which was 95% pure was added to this solution over a 40-min. period at 9–11° while running a total amount of 2 mmoles (flow meter) of oxygen into the mixture and stirring vigorously. The reaction mixture was maintained at 20° for 35 min. About 3% of the product was removed for analytical purposes and dry ether added to the remainder to give a total volume of 800 ml. During 5 min. of vigorous stirring, 60.8 g. (0.6 mole) of triethylamine was added at 4–10°; the mixture was kept at 22–24° for 0.5 hr. and 200 ml. of 2 *N* sulfuric acid was added at 10–20° while stirring with cooling. The mixture was extracted with ether and the ethereal solution washed with sodium bicarbonate solution and water. The ether and water were vacuum evaporated; and the residue (88.22 g.) was chromatographed on silicic acid with hexane eluent, yielding 65.95 g. (77% yield) of 96–100% spectrally pure 1-nitro-1-octadecene, m.p. 32.0–33.5°. An analytically pure sample melted at 34.5–35°, m.p. reported[10]: 38°.

Anal. Calcd. for $C_{18}H_{35}NO_2$: C, 72.67; H, 11.86; N, 4.71. Found: C, 72.91; H, 11.85; N, 4.47.

The hydrolysis of an aliquot of the crude dinitrogen tetroxide–olefin reaction product for the nitroalcohol determination was carried out by stirring the ethereal reaction mixture with an excess of 2*N* sulfuric acid for 4 hr. at 23°. The hydrolysis mixture was extracted with ether, worked up as described for the synthesis of V[10] and analyzed for V.

(b) *Via* **Dehydration of Nitro alcohol.**—A mixture of 2.00 g. (6.35 mmoles) of 1-nitro-2-octadecanol and 1.88 g. (12.7 mmoles) of phthalic anhydride was heated for 70 min. at 175–180°. The dark reaction product was extracted with hexane and the solution chromatographed on silicic acid, yielding 0.93 g. (52%) of 1-nitro-1-octadecene, m.p. 30–34°. The structure was confirmed by its infrared spectrum.

TABLE III

ELIMINATION REACTIONS

Run	Base	Starting material	Reaction time, min.	Mole % yield or recovery of VI
1	NH_3	VI	120	80[c]
2	$N(C_2H_5)_3$	VI	120	95
3	NH_3	II[a]	120	60[c]
4	$N(C_2H_5)_3$	II[a]	15	92
5	NH_3	III	30	80[c]
6	NH_3	I[b]	15	95
7	$N(C_2H_5)_3$	2II[a] 3I[b]	34	94
8	$N(C_2H_5)_3$	2II[a] 3I[b]	2.5	94

[a] The starting material consists of 88% II, 8% V, and 4% other impurities. [b] The starting material contains less than 10% of VI. [c] The major by-products were saturated nitro compounds.

In the experiments with triethylamine, concentrations of 6–12% of nitro compounds in ether (except run 8: 2%) and mole ratios of triethylamine to nitro compounds of 1–2 (except run 8: 150) were used. In the elimination reactions with ammonia 0.2–0.3 mmole of the starting material was dissolved in 1 ml. of ether. After addition of 3–4 ml. of 1% aqueous ammonia, containing about 2 mmoles of ammonia, at 23°, the heterogeneous mixture was shaken at intervals. The reactions with both bases were quenched with dilute sulfuric acid or aqueous ammonium chloride solution at the times given, and the aqueous phase was extracted with ether several times; the combined ethereal solutions were washed with sodium bicarbonate and water, the ether and water were evaporated *in vacuo*, and infrared spectra of the crude products were calculated for nitro-olefin content by the ratio method. The yields of nitro-olefin given in Table III represent mole % nitro-olefin content of the isolated crude yields, which were at least 95%. In several runs, the recovery from work-up was quantitative; and the crude product melted only 2° lower than an analytically pure sample of VI.

1-Nitrocycloöctene.—Cycloöctene (44.40 g., 0.40 mole), which contained 4.6% cycloöctane, was added to a solution of 39.28 g. (0.427 mole) of dinitrogen tetroxide in 150 ml. of dry ether over a 24-min. period at 9–12° while bubbling 13 mmoles of oxygen through the solution. After addition of 25 ml. of ether and stirring of the yellow solution for 0.5 hr. at 10°, 121 g. (1.2 moles) of triethylamine was added at 4–12°. The mixture was kept at 24° for 0.5 hr., cooled to 3°, diluted with 150 ml. of ether, and quenched with 1.2 moles of acetic acid dissolved in 200 ml. of water. After work-up as described for 1-nitro-1-octadecene and removal of the cycloöctane *in vacuo*, 61.0 g. of yellow oil remained. Pure 1-nitrocycloöctene was obtained by chromatography on silicic acid and subsequent distillation, b.p. 60°/0.2 mm., $n^{20}D$ 1.5116; infrared data are given in Table II. The infrared analysis of the crude oil showed that the yield of 1-nitrocycloöctene in this reaction was 96%. A slow decomposition with simultaneous precipitation of a solid occurred upon standing for several weeks at 23°.

Anal. Calcd. for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.84; H, 8.27; N, 8.80.

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The Formation of a Chromanone and Fluoro Ketones in the Reaction of Diazo Ketones with Boron Trifluoride

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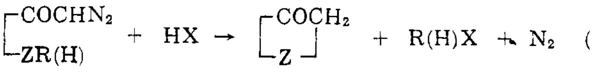
The reaction of 1-diazo-3-(*o*-anisyl)-2-propanone with boron trifluoride or a catalytic amount of sulfuric acid gives 3-chromanone as the major product; with other acids mainly open-chain products are formed. Other diazo ketones with boron trifluoride in ether give mixtures of an ethoxy ketone and a fluoro ketone.

The normal reaction of a diazo ketone with an acid (HX) to give a substituted methyl ketone (equation 1) is frequently subverted by the formation of cyclic products when a nucleophilic center is present at an α′ or β′ position (equation 2). Four-membered heterocyclic ketones are obtained from α′-hydroxydiazo ketones[2,3] or 3-diazoacetylpyrazolines[4,5] on treatment with acetic acid or mineral acids. Open-chain products are not obtained in the latter reaction, even on addition of excess nucleophile (X^-)[5]; the pronounced tendency for cyclization is unusual in the formation of a four-membered ring. The facile formation of a five-membered ring by this process has

$$RCOCHN_2 + HX \longrightarrow RCOCH_2X + N_2 \qquad (1)$$



$$\left[\begin{array}{l}\text{COCHN}_2\\ \text{ZR(H)}\end{array}\right. + HX \rightarrow \left[\begin{array}{l}\text{COCH}_2\\ \text{Z}\end{array}\right] + R(H)X + N_2 \qquad (2)$$

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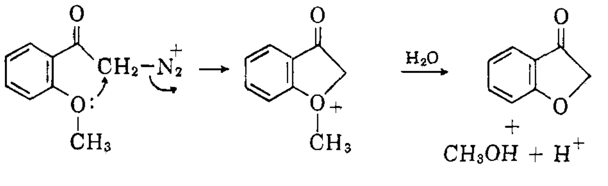
been observed most often in the reactions of *o*-substituted diazoacetophenones, which lead to coumaranones in high yields.[6–8] Only catalytic amounts of acid are required in the conversion of *o*-methoxy-ω-diazoacetophenone to coumaranone, since the proton is recovered when methanol is split off by solvolysis of the oxonium intermediate.[8]



Formation of a six-membered ring is less common. A recent example is provided by the work of Bhati,[9] who obtained isochromanediones from the reaction of *o*-diazoacetylbenzoic acids with hydriodic acid. It has been suggested[10] that the conversion of *o*-nitrodiazoacetophenone to N-hydroxyisatin[11] may proceed by initial formation of a six-membered oxazine intermediate. However, in the attempted ring closure of 1-diazo-3-(*o*-anisyl)-2-propanone (I) to 3-chromanone (VI) with hydrochloric or hydrobromic acids only the open-chain products, 1-chloro- and 1-bromo-3-(*o*-anisyl)-2-propanone, were isolated.[7]

In order to define further the scope of these cyclization reactions, particularly with respect to the formation of larger heterocyclic rings, we first reinvestigated the reactions of 1-diazo-3-(*o*-anisyl)-2-propanone (I) with other acids. In line with the earlier work, ethereal acetic acid gave only the open-chain product. The acetoxymethyl ketone Va was characterized by infrared and n.m.r. spectra and the formation of the 2,4-dinitrophenylosazone. In the reaction of I with one equivalent of concentrated sulfuric acid in ether solution, the major product (19%) was a solid which on hydrolysis liberated sulfate ion and the hydroxymethyl ketone Vc, and was thus the dialkyl sulfate Vb. A similar reaction was previously noted by Newman and Beal,[12] who obtained a solid sulfate from the reaction of 1-diazo-4-phenyl-2-butanone with concentrated sulfuric acid.

A minor liquid compound from the reaction with concentrated sulfuric acid was obtained in larger amounts, together with the hydroxy ketone Vc, when I was treated with a catalytic amount of sulfuric acid in aqueous dioxane, and was virtually the only product isolated in the reaction of I with 1.5 moles of boron trifluoride in ether. The infrared spectrum (5.78 μ) and the proton n.m.r. spectrum (three peaks at 3.10 τ, 5.68 τ, and 6.48 τ in the ratio 2:1:1, corresponding to four aromatic protons and two unsplit methylene groups) indicated that this compound was the desired 3-chromanone (VI); and this was confirmed by the correspondence in properties and derivatives with those previously reported for material made in another way.[7] The identification of this compound in the other reaction mixtures was established by peak enhancement in the vapor phase chromatograms.

The yields of 3-chromanone in the four reactions, as estimated by quantitative vapor phase chromatography on a silicone column after initial distillation, are summarized in Table I. In all the reactions a substantial amount of undistillable tar was present, and the reported yields may be somewhat lower than those actually present in the crude products.

TABLE I

Acid	Equivalent ratio acid/diazo ketone	Solvent	Yield, % Chromanone	 Open-chain product
Acetic	3.4	Ether	..	42
Sulfuric	1.0	Ether	4	19
Sulfuric	0.04	Aqueous dioxane	15	45
BF$_3$	1.5	Ether	35	..

In contrast to the lower homolog, *o*-methoxydiazoacetophenone, which under all acid conditions studied gives only the cyclic product, the reactions of the diazo ketone show an interesting balance between the competing paths (equations 1 and 2). The mechanisms involved in the reactions of diazocarbonyl compounds with acids have been discussed by Huisgen,[13] who distinguished the "catalytic reaction" (equation 3) in which the products are independent of the nucleophilic species present, and the "stoichiometric reaction" (equation 4) in which the nature and concentration of the nucleophile play a commanding role.[14]

$$\mathrm{RCOCHN_2 + H^+ \longrightarrow RCOCH_2{}^+ + N_2 \xrightarrow{H_2O} RCOCH_2OH + H^+} \quad (3)$$

$$\mathrm{RCOCHN_2 + HA \longrightarrow RCOCH_2A + N_2} \quad (4)$$

The conditions employed in the reaction of I with dilute sulfuric acid were chosen to correspond to the catalytic reaction (equation 3), while the reactions with glacial acetic acid and concentrated sulfuric acid quite evidently corresponded to equation 4. In the latter reactions the results are in accord with the relative nucleophilic capabilities of acetate ion and bisulfate ion. With the very weakly nucleophilic bisulfate ion, participation of the neighboring methoxy group becomes a significant reaction; in acetic acid no more than a trace of the chromanone was produced. Cyclization clearly becomes much more important under the catalytic conditions, even though nucleophilic solvent is available. This is consistent with the view that the stoichiometric reactions, in solvents of lower dielectric strength, involve a rather closely associated ion pair III, in which competition of a neighboring group is less favorable than in the solvated diazonium ion II. The reaction of I with boron trifluoride etherate represents essentially the limiting case, in which no effective nucleophile is present, and thus ring closure is the only reaction observed. The formation of the cyclic ether VI must involve the oxonium ion IV in the reactions with sulfuric acid, or the oxonium fluoroborate

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VII in the case of boron trifluoride, followed by nucleophilic attack at the methyl group. The hydroxy ketone Vc is probably derived by hydrolysis of the oxonium ion IV, since the anchimerically assisted conversion of the diazonium ion II to the IV would be expected to be faster than direct solvolysis of II.

The success of the cyclization reaction of I with boron trifluoride encouraged us to attempt the preparation of benzoxepanone from the next higher homolog. A diazo ketone was prepared in the usual way from *o*-methoxyhydrocinnamoyl chloride and was treated without isolation with boron trifluoride etherate. Only a very small amount of volatile product could be distilled from the dark reaction mixture. The proton n.m.r. spectrum of the major component in the distillate contained, among other peaks, a 2-proton doublet at 5.45 τ with $J = 47$ c.p.s. This feature clearly indicated the presence of the $COCH_2F$ grouping,[15] and analysis of the 2,4-dinitrophenylhydrazone confirmed the composition of 1-fluoro-4-(*o*-anisyl)-2-butanone. There was no indication of the formation of the seven-membered cyclic ether.

Although kinetic data have not been obtained, it seems quite plain from the product data in this and previous work[6–8] that the importance of *o*-methoxy participation of this reaction falls off sharply in the order of ring size $5 > 6 \gg 7$. This is entirely consistent with the order observed in the solvolysis of ω-methoxy bromobenzenesulfonates.[16] It must be noted, however, that in the latter solvolyses, anchimeric assistance is negligible when a four-membered ring is involved—*e.g.*, 3-methoxypropyl brosylate; while in the diazo ketone reactions, formation of a four-membered ring is quite favorable, as mentioned above, and substantial rate enhancement due to an α'-substituent has been observed in one case of four-membered ring formation.[5]

The unexpected isolation of a fluoro ketone in this reaction prompted the examination of the reactions of the two unsubstituted phenyl diazo ketones VIII and IX with boron trifluoride. These reactions were also of interest from the standpoint of possible cyclization to an indanone[17] and a tetralone,[18] respectively, both of which have been observed in other cases.

In both reactions, two products were obtained in approximately equal amounts (20–30% yields). The lower-boiling products contained fluorine and showed the characteristic n.m.r. splitting with a J value of 47 c.p.s. for α-fluoro ketones. The structures of the fluoro ketones were established as X and XI by conversion to the corresponding methyl ketones. Prolonged refluxing with sodium iodide in acetone led to the iodo ketones, which were then reduced with concentrated hydriodic acid; phenylacetone and 4-phenyl-2-butanone were characterized as the dinitrophenylhydrazones.

The presence of a doublet in the proton n.m.r. spectrum of 1-fluoro-2-phenyl-2-propanone at 6.33, with $J = 3.2$ c.p.s. for methylene alpha to phenyl and carbonyl, is interesting since it demonstrates spin-spin splitting of hydrogen by fluorine separated by four bonds. This type of long-range splitting has been observed in the C-19 methyl signal of 6-fluoro steroids.[19] The F^{19} n.m.r. spectrum[20] of 1-fluoro-3-phenyl-2-propanone showed a triplet further split into triplets, with J values of 47 and 3.2 c.p.s., respectively. This confirms the four-bond spin-spin splitting of this fluoro ketone.

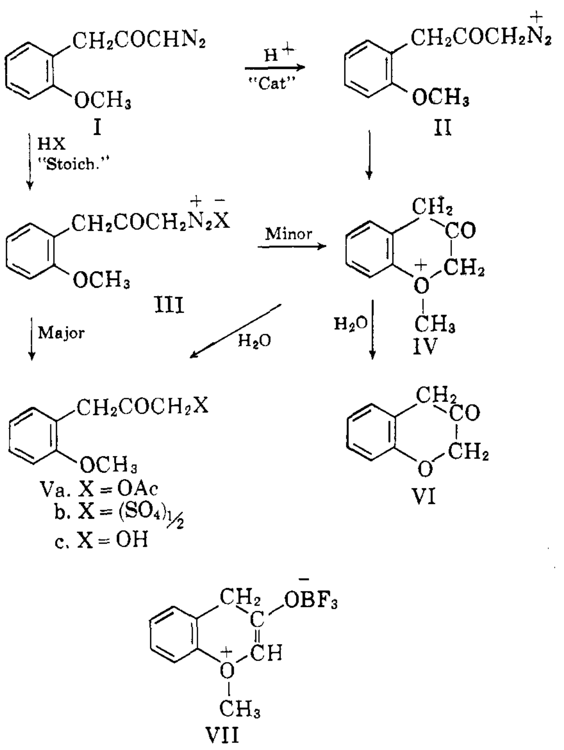

Figure 1

The higher-boiling fractions in each case were also ketonic, and the proton n.m.r. spectra and analyses indicated that they were the ethoxy ketones XII and XIII. Traces of other components were present in the v.p.c. tracings of both reaction mixtures, but no other compounds were identified.

$$\underset{\substack{\text{VIII.}\ n = 1\\ \text{IX.}\ n = 2}}{C_6H_5(CH_2)_nCOCHN_2} + BF_3 \xrightarrow{\text{EtOEt}} \underset{\substack{\text{X.}\ n = 1\\ \text{XI.}\ n = 2}}{C_6H_5(CH_2)_nCOCH_2F}$$

$$\underset{\substack{\text{XII.}\ n = 1\\ \text{XIII.}\ n = 2}}{C_6H_5(CH_2)_nCOCH_2OEt}$$

The formation of these products reveals two hitherto unrecognized paths in the reactions of diazo ketones with boron trifluoride. The formation of α-alkoxy ketones in the reaction of diazo ketones with alcoholic boron trifluoride was reported some years ago by Newman and Beal,[12] and represents a useful preparative method; but the reaction with boron trifluoride etherate was reported to give only tars. Very recently, the formation of an indanone has been observed with boron trifluoride in ether when two additional phenyl substituents are present in the α'-position.[17] After our work was completed, the reaction of diazoacetophenone with boron trifluoride in ether was reported to lead to a bisphenacyldiazonium–boron trifluoride

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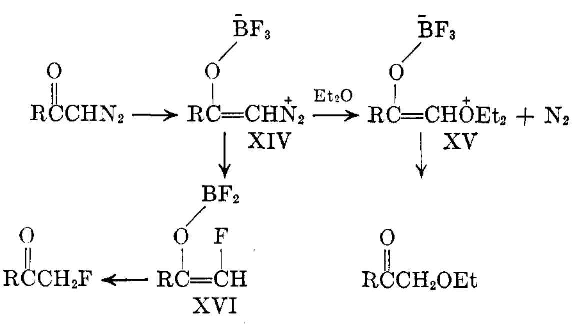

Figure 2

complex by loss of one mole of nitrogen, followed by a second condensation to an azobisfuran in unspecified yield.[21]

The course of the reaction of the diazo ketones VIII and IX is interpreted as indicated in Figure 2. Nucleophilic attack by ether at the diazo carbon of XIV would lead to the oxonium ion XV and subsequently to the ethoxy ketone, a path typical of the cleavage of ethers with powerful electrophiles. The detachment of a fluoride nucleophile in the production of the fluoroketones through XVI is reminiscent of the formation of boron difluoride chelates of 1,3-dicarbonyl compounds.[22] A very similar reaction involving the transfer of fluoride ion from boron to carbon has been observed[23] in the formation of fluorohydrins from steroidal epoxides.[24]

Experimental

1-Acetoxy-3-(*o*-anisyl)-2-propanone (Va).—*o*-Methoxyphenylacetyl chloride was prepared in 86% yield from *o*-methoxyphenylacetic acid[25] by refluxing for 30 min. with thionyl chloride, b.p. 105–110° (0.70 mm.)

A solution of 1 diazo-3-(*o*-anisyl)-2-propanone[8] (I) was obtained by addition of 7.36 g. (0.04 mole) of the acid chloride to an excess (0.16 mole) of diazomethane in ether.[26] After standing for 2 days, 10 ml. of glacial acetic acid was added and the solution was stored for another day. Evaporation of the ether and rapid distillation through a small Vigreux column at 0.50 mm. afforded four fractions: b.p. (1) 125–130°, 2.50 g.; (2) 132–139°, 0.7 g.; (3) 139–153°, 0.5 g.; and (4) 153–180°, 0.4 g. Vapor phase chromatography[27] of fraction 1 showed a major component (80%) and two unidentified minor peaks with shorter retention times. Fractions 2 and 3 were homogeneous by vapor phase chromatography and the single component corresponded to the major peak of 1. From the area under the peaks and the weight of the fractions, the yield of Va was estimated as 42%. Fraction 2, used for infrared spectrum[28] (and n.m.r.), showed strong absorption bands at 5.70 and 5.83 μ (C=O) and at (7.8–8.2 μ (ester and Ar—O—R). The proton n.m.r. spectrum[29] (20% deuteriochloroform) showed a multiplet at 2.73 τ and singlets at 5.31, 6.25, 6.35, and 7.93 τ with relative intensities 5:2:3:2:3, corresponding to C_6H_5, $—COCH_2O—$, $CH_3O—$, $Ar—CH_2CO—$ and $—COCH_3$, respectively.

Fraction 2 was converted to the semicarbazone (69% yield), m.p. 147–148°, after recrystallization from methanol.

Anal. Calcd. for $C_{13}H_{17}N_3O_4$: C, 55.90; H, 6.14; N, 15.05. Found: C, 55.65; H, 6.03; N, 15.07.

Fraction 1 was converted to the 2,4-dinitrophenylosazone, m.p. 259–260°, after recrystallization from acetic acid.

Anal. Calcd. for $C_{22}H_{18}N_8O_9$: C, 49.07; H, 3.37. Found: C, 49.57; H, 3.55.

3-Chromanone (VI) and 1-Hydroxy-3-(*o*-anisyl)-2-propanone (Vc).—1-Diazo-3(*o*-anisyl)-2-propanone (I) was prepared from 0.01 mole of the acid chloride. After evaporation of the ether, I was dissolved in 40 ml. of dioxane and 100 ml. of water. Twenty-one milliliters of 0.192 *N* sulfuric acid (0.004 eq.) was added to this solution over a 5-min. period with stirring. After a period of 20 hr., 0.079 mole of nitrogen had been collected over water and the rate of gas evolution was negligible. The dioxane was evaporated and the residue extracted with ether. After drying, the ether was evaporated and the product distilled at 0.5 mm. to give four fractions: b.p. (1) 82°, 0.51 g.; (2) 90–112°, 1.29 g.; (3) 113–118°, 2.63 g.; and (4) 114°, 0.38 g.

On the silicone column, fraction 1 gave one sharp peak with a shoulder; the major component was identified as 3-chromanone (15% yield) by conversion to the semicarbazone (48% yield), m.p. 188–189° after recrystallization from methanol (lit.,[7] m.p. 188.5°).

Anal. Calcd. for $C_{10}H_{11}N_3O_2$: C, 58.55; H, 5.40; N, 20.48. Found: C, 58.21; H, 5.15; N, 20.28.

The infrared spectrum of VI contained bands at 5.78 μ (C=O), 8.00 μ (Ar—O—R), and 9.52 μ (R—O—R). There was also a weak band at 2.87 μ, suggesting contamination by the hydroxy compound Vc. The proton n.m.r. spectrum (20% deuteriochloroform) showed a multiplet at 3.10 τ and singlets at 5.68 and 6.48 τ, relative intensities 2:1:1, corresponding to aryl, $—COCH_2O—R$ and $ArCH_2CO$ protons, respectively. There were also two minor peaks; one at 6.20 τ was apparently due to methoxy, representing 10% of Vc as an impurity.

Fraction 3 showed two peaks by gas chromatography. The major component with longer retention time was characterized as 1-hydroxy-3-(*o*-anisyl)-2-propanone as follows. Oxidation with periodic acid indicated 80% purity. The infrared spectrum showed strong absorption at 2.85 μ (OH); 5.80 μ (C=O); and 8.00 μ (Ar—O—R). The proton n.m.r. spectrum (20% deuteriochloroform) showed a multiplet at 3.10 τ and single peaks at 5.74, 6.23, 6.33, and 6.72 τ, relative intensities 4:2:3:2:1; corresponding to aryl, $—COCH_2OH$, $—OCH_3$, $ArCH_2CO—$, and OH, respectively. The alcohol was further characterized by conversion to the 2,4-dinitrophenylosazone whose infrared spectrum was identical with that of the 2,4-dinitrophenylosazone from Va. The yield of Vc was estimated to be 19% from vapor phase chromatography peak area. The minor component in fraction 3 was proved to be VI by peak enhancement.[30]

Di(*o*-anisyl)-β-ketopropyl sulfate (Vb).—To an ether solution of I from 0.04 mole of the acid chloride was added 2.04 g. (0.04 equiv.) of concd. sulfuric acid. Some tar was formed which was insoluble in both water and ether. The ether solution was washed twice with water, dried over anhydrous sodium sulfate, and evaporated. Benzene was added and evaporated to remove the last traces of water. The solid was filtered and recrystallized from benzene to give 1.62 g. (19% yield) of white crystals of Vb, m.p. 113°.

Anal. Calcd. for $C_{20}H_{22}SO_8$: C, 56.87; H, 5.25. Found: C, 56.84; H, 5.19.

The mother liquor was evaporated and distilled at 0.5 mm.: b.p. (1) 83–87°, 0.43 g.; (2) 100–104°, 0.34 g. Fraction 1 showed two peaks of nearly equal area on vapor phase chromatography with two peaks of nearly equal area on vapor phase chromatography with 10-ft. silicone column. The peak with shorter retention time proved to be 3-chromanone by peak enhancement. Fraction 1 yielded a semicarbazone (40% yield), m.p. 181–183°, after three recrystallizations from methanol, whose infrared spectrum was identical with that of the semicarbazone of VI.

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[24] The possibility that the fluoro ketones arise by reaction with hydrogen fluoride formed by hydrolysis of boron trifluoride with ambient moisture seems remote. The liberation of fluoride ion from the strong acid HBF_3OH is slow, and, if this were the pathway, the α-hydroxy ketone, rather than the fluoro ketone, would be expected.

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[27] The chromatograms were obtained with a 10-ft. column packed with GE-SF96 silicone suspended on firebrick, using a Wilkens Aerograph Master A-100 instrument; we appreciate the helpful advice of Mr. N. Heindel on vapor phase chromatography.

[28] The infrared spectra were determined with a Baird Model B recording spectrometer fitted with a sodium chloride prism.

[29] N.m.r. spectra were obtained at 60 Mc. with Varian A-60 instrument; we are grateful for helpful discussions of the data with Dr. H. C. Beachell.

[30] Fraction 1 from boron trifluoride reaction was used as authentic VI for peak enhancement.

Fraction 2 gave three peaks with gas chromatography. The first peak (second largest area) had the shortest retention time, the same as 3-chromanone; the second peak (largest area) was unidentified; the third peak was a minor one. The second peak represented approximately a 10% yield of the unidentified product. Fraction 2 formed a semicarbazone in very low yield, whose infrared spectrum was identical with that of the semicarbazone of 1-hydroxy-3-(*o*-anisyl)-2-propanone. The yield of 3-chromanone was estimated as 4% by vapor phase chromatography.

Hydrolysis of Di(*o*-anisyl)-β-ketopropylsulfate.—One gram of Vb was refluxed with 1 ml. of concd. hydrochloric acid and 10 ml. of water for 5 hr. on the steam bath. The product was extracted with ether and distilled. Gas chromatography of the distillate showed a major peak corresponding to Vc and some minor peaks caused by rearrangement of the α-hydroxy ketone.

3-Chromanone (VI) Using Boron Trifluoride Etherate.—To 4.32 g. (0.03 mole) of boron trifluoride etherate[31] dissolved in 100 ml. of anhydrous ether was added a solution of I (prepared from 0.02 mole of acid chloride without isolation) in 10 ml. of anhydrous ether; nitrogen was rapidly evolved. The ether layer was washed with water, dried, and evaporated. Benzene was added and evaporated to complete the drying. The residue was distilled at 0.50 mm.: b.p. (1) 84–88°, 1.04 g.; (2) 88–113°, 0.13 g.; (3) 113–116°, 0.41 g.; (4) residue, 0.43 g. Fraction 1 was shown to be homogeneous by gas chromatography and yielded a semicarbazone (78% yield), m.p. 183–185°, identical by infrared spectrum with the semicarbazone of 3-chromanone. The yield of VI was 35%. Fraction 3 showed four peaks, one of which proved to be VI; another corresponded to 1-hydroxy-3-(*o*-anisyl)-2-propanone (Vc) by peak enhancement.[32] The estimated yield of Vc was 2%.

1-Fluoro-4-(*o*-anisyl)-2-butanone.—β-(*o*-Anisyl)propionyl chloride, b.p. 110° (0.75 mm.), was prepared in 80% yield by treatment of *o*-methoxyhydrocinnamic acid (m.p. 88–89°) with thionyl chloride. An ether solution of 1-diazo-4-(*o*-anisyl)-2-butanone was prepared, without isolation of the diazo ketone, by addition of 19.8 g. (0.10 mole) of β-(*o*-anisyl)propionyl chloride to 0.04 mole of diazomethane. To 14.2 g. (0.10 mole) of boron trifluoride etherate in 225 ml. of anhydrous ether was added rapidly the diazo ketone in 85 ml. of anhydrous ether at ice bath temperature. After the usual 2-hr. period of standing at room temperature, the product was worked up as in previous experiments to yield two fractions boiling at 0.8 mm.: b.p. (1) 116–121°, 0.76 g.; (2) 122–134°, 1.44 g.

The infrared spectrum of fraction 1 had bands at 5.72 and 5.78 μ (C═O); 8.00 μ (Ar—O—R); 9.47 and 9.64 μ (C—F). The proton n.m.r. spectrum (20% carbon tetrachloride) showed a multiplet at 3.08 τ for aromatic protons; a doublet at 5.45 τ, with $J = 47$ c.p.s. for methylene between carbonyl and fluorine; a singlet at 6.32 τ for methoxy, and a multiplet at 7.25 τ for the two methylenes between phenyl and carbonyl. The relative intensities were 4:2:3:4, respectively. There were a few very small peaks, one of them, a triplet, was recognized as the methyl of the ethyl group at 8.88 τ, representing 10% of 1-ethoxy-4-(*o*-anisyl)-2-butanone as impurity. Fraction 1 afforded a 2,4-dinitrophenylhydrazone, m.p. 148–149°.

Anal. Calcd. for $C_{17}H_{17}N_4FO_5$: C, 54.25; H, 4.57; F, 5.05. Found: C, 54.47; H, 4.52; F, 3.98.

1-Fluoro-3-phenyl-2-propanone (X) and 1-Ethoxy-3-phenyl-2-propanone (XII).—1-Diazo-3-phenyl-2-propanone (VII) was prepared by addition of 46.5 g. (0.30 mole) of phenylacetyl chloride to an excess (0.80 mole) of diazomethane in ether. After standing for a day, the ether was evaporated to yield the diazo ketone, m.p. 43–44°.[33] The diazo ketone was dissolved in 250 ml. of anhydrous ether and added in 3 min. to 42.6 g. (0.30 mole) of boron trifluoride etherate in 675 ml. of anhydrous ether at ice bath temperature. Nitrogen evolution was very rapid. Two hours later, the ether solution was washed with water, with sodium carbonate solution, and again with water. Three fractional distillations through a small Vigreux column at 2 mm. gave three fractions: b.p. (1) 97–99°, 6.70 g.; (2) 99–120°, 6.80 g.; (3) 120–122°, 8.90 g. Before analysis these fractions were combined with the corresponding fractions of another run and fractionally distilled twice more. Fraction 1 gave a positive test for fluorine on sodium fusion and a negative test with periodic acid. The infrared spectrum showed bands at 5.70 and 5.76 μ (C═O); 9.48 and 9.64 μ (C—F). Before running the n.m.r., fraction 1 was further purified by preparative vapor chromatography on a 5-ft. silicone-on-Chromosorb column at 220°. The proton n.m.r. spectrum (20% carbon tetrachloride) showed a multiplet at 2.90 τ for aromatic protons, a doublet at 5.39 τ, with $J = 47$ c.p.s. for methylene between carbonyl and fluorine, and a doublet at 6.33 τ, with $J = 3.2$ c.p.s. for methylene *alpha* to phenyl and carbonyl. The relative intensities were 5:2:2. The two preparations yielded 1-fluoro-3-phenyl-2-propanone (X) in 22.5 and 23.4% yield, respectively. Further characterization of fraction 1 involved conversion to the 2,4-dinitrophenylhydrazone, m.p. 96–97°.

Anal. Calcd. for $C_{15}H_{13}N_4FO_4$: C, 54.22; H, 3.94; F, 5.72. Found: C, 54.56; H, 4.40; F, 5.55.

Conversion of X to phenylacetone was accomplished by refluxing 200 mg. of fraction 1 with 5 ml. of 15% sodium iodide in acetone for 48 hr. The acetone was evaporated and the residue treated with 50 ml. of chloroform and 10 ml. of 57% hydriodic acid. After washing the chloroform solution with saturated potassium iodide solution and dilute sodium thiosulfate solution, the solvent was evaporated, and the residue was converted to 201 mg. (47% yield) of the 2,4-dinitrophenylhydrazone, m.p. 147–148°; mixed melting point with the derivative of authentic phenylacetone was not depressed.

Fraction 3 was characterized as 1-ethoxy-3-phenyl-2-propanone (XII) by infrared spectrum 5.75 μ (C═O); 8.95 μ (R—O—R). The proton n.m.r. spectrum (20% deuteriochloroform) showed a multiplet at 2.80 τ for aromatic protons; a singlet at 5.98 τ for methylene alpha to phenyl and carbonyl; a singlet at 6.30 τ for methylene between carbonyl and ether oxygen; a quadruplet at 6.55 τ, with $J = 7$ c.p.s. for methylene of ethyl group; and a triplet at 8.82 τ, with $J = 7$ c.p.s. for methyl of ethyl group. The relative intensities were 5:2:2:2:3:. Fraction 3 formed a 2,4-dinitrophenylhydrazone, m.p. 133–134°.

Anal. Calcd. for $C_{17}H_{18}N_4O_5$: C, 56.98; H, 5.06; N, 15.64. Found: C, 57.22; H, 5.40; N, 15.48.

The yield of XII was 23.1% and 31.9% for the two preparations.

1-Fluoro-4-phenyl-2-butanone (XI) and 1-Ethoxy-4-phenyl-2-butanone (XIII).—1-Diazo-4-phenyl-2-butanone[34] (IX) from 0.30 mole of hydrocinnamoyl chloride was added without isolation to 0.3 mole of boron trifluoride etherate and the product worked up as in the previous experiment. Three fractional distillations at 2 mm. gave three fractions: (1) b.p. 102–110°, 7.1 g.; (2) 110–128°, 1.8 g.; (3) 128–134°, 8.5 g.

Fraction 1 was redistilled and the center cut passed through a 5-ft. silicone preparative column. The infrared spectrum of this purified sample showed bands at 5.75 μ (C═O) and 9.47 μ (C—F). The proton n.m.r. spectrum (neat) was consistent with 1-fluoro-4-phenyl-2-butanone. There was a doublet in 5–6 τ range for methylene between carbonyl and fluorine, with $J = 47$ c.p.s. Fraction 1 yielded a 2,4-dinitrophenylhydrazone, m.p. 146–148°.

Anal. Calcd. for $C_{16}H_{15}N_4FO_4$: C, 55.49; H, 4.56; N, 16.17; F, 5.49. Found: C, 55.38; H, 4.44; N, 16.02; F, 6.03.

The yield of XI was 16.2%. The structure of XI was further proved by conversion to the 2,4-dinitrophenylhydrazone of 4-phenyl-2-butanone (45% yield), m.p. 123–125° (lit.,[35] 128.5–129°), following the procedure of the previous experiment.

Fraction 3 had absorption bands at 5.80 μ (C═O); 9.00 μ (R—O—R). The proton n.m.r. spectrum was consistent with 1-ethoxy-4-phenyl-2-butanone (yield 16.2%). The 2,4-dinitrophenylhydrazone melted at 115–117°.

Anal. Calcd. for $C_{18}H_{20}N_4O_5$: C, 58.06; H, 5.41; N, 15.05. Found: C, 58.33; H, 5.67; N, 14.90.

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[31] The boron trifluoride etherate was distilled just prior to use, b.p. 126°.

[32] Fraction 3 from the water dioxane run was used for peak enhancement of Vc.

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