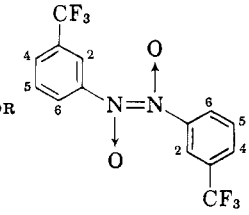
TABLE I

N.M.R. DATA FOR



H atom	τ[a]	Mult.	J[b]
2	1.57	b	...
4	2.39	s	...
5	2.38	AB	7.6
6	1.50	AB	7.6

ϕ[c] for F atom of CF_3 = 63.62

b = broad
s = sharp
AB = type system[b]

[a] See ref. 6. [b] See ref. 7. [c] See ref. 8.

(2.5 moles) contained in a three-necked round-bottom flask fitted with a reflux condenser, stirrer, and dropping funnel. The dropping funnel was replaced by a thermometer and reaction was allowed to occur for an additional 24 hr. at 85°. The excess ethyl mercaptan and diethyl disulfide were removed by steam distillation. The residual aqueous alkaline mixture was extracted with benzene. The aqueous layer was discarded and the benzene layer was evaporated to dryness. The residue was dissolved in *n*-hexane and the solution passed through a 72 × 1 in. column filled with activated alumina. The column was developed with hexane. The first three 1-l. fractions contained 20 g. of sulfur-free white compound that melted at 48.5–49.0° after recrystallization from methanol. Fractions 4 and 5 contained 5 g. of a mixture of products, m.p. 45–60°. The infrared spectra of these fractions indicated that they were a mixture of the compound melting at 48.5–49.0° and the azoxy compound eluted next from the column. Fraction 6 contained 1.5 g. of a yellow compound (m.p. 127–129°). The compound was recrystallized from ethanol to give yellow crystals (m.p. 130–131°) that were identified as 4,4′-diethylmercapto-3,3′-ditrifluoromethylazoxybenzene by elemental analysis and by comparison of the infrared spectrum with those of similar azoxy compounds.[9] The compound gave a deep red-purple color when dissolved in concentrated sulfuric acid indicative of an aromatic azoxy containing alkyl mercapto-substituent in the *para* position.[9]

Anal. Calcd. for $C_{18}H_{16}ON_2S_2F_3$: C, 47.57; H, 3.55; S, 14.12. Found: C, 47.2; H, 4.0; S, 13.8.

Elemental analysis of the white compound melting at 48.5–49.0° indicated an empirical formula of $C_7H_4ONF_3$.

Anal. Calcd. for $C_{14}H_8O_2N_2F_6$: C, 47.98; H, 2.30; N, 8.00; O, 9.14; F, 32.55; mol. wt., 350. Found: C, 48.3; H, 2.49; N, 7.74; O, 8.98; F, 33.0; mol. wt., 356.

The molecular weight at 5° and at 80° was measured as 356 but the value decreased steadily when solvents of increasing boiling points were used, indicating that dissociation increased with temperature above 80°. The infrared spectrum and n.m.r. data for this compound are shown in Fig. 1 and Table I, respectively.

A sample of this compound (m.p. 48.5–49.0°) was distilled at atmospheric pressure (b.p. 295°) and showed no color formation in the vapor state or when melted. The distillate was crystallized from methanol in the form of long white thin needles (m.p. 44–46°), indicating that only little decomposition had occurred.

One gram of this compound (m.p. 48.5–49.0°) was reduced with zinc at reflux temperature for 4 hr. in 40 cc. of 10% aqueous hydrochloric acid. The solution was cooled to room temperature, made strongly alkaline, and then extracted with ether. The ether extract was dried with magnesium sulfate, separated by filtration, and evaporated to dryness. The residual oil was made to react with acetic anhydride to give the corresponding amide. The product was crystallized from aqueous methanol and then from hexane in the form of white platelets (0.9 g., m.p. 102.5–103.5°). The compound was identified as *m*-trifluoromethylacetanilide (no depression in melting point when mixed with an authentic sample).

Reduction with Zinc in Aqueous Ammonium Chloride.—Powdered zinc (0.46 mole) was added slowly to a cold mixture of *m*-trifluoromethylnitrobenzene (0.16 mole), water (500 cc.), and ammonium chloride (0.28 mole) contained in a 1-l. three-necked round-bottom flask fitted with a stirrer, reflux condenser, and an adapter for addition of solids. The mixture was allowed to react at room temperature for 6 hr. A small amount of m-$CF_3C_6H_4NH_2 \cdot ZnCl_2$ precipitated from solution, and was removed by filtration. The mother liquor was acidified with dilute aqueous hydrochloric acid and then extracted with ether. The ether extract was evaporated to dryness. The residual oil was crystallized from a methanol–water solution and 10 g. (36%) of *m*-trifluoromethylnitrosobenzene was isolated in the form of tiny slightly orange needles, m.p. 44–46°.

The aqueous acid layer from which *m*-trifluoromethylnitrosobenzene was removed by extraction with ether was made alkaline and re-extracted with ether. The ether layer was evaporated to dryness and the residue treated with acetic anhydride. The acetylated product was recrystallized from water. The compound (7 g., 22%) was isolated in the form of white platelets (m.p. 87–88°). The compound resolidified when a crystal of *m*-trifluoromethylacetamide, m.p. 102–103°, was added to the melt. This white solid remelted at 102–103°.

Reduction with Alkaline Ethanol.—A mixture of *m*-trifluoromethylnitrobenzene (0.18 mole), water (100 cc.), sodium hydroxide (0.6 mole), and ethanol (0.5 mole) was allowed to react at reflux temperature for 24 hr. to give a deep red solution. The solution was diluted with water and extracted with benzene. The aqueous layer was discarded and the organic layer was evaporated to dryness. The red crystalline residue was dissolved in hexane and separated by chromatography as described previously to give *m*-trifluoromethylnitrosobenzene in the form of orange tinted delicate needles (10.5 g., m.p. 48.0–48.5°).

Acknowledgment.—The authors are indebted to Dr. G. V. D. Tiers for interpretation of the n.m.r. data. The elemental analyses and molecular weight determinations were done by the Carl Tiedke Laboratory of Teaneck, New Jersey, and by the Analytical Department of the M. W. Kellogg Company.

(6) G. V. P. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

(7) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 119.

(8) G. Filipovich and G. V. D. Tiers, *J. Phys. Chem.*, **63**, 761 (1959).

(9) H. R. Davis, J. W. Copenhaver, W. E. Hanford, and H. F. Lederle, 121st National Meeting of American Chemical Society, Buffalo, N. Y., March, 1952, p. 66-K.

On the Modified Oppenauer Oxidation

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The use of acidic reagents for oxidation of a hydroxyl group to a carbonyl function has sometimes failed with compounds containing basic nitrogen atoms,[2] particularly if the nitrogen is in the immediate vicinity of the hydroxyl. The difficulty is not necessarily circumvented by oxidation under the basic conditions of the Oppenauer procedure since the aluminum alkoxide is capable of complexing with the nitrogen[3,4a] and in some

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(2) *Inter alia* (a) quinine: P. Rabe, W. Naumann, and E. Kuliga, *Ann.* **364**, 345 (1909); (b) buphanamine: L. G. Humber and W. I. Taylor, *Can. J. Chem.*, **33**, 1268 (1955); codeine: F. Ach and L. Knorr, *Ber.*, **36**, 3070 (1903).

(3) (a) quinine: R. L. McKee and H. R. Henze, *J. Am. Chem. Soc.*, **66**, 2021 (1944); (b) 1,2-aminoalcohols: R. E. Lutz, R. H. Jordan, and W. L. Truett, *ibid.*, **72**, 4085 (1950); (c) *cis*- and *trans*-1-amino-2-indanols: R. E. Lutz and R. L. Wayland, *ibid.*, **73**, 1639 (1951).

TABLE I
THE MODIFIED OPPENAUER OXIDATION OF QUININE

Reaction	Ketone, mole ratio to quinine	Base, mole ratio to quinine	Solvent	Temp.	Time, hr.	% Yield, crude product	% Quininone in product
1	Benzophenone, 5.0	K–O–*t*-Bu, 2.5	Benzene	R.t.[a]	1	81	9–25
2	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	Benzene	R.t.	0.5	82	82
3	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	Benzene	R.t.	1	97	88
4	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	Benzene	R.t.	12	88	96
5	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	Benzene	Reflux	2 min.	80	66
6	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	Benzene	Reflux	10 min.	85	100
7	Fluorenone, 5.0	K–O–*t*-Bu, 1.0	Benzene	R.t.	1	76	36
8	Fluorenone, 5.0	K–O–*t*-Bu, 0.1	Benzene	R.t.	1	73	2.7
9	Benzophenone, 5.0	K–O–*t*-Bu, 2.5	*t*-BuOH	R.t.	6	93	0
10	Benzophenone, 5.0	K–O–*t*-Bu, 2.5	*t*-BuOH	Reflux	0.5	92	1.8
11	Benzophenone, 5.0	K–O–*t*-Bu, 2.5	*t*-BuOH	Reflux	4.5	85	8
12	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	*t*-BuOH	R.t.	4	93	2–3
13	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	*t*-BuOH	Reflux	0.5	83	48
14	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	*t*-BuOH	Reflux	4	92	91
15	Quinone, 4.0	K–O–*t*-Bu, 2.5	Benzene	R.t.	0.5	69	1.7
16	Quinone, 4.0	K–O–*t*-Bu, 2.5	Tetrahydrofuran	R.t.	1	72	0.8
17	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	Tetrahydrofuran	R.t.	1	89	43
18	Fluorenone, 5.0	Al–(O–*t*-Bu)$_3$, 1.2	Benzene	R.t.	1	72	0
19	Fluorenone, 5.0	Al–(O–*i*-Pr)$_3$, 1.4	Benzene	Reflux	2	74	0
20	Fluorenone, 5.0	None	Benzene	R.t.	1	78	...
21	Fluorenone, 5.0	None	Benzene	R.t.	1	80	...
22	Fluorenone, 5.0	K–O–*t*-Bu, 2.5	$Me_2S \rightarrow O$	R.t.	0.1	99	0

[a] R.t. = room temperature.

manner stabilizing the amino alcohol. To avoid these difficulties, Woodward substituted potassium *t*-butoxide for the aluminum alkoxide in the Oppenauer oxidation.[4] However, this modification, which is conducted at the reflux temperature of a benzene solution for several hours, is limited to the preparation of those carbonyl compounds not sensitive to heat and strong base.

Some time ago this problem arose in the course of work on amino alcohols among the *Amaryllidaceae* alkaloids. A study of the modified Oppenauer oxidation of quinine was made with the purpose of finding milder conditions for the reaction. Quinine was chosen because it is a typical amino alcohol not oxidized by the usual Oppenauer conditions[3a] but readily oxidized by the potassium *t*-butoxide–benzophenone modification,[4a] and because the yield of ketone, quininone, could be determined conveniently by ultraviolet spectroscopy (see Experimental). The results of the study are summarized in Table I.

The most significant finding was that use of the more rapid hydride acceptor, fluorenone,[5] permits the reaction time and temperature to be decreased considerably. Thus, oxidations can be carried out in benzene solution at room temperature in one-half to one hour (reactions 2 and 3) or within about five minutes at reflux temperature (reactions 5 and 6). With the more powerful but slower hydride acceptor, quinone,[5] no appreciable oxidation occurred at room temperature (reaction 15). As expected, attempts to use the weaker, complex-forming aluminum alkoxides at room temperature or at reflux gave no oxidation (reactions 18 and 19). Furthermore, even with potassium *t*-butoxide, about 2.5 equivalents of base were required for rapid oxidation (compare reactions 7 and 8 with 3). The room temperature reactions were strongly inhibited by *t*-butyl alcohol (reaction 12), although the oxidation can be carried out in this solvent at reflux (reaction 14) if fluorenone is used. The rate of oxidation was faster in benzene (reaction 3) than in tetrahydrofuran (reaction 17) or dimethylsulfoxide (reaction 22).[6]

Since this work was completed, a number of oxidations have been done under these milder conditions, and some of these are listed in Table II. In spite of the strong base used there has been only one case of condensation to produce a fluorenylidene derivative (Table II, haemanthamine) and no case of ketone self condensation. Base-catalyzed β-elimination can take place as in the oxidation of montanine and coccinine, and some special ketonic systems (caranine) are oxidized further by fluorenone or air under the strongly basic conditions. The reactions are run in a nitrogen atmosphere in view of the ease of air oxidation of ketones in the presence of potassium *t*-butoxide.[7]

In general, good yields of oxidation products have been obtained (Table II). However, the large size of the fluorenone molecule, which must approach quite

(4) (a) R. B. Woodward, N. L. Wendler, and F. V. Brutschy, *J. Am. Chem. Soc.*, **67**, 1425 (1945); (b) R. B. Woodward and E. C. Kornfeld, *ibid.*, **70**, 2513 (1948); (c) H. Rapoport, R. Naumann, E. R. Bissell, and R. M. Bonner, *J. Org. Chem.*, **15**, 1103 (1950).

(5) R. H. Baker and H. Adkins, *J. Am. Chem. Soc.*, **62**, 3305 (1940).

(6) D. J. Cram, M. R. V. Sahyun, and G. R. Knox [*J. Am. Chem. Soc.* **84**, 1734 (1962)] have found the use of dimethyl sulfoxide or tetrahydrofuran as solvent to increase the rate of several reactions. In the Oppenauer reaction benzene is superior to either of these solvents, probably for the same reason these authors suggest for the superiority of tetrahydrofuran over dimethyl sulfoxide in the Cope elimination; less solvation energy of the potassium quinine alkoxide has to be overcome in going to the transition state for hydride transfer to fluorenone.

(7) E. J. Bailey, D. H. R. Barton, J. Elks, and J. F. Templeton, *J. Chem. Soc.*, 1578 (1962).

TABLE II

OXIDATIONS BY THE MODIFIED OPPENAUER METHOD

Compound Oxidized	Product	Yield, %
α-Dihydrocaranine	α-Dihydrocaranone	65[a]
Caranine	a Phenanthridinium betaine	86[b]
Dihydroundulatine	Epioxodihydroundulatine	75[c]
Montanine	Dehydrococcinine	60[d]
Coccinine	Dehydrococcinine	35[d]
Dihydrobuphanamine	Oxodihydrobuphanamine	58[e]
Dihydrohaemanthamine	Fluorenylideneoxodihydrohaemanthamine	...[f]
Yohimbine	Yohimbinone	51[g]
β-Yohimbine	Yohimbinone	17[g]
Corynanthine	Yohimbinone	18[g]
Deoxyajmaline	Deoxyajmalone	85[h]
Dihydroambelline	Recovered starting material	81[i]
Falcatine	Recovered starting material	...[j]
Dihydrocrinine	Oxodihydrocrinine	51[k]
Cholesterol	Δ⁴-3-Cholestenone	44[l]
Crinamine	Recovered starting material	45[i]

[a] E. W. Warnhoff and W. C. Wildman, *J. Am. Chem. Soc.*, **79**, 2192 (1957). [b] H. M. Fales, E. W. Warnhoff, and W. C. Wildman, *ibid.*, **77**, 5885 (1955). [c] E. W. Warnhoff and W. C. Wildman, *ibid.*, **82**, 1472 (1960). [d] Y. Inubushi, H. M. Fales, E. W. Warnhoff, and W. C. Wildman, *J. Org. Chem.*, **25**, 2153 (1960). [e] H. M. Fales and W. C. Wildman, *ibid.*, **26**, 881 (1961). [f] H. M. Fales, personal communication. [g] M.-M. Janot, R. Goutarel, E. W. Warnhoff, and A. LeHir, *Bull. soc. chim. France*, 637 (1961). [h] M. F. Bartlett, R. Sklar, W. I. Taylor, E. Schlittler, R. L. S. Amai, P. Beak, N. V. Bringi, and E. Wenkert, *J. Am. Chem. Soc.*, **84**, 622 (1962). [i] E. W. Warnhoff, unpublished work. [j] W. C. Wildman, personal communication. [k] W. C. Wildman, *J. Am. Chem. Soc.*, **80**, 2567 (1958). [l] Present work.

close to the hydroxyl bearing carbon for hydride transfer, makes the reaction subject to stringent steric requirements, and there are several examples of amino alcohols not oxidized under these conditions (Table II, dihydroambelline, crinamine, and falcatine). In some of these cases (crinamine[8] and dihydroambelline[9]) the chromic acid–pyridine reagent has proved a successful alternative.

The potassium *t*-butoxide need not be freshly prepared as long as it has been protected from moisture and carbon dioxide. Commercially available alkoxide[10] should meet these requirements. The use of sublimed potassium *t*-butoxide is indicated whenever the alcohol to be oxidized contains a group which might react with the hydroxide or carbonate invariably present in unsublimed material (yohimbine, β-yohimbine, corynanthine, Table II).

The method is most readily applied to amino alcohols which can be separated by acid extraction from the fluorenone–fluorenol mixture. However, nonbasic alcohols, *e.g.*, cholesterol, can be oxidized and purified by chromatography, distillation, or sublimation. During the reaction even at room temperature some fluorenone is cleaved by base to 2-biphenylcarboxylic acid and this must be taken into account in isolation of acidic oxidation products.

Experimental

Reagents.—*t*-Butyl alcohol was distilled from sodium. Commercial fluorenone, benzophenone, and quinine were used without purification. Reagent grade benzene was dried over sodium.

Typical Oxidation Procedure.—Potassium metal (0.5 g., 0.012 g.-atom) was dissolved in 30 ml. of *t*-butyl alcohol. The excess alcohol was removed by distillation at atmospheric pressure and then at aspirator vacuum. The solid potassium *t*-butoxide was dried at 120–130° at aspirator vacuum for 15–30 min.

To the dry *t*-butoxide was added 1.62 g. (5.0 mmoles) of dry quinine, 40 ml. of dry benzene (tetrahydrofuran or dimethyl sulfoxide), 4.50 g. (25 mmoles) of dry fluorenone, and a magnetic stirring bar. The reaction mixture was immediately put under a nitrogen atmosphere and stirred (with or without heating) for the period specified in Table I. The reaction mixture turned an opaque brown on mixing. The oxidation was terminated by the addition of 30–50 ml. of water, whereupon the color lightened to an orange-yellow.

The reaction mixture was diluted with 30–50 ml. of ether, and the two phases were separated. The aqueous layer was washed with two portions of ether. The combined organic layers were extracted with four portions of 5% hydrochloric acid. The combined aqueous acid solutions were washed twice with ether and poured into a mixture of ice and concentrated ammonium hydroxide solution. The white precipitate was extracted with three portions of ether. The ether extract was washed three times with saturated sodium chloride when the last wash was neutral. The dried (magnesium sulfate) ether solution was evaporated at reduced pressure. The yield of product varied from 70–97%.

The per cent of quininone in the product was determined from the ultraviolet extinction coefficient in absolute ethanol at 360 mμ. At this wave length pure quinine had no absorption while quininone had ε 3760. This analytical procedure was shown to be accurate to ±1% by measurements on known mixtures of quinine and quininone.

In the case of the reactions run in *t*-butyl alcohol, most of the alcohol was evaporated at reduced pressure before addition of water and ether and work-up.

The product from reaction 4, Table I, was chromatographed on 30 g. of alumina. Benzene–hexane (1:1) and pure benzene eluted **quininone**, m.p. 99–104° (hot stage), after recrystallization from cyclohexane.

When a reaction was carried out for 1 hr. at room temperature exactly as described above except that the quinine was omitted, there was recovered from the basic aqueous layer after acidification 0.59 g. of **2-biphenylcarboxylic** acid whose infrared spectrum in chloroform was identical with that of an authentic sample.

Oxidation of Cholesterol.—A mixture of the potassium *t*-butoxide prepared from 0.5 g. of potassium, 4.50 g. of dry fluorenone, 2.02 g. of dry cholesterol, and 40 ml. of dry benzene was put under nitrogen and stirred with a magnetic stirring bar for 1 hr. at room temperature. The reaction mixture was diluted with water and ether. The ether layer was separated, dried, and evaporated to leave 6.35 g. of yellow oil. Crystallization from cyclohexane removed 2.99 g. of fluorenone in three crops. The filtrate was then chromatographed on 100 g. of alumina. Pure benzene eluted **Δ⁴-3-cholestenone** which was recrystallized from cyclohexane to give 0.90 g. (44%), m.p. 80–82° undepressed on admixture with an authentic specimen.

(8) H. M. Fales and W. C. Wildman, *J. Am. Chem. Soc.*, **82**, 197 (1960)
(9) P. Naegeli, E. W. Warnhoff, H. M. Fales, R. E. Lyle, and W. C. Wildman, *J. Org. Chem.*, **28**, 206 (1963).
(10) MSA Research Corporation, Callery, Pa.

Cleavage–Elimination of Diphenylmethane from 7,7-Diphenylbicyclo[3.2.0]hept-2-en-6-one in Base[1]

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During an investigation into the synthesis and chemistry of certain strained bicyclic and polycyclic systems, we had occasion to study various methods of removing the carbonyl group from the product of the cycloaddi-

(1) From the M. S. thesis of A. C. Kovelesky, Kansas State University, 1962.