Jacobsen-Type Rearrangements in Aromatic Trichloromethylations[1]

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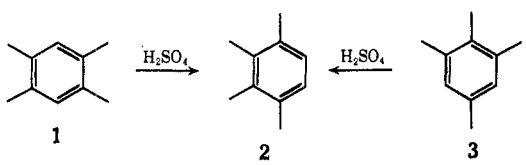
Trichloromethylation of 2-X-1,3,5-trimethylbenzenes by CCl_4–$AlCl_3$, followed by methanolysis, affords substituted methyl benzoates in >90% yields. When X = H, no alkyl rearrangement occurred, methyl 2,4,6-trimethylbenzoate being the sole product. But when X = F, Cl, or Br, there was formed in addition to methyl 3-X-2,4,6-trimethylbenzoate a minor product, methyl 4-X-2,3,5-trimethylbenzoate. Electrophilic attack by CCl_3^+ para to the halogen, followed by a Wagner–Meerwein 1,2-methyl migration, accounts for the rearrangement products. Their amount increases (Br, 7%; Cl, 12%; F, 30%) as the ability of the halogen to stabilize an adjacent positive charge in the intermediate benzenonium ion increases.. The trichloromethylation reaction is a good, nonreversible model for study of Jacobsen-type rearrangements.

Part A

Despite its venerability[3] the Jacobsen rearrangement is still poorly understood by modern mechanistic standards.[4] The reaction is typified by the isomerization of durene (1) or isodurene (2) to prehnitene (3) in the presence of concentrated sulfuric acid. The products are usually vicinally substituted; the hydrocarbons are



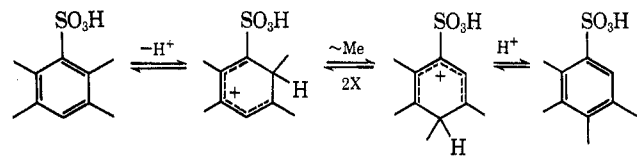
recovered from the actual products, which are sulfonic acids, by steam distillation. Methyl, ethyl, and methylene groups migrate, but secondary and tertiary alkyl groups (*i.e*, isopropyl and *tert*-butyl) are eliminated. Halogens (except F[4a]) may also migrate.[4,5] Disproportionation of halogens[4,6] and alkyl groups[4,5,7] also occurs; with methyl groups, this reaction may proceed *via* diarylmethane intermediates.[8]

Though numerous mechanisms for the Jacobsen rearrangement have been suggested,[4b-d] none is firmly established. Those most frequently proposed are summarized in Chart I,[9-11] using the conversion of **1** → **3** as an example.

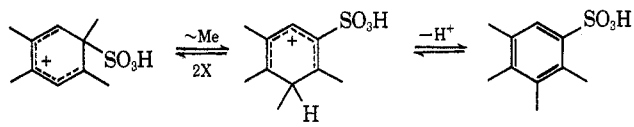
Of these, A and/or B are the most likely.[12] C requires that the desulfonation of prehnitenesulfonic acid be slow relative to the isomeric sulfonic acids; S^{35} labeling experiments[11] show this not to be the case. D rests mainly on the detection of SO_2 and oxidation products (from

CHART I

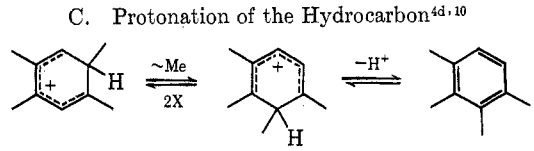
A. Protonation of the Sulfonic Acid[9]



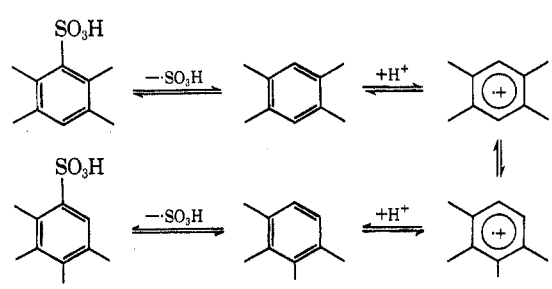
B. Sulfonation at a Substituted Position[4b]



C. Protonation of the Hydrocarbon[4d,10]

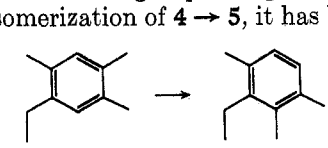


D. Radical–Cation Intermediate[11]



$\cdot SO_3H \rightarrow SO_2 + \cdot OH$?), and of esr signals due to hydrocarbon cation radicals. The mechanism by which the latter are presumed to isomerize is obscure, and the experimental observations have not been demonstrated to be associated with the main reaction path.

Some very basic mechanistic information is often lacking, even for mechanisms A and B. Frequently it is not even clear which group is migrating. For example, in the isomerization of **4** → **5**, it has been asserted[4c]



that the ethyl group migrates in preference to methyl, but this has not been established experimentally.[13]

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(1) We express appreciation to the National Science Foundation for financial support of this research.

(2) Du Pont Teaching Fellow, M. S. U., 1965–1966.

(3) O. Jacobsen, *Chem. Ber.*, **19**, 1209 (1886).

(4) For reviews, see (a) L. I. Smith, *Org. React.*, **1**, 370 (1942); (b) M. J. S. Dewar in "Molecular Rearrangements," Part I, P. deMayo, Ed., Interscience, New York, N. Y., 1963, pp 299–306; (c) H. J. Shine, "Aromatic Rearrangements," Elsevier Publishing Co., Amsterdam, 1967, pp 23–32, 48–55; (d) H. Suzuki, *Bull. Chem. Soc. Jap.*, **36**, 1642 (1963).

(5) L. I. Smith and C. L. Moyle, *J. Amer. Chem. Soc.*, **58**, 1 (1936).

(6) J. Herzig, *Monatsh. Chem.*, **2**, 192 (1881); for recent examples, see R. Goto and H. Suzuki, *Nippon Kagaku Zasshi*, **84**, 167 (1963); H. Suzuki and R. Goto, *ibid.*, **84**, 284 (1963); H. Suzuki, K. Maruyama, and R. Goto, *Bull. Chem. Soc. Jap.*, **38**, 1590 (1965).

(7) O. Jacobsen, *Chem. Ber.*, **20**, 896 (1887); L. I. Smith and A. R. Lux, *J. Amer. Chem. Soc.*, **51**, 2994 (1929).

(8) H. Suzuki and Y. Tamura, *Chem. Commun.*, 244 (1969); H. Suzuki, Y. Tamura, and A. Sera, *Bull. Chem. Soc. Jap.*, **42**, 851 (1969); H. Suzuki, *ibid.*, **42**, 2618 (1969).

(9) E. N. Marvell and B. M. Graybill, *J. Org. Chem.*, **30**, 4014 (1965).

(10) M. Kilpatrick and M. Meyer, *J. Phys. Chem.*, **65**, 1312 (1961).

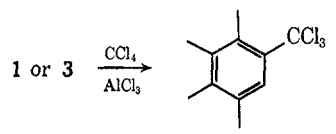
(11) F. Bohlmann and J. Riemann, *Chem. Ber.*, **97**, 1915 (1964).

(12) An alternative to A, sulfonation of the sulfonic acid, cannot be ruled out.

(13) A. Tohl and D. von Karchowski, *Chem. Ber.*, **25**, 1530 (1892); L. I. Smith and M. A. Kiess, *J. Amer. Chem. Soc.*, **61**, 989 (1939).

The major stumbling blocks to mechanistic studies on the Jacobsen reaction as usually considered are (a) the well-known reversibility of sulfonations, (b) the presence of two electrophiles, H^+ and a sulfonating species (SO_3, SO_3H^+, etc.), with the resulting uncertainty about which is required at what stage of the mechanism, and (c) oxidation, which may lead to SO_2, tars, and a less than clean reaction.

To avoid these difficulties, we have begun a systematic study of aromatic trichloromethylation[14] which also gives Jacobsen-like rearrangements.[15] For example, durene (**1**) or isodurene (**2**) gives mainly trichloromethylprehnitene (**6**). The reaction has the advantage that a new carbon–carbon bond is formed with the



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electrophile (CCl_3^+), a process likely to be less reversible than sulfonation. The initial product $ArCCl_3$ reacts with the Lewis acid, used in excess, to form $ArCCl_2^+$, thus being effectively removed from further reaction.[14,16] Work-up by methanolysis gives esters readily separated and analyzed by vpc and spectroscopic methods.

In this paper we describe the trichloromethylation of **7** (X = H, CH_3, F, Cl, and Br); the substituents, particularly the halogens, serve as a label to determine the position of electrophilic attack and identify the migrating group.

Results and Discussion

Each compound **7** was added, in CCl_4 solution, to a twofold excess of $AlCl_3$ slurried in CCl_4, at 40°. After 2 hr the trichloromethyl compounds were isolated and methanolyzed, and the resulting methyl esters were separated (vpc), analyzed, and identified by comparison with authentic samples. Isolated yields of esters were 90% or greater; no tars or undesirable side products were produced.

The structures and percentages of products are summarized in Chart II.

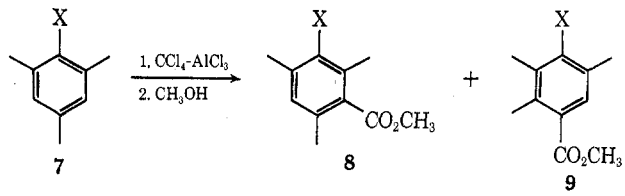
The product from mesitylene (**7-H**) was pure methyl 2,4,6-trimethylbenzoate, but the halomesitylenes and isodurene gave, in addition to the expected product **8**, a Jacobsen-like rearrangement product **9**. The structure of **9** was proved conclusively by independent synthesis when X = CH_3 and F (for the latter, see Part B), but is assumed by analogy for X = Cl and Br.

The reaction is assumed to involve an electrophilic substitution by CCl_3^+, or its equivalent, say

$$\overset{\delta+}{CCl_3}\cdots Cl\cdots\overset{\delta-}{AlCl_3}$$

The preferred intermediate in all cases is structure A, in which the positive charge is stabilized by three

CHART II

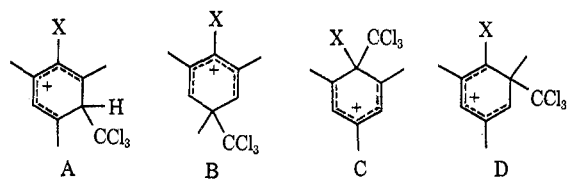


7 **8** **9**

X	% product	
H	100	0
CH_3	73[a]	25[a]
F	70	30
Cl	88	12
Br	93	7

[a] These yields are normalized from 90 to 100%. Some disproportionation (10%) to methyl 2,4,6-trimethylbenzoate and methyl pentamethylbenzoate occurred. The third isomerization product, 2%, was methyl 2,3,5,6-tetramethylbenzoate. No disproportionation or other isomerization products were observed in any of the other cases.

methyl groups in the ortho and para positions. Proton loss leads, after methanolysis, to **8**. Intermediate C is



A B C D

also stabilized by three methyls and may be important when X is methyl, but not when X is halogen, since the halogen-bearing ring carbon should be electron deficient and a poor site for electrophilic attack.[17] Intermediate D is excluded when X = halogen or H, since no products expected from this intermediate were observed. When X = halogen, the minor products (**9**) are derived from intermediate B, by 1,2-methyl migration, proton loss, and methanolysis. The percentage of **9** decreases as the ability of the halogen to stabilize an adjacent carbonium ion decreases, being greatest as expected[18,19] when X = F. Competitive rate experiments show that **7-F** reacts at approximately the same rate (k_{rel} = 1.0 ± 0.1) as **7-CH_3**, whereas the rate falls off for **7-Cl** (0.36 ± 0.05) and **7-Br** (0.21 ± 0.03).

We conclude that the Jacobsen-like rearrangement in these trichloromethylations occurs by attack of the electrophilic CCl_3^+ on an already substituted aromatic ring position, followed by 1,2-methyl migration and proton loss (perhaps most analogous to mechanism B in the introduction).

Part B

Structures of the Major Products (8).—Compounds **8-H** and **8-CH_3** were identified by comparison (ir, nmr, and retention time) with authentic samples synthesized

(14) H. Hart and R. W. Fish, *J. Amer. Chem. Soc.*, **82**, 5419 (1960); H. Hart and R. W. Fish, *ibid.*, **83**, 4460 (1961); H. Hart, J. A. Hartlage, R. W. Fish, and R. R. Rafos, *J. Org. Chem.*, **31**, 2244 (1966).

(15) Suzuki[4d] has generalized the term Jacobsen rearrangement beyond the usual sulfonations, to include a variety of anomalous electrophilic substitutions which involve inter- and/or intramolecular group migrations.

(16) H. Volz and M. J. Volz de Lecca, *Tetrahedron Lett.*, 3413 (1965).

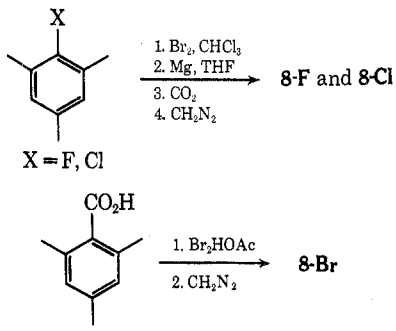
(17) One cannot, from the present work, exclude the possibility that **8** arises in part from C followed by two migrations of X, though, in the second step, X (halogen) would have to migrate exclusively in preference to CH_3. This seems unlikely, and no product with X ortho to the carbomethoxy group was observed.

(18) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1962, p 168.

(19) G. A. Olah and T. E. Kiovsky, *J. Amer. Chem. Soc.*, **89**, 5692 (1967); G. A. Olah and T. E. Kiovsky, *ibid.*, **90**, 2583 (1968).

by literature procedures.[20,21] Compounds **8-F**, **8-Cl**, and **8-Br**, previously unknown, were synthesized by the sequence in Scheme I. The ir and nmr spectra were

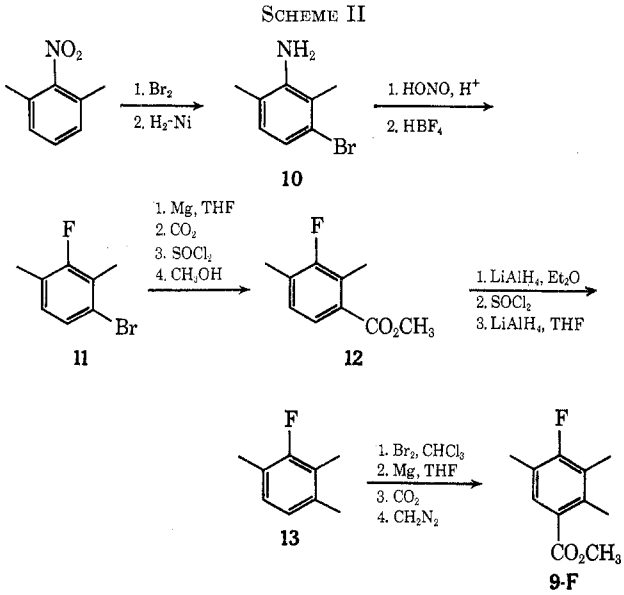
SCHEME I



unexceptional and identical with those of the major trichloromethylation–methanolysis products.

Structures of the Minor Products (9).—Compound **9-CH$_3$** from the trichloromethylation of isodurene was identical (ir, nmr) with authentic[21] methyl 2,3,4,5-tetramethylbenzoate. Compound **9-F**, previously unknown, was synthesized from 2-nitro-1,3-dimethylbenzene, according to Scheme II. Bromination gave

SCHEME II



4-bromo-2-nitro-1,3-dimethylbenzene; the position of the bromine was clearly ortho, para to the methyls, and meta to the nitro, as shown by the AB aromatic proton pattern (doublets at τ 2.21 and 2.79, J = 6 Hz). This pattern was also evident in the amine **10**. The nmr spectrum of the bromination product of **13** showed that the bromine had entered the ring para to the fluorine, because the remaining aromatic proton appeared as a doublet at τ 3.00, J_{HF} = 7.8 Hz (characteristic of meta, not para J_{HF}).[22] Similarly, the aromatic proton in **9-F** appeared as a doublet at τ 2.60, J_{HF} = 8.1 Hz. Synthetic **9-F** and that obtained from the trichloromethylation–methanolysis of **7-F** were identical in all respects.

Because of the length of this synthesis, it was not repeated for X = Cl or Br; the structures of the minor products from **7-Cl** and **7-Br** are assumed to be analogous to that from **7-F**.

Further Discussion.—As stated in Part A, trichloromethylation (in contrast to sulfonation) is probably irreversible. The reactions are heterogeneous. Normally a dilute CCl_4 solution of the aromatic compound is added to a stirred suspension of a twofold excess of $AlCl_3$ in CCl_4. The mixture almost immediately develops a red-orange color, which changes to deep purple as the reaction proceeds. The color resides in a lower, semisolid phase (often spread on the vessel walls by the stirrer). The upper, CCl_4 layer remains almost colorless. All of the reaction product appears to be complexed with the $AlCl_3$ in the colored layer, because separate hydrolysis of the colorless layer affords no trichloromethylation product whatever. Therefore, it appears that as soon as $ArCCl_3$ is produced, it reacts with the excess $AlCl_3$ present to form $ArCCl_2^+$ $AlCl_4^-$.

Hydrolysis of the lower layer gives mainly $ArCCl_3$; in this step, chloride competes effectively with water, and very little $ArCO_2H$ is formed.

Evidence for interaction between CCl_4 and $AlCl_3$ has been presented by Willard,[23] who found rapid Cl^{36} exchange between liquid CCl_4 and solid $AlCl_3$, even at $-21°$. Since no exchange occurred between the vapors (140°, 9 hr), an $AlCl_3$ surface is essential. The authors favor an exchange mechanism in which an induced dipolar CCl_4 molecule is adsorbed on the $AlCl_3$ lattice at a charge site. This adsorption may furnish an incipient source of CCl_3^+ needed for the trichloromethylations.

Experimental Section[24]

Starting Materials.—Fluoromesitylene was prepared from the amine *via* the diazonium tetrafluoborate:[25] nmr τ 3.47 (d, 2, J_{HF} = 6.8 Hz, arom), 7.86 (br m, 9, CH_3's). Chloromesitylene was prepared by chlorination of mesitylene:[25a] nmr τ 3.41 (s, 2, arom), 7.81 (s, 6, *o*-CH_3's), 7.92 (s, 3 H, *p*-CH_3). Bromomesitylene was prepared by brominating mesitylene:[26] nmr τ 3.25 (s, 2, arom), 7.72 (s, 6, *o*-CH_3's), 7.91 (s, 3, *p*-CH_3).

General Trichloromethylation Procedure.—A solution of the aromatic compound in carbon tetrachloride was added dropwise to a stirred slurry of aluminum chloride (anhydrous, twice the molar amount of aromatic compound) in carbon tetrachloride, at 40.0 ± 0.1°. After addition, the mixture was stirred for 2 hr and then hydrolyzed by pouring it into ice water. The organic layer was dried ($MgSO_4$) and concentrated to half its volume, methanol was added, and the mixture was refluxed overnight. Evaporation of the solvent left a residue of substituted methyl benzoate(s) which was analyzed directly by vpc (usually 5 ft × 0.25 in. 20% SF-96 on Chromosorb W, He carrier gas, 40 psi, 175°). Products were also isolated by vacuum distillation or recrystallization. In the following specific cases, amounts are given, and conditions are stated only if they deviate from those given in the general procedure.

(20) M. L. Bender and R. S. Dewey, *J. Amer. Chem. Soc.*, **78**, 317 (1956).

(21) The tetramethylbenzoic acids were prepared by procedures analogous to that given for mesitoic acid in "Organic Syntheses," Coll. Vol. III, Wiley, New York, N. Y., 1955, p 533; the acids were converted to methyl esters with diazomethane or by methanolysis of the acid chlorides. Melting points agreed with those in the literature: see L. I. Smith and J. J. Rosenbaum, *J. Amer. Chem. Soc.*, **73**, 3843 (1951).

(22) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Pergamon Press, Oxford, 1969, p 349.

(23) C. H. Wallace and J. E. Willard, *J. Amer. Chem. Soc.*, **72**, 5275 (1950); M. Blau and J. E. Willard, *ibid.*, **73**, 442 (1951).

(24) All melting points are uncorrected. Analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Infrared spectra were calibrated against polystyrene and nmr spectra against tetramethylsilane as an internal reference.

(25) (a) E. T. McBee and R. E. Leech, *Ind. Eng. Chem.*, **39**, 393 (1947); (b) G. Balz and G. Schiemann, *Chem. Ber.*, **60**, 1186 (1927).

(26) L. I. Smith, "Organic Syntheses," Coll. Vol. II, Wiley, New York, N. Y., 1943, p 95.

Trichloromethylation of Mesitylene (7-H) and Subsequent Methanolysis.—Mesitylene (4.76 g, 0.039 mol) in 200 ml of CCl_4, aluminum chloride (10.58 g, 0.079 mol) in 200 ml of CCl_4, 500 ml of ice water, 150 ml of methanol. A single vpc peak (150°, ret. time 5.3 min) was observed. Distillation gave 6.31 g (90%) of methyl 2,4,6-trimethylbenzoate, bp 72–73° (0.15 Torr), identical in ir, nmr, and retention time with an authentic sample.[20]

Trichloromethylation of Isodurene (7-CH_3), and Subsequent Methanolysis.—Isodurene (6.7 g, 0.05 mol) in 100 ml of CCl_4, aluminum chloride (13.3 g, 0.1 mol) in 100 ml of CCl_4, 100 ml of methanol. The crude product (9.10 g, 95%) gave vpc peaks assigned as follows (ret. time in min, %): methyl 2,4,6-trimethylbenzoate (5.3, 3–5), methyl 2,3,4,6- and 2,3,5,6-tetramethylbenzoates (10.3, 66 and 2%, respectively, as determined by nmr), methyl 2,3,4,5-tetramethylbenzoate (13.9, 22), and methyl pentamethylbenzoate (16.0, 5–7). All products were identified by comparison of ir, nmr, and retention times with those of authentic samples.

Trichloromethylation of Fluoromesitylene (7-F), and Subsequent Methanolysis.—Fluoromesitylene (1.38 g, 0.01 mol) in 75 ml of CCl_4, aluminum chloride (2.68 g, 0.02 mol) in 75 ml of CCl_4, 100 ml of ice water, 100 ml of methanol. The vpc peaks (ret. time in min, %) were assigned as follows: methyl 3-fluoro-2,4,6-trimethylbenzoate (7.8, 70) and methyl 4-fluoro-2,3,5-trimethylbenzoate (9.3, 30). The compounds were identical (ir, nmr, retention time) with authentic samples prepared as described below.

Methyl 3-Fluoro-2,4,6-trimethylbenzoate (8-F).—A solution of 2-bromo-4-fluoro-1,3,5-trimethylbenzene[27] (3.0 g, 0.014 mol) in 25 ml of dry tetrahydrofuran was added to a stirred suspension of magnesium (0.34 g, 0.014 g-atom) in 10 ml of THF. The mixture was refluxed (1 hr); CO_2 was passed in until the mixture became white. The mixture was acidified (6 *N* HCl), extracted with ether, dried ($MgSO_4$), and evaporated. The residue of **3-fluoro-2,4,6-trimethylbenzoic acid** was recrystallized from aqueous acetone to yield 0.51 g (20%), mp 140.5–141.0°.

Anal. Calcd for $C_{10}H_{11}FO_2$: C, 65.95; H, 6.04; neut equiv, 182. Found: C, 65.94; H, 6.13; neut equiv, 180.7.

The acid was converted, *via* diazomethane, to methyl 3-fluoro-2,4,6-trimethylbenzoate which was purified by vpc: mp 12.0–12.5°; ir 1724 cm^{-1}; nmr τ 3.27 (d, 1, J_{HF} = 7.1 Hz, arom), 6.19 (s, 3, OCH_3), 7.82–7.87 (m, 9, CH_3's).

Anal. Calcd for $C_{11}H_{13}FO_2$: C, 67.32; H, 6.69. Found: C, 67.25; H, 6.72.

4-Bromo-2-fluoro-1,3-dimethylbenzene (11).—A solution of 3-bromo-2,6-dimethylaniline[28] (33.2 g, 0.166 mol) in 200 ml of water containing 25 ml of 18 *M* sulfuric acid was cooled to 3° and solid sodium nitrite was added until an excess was indicated (starch–iodide). The solution was filtered, 55 g of 47% fluoroboric acid was added, and the white precipitate was collected, washed successively (100 ml) with water, ethanol, and ether, and dried in a vacuum desiccator over P_2O_5 for 5 hr. The dry powder was gently heated in a large flask fitted with an efficient condenser. The solid decomposed smoothly, to leave a liquid which was dissolved in ether, washed (20% NaOH, water), and dried ($MgSO_4$). Evaporation of the ether and distillation of the residue gave 25.8 g (0.127 mol, 77%) of **4-bromo-2-fluoro-1,3-dimethylbenzene:** bp 38–39° (0.8 Torr); nmr τ 2.6–3.3 (m with peaks at 2.68, 2.91, 3.01, 3.16, and 3.29, 2, arom), 7.74 (d, 3, J_{HF} = 2.6 Hz), 7.92 (d, 3, J_{HF} = 2.3 Hz).

Anal. Calcd for C_8H_8BrF: C, 47.31; H, 3.98. Found: C, 47.41; H, 4.09.

Methyl 3-Fluoro-2,4-dimethylbenzoate (12).—A solution of **11** (37.6 g, 0.185 mol) in 50 ml of anhydrous tetrahydrofuran was added dropwise to a stirred slurry of magnesium (4.5 g, 0.185 g-atom) in 50 ml of THF. When the Grignard reagent was completely formed, the solution was poured over excess crushed Dry Ice. Work-up gave 29.0 g (0.172 mol, 93%) of crude **3-fluoro-2,4-dimethylbenzoic acid.** Two recrystallizations from aqueous acetone gave needles, mp 140.5–141.0°.

Anal. Calcd for $C_9H_9FO_2$: C, 64.27; H, 5.40; neut equiv, 168. Found: C, 64.32; H 5.27; neut equiv, 166.6.

The acid (20 g, 0.119 mol) was refluxed for 1 hr with thionyl chloride (30 g, 0.252 mol), excess thionyl chloride was removed by distillation, methanol (100 ml) was added, and the mixture was refluxed for 1 hr. Work-up gave 18.4 g (0.101 mol, 85%) of **methyl 3-fluoro-2,4-dimethylbenzoate:** bp 53–54° (0.15 Torr); ir 1718 cm^{-1}; nmr τ 2.21 (d, 1, J = 7.8 Hz, arom 6-H), 2.82 (t, 1, J_{HH} and J_{HF} = 7.8 Hz, arom 5-H), 6.06 (s, 3, OCH_3), 7.46 (d, 3, J_{HF} = 2.7 Hz, methyl at C-2), 7.70 (d, 3, J_{HF} = 2.3 Hz, methyl at C-4).

Anal. Calcd for $C_{10}H_{11}FO_2$: C, 65.91; H, 6.10. Found: C, 65.80; H, 6.13.

3-Fluoro-1,2,4-trimethylbenzene (13).—A solution of **12** (14 g, 0.077 mol) in 50 ml of anhydrous ether was added dropwise to a slurry of $LiAlH_4$ (5.85 g, 0.154 mol) in 300 ml of ether, after which the mixture was refluxed (1 hr). Customary work-up gave a liquid residue which solidified on standing. Distillation gave 9.45 g (0.063 mol, 80%) of **3-fluoro-2,4-dimethylbenzyl alcohol,** bp 74–75° (0.3 Torr). Recrystallization from petroleum ether yielded platelets: mp 37–38°; ir 3320 (br) cm^{-1}; nmr τ 3.00, 3.05 (s, 2, arom), 5.55 (s, 2, CH_2), 5.82 (s, 1, OH), 7.75 (d, 3, J_{HF} = 2.1 Hz, arom CH_3), 7.88 (d, 3, J_{HF} = 2.2 Hz, arom CH_3).

Anal. Calcd for $C_9H_{11}FO$: C, 70.10; H, 7.20. Found: C, 70.16; H, 7.11.

The alcohol (9.3 g 0.062 mol) was treated cautiously with 25 ml of thionyl chloride. When the spontaneous reaction subsided, the mixture was refluxed (1 hr). Work-up gave 8.1 g (0.047 mol, 76%) of **3-fluoro-2,4-dimethylbenzyl chloride:** bp 49–50° (0.35 Torr); nmr τ 2.90, 2.94 (s, 2, arom), 5.43 (s, 2, CH_2), 7.71 (t, from overlapping doublets, 6, J_{HF} = 2.4 Hz, arom CH_3's).

Anal. Calcd for $C_9H_{10}ClF$: Cl, 20.53. Found: Cl, 20.38.

A solution of the benzyl chloride (8.0 g, 0.046 mol) in 25 ml of dry THF was added dropwise to a stirred suspension of $LiAlH_4$ (0.95 g, 0.025 mol) in 25 ml of THF. Addition was followed by 1 hr reflux. Work-up gave 5.79 g (0.042 mol, 91%) of **3-fluoro-1,2,4-trimethylbenzene:** bp 54–55° (15 Torr); $n^{25}D$ 1.4858; nmr τ 3.03 (d, 1, J_{HF} = 6 Hz, arom 5-H), 3.08 (s, 1, arom 6-H), 8.65–8.90 (m, 9, arom CH_3's).

Anal. Calcd for $C_9H_{11}F$: C, 78.21; H, 8.04. Found: C, 78.24; H, 8.15.

Methyl 4-Fluoro-2,3,5-trimethylbenzoate (9-F).—To a solution of **13** (5.0 g, 0.037 mol) in 50 ml of chloroform was added dropwise with stirring a solution of bromine (5.9 g, 0.037 mol) in 50 ml of chloroform. After 3 hr at room temperature, excess bromine was removed with 10% sodium bisulfite. The clear mixture was washed (H_2O), dried ($MgSO_4$), and distilled to yield 6.83 g (0.030 mol, 81%) of **6-bromo-3-fluoro-1,2,4-trimethylbenzene:** bp 95–96° (10 Torr); $n^{25}D$ 1.5365; nmr τ 3.00 (d, 1, J_{HF} = 7.8 Hz, arom), 7.79 (s, 3, arom CH_3), 7.89 (br s, 6, arom CH_3's).

Anal. Calcd for $C_9H_{10}BrF$: C, 49.78; H, 4.65. Found: C, 49.88; H, 4.66.

A solution of the bromofluoride (3.0 g, 0.014 mol) in 10 ml of dry THF was added to a suspension of magnesium (0.34 g, 0.014 g-atom) in 25 ml of THF. After 1 hr reflux, the mixture was poured over crushed Dry Ice. Customary work-up gave crude **4-fluoro-2,3,5-trimethylbenzoic acid** (1.29 g, 50%) which, after two sublimations (0.1 Torr, 100°), was pure, mp 167–168°; ir 3300–2400 cm^{-1} (br).

Anal. Calcd for $C_{10}H_{11}FO_2$: C, 65.91; H, 6.10; neut equiv, 182. Found: C, 65.93; H, 6.08; neut equiv, 182.5.

An ether solution of the acid (0.5 g, 0.003 mol) was treated with diazomethane. The ester was purified by vpc (5 ft × 0.25 in. 20% SE-30, 180°) to give **methyl 4-fluoro-2,3,5-trimethylbenzoate (8-F):** mp 19.0–19.5°; ir 1725 cm^{-1}; nmr τ 2.60 (d, 1, J_{HF} = 8.1 Hz), 6.25 (s, 3, OCH_3), 7.62 (s, 3, C-2 methyl), 7.80–7.92 (m with 3 peaks due to HF coupling, 6, C-3 and C-5 methyls).

Anal. Calcd for $C_{11}H_{13}FO_2$: C, 67.32; H, 6.69. Found: C, 67.26; H, 6.65.

Trichloromethylation of Chloromesitylene (7-Cl) and Subsequent Methanolysis.—Chloromesitylene (15.5 g, 0.10 mol) in 100 ml of CCl_4, aluminum chloride (26.6 g, 0.2 mol) in 100 ml of CCl_4, 500 ml of ice water. The crude trichloromethyl product weighed 25.7 g (0.094 mol, 94%). After methanolysis (100 ml of methanol) the product was analyzed by vpc using a 20% Carbowax 20 M on Chromosorb W column, 175°. The vpc peaks (ret. time in min, %) were assigned as follows: methyl 3-chloro-2,4,6-trimethylbenzoate (54.6, 88) and methyl 4-chloro-2,3,6-trimethylbenzoate (71.4, 12). The former was identical (ir, nmr, retention time) with an authentic sample prepared as described below.

(27) G. Grassini, G. Illuminati, and G. Marino, *Gazz. Chim. Ital.*, **86**, 1138 (1956).

(28) K. Auwers, and T. Markovits, *Chem. Ber.*, **41**, 2332 (1908); E. Noelting, A. Braun, and G. Thesmar, *ibid.*, **34**, 2261 (1901).

Methyl 3-Chloro-2,4,6-trimethylbenzoate (8-Cl).—To a solution of chloromesitylene (31.0 g, 0.20 mol) in 100 ml of chloroform was added, at room temperature, a solution of bromine (35 g, 0.22 mol) in 50 ml of chloroform, in an apparatus equipped with an HBr trap. After being stirred for 3.5 hr, the mixture was washed ($NaHSO_3$, H_2O) and dried ($MgSO_4$). Distillation afforded 33.1 g (0.14 mol, 71%) of **2-bromo-4-chloro-1,3,5-trimethylbenzene**, bp 128–129° (10.5 Torr). The distillate solidified and, after recrystallization from pentane, yielded crystals: mp 57.5–58°; nmr τ 3.13 (s, 1, arom), 7.50, 7.72, 7.86 (s, 3 each, arom CH_3's).

Anal. Calcd for $C_9H_{10}BrCl$: C, 45.89; H, 4.29. Found: C, 46.38; H, 4.51.

A solution of the bromochloride (30 g, 0.129 mol) in 150 ml of dry ether was added dropwise to a suspension of magnesium (3.15 g, 0.129 g-atom) in 150 ml of ether. Reaction was initiated with ethylmagnesium iodide. After Grignard formation was complete, the mixture was poured over crushed Dry Ice. The usual work-up afforded, after two recrystallizations from aqueous acetone, 16.8 g (0.085 mol, 66%) of 3-chloro-2,4,6-trimethylbenzoic acid, mp 145–146° (lit.[29] value 143.5–144.0°).

The acid (5 g, 0.025 mol) in ether was treated with diazomethane. Work-up gave 5.15 g (0.024 mol, 96%) of crude **methyl 3-chloro-2,4,6-trimethylbenzoate (8-Cl)**. Two recrystallizations from petroleum ether (30–60°) gave pure ester: mp 34–34.5°; ir 1725 cm^{-1}; nmr τ 3.19 (s, 1, arom), 6.20 (s, 3, OCH_3), 7.73 (br s, 6, arom CH_3's), 7.83 (s, 3, arom CH_3).

Anal. Calcd for $C_{11}H_{13}ClO_2$: C, 62.12; H, 6.17. Found: C, 62.10; H, 6.11.

Trichloromethylation of Bromomesitylene (7-Br) and Subsequent Methanolysis.—Bromomesitylene (2.01 g, 0.010 mol) in 50 ml of CCl_4, aluminum chloride (2.70 g, 0.020 mol) in 50 ml of CCl_4, 500 ml of ice water, 100 ml of methanol, 20% SE-30 column. In addition to some recovered starting material (ret. time 6.4 min, 8%), two products were obtained, methyl 3-bromo-2,4,6-trimethylbenzoate (24.8 min, 93%) and 4-bromo-2,3,5-trimethylbenzoate (27.8 min, 7%). The former was identical (ir, nmr, retention time) with an authentic sample prepared as described below.

Methyl 3-Bromo-2,4,6-trimethylbenzoate (8-Br).—An ether solution of 3-bromo-2,4,6-trimethylbenzoic acid[29] was treated with diazomethane. The usual work-up afforded a 96% yield of **methyl 3-bromo-2,4,6-trimethylbenzoate**: mp (30–60° petroleum ether) 42.5–43°; ir 1713 cm^{-1}; nmr τ 3.21 (s, 1, arom), 6.22 (s, 3, OCH_3), 7.70 (br s, 6, arom CH_3's), 7.86 (s, 3, arom CH_3).

Anal. Calcd for $C_{11}H_{13}BrO_2$: C, 51.36; H, 5.06. Found: C, 51.49; H, 5.21.

Relative Trichloromethylation Rates.—A suspension of aluminum chloride (2.68 g, 0.020 mol) in 75 ml of carbon tetrachloride was allowed to thermally equilibrate at 40.0 ± 0.1°. A mixture of 0.005 mol each of isodurene and 1 mol of the halomesitylenes in 75 ml of carbon tetrachloride was similarly brought to temperature; the solutions were quickly mixed, stirred for 5 min, and quenched by adding 100 ml of ice water. Solvent was evaporated from the organic layer and the residue was refluxed (2 hr) with 100 ml of aqueous acetone (1:1). The mixture was made strongly alkaline, and unreacted aromatics were extracted with ether and analyzed by vpc.

Registry No.—**8-Br**, 26584-20-3; **8-Cl**, 26584-21-4; **8-F**, 26584-22-5; **8-F** (acid), 26584-23-6; **9-F**, 26584-24-7; **9-F** (acid), 26584-25-8; **11**, 26584-26-9; **12**, 26584-27-0; **12** (acid), 26583-81-3; **13**, 26630-72-8; 3-fluoro-2,4-dimethylbenzy alcohol, 26583-82-4; 3-fluoro-2,4-dimethylbenzyl chloride, 26583-83-5; 6-bromo-3-fluoro-1,2,4-trimethylbenzene, 26583-84-6; 2-bromo-4-chloro-1,3,5-trimethylbenzene, 26583-85-7.

(29) F. M. Beringer and S. Sands, *J. Amer. Chem. Soc.*, **75**, 3319 (1953).

Reduction with Metal-Ammonia Combinations. III.[1] Synthesis of β- and γ-Alkylthiomercaptans from 1,3-Dithiolanes and 1,3-Dithianes

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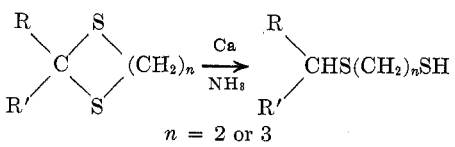
Eleven 1,3-dithiolanes and four 1,3-dithianes have been reduced with calcium in liquid ammonia to give β- and γ-alkylthiomercaptans, $RS(CH_2)_nSH$ (n = 2 or 3), respectively, in high yields.

Part A

Recently, the calcium–ammonia reduction of 1,3-oxathiolanes and 1,3-oxathianes has been reported[1] as a fairly general preparative method for β- and γ-alkoxy mercaptans, respectively. It is evident that selective cleavage of the C–S bond of 1,3-dithiolanes and 1,3-dithianes (Scheme I) would provide a convenient route

SCHEME I



n = 2 or 3

to β-alkylthioethyl and γ-alkylthiopropyl mercaptans. *A priori*, it was not evident whether cleavage of only one of the four C–S bonds in the starting materials shown in Scheme I could be achieved and at the inception of this work there was only one report[2] of such a selective reduction (of 2,2-dimethyl-4-hydroxymethyl-1,3-dithiolane), whereas there were several known instances where reduction led to complete desulfurization[3] or to more complicated products.[4] While this work was in progress,[5] Owen and coworkers[6] published additional examples involving selective cleavage of 2,2-dimethyl-1,3-dithiolanes (Scheme I, R = R′ = CH_3) whereas total cleavage (Scheme II) occurred with 2-methyl- and 2-phenyl-1,3-dithiolanes (R = R′ = H or R = C_6H_5; R′ = H).

As the data in Table I show, reduction according to

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(1) Paper II [E. L. Eliel and T. W. Doyle, *J. Org. Chem.*, **35**, 2716 (1970)] contains an extensive survey of the background literature.

(2) L. W. C. Miles and L. N. Owen, *J. Chem. Soc.*, 2938 (1950).

(3) (a) L. A. Stocken, *ibid.*, 592 (1947); (b) R. E. Ireland, T. I. Wrigley, and W. G. Young, *J. Amer. Chem. Soc.*, **80**, 4604 (1958); (c) N. S. Crossley and H. B. Henbest, *J. Chem. Soc.*, 4413 (1960); (d) R. D. Stolow and M. M. Bonaventura, *Tetrahedron Lett.*, 95 (1964). These reports refer either to benzylic (a) or allylic (b) thioacetals or -ketals or involve reduction with lithium in ethylamine (c, d).

(4) Q. F. Soper, W. E. Buting, J. E. Cochran, and A. Pohland, *J. Amer. Chem. Soc.*, **76**, 4109 (1954); A. Schönberg, E. Petersen, and H. Kaltschmitt, *Ber.*, **66B**, 233 (1933); the latter report involves sodium in ether.

(5) Preliminary report: E. L. Eliel, T. W. Doyle, R. A. Daignault, and B. C. Newman, *J. Amer. Chem. Soc.*, **88**, 1828 (1966).

(6) E. D. Brown, S. M. Iqbal, and L. N. Owen, *J. Chem. Soc. C*, 415 (1966).