very intense and characteristic sulfinate ester stretching band at about 1140 cm.$^{-1}$.

The sulfoxide was recrystallized several times from n-hexane to give pure II; m.p. 80.0–80.5°, $\nu_{max}^{CHCl_3}$ 1035 cm.$^{-1}$ (sulfoxide stretching). N.m.r. (25% in CHCl$_3$) is in τ-units: triplet, 6.57, $J = 7$ c.p.s. (N–CH$_2$–); singlet, 7.12 (N–CH$_3$); multiplet, 7.23–7.53 (–CH$_2$–SO–); singlet, 7.53 (CH$_3$–SO–); pentuplet, 8.03, $J = 7$ c.p.s. (–CH$_2$–CH_2–CH$_2$–). The n.m.r. assignments were made by comparison with the spectrum of N-methyl-N-propyl-aniline.

Anal. Calcd. for C$_{11}$H$_{17}$NOS: C, 62.52; H, 8.11. Found: C, 62.51; H, 8.04.

The rotation went to zero as the recrystallization proceeded while the rotation of the oil from the mother liquors became more levorotatory. A racemic compound preferentially crystallized from the n-hexane. To circumvent this problem, the crude sulfoxide (5.5 g.) was distilled through a small Vigreux column. N-Methyl-N-propylaniline (0.9 g.) from the hydrolysis of the Grignard reagent was obtained as the first fraction, b.p. about 60° (0.5 mm.), lit.[19] b.p. 95–98° (10 mm.). The infrared and n.m.r. spectra were identical with those obtained from an authentic sample. The column was removed and the remainder of the material distilled to give II (2.2 g.); b.p. about 180° (0.6 mm); m.p. 75–78°; $[\alpha]^{28}$D −12 ± 1° (c 2.54, acetone); O.R.D. (c 1.85, ethanol) gave a negative plain curve: $[\phi]_{600}$ −23°, $[\phi]_{500}$ −30°, $[\phi]_{400}$ −54°, $[\phi]_{350}$ −90°, $[\phi]_{340}$ −97°. Addition of

(19) R. L. Bent, *et. al., J. Am. Chem. Soc.,* **73**, 3100 (1951).

gaseous hydrogen chloride to the ethanol solution to form the hydrochloride salt did not change the O.R.D. values indicating that the aniline group probably does not influence the sulfoxide chromophore very much.

The n.m.r. spectrum of the distilled sulfoxide was identical with that obtained from the recrystallized sulfoxide. Addition of 5% of (−)-menthol to the recrystallized sulfoxide gave a mixture whose n.m.r. spectrum clearly revealed the methyl groups of the menthol. In order to have $[\alpha]$D −12°, the distilled sulfoxide would need to be contaminated with 20% (−)-menthol or 10% (−)-menthyl methanesulfinate. The n.m.r. spectrum ruled out such contamination.

Several repetitions of the reaction always gave levorotatory II. Addition of the ester to the Grignard reagent gave identical results: rotation of II, $[\alpha]^{25}$D −11 ± 1° (c 2.07, acetone).

Instruments.—The infrared spectra were obtained on Perkin-Elmer Model 21 and Model 337 spectrophotometers, the n.m.r. spectra on a Varian Model A-60 spectrometer, and the O.R.D. curves on a Rudolph Model 260/655/850/810-614 recording spectropolarimeter.

The Chlorination of Active Hydrogen Compounds with Sulfuryl Chloride.
I. Ketones

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A number of ketones possessing α-hydrogen atoms are readily chlorinated by sulfuryl chloride to yield α-chloro ketones according to R—C(O)—CHR$_2$ + SO$_2$Cl$_2$ → R—C(O)—CClR$_2$ + SO$_2$ + HCl. In general, the order of preferred substitution is methine > methylene > methyl. In several cases, α,α-dichloro ketones were the major products. The chlorination is sensitive to steric factors as well as electronic ones; *e.g.*, 1,2,3-triphenylpropanone-1 did not react even when dissolved in an excess of sulfuryl chloride. An acid-catalyzed ionic mechanism is proposed to explain the experimental results.

A few isolated examples of the chlorination of active hydrogen compounds by sulfuryl chloride can be found.[1-7] The compounds studied (and the products obtained) included malonic esters[1,2] (chloromalonates), methyl ethyl ketone[3] (3-chlorobutanone-2), acetone[4] (1-chloropropanone-2 and 1,1-dichloropropanone-2), cyclopentyl phenyl ketone[5] (α-chlorocyclopentyl phenyl ketone), methyl and ethyl levulinate[6] (chlorination of the methylene group α to the keto carbonyl), and β-diketones[7] (2,2-dichloro-1,3-diketones). In all cases but one,[4] a single product was isolated and/or reported even though more than one α-methyl, methylene, or methine group was often present.

In order to gain a better understanding of the scope and limitations of the chlorination of active hydrogen compounds with sulfuryl chloride, a variety of ketones have been subjected to this reaction and the results are reported here.

Results

A total of nine different ketones was used in this investigation and the chlorinated products obtained from them are summarized in Table I. In every case chlorination occurred exclusively in the α-positions.

The "linear" ketones, acetone, methyl ethyl ketone, and diethyl ketone, each gave several products upon treatment with an equimolar amount of sulfuryl chloride. However, the major product[8] from each was the α,α-dichloro derivative [1,1-dichloropropanone-2 (60–70%), 3,3-dichlorobutanone-2 (48%), and 2,2-dichloropentanone-3 (58%), respectively]. The other products from the chlorination of methyl ethyl ketone and diethyl ketone consisted of nearly equal amounts of the α,α'-dichloro and monochloro derivatives. The methylene protons of methyl ethyl ketone were substituted much more readily than the methyl protons. On the other hand, very little 1,3-dichloropropanone-2 was formed

(1) A. K. Macbeth, *J. Chem. Soc.,* 1116 (1922).

(2) K. G. Naik and N. T. Talati, *J. Indian Chem. Soc.,* **8**, 203 (1931).

(3) E. R. Buchman, A. O. Reims, and H. Sargent, *J. Org. Chem.,* **6**, 764 (1941).

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(5) G. Cauquil and J. Rouzaud, *Compt. rend.,* **237**, 1720 (1953).

(6) H. Yasuda, *J. Sci. Res. Inst.* (Tokyo), **513**, 32 (1957).

(7) E. Gudriniece, G. Vanags, A. Kurzemnicks, and Z. Grants, *Izv. Vysshikh Uchebn. Zavedenii Khim. i Khim. Tekhnol.,* **3**, 119 (1960); *Chem. Abstr.,* **54**, 17,352.

(8) The per cent yields given, unless otherwise specified, are based upon the relative quantity of chlorinated products which were obtained. The actual yields in terms of conversion of sulfuryl chloride were generally high, *i.e.*, >80%.

TABLE I

PRODUCTS FROM THE CHLORINATION OF KETONES WITH SULFURYL CHLORIDE

Ketone	$\dfrac{\text{moles of SO}_2\text{Cl}_2}{\text{moles of R}_2\text{C}=\text{O}}$	Products (% yield)[a]
Acetone	1	1,1-Dichloropropanone-2 (58), 1-chloropropanone-2 (41)
Acetone	1[b]	1,1-Dichloropropanone-2 (61), 1-chloropropanone-2 (38)
Acetone	2	1,1-Dichlorobutanone-2 (72), 1,1,3-trichloropropanone-2 (20), 1,3-dichloropropanone-1 (6)
Methyl ethyl ketone	1	3,3-Dichlorobutanone-2 (48), 1,3-dichlorobutone-2 (27), 3-chlorobutanone-2 (19)
Methyl ethyl ketone	2	3,3-Dichlorobutanone-2 (42), 1,1-dichlorobutanone-2 (7), 1,3-dichlorobutanone-2 (46)
Diethyl ketone	1	2,2-Dichloropentanone-3 (58), 2,4-dichloropentanone-3 (20, meso and dl isomers), 2-chloropentanone-3 (15)
Methyl isopropyl ketone	1	3-Chloro-3-methylbutanone-2 (77), 1-chloro-1-methylbutanone-2 (15)
Diisopropyl ketone	1	2-Chloro-2,4-dimethylpentanone-3 (95), 2,4-dichloro-2,4-dimethylpentanone-3 (~5)
Desoxybenzoin	1	Desyl chloride (~100)
Phenylacetone	1	1-Phenyl-1-chloropropanone-2 (95), 1-phenyl-3-chloropropanone-2 (trace), 1,3-dichloro-1-phenylpropanone-2 (trace)
1,1-Diphenylacetone	1[c]	1,1-Diphenyl-1-chloropropanone-2 (53)[d]
1,1-Diphenylacetone	1[e]	1,1-Diphenyl-1-chloropropanone-2 (77)[f]
Phenylacetone + acetone	0.5[g]	1-Phenyl-1-chloropropanone-2 (82), 1-chloropropanone-2 (14)
1,2,3-Triphenylpropanone-1	1[h]	No reaction
1,2,3-Triphenylpropanone-1	3[e]	No reaction

[a] Per cent yields are based on sulfuryl chloride. [b] Acetone added to sulfuryl chloride; the opposite order of addition was used in all other cases. [c] Carbon tetrachloride was used as solvent. [d] This yield was obtained after 6 hr. [e] No solvent was used. [f] This yield was obtained after 24 hr. [g] An equimolar quantity of each ketone was used. [h] Reactions were attempted in benzene and carbon tetrachloride solutions.

during the chlorination of acetone. When acetone was chlorinated by slowly adding it to sulfuryl chloride, rather than by the inverse procedure, no significant differences in the yields or product distribution were found.

Both acetone and methyl ethyl ketone reacted with an excess (twofold) of sulfuryl chloride. The major product in the case of acetone was again the α,α-dichloro derivative (72%), and the next major product was the trichlorinated compound (20%), 1,1,3-trichloropropanone-2. Under these conditions methyl ethyl ketone gave essentially equal amounts of 3,3-dichlorobutanone-2 (42%) and 1,3-dichlorobutanone-2 (46%).

The branched ketones, methyl isopropyl ketone and diisopropyl ketone, each gave a monochloro derivative as the major product (in total yields of 87% and 95%, respectively). The methine proton of methyl isopropyl ketone was replaced more readily than the methyl protons. Since there are three methyl protons and one methine proton and since the ratio of methine substitution to methyl substitution was 5.1:1 (77 vs. 15%), it is apparent that the methine proton is ~15 times as reactive as the methyl protons in this reaction.

Both desoxybenzoin and phenylacetone reacted rapidly and exothermally with an equimolar amount of sulfuryl chloride. The former gave desyl chloride in virtually quantitative yield. Practically no α,α-dichlorodesoxybenzoin was produced. Similarly, the major product (95%) from phenylacetone was 1-phenyl-1-chloropropanone-2, and very little (~3%) 1,1-dichloro-1-phenyl-propanone-2 and 1-chloro-3-phenylpropanone-2 (trace) were formed.
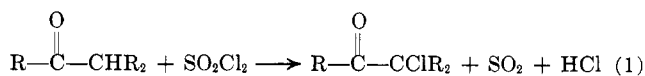
The reaction of 1,1-diphenylacetone with sulfuryl chloride either neat or in carbon tetrachloride was very slow and the sole product was 1,1-diphenyl-1-chloro-propanone-2. No reaction occurred over 3–12-hr. periods when 1,2,3-triphenylpropanone-1 was dissolved in a threefold excess of sulfuryl chloride or when attempts were made to carry out the chlorination in benzene or carbon tetrachloride.

Finally, a competitive chlorination between acetone and phenylacetone showed the latter to be much more reactive. Considering only the acetone methyl groups (and not that from phenyl acetone) and the phenyl acetone methylene group, there is a statistical factor of 3 in favor of acetone. Since ~6 times as much 1-phenyl-1-chloropropanone-2 as 1-chloropropanone-2 was formed, the methylene protons of the former are ~18 times more susceptible to substitution in this reaction than the methyl protons of acetone.
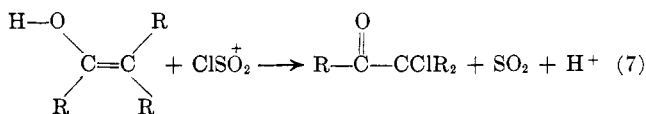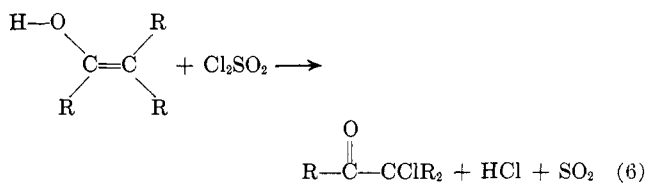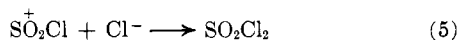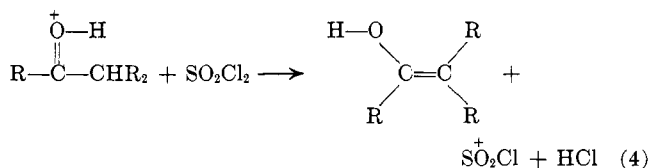
Discussion

The experimental conditions (relatively low temperatures), the preponderance of α,α-dichloro ketones as products in many cases, exclusive α-chlorination, and sensitivity to steric factors clearly indicate that the chlorination of ketones by sulfuryl chloride proceeds via an ionic mechanism. Acid catalysis is most likely involved. One of the acids, hydrogen chloride, is generated during the reaction via eq. 1, following.

$$\underset{\text{O}}{\overset{\text{O}}{\underset{\|}{R-C}}}-CHR_2 + SO_2Cl_2 \longrightarrow R-\overset{\text{O}}{\overset{\|}{C}}-CClR_2 + SO_2 + HCl \quad (1)$$

Accordingly, the following reaction sequence[9] (eq. 2–7) is plausible.

$$R-\overset{\text{O}}{\overset{\|}{C}}-CHR_3 + HCl \rightleftharpoons R-\overset{\overset{+}{O}-H}{\overset{\|}{C}}-CHR_2 + Cl^- \quad (2)$$
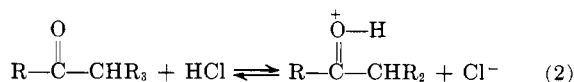
(9) The possibility that sulfuryl chloride can catalyze the enolization is not ruled out per se; however, it is felt that the over-all explanation would not differ significantly from the one shown in eq. 2–7, should this be a catalyst as well as hydrogen chloride.

$$\underset{R}{\overset{\overset{+}{O}-H}{\underset{\|}{R-C-CHR_2}}} + Cl^- \longrightarrow \underset{R}{\overset{H-O}{\underset{R}{\diagdown}}}C=C\underset{R}{\overset{R}{\diagup}} + HCl \quad (3)$$
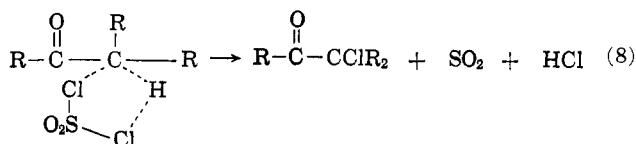
$$\underset{R}{\overset{\overset{+}{O}-H}{\underset{\|}{R-C-CHR_2}}} + SO_2Cl_2 \longrightarrow \underset{R}{\overset{H-O}{\underset{R}{\diagdown}}}C=C\underset{R}{\overset{R}{\diagup}} +$$

$$\overset{+}{S}O_2Cl + HCl \quad (4)$$

$$\overset{+}{S}O_2Cl + Cl^- \longrightarrow SO_2Cl_2 \quad (5)$$

$$\underset{R}{\overset{H-O}{\underset{R}{\diagdown}}}C=C\underset{R}{\overset{R}{\diagup}} + Cl_2SO \longrightarrow$$

$$\overset{O}{\underset{\|}{R-C-CClR_2}} + HCl + SO_2 \quad (6)$$

$$\underset{R}{\overset{H-O}{\underset{R}{\diagdown}}}C=C\underset{R}{\overset{R}{\diagup}} + Cl\overset{+}{S}O_2 \longrightarrow \overset{O}{\underset{\|}{R-C-CClR_2}} + SO_2 + H^+ \quad (7)$$
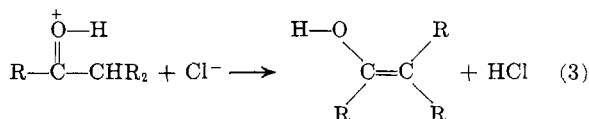
The equilibrium shown in eq. 2 is well known.[10] The same enolic intermediate is formed in eq. 3 and 4, which differ only in the mode of abstraction of the proton. It has been shown[11-13] that halide ions, e.g., chloride and bromide, can function as bases in the manner shown in eq. 3. On the other hand, sulfuryl chloride has been found to catalyze the condensation of aldehydes[14] and the Pechman reaction.[15] Whether either or both eq. 3 and 4 actually are involved can best be resolved by a detailed kinetic analysis of the system.

An alternate path for substitution conceivably could involve a concerted reaction (eq. 8) which proceeds

$$\overset{O}{\underset{\|}{R-C}}\underset{\underset{O_2S-Cl}{\overset{|}{Cl}}}{-}\overset{R}{\underset{\overset{}{}}{\overset{|}{C}}}-R \rightarrow \overset{O}{\underset{\|}{R-C-CClR_2}} + SO_2 + HCl \quad (8)$$

through a cyclic transition state. In the case of the chlorination of methyl isopropyl ketone, the major product was 2-chloro-2-methylbutanone-3 rather than the product from substitution on the methyl group, 1-chloro-3-methylbutanone-2. Since the two electron-releasing methyls of the isopropyl group make the methine carbon more nucleophilic while decreasing the acidity of the methine proton (relative to the carbon and protons of the methyl group), it would be concluded that, if eq. 8 applies, chloronium transfer (bond making) is more important than proton abstraction (bond breaking). On the other hand, chlorination of acetone gave 1,1-dichloropropanone-2 as the major

product. Thus, in this case, the protons of the CH_2Cl group were much more susceptible to reaction than those of a corresponding methyl group. If this result is explained in terms of eq. 8, it is apparent that a conclusion directly opposite that which was obtained from the chlorination of methyl isopropyl ketone will be reached; i.e., "bond breaking" is more important than "bond making." Therefore, eq. 8 does not offer a consistent explanation of the experimental observations.

While it has not been proved conclusively that chlorinations with sulfuryl chloride proceed via eq. 2–7, it should be pointed out that these are formally similar to the pathways proposed to explain other acid-catalyzed halogenations, e.g., bromination with bromine.[11] On the other hand, the possibility that molecular chlorine from $SO_2Cl_2 \rightleftarrows SO_2 + Cl_2$ is actually an important component of this chlorination system can be ruled out because this does not appear to be important at much higher temperatures in free-radical chlorinations.[16]

Steric considerations are also of considerable importance in chlorination of ketones with sulfuryl chloride. For example, the electronic arguments which might explain the formation of large quantities of 1,1-dichloropropanone-2 during the chlorination of acetone would lead one to expect that large amounts of 1,1,1-trichloropropanone-2 would also be formed; however, only trace amounts arose even in the presence of an excess of sulfuryl chloride. Similarly, the major product from the chlorination of phenylacetone was 1-chloro-1-phenylpropanone-2 (95% yield) rather than a dichloro derivative. The same result was obtained with desoxybenzoin. The more hindered ketone, 1,1-diphenylacetone, gave 1,1-diphenyl-1-chloropropanone-2 as the sole product, but the reaction was notably slower than in the case of the other ketones even in an excess of sulfuryl chloride. While 1,2,3-triphenylpropanone-1 is nearly as hindered as 1,1-diphenylacetone, it lacks the driving force derived from the formation of an enolic intermediate conjugated with two benzene rings; consequently, it failed to react. Since it is unlikely that protonation of a carbonyl group is subject to steric inhibition, it is possible that this effect arises from hindrance to the approach of a halide ion or sulfuryl chloride molecule in the proton abstraction steps (eq. 3 and 4).

Finally, it is worth emphasizing that chlorinations of ketones with sulfuryl chloride are simple reactions to perform, the yields are generally very high, and, in many cases, the position of substitution is quite selective. Thus, sulfuryl chloride is a very useful reagent for the preparation of a variety of chlorinated ketones.

Experimental

General.—All of the ketones used in this investigation, except 1,2,3-triphenylpropanone-1 whose preparation is described below, were commercially available and were used as received. Melting points are corrected but boiling points are not. Elemental analyses were performed by the Schwarzkopf Microanalytical Laboratories, Woodside, N. Y., or by the Galbraith Laboratories, Inc., Knoxville, Tenn. Nuclear magnetic resonance spectra were obtained on a Varian Associates A-60 spectrometer (60 Mc., 37 ± 1°). The spectra were taken of the neat liquids or of carbon tetrachloride solutions, and tetramethylsilane (TMS) was

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(16) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957 pp. 380–381.

used as an internal reference.[17] Both preparative and analytical gas chromatography (v.p.c.) measurements were made with a column composed of 20% Ucon polar, 50-HB-2000 (60–80 mesh) on a Chromosorb-P support.

Chlorination of Acetone.—Acetone (58 g., 1 mole) was placed in a 300-ml. round-bottom flask equipped with a condenser (protected from the atmosphere with an anhydrous calcium chloride drying tube), dropping funnel, and magnetic stirrer. Sulfuryl chloride (135 g., 1 mole) was added dropwise over a period of 50 min. The reaction was very exothermic and the temperature was maintained between 30 and 40° by controlling the rate of addition. Both sulfur dioxide and hydrogen chloride were rapidly evolved during the reaction. After the addition was complete, the dark brown solution was distilled. The major portion of the product, after the removal of the unconverted acetone, boiled at 117–118° and weighed 95 g. Elemental analysis indicated that this was a mixture of a mono- and dichlorinated acetone.

Anal. Found: C, 49.8; H, 3.93; Cl, 49.8.

Vapor phase chromatography (v.p.c.) showed that the two major peaks with relative areas of 41 and 58% were present along with with a minor peak ($\sim$1%) due to a higher boiling substituent. From a comparison of retention times[18] it was found that the largest peak (58%) was due to 1,1-dichloropropanone-2, and the next largest peak (41%) was due to 1-chloropropanone-2. The identity of the trace ($\sim$1%) substituent was not definitely established, but it may have been 1,1,1-trichloropropanone-2.

The reaction conducted with the reverse mode of addition, *i.e.*, addition of acetone to sulfuryl chloride, exhibited the same characteristics as described above and was analyzed in the same way (Table I).

The reaction conducted with a sulfuryl chloride–acetone ratio of 2 was performed by the dropwise addition of sulfuryl chloride (0.5 mole) to the acetone (0.25 mole) as described above. After the addition was complete the reaction mixture was allowed to stir at room temperature overnight. Fractionation was performed through a 14-in. Vigreux column. The first fraction was 1,1-dichloropropane-2, b.p. 117–118°, n^{25}D 1.4463, which was obtained in 72% yield (22.8 g.)

Anal. Calcd. for $C_3H_4Cl_2O$: C, 28.38; H, 3.15; Cl, 55.95. Found: C, 27.94; H, 3.29; Cl, 55.82.

The n.m.r. (neat liquid) spectrum of this material consisted of two singlets, τ 7.54 and 3.85, with relative intensities of 3.1:1, respectively.

The next fraction, 6% (1.9 g.), was 1,3-dichloropropanone-2, b.p. 78–80° (30 mm.), n^{25}D 1.4795, lit.[19] n^{46}D 1.4711.

The n.m.r. spectrum of this compound consisted of a sharp singlet, τ 5.55. No methyl group absorptions (7.25 μ) were present in the infrared spectrum.

The final fraction was 1,1,3-trichloropropanone-2, b.p. 91–94° (30 mm.), n^{25}D 1.4695, lit.[20] n^{20}D 1.4711, obtained in 20% yield (8.1 g.). The n.m.r. spectrum (neat liquid) of this compound consisted of two singlets, τ 5.30 and 3.61, in the ratio of 2.01:1, respectively. No methyl group absorption (7.25 μ) appeared in the infrared spectrum.

Chlorination of Methyl Ethyl Ketone.—The experimental procedure was identical with that used in the case of acetone. The dropwise addition of sulfuryl chloride (1 mole) of the ketone (1 mole) resulted in an exothermic reaction which was kept below 40° by controlling the rate of addition (40 min.). The reaction mixture was distilled through a 14-in. Vigreux column and 35 g. of methyl ethyl ketone was recovered. The residue was separated by preparative v.p.c. The first component (19%) was 3-chlorobutanone-2, n^{25}D 1.4158, lit.[21] n^{26}D 1.4168. The n.m.r. spectrum of this material consisted of a quartet, τ 5.25; singlet, 7.85; and a doublet, 8.95; in the relative intensity ratios

of 1:2.95:2:98 (1:3:3), respectively. The next component (48%) was 3,3-dichlorobutanone-2.

Anal. Calcd. for $C_4H_6Cl_2O$: C, 34.00; H, 4.26; Cl, 50.40. Found: C, 33.78; H, 4.11; Cl, 50.66.

The n.m.r. spectrum (carbon tetrachloride solution) of this compound consisted of 2 singlets, τ 7.48 and 7.88, with a relative intensity ratio of 1:1.05, respectively. The infrared spectrum showed a strong methyl absorption at 7.25 μ.

The highest boiling component (27%) was 1,3-dichlorobutanone-2, n^{25}D 1.4625, lit.[20] n^{20}D 1.4650. The n.m.r. spectrum of this compound (carbon tetrachloride solution) consisted of a quartet, τ 5.25; singlet, 5.60; and a doublet, 8.46; in the relative intensity ratios of 1:2.1:2.98 (1:2:3), respectively.

The experiment above was repeated with a sulfuryl chloride–methyl ethyl ketone ratio of 2. After stirring overnight the components were again separated *via* preparative v.p.c. The first component (42%) was 3,3-dichlorobutanone-2. The second component (7%) was considered to be 1,1-dichlorobutanone-2 on the basis of its n.m.r. spectrum (carbon tetrachloride solution): singlet, τ 3.70; quartet, 7.11; and triplet, 8.78; with relative intensity ratios of 1:2.1:3.05 (1:2:3), respectively. The final component (46%) was 1,3-dichlorobutanone-2.

Chlorination of Diethyl Ketone.—The dropwise addition of 1 mole of sulfuryl chloride to 1 mole of diethyl ketone was very exothermic and was performed over a period of 1.33 hr. At no time was the temperature of the reaction allowed to exceed 40°. The reaction mixture was light yellow at the end of the addition. The system was separated by preparative gas chromatography. Four major components were detected. The first of these was diethyl ketone. The second (15%) was considered to be 2-chloropentanone-3 on the basis of its n.m.r. spectrum (carbon tetrachloride solution): quartet, τ 5.69; multiplet,[21] 7.30; doublet, 8.42; and triplet, 8.93; in the relative intensity ratios of 1:2.05:3.1:3.09, respectively. The third component (58%) was 2,2-dichloropentanone-3.

Anal. Calcd. for $C_5H_8Cl_2O$: C, 38.70; H, 5.16; Cl, 45.75. Found: C, 38.41; H, 5.12; Cl, 45.98.

The n.m.r. spectrum (neat liquid) of this material consisted of a quartet, τ 7.02; singlet, 7.83; and a triplet, 8.81; in the relative intensity ratios of 2:2.90:3.00, respectively. The final component (20%) was 2,4-dichloropentanone-3.

Anal. Calcd. for $C_5H_8Cl_2O$: C, 38.7; H, 5.16; Cl, 45.75. Found: C, 38.48; H, 4.98; Cl, 46.05.

The n.m.r. spectrum (neat liquid) of this compound was unusual and consisted essentially of a complex multiplet (τ $\sim$5.20) and another multiplet, consisting of four sharp lines of nearly equal intensity (τ $\sim$8.38). The peaks were in a total intensity ratio of 1:3, respectively (actually 1:3.15). No triplets were present (ruling out methylene groups). Consequently, the compound appears to be 2,4-dichloropentanone-3. The complexity of the spectrum can be explained on the basis of the presence of equal amounts of *meso* and *dl* isomers.

Chlorination of Methyl Isopropyl Ketone.—Sulfuryl chloride (0.5 mole) was added dropwise over a period of 25 min. to 0.5 mole of methyl isopropyl ketone. Heat was evolved (the temperature rose to $\sim$40°) and the reaction mixture became red. Stirring was continued for 1 hr. after the addition was complete. Analysis was done by means of v.p.c. which indicated three major components: methyl isopropyl ketone (8%), 3-chloro-3-methylbutanone-2 (77%), and 1-chloro-3-methylbutanone-2 (15%). The two chlorinated products were also separated by distillation through a 12-in., helice-packed distillation column. The major product, 3-chloro-3-methylbutanone-2, b.p. 143–145°, n^{25}D 1.4378 (lit.[20] b.p. 142–143°, n^{20}D 1.4390), was obtained in 60% yield (36.2 g.). The n.m.r. spectrum (neat liquid) of this compound consisted of two sharp singlets, τ 7.65 and 8.31, in the ratio of 1:2.11, respectively. The minor component, 1-chloro-3-methylbutanone-2, b.p. 74–76° at 40 mm., lit.[22] b.p. 58° at 30 mm., was obtained in 6% yield (3.6 g.). The n.m.r. spectrum of this compound (neat liquid) consisted of a singlet, τ 5.72; multiplet, 7.15; and doublet, 8.83; in the ratio of 1.95:1:6.31, respectively. A viscous, dark residue remained after the distillation.

Chlorination of Diisopropyl Ketone.—The experimental procedure was identical with that used in the chlorination of methyl

(17) Strictly speaking, the τ-scale for expressing chemical shifts in reference to TMS (τ 10.0) is usually applied to measurements made in an inert solvent, *e.g.*, carbon tetrachloride; *cf.* G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1150 (1958). Furthermore, the line positions of the protons in halogenated ketones are noticeably solvent dependent (private communication from Dr. B. L. Shapiro). Therefore, many of the τ-values given here are approximate.

(18) Monochloroacetone used as a standard for the v.p.c. measurements was synthesized through the reaction of sulfuryl chloride with a twentyfold excess of acetone.[4]

(19) W. Polaczkowa and Z. Bankowska, *Roczniki Chem.*, **30**, 119 (1956).

(20) G. B. Bachman and T. Hokama, *J. Org. Chem.*, **25**, 178 (1960).

(21) The multiplet peaks for the CH_2 group, rather than the simple first-order quartet, arise because the two protons are not magnetically equivalent: *cf.* E. I. Snyder, *J. Am. Chem. Soc.*, **85**, 2624 (1963).

(22) M. Thiel, F. Ansinger, and G. Peckling, *Ann. Chem.*, **611**, 131 (1958).

isopropyl ketone. From 0.5 mole of ketone and 0.5 mole of sulfuryl chloride there was obtained 57.3 g. (84%) of 2-chloro-2,4-dimethylpentanone-3, b.p. 143–145°, lit.[23] b.p. 142–143°. The n.m.r. spectrum (neat liquid) of this compound consisted of a multiplet, τ 6.55; ·singlet, 8.31; doublet, 8.34; in the ratio of 1:5.83:5.78, respectively. A higher boiling compound (approximately 5% yield), presumably 2,4-dichloro-2,4-dimethylpentanone-3, was detected *via* v.p.c. The yield of the main product, 2-chloro-2,4-dimethylpentanone-3 was 94% according to v.p.c.

Chlorination of Desoxybenzoin.—Sulfuryl chloride (0.5 mole) was added dropwise to 0.5 mole of desoxybenzoin over a period of 20 min. The rate of addition was such that the temperature of the reaction mixture did not exceed 40°. The viscous yellow liquid which formed was stirred at room temperature (~22°) for 2 hr. It slowly solidified to a white crystalline solid. The temperature rose to 55° during the course of the solidification (~20 min.). The yield of crude product was 117 g. A portion of this material was recrystallized from petroleum ether (b.p. 60–70°) to yield white needles, m.p. 65.0–65.5°. A mixture of this material with deoxybenzoin had m.p. 37–39°. An analytical sample (m.p. 66–66.25°) was obtained by recrystallizing the crude product three times from petroleum ether. A mixture with authentic desyl chloride melted at 66–67°.

Chlorination of Phenylacetone.—Phenylacetone (0.25 mole) was chlorinated by the dropwise addition to it of 0.25 mole of sulfuryl chloride. The reaction was exothermic and the addition was conducted over a period of 25 min. at such a rate that the temperature did not exceed 40°. Upon distillation there was obtained 40.2 g. (95%) of 1-chloro-1-phenylacetone, b.p. 123–124° at 30 mm., $n^{25}D$ 1.5339. The n.m.r. spectrum of this compound consisted of two singlets, τ 4.53 and 7.42, as well as the aromatic protons below τ 3 in the intensity ratio of 1:3.12:5.34, respectively. Analysis by v.p.c. indicated that ~3% of 1-phenylpropanone-2 and trace amounts of two higher boiling components, presumably 1-phenyl-3-chloropropanone-2 and 1,1-dichloro-1-phenylpropanone-2, were also present.

Chlorination of 1,1-Diphenylacetone.—Reactions were conducted with 0.05 mole of ketone and 0.05 mole of sulfuryl chloride in carbon tetrachloride solvent or without solvent. The reaction in carbon tetrachloride (50 ml.) was terminated after 6 hr. (at room temperature) by pouring the reaction solution onto 200 g. of a mixture of ice and water. The carbon tetrachloride layer was removed and then dried over anhydrous calcium chloride. Removal of the carbon tetrachloride *in vacuo* left a light yellow liquid residue which was separated by preparative gas chromatography into two components. The first of these was unconverted 1,1-diphenylacetone while the second was 1,1-diphenyl-1-chloropropanone-2. This structure was assigned on

the basis of the infrared spectrum, which showed strong methyl absorption at 7.25 μ; the n.m.r. spectrum (carbon tetrachloride solution), which showed aromatic protons at τ ~2.8 and a sharp singlet at 7.75, in the ratio of 3.71:1, respectively; as well as the elemental analysis which showed that the compound contained only one chlorine atom.

Anal. Calcd. for $C_{15}H_{13}ClO$: C, 73.70; H, 5.32; Cl, 14.50. Found: C, 73.58; H, 5.19; Cl, 14.48.

The yield of 1,1-diphenyl-1-chloropropanone-2 under these conditions was 53%. In a similar reaction conducted without solvent the yield of the same product was 77% after 24-hr. reaction at room temperature. Only traces (<1%) of a slightly higher boiling product, presumably 1,1-diphenyl-3-chloropropanone-2, were detected.

Synthesis of 1,2,3-triphenylpropanone-1.—Desoxybenzoin (98 g., 0.5 mole) was dissolved in 300 ml. of refluxing, anhydrous ethanol which contained 28 g. (0.5 mole) of potassium hydroxide. Benzyl chloride (64 g., 0.505 mole) was added dropwise to the refluxing solution over a period of 1 hr. The mixture was stirred and refluxed an additional 4 hr. after the addition. The reaction mixture was allowed to cool to room temperature, and then it was diluted with 1 l. of cold water. Crude 1,2,3-triphenylpropanone-1 (115 g., 80%) separated in the form of a tan crystalline solid. It was recrystallized from petroleum ether in the form of fine white needles, m.p. 125°, lit.[24] m.p. 122.

Attempted Chlorination of 1,2,3-Triphenylpropanone-1.—Attempts were made to chlorinate the compound in benzene, in carbon tetrachloride, and without solvent in a threefold excess of sulfuryl chloride. No evidence of reaction was found (no hydrogen chloride or sulfur dioxide evolution). In each case the starting ketone could be recovered without change (infrared and mixture melting point) after 24 hr. at room temperature.

Chlorination of a Mixture of Acetone and Phenylacetone.—Sulfuryl chloride (34 g., 0.25 mole) was added dropwise over a period of 30 min. to a well-stirred mixture of acetone (0.25 mole) and phenylacetone (0.25 mole). The temperature of reaction was kept below 40° by adjusting the rate of addition. Stirring was continued for 1 hr. after addition and then the crude mixture (a light yellow liquid) was analyzed by v.p.c. It consisted of 82% of 1-phenyl-1-chloroacetone, 14% of 1-chloropropanone-2, and traces of other components (yields are based on sulfuryl chloride).

(23) F. Asinger, M. Thiel, and V. Tesar, *Ann. Chem.*, **619**, (1958).

(24) A. McKenzie, R. Roger, and G. O. Wills, *J. Chem. Soc.*, 779 (1926)

Nitration and Acetylation of 9-Alkylfluorenes[1]

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The products from nitration and acetylation of some 9-alkylfluorenes have been investigated. Nitration gave either 2-nitro derivatives (12–38% yield) or 2,9-dinitro (tentative assignment) derivatives (33–60% yield). Monoacetylation occurred in 60–75% yield. Successive steps of oxime formation and Beckmann rearrangement converted the acetyl derivatives into acetylamino compounds. In one case (9-methylfluorene), the acetyl group was shown to occupy the 2-position. Air oxidation of the monoacetyl-9-ethylfluorene gave a crystalline product, assigned the structure of 2-acetyl-9-ethyl-9-fluorenyl hydroperoxide.

The high carcinogenic activities of 2-fluorenamine and related compounds have been recognized for some years.[4] In this respect, it seemed of interest to prepare similar derivatives of 9-alkylfluorenes for biological investigations. The present study is concerned with

the syntheses and structural determinations of primary substitution products of 9-alkylfluorenes, obtained through processes of nitration and acetylation of the parent hydrocarbons Ia–d (Scheme I).

In an effort to prepare 2-nitro-9-alkylfluorenes, we followed the same general procedure (concentrated

(4) E. K. Weisburger and J. H. Weisburger, "Advances in Cancer Research," Vol. 5, J. P. Greenstein and A. Haddow, Ed., Academic Press, Inc., New York, N. Y., 1958, pp. 331–431.