldehyde. The benzaldehyde-aluminum chloride complex was maintained at 75-85°, by regulating first the rate of addition of benzaldehyde to aluminum chloride (25 min.) and second the rate of addition of chlorine (120 min.). At the end of the addition, the mixture was maintained at 80° by means of an oil bath and stirred for 3 more hours. The complex was decomposed in the usual manner, and 3-chlorobenzaldehyde was obtained: b.p. 93-96° at 15 mm., 31.0 g., 43% conversion, 59% yield; m.p. of phenylhydrazone 133-135°, reported[39] m.p. 134-135°; m.p. of semicarbazone 227-228°, reported[39] 228°; m.p. of 3-chlorobenzoic acid 155-156°, neutral equivalent 156.2, reported[39] m.p. 158° and neutral equivalent 156.5. The refractive indices of various fractions were not taken because of ease of air-oxidation of the aldehyde.

Dichlorination of acetophenone. The ratio of reagents was aluminum chloride 2, chlorine 2.3, and ketone 1. The complex was maintained at 50° by means of a Glascol heater and at a somewhat higher temperature toward the end of the addition of chlorine. The addition was complete in 12 hr. If the rate of addition were made faster, some chlorine gas tended to escape in effluent gases. By means of fractionation in a Helipak column, 2,5-dichloroacetophenone was obtained in 43% yield: b.p. 71-72.5° at 2 mm., n_D^{25} 1.5595, oxime m.p. 127-130°, rearranged to 2,5-dichloroacetanilide, m.p. 133-133.5°; reported[53] m.p. of oxime 130° and of 2,5-dichloroacetanilide 133°. Apparently, no other dichloro isomer was formed as judged from b.p. and refractive indices, although some crude mono- and tri-chlorinated compounds were isolated.

Dichlorination of 4-methylacetophenone. The ratio of reagents was ketone 1, aluminum chloride 2.5, and chlorine 2. The mixture was maintained at 55° throughout the 4-hr. period of addition of chlorine. This temperature probably was not quite high enough to give complete mixing and a maximum yield. The chlorinated complex was difficult to remove from the flask. The slurry of ice and hydrochloric acid therefore was added *all at once* to the chilled flask containing the complex. If only a small portion of ice were added, strong local heating occurred at the interface of complex and water. The complex was usually decomposed after standing in contact with water overnight and after some stirring the next day. This reverse method of decomposition was used whenever the complex was too difficult to remove from flask. The crude product was stripped from the tar and fractionated in the usual manner. 3-Chloro-4-methylacetophenone (b.p. 88-107° at 3 mm., 7.2 g., 13%, m.p. 45-46° after recrystallization from pentane, reported[48] m.p. the same), 3,5-dichloro-4-methylacetophenone (b.p. 108-111° at 3 mm., 8.3 g., 15%, m.p. 66-67°; oxidized to acid, m.p. 191-192°, neutral equivalent 204, calcd. 205; oxime m.p. 153.5-154° which was rearranged to 3,5-dichloro-4-acetotoluidide m.p. 220-221°, reported m.p. 220°), and trace amounts of hexachlorobenzene, m.p. 230°, were obtained. The latter was separated by its ready elution from an alumina column. The remainder of the product was a solid of wide m.p. range.

Trichlorination of acetophenone. The mole ratio was ketone 1, aluminum chloride 2.5, and chlorine 3. The temperature of mixture was maintained at about 40° throughout the 9 hr. required for the addition of chlorine. The complex was decomposed by adding the slurry of ice and acid to the flask as described in previous section. The crude oil, stripped from the small amount of residue was separated by means of a Todd column, monel spiral, 5/1 reflux ratio into the following compounds:

Crude 2,5-dichloroacetophenone: 11 g., 17%, n_D^{25} 1.5592-1.5602.

Crude 2,3,5-trichloroacetophenone: 29.5 g.; 38% crude yield, refractionated to constant refractive index, b.p. 132° at 7 mm., n_D^{25} 1.5720.

Anal. Calcd. for $C_8H_5Cl_3O$: Cl, 47.7. Found: Cl, 47.3.

The ketone was oxidized with sodium hypobromite to 2,3,5-trichlorobenzoic acid: m.p. 162.5-163°, neutral equivalent 225, reported[39] m.p. 163°, theoretical neutral equivalent 223.5. The oxime, m.p. 143-145°, was rearranged in polyphosphoric acid to 2,3,5-trichloroacetanilide, m.p. 173°.

2,3,5,6-Tetrachloroacetophenone. This isomer was separated from the 2,3,4,5 isomer by its lower b.p. (ca. 130° at 5 mm.) in the Todd still and by its difference in crystal habit (rhombic plates from aqueous ethanol which could be handpicked). The yield of 2,3,5,6-tetrachloroacetophenone was 22%, m.p. 61.5-62.5°.

Anal. Calcd. for $C_8H_4Cl_4O$: Cl, 55.0. Found: Cl, 54.83.

The ketone failed to form an oxime and a 2,4-dinitrophenylhydrazone by the usual methods and failed also to form the corresponding acid by hypobromite oxidation. However, it was converted to 2,3,5,6-tetrachlorobenzoic acid by means of oxidation in pyridine-water-potassium permanganate solution[54]: m.p. 181.5-182° after two recrystallizations from water; calcd. neutral equivalent 257.9; found, 255. The ketone was also cleaved to 1,2,4,5-tetrachlorobenzene, m.p. and mixed m.p. with authentic sample, 139-139.5° by means of 50% potassium hydroxide in aqueous alcohol after the method of Lock.[55]

2,3,4,5-Tetrachloroacetophenone. This ketone was higher boiling than the 2,3,5,6-isomer (b.p. *ca.* 133° at 5 mm.) and was recrystallized from pentane: 5% yield of colorless needles, m.p. 74-75.5°.

Anal. Calcd. for $C_8H_4Cl_4O$: Cl, 55.0. Found: Cl, 54.69.

The ketone was converted by potassium permanganate in aqueous pyridine[54] to 2,3,4,5-tetrachlorobenzoic acid; m.p. and reported[48] m.p. 194-194.5°, neutral equivalent 256.5, calcd. 257.9. Huntress[39] reports the m.p. as 186°. The oxime, m.p. 172-174°, was rearranged in polyphosphoric acid to 2,3,4,5-tetrachloroacetanilide: m.p. 165-166°, reported[48] m.p. 160-162°. Further statements are made about the two tetrachloro ketones in the following two sections.

Exhaustive chlorination of acetophenone. The mole ratio was ketone 1, aluminum chloride 2, and excess chlorine led directly from the tank to the reaction mixture. The mixture was maintained at 50° during the period of addition, 18 hr. The complex solidified before the addition of chlorine was complete.

The crude product was distilled under vacuum with separation into a liquid fraction, b.p. 107-111° at 1 mm., consisting mostly of di- and trichlorinated ketones, and a solid fraction, b.p. 112-115° at 1 mm., consisting of a mix-

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(52) M. Gomberg and J. C. Bailar, *J. Am. Chem. Soc.*, **51**, 2232 (1929).

(53) T. De Crauw, *Rec. trav. chim.*, **50**, 753 (1931).

(54) J. Cymerman-Craig, J. W. Loder, and B. Moore, *Austral. J. Chem.*, **9**, 222 (1956). The mixture was refluxed rather than held at 15°.

(55) S. Lock, *Ber.*, **68**, 1505 (1935).

ture of 2,3,5,6- and 2,3,4,5-tetrachloro ketones. The mixture of tetrachloro ketones was treated with 2,4-dinitrophenylhydrazine in acidic aqueous ethanol, and the 2,4-dinitrophenylhydrazone of 2,3,4,5-tetrachloroacetophenone (14 g., 13% of yellow-orange needles, m.p. 270° with Kofler hot stage apparatus) separated from the unreacted tetrachloro ketone by virtue of its insolubility in pentane. The 2,3,5,6-tetrachloroacetophenone, remaining in the pentane layer, was recovered by concentration of the pentane, treatment of the concentrate with Norit, and recrystallization: white plates m.p. 60–62°, 57 g., 54%. No pentachloroacetophenone was detected.

Exhaustive chlorination of p-methylacetophenone. The reaction was carried out as above except that the reaction mixture was maintained at 85° for 5 hr. and then at 95° for 1 hr. The flow-rate of chlorine was increased as the temperature was raised. At the end of the sixth hour, the mixture froze to hard brick-red lumps which stopped the flow of chlorine. Chlorine escaped from the sulfuric acid trap into the hood. The crude solid obtained from the ether extract was stripped from the tar (9 g.) by distillation at 1-mm. pressure. The distillate was solid and weighed 78.4 g. Recrystallization of a small amount from hexane gave crystals of mixed form, m.p. 93–98°. Forty g. of the crude mixture was separated by chromatography in a 30 × 6.5 cm. column containing 900 g. of Alcoa Activated Alumina, Grade F-20 using 1.5 liters of hexane as a wash solvent. The washing was terminated after the first fraction had been eluted from the column. The eluate was concentrated and recrystallized from hexane yielding hexachlorobenzene: needles, m.p. and mixed m.p. with authentic sample 229.5–230.5°; analysis for chlorine identical to authentic substance; prorated yield 9%. The alumina was then extruded and extracted with hexane by means of a Soxhlet apparatus. The crude solid, m.p. 91–92°, obtained by extraction tended to discolor on the surface. Recrystallization from ethanol gave 2,3,5,6-tetrachloro-4-methylacetophenone: plates, 31 g., prorated yield 67%, m.p. 98.5–99.5°. The purified compound did not discolor.

Anal. Calcd. for $C_9H_6Cl_4O$: Cl, 52.1. Found: Cl, 51.67.

The ketone was converted to 2,3,5,6-tetrachlorotoluene (m.p. 93.5–94°, tough fibrous needles very difficult to crush; reported[56] m.p. 94°) by the method of Lock.[55]

Iodination of acetophenone. Iodine failed to react with acetophenone in the presence of swamping amounts of aluminum chloride. Only acetophenone with a small amount of polymeric material was recovered. Iodine monochloride however, was found to react to give mixtures of 3-chloro- and 3-iodoacetophenones. Iodine monochloride was made by the Inorganic Syntheses method.[57] Care was taken to add only small portions of iodine during the earlier stages of addition.[58] The mole ratio was ketone 1, $AlCl_3$ 2.5, ICl 1.5. The reaction mixture was held at room temperature while iodine monochloride was added dropwise over a period of 70 min. The contents were stirred for several hours longer and then allowed to stand overnight. The ether extract was washed with sodium bisulfite solution in addition to the usual water and sodium bicarbonate washes. The ether residue was separated by fractionation in an 8-in. column filled with Helipak filling at 1.5 mm. Acetophenone (b.p. 62–70° at 1.5 mm., 11.5 g., 28%, n_D^{25} 1.5312) and crude 3-chloroacetophenone (b.p. 87–96° at 1.5 mm., n_D^{25} 1.5440–1.5490, 22 g., 47%) were separated. The residue was distilled in a short-path apparatus at 1.5 mm., yielding crude 3-iodoacetophenone: b.p. 112–120° at 1.5 mm., n_D^{25} 1.6188, 12.5 g., 15%. Distillation through a Helipak column promoted decomposition of the iodo ketone. Redistillation of 3-chloroacetophenone gave the pure compound: b.p. 61–63° at 0.5 mm., n_D^{25} 1.548, oxime m.p. 87.5–88.5°. Slow redistillation of 3-iodoacetophenone from a short-path apparatus at 0.5 mm. gave the pure compound: colorless liquid, b.p. 85–86° at 0.5 mm., m.p. 27.5–29.5°, n_D^{25} 1.620, d_{25}^{25} 1.754, reported[51] a dark liquid, b.p. 102° at 2 mm. The iodoketone was quite heat-sensitive, turning yellow when warmed on a porcelain spatula and turning to a liquid on storage for a year in a brown bottle.

The formation of both 3-chloro- and 3-iodoacetophenone from iodine monochloride suggested that the latter was disproportionated by the catalyst to unreactive iodine and chlorine. To check this possibility, iodine monochloride was mixed with an equimolecular portion of aluminum chloride and this mixture introduced portionwise into the flask containing the ketone-aluminum chloride complex. The yields of ketones of comparable purity to the ordinary runs were 32% 3-chloroacetophenone and 6.5% 3-iodoacetophenone. This result together with the fact that the yield of iodo ketone is greater with more reactive ketones (see next section) strengthens the suggestion that iodine monochloride undergoes disproportionation in the presence of aluminum chloride. Reducing the molar ratio of aluminum chloride, however, reduced the yield of both 3-chloro- and 3-iodoacetophenones. The concentration of a single ketone in a mixture of two ketones could be estimated from the refractive index as shown. The per cent of 3-chloroacetophenone in acetophenone had refractive indices, n_D^{25}, as follows: 100%, 1.5479; 73.1%, 1.5427; 27.6%, 1.5354; 0%, 1.5319. The per cent of 3-iodoacetophenone in 3-chloroacetophenone had refractive indices as follows: 100%, 1.6199; 77.1.%, 1.5966; 50.9%, 1.5765.

Iodination of 4-methylacetophenone. The molar ratio was ketone 1, aluminum chloride 2, and iodine monochloride. 1.2. The reaction mixture was held at 80° ± 3° during the addition of iodine monochloride (30 min.). Some heat of reaction was noticeable. A small amount of iodine sublimed on walls, and evolution of hydrogen chloride was very rapid. The work-up of halogenated ketones was the same as usual except a wash with aqueous sodium bisulfite was done first. The separation of ketones was accomplished by very slow distillation in a 3-in. Vigreux column. Crude 4-methylacetophenone (b.p. 60° at 1 mm., 22 g., 36%, n_D^{25} 1.5393), crude 3-chloro-4-methylacetophenone (b.p. 72–80° at 1 mm., 18 g., 25%, recrystallized from hexane, m.p. 43–44°, reported[58] m.p. 44–45°, oxime m.p. 94.5–95.5°, reported[58] m.p. 96–97°; 2,4-dinitrophenylhydrazone: orange colored needles, m.p. 245–247.5°), and crude 3-iodo-4-methylacetophenone (b.p. 106° at 1 mm., 41 g., 36%; recrystallization from an equal volume of hexane with seeding gave dense transparent cubes, m.p. 41.5–42°, yellowing slightly on storage for a year in a brown bottle; n_D^{25} of supercooled liquid 1.617; oxime: needles with yellow-green cast, m.p. 107–107.5°; 2,4-dinitrophenylhydrazone: burnt-orange colored needles from nitrobenzene, m.p. 270–272°, dec.) were obtained.

Analysis of 3-iodo-4-methylacetophenone. Calcd. for C_9H_9IO: I, 48.8. Found: 48.72%.

With more precise fractionation, greater amounts of each ketone probably could be obtained; intermediate fractions were not counted in % yield. A run was also made in which the reaction mixture was maintained at room temperature. The yields of ketones comparable in purity to first run were as follows: 18% recovered 4-methylacetophenone, 22% 3-chloro-4-methylacetophenone, and 23% 3-iodo-4-methylacetophenone.

Aluminum bromide as a catalyst. 3-Bromoacetophenone was obtained in 77% yield, b.p. 80° at 0.5 mm., n_D^{25} 1.5729 by using anhydrous aluminum bromide (Fluka) in place of aluminum chloride.

Attempted use of sulfuric acid. Acetophenone (24 g.) was added dropwise to 100% sulfuric acid (55 ml.) held at ice temperature. Bromine (34 g.) was then added and the

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(57) J. Cornog and R. A. Karges, *Inorganic Syntheses*, 1, 165 (1939).

(58) Aqueous ammonia was found to be a much more efficacious reagent than 6*N* hydrochloric acid in removing iodine monochloride from the skin.

mixture allowed to come to room temperature during the next 6 hr. Bromine was found to be insoluble in sulfuric acid. The mixture was quenched in crushed ice and worked up in the usual manner. The lachrymatory oil was treated with diethylamine in ether by the method of Lutz[41] to remove phenacyl bromide. After this treatment, only a small amount of acetophenone (b.p. less than 62° at 1 mm.) was obtained.

A mixture of sulfuric acid (184 g.) and anhydrous aluminum chloride (45.7 g.) was also used as a catalyst. The mixture evolved hydrogen chloride and became solid. An additional 100 ml. of sulfuric acid was added to make the system fluid. Acetophenone (40.4 g.) was added dropwise forming a yellow orange complex. Bromine (53.7 g.) was added with stirring over a one hour period and this mixture was allowed to stir overnight. Phenacyl bromide, b.p. 71–73° at 1.5 mm., 30.5 g., 45%, was obtained as a solid. No higher boiling fraction was present in more than a gram quantity.

Chlorosulfonic acid was found to give a completely water-soluble product within the space of 20 min. followed by the addition of bromine within a space of 25 min.

Attempted use of boron trihalides. Boron trichloride (Matheson, 142 g., 1.2 mole) was condensed in a three-necked flask cooled by a slurry of Dry Ice and acetone. Acetophenone (90 g., 0.75 mole) was added dropwise forming a yellow orange colored soluble complex. Bromine (120 g., 0.75 mole) was added dropwise over a period of 20 min. No hydrogen bromide was evolved. The reaction mixture was then allowed to warm up to room temperature over a period of 6 hr. Most of the boron trichloride and some of the bromine evaporated during this period. No product except acetophenone and solid phenacyl bromide (b.p. 71–73° at 1.5 mm.) was obtained. As little as 5 g. of 3-bromoacetophenone would have been detected by the method of isolation.

Boron trifluoride was passed rapidly into 90 g., 0.75 mole of acetophenone. Sufficient heat was liberated to necessitate cooling. After 45 minutes of saturating the mixture with boron trifluoride, bromine (120 g., 0.75 mole) was added dropwise. Some hydrogen bromide seemed to be evolved together with bromine vapor. After six hours of stirring, the mixture became semi-solid and greenish black in color. The usual procedure of isolation gave a dark polymerized mass from which only a few grams of lachrymatory oil could be distilled.

Attempted use of stannic chloride in chlorination of benzaldehyde. Benzaldehyde (51.9 g., 0.49 mole) was added dropwise to 454 g., 1.74 moles of stannic chloride to form a creamy, white slurry that was easily stirred. The heat of reaction seemed comparable to that of benzaldehyde and aluminum chloride. Chlorine (43.8 g., 0.49 mole) was bubbled through the mixture over a period of 3 hr. and the mixture was stirred an additional 5 hr. After the usual isolation, benzaldehyde (b.p. 69° at 15 mm., 37 g., 71%) was first removed leaving a semisolid residue (3 g.) in still pot. The residue was oxidized in quantitative yield to benzoic acid, m.p. and mixed m.p. 122°.

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NASHVILLE 5, TENN.

[CONTRIBUTION FROM UNIVERSITY COLLEGE FOR GIRLS, EIN SHAMS UNIVERSITY,
AND SCHOOL OF PHARMACY, LONDON UNIVERSITY]

Synthesis of Decahydro-5,6-benzindan-1-yl Acetoxymethyl Ketone and 1-Acetoxydecahydro-4,5-benzindan-1-yl Methyl Ketone

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Decahydro-5,6-benzindan-1-yl acetoxymethyl ketone and 1-acetoxydecahydro-4,5-benzindan-1-yl methyl ketone were synthesized from 1-carbethoxy-4,5,6,7,1′,2′,3′,4′-octahydro-5,6-benzindan-3-one and decahydro-4,5-benzindan-1-one, respectively. These compounds are of interest as analogs of adrenal cortical hormones.

Adrenal cortical hormones usually have a —CO-CH_2R side chain and an R′ group (where R and R′ = H or OH) attached to the carbon atom at position 17 in the cyclopentanoperhydrophenanthrene nucleus. Moreover, the presence of cortical activity has been demonstrated in perhydroindan-1-yl hydroxymethyl ketone[2] I in the life maintenance test. In view of these observations and because the optimum skeleton upon which to attach the side chain has not been determined, it was decided to attempt the preparation of such derivatives of decahydrobenzindans which may be regarded as analogs of the cyclopentanoperhydrophenanthrene nucleus. Thus, decahydro-5,6-benzindan-1-yl acetoxymethyl ketone and 1-acetoxy-decahydro-4,5-benzindan-1-yl methyl ketone were synthesized according to the following scheme.

Clemmensen reduction of 1-carbethoxy-4,5,6,-7,1′,2′,3′,4′-octahydro-5,6-benzindan-3-one[3] II gave mainly an unsaturated ester tentatively assigned the constitution III. A trace of another product was also isolated and shown to be the paraconic acid X. With regard to the absorption properties of the unsaturated ester III, attention was drawn to the investigation of Ungnade and Ortega,[4] which has established that α,β-unsaturated acids or esters in alcoholic solution show a distinct maximum in the region between 210–225 mμ ($E \approx 9000$).

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