mole) of N-bromosuccinimide in 500 ml. of carbon tetrachloride there was added 100 mg. of benzoyl peroxide. The mixture was stirred and heated under reflux on the steam bath for 1 hr. in the presence of two No. 2 Photoflood lamps. The succinimide was collected by filtration. Evaporation of the solvent from the filtrate left a tan solid residue which was recrystallized from methanol to yield 15 g. (39%) of pale yellow crystals, m.p. 125–126°.

Anal. Calcd. for $C_{19}H_{24}BrNO_2$: C, 60.32; H, 6.40; N, 3.70. Found: C, 60.28; H, 6.35; N, 3.61.

2-(1-Nonenyl)cinchoninic Acid (IIIb).—To 25 g. (0.066 mole) of 2-(1-bromononyl)cinchoninic acid there were added 50 g. of finely ground potassium hydroxide and 125 ml. of *t*-butyl alcohol. The mixture was stirred and heated under reflux for 1 hr., during which time a viscous mass of salt had formed on the bottom and sides of the flask. The mixture was diluted with 100 ml. of water and acidified to pH 2 with dilute sulfuric acid. The solid was collected by filtration and washed well with water to remove the residual salts. Recrystallization from methanol gave 16.2 g. (82%) of light yellow crystals, m.p. 137–138°.

Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80. Found: C, 77.00; H, 7.94.

4-Amino-2-(1-nonenyl)quinoline (IVb).—To a solution of 2.97 g. (0.01 mole) of 2-(1-nonenyl)cinchoninic acid and 1.38 ml. (0.01 mole) of triethylamine in 25 ml. of tetrahydrofuran at 5° there was added dropwise 1.4 g. (0.013 mole) of ethyl chloroformate. The mixture was stirred for 0.5 hr. while a solution of 0.86 g. (0.013 mole) of sodium azide in 20 ml. of water was added dropwise. After stirring an additional hour at 5°, the solution was poured onto 100 g. of cracked ice and the azide was extracted into ether. A few milliliters of saturated sodium chloride solution was added to break up the resulting emulsion. The organic layer was separated and dried over anhydrous magnesium sulfate. Anhydrous methanol (10 ml.) was added to the filtered solution and the ether was removed under reduced pressure. The residue was boiled for 2 hr. with 10 ml. of anhydrous methanol in 35 ml. of benzene. The benzene was removed under reduced pressure and the carbamate was heated under reflux for 5 hr. in aqueous methanolic potassium hydroxide prepared from 2 g. of potassium hydroxide pellets, 20 ml. of methanol, and 5 ml. of water. The mixture was diluted with 50 ml. of water and the amine was extracted into ether. The ether was removed under reduced pressure and the residue was dissolved in 20 ml. of acetone. The pH was adjusted to 2 by the addition of dilute (1:1) nitric acid. The amine salt was collected by filtration and washed with acetone to yield 1.07 g. (33%) of off-white crystalline 4-amino-2-(1-nonenyl)quinoline nitrate, m.p. 163–164°.

Anal. Calcd. for $C_{18}H_{25}N_3O_3$: C, 65.23; H, 7.60; N, 12.68. Found: C, 65.58; H, 7.70; N, 12.63.

2-(1-Nonenyl)-4-quinolinol (Vb, Pyo III).—To a light yellow solution of 2.64 g. (0.08 mole) of 4-amino-2-(1-nonenyl)quinoline nitrate dissolved in 20 ml. of trifluoroacetic acid at 5° there was added 0.52 g. (0.08 mole) of sodium nitrite. After the deep red solution was stirred for 0.5 hour at 5°, 7 ml. of water was added all at once, and the solution was stirred for an additional 0.5 hour. The mixture was poured into 50 ml. of water and extracted with ether. The ether layer was separated, washed with water, and evaporated under reduced pressure to obtain a red oil. The oil was dissolved in 25 ml. of acetone and diluted with a saturated aqueous sodium carbonate solution to pH 9. The tan crystals were collected by filtration, washed with water, and dissolved in 20 ml. of methanol. After a carbon treatment, the filtrate was evaporated to obtain a yellow crystalline solid. Recrystallization from acetone yielded 1.2 g. (56%) of pale yellow needles, m.p. 151–152°.

Anal. Calcd. for $C_{18}Y_{23}NO$: C, 80.25; H, 8.61; N, 5.20. Found: C, 80.05; H, 8.60; N, 5.08.

The infrared spectrum was identical with the spectrum of authentic 2-(1-nonenyl)-4-quinolinol (Pyo III).[2] The *trans* character of the double bond in the nonenyl side chain was clearly shown by the strong band at 965 cm.$^{-1}$ which is characteristic of a *trans*-disubstituted ethylene.[11] Likewise the other compounds bearing alkenyl groups showed a similar absorption band. Lack of absorption in the region of 690 cm.$^{-1}$ indicated the absence of *cis* isomer in every case.

Acknowledgment.—The authors wish to thank Richard M. Downing for the microanalyses and Donald Evans and David Whitehead for the infrared spectra.

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[11] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y. 1958, p. 45.

A Convenient Synthesis of Tricyclic 2-Quinolizidones[1]

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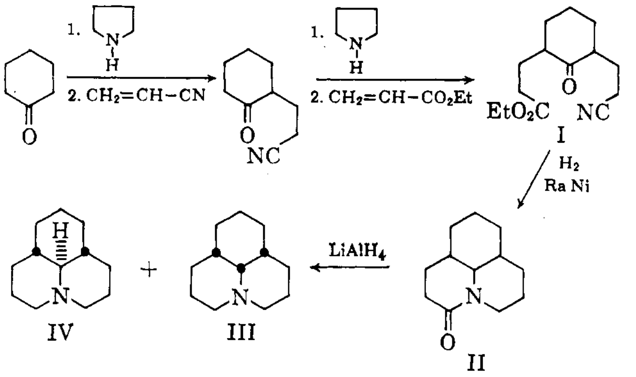
We have previously shown the utility of our quinolizidine synthesis in the preparation of matrine,[2] matridine,[3] and various tricyclic systems with nitrogen at a bridgehead.[4] This work reports a modification of that scheme which allows its application to the synthesis of 2-quinolizidones typified by II.

This new route is outlined below.



The steps are all unexceptional and follow closely the basic pathway we investigated earlier. Key in the synthesis is the Stork enamine synthesis[5] for the preparation of I and the reductive cyclization of I to provide II. We have discussed the latter reaction previously.[4]

The structure and stereochemistry of the quinolizidone (II) were established by lithium aluminum hydride reduction of II to a mixture of hexahydrojulolidines, which consisted of 60% III and 40% IV.

Experimental[6]

Ethyl β-[2-(1-Oxo-6-cyanoethyl)]cyclohexylpropionate (I).—The pyrrolidine enamine was prepared by refluxing 35 g. (0.23 mole) of the above ketone with 57 g. (0.81 mole) of pyrrolidine in 200 ml. of anhydrous benzene. After 18 hr. the theoretical amount of water had been collected in an azeotrope separator. The excess pyrrolidine and benzene were removed *in vacuo* and

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[1] We wish to acknowledge the support of this research by the National Institutes of Health through Research Grant RG-7902. This work was taken in part from the M.S. Dissertation of B. A. Hall and the Ph.D. Dissertation of K. P. Singh.

[2] L. Mandell, K. P. Singh, J. T. Gresham, and W. Freeman, *J. Am. Chem. Soc.*, **85**, 2682 (1963).

[3] L. Mandell and K. P. Singh, *ibid.*, **83**, 1766 (1961).

[4] L. Mandell, J. U. Piper, and K. P. Singh, *J. Org. Chem.*, **28**, 3440 (1963).

[5] G. Stork, A. Brizzolera, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

[6] Melting points and boiling points are uncorrected. Elemental analyses were done by Drs. G. Weiler and F. B. Strauss, Oxford, England.

the crude enamine was taken up in 200 ml. of N,N-dimethylformamide. Twenty-three grams (0.23 mole) of ethyl acrylate was added dropwise to the enamine solution at reflux and the reaction mixture was refluxed for 40 hr. The solvent was removed *in vacuo* on a steam bath and the enamine was hydrolyzed by refluxing for 2 hr. with 150 ml. of water and 8 ml. of glacial acetic acid. After cooling, the mixture was extracted thoroughly with ether and the ether extract was washed with dilute acid, base, and water, and finally dried over sodium sulfate. The ether was removed and the residue was distilled to afford 18.6 g., b.p. 160–162° at 1 mm. Allowing for recovered starting material the yield was 63%.

Anal. Calcd. for $C_{14}H_{21}NO_3$: C, 66.9; H, 8.4; N, 5.6. Found C, 66.9; H, 8.5; N, 5.6.

3-Oxohexahydrojulolidine (II).—Twenty grams (0.80 mole) of I was hydrogenated in 100 ml. of absolute ethanol at 1800 p.s.i. and 125° using 7 g. of W-7 Raney nickel as catalyst. The catalyst was removed by filtration, the solvent was removed *in vacuo,* and the residue was distilled, giving 8.3 g. (54%) of II, b.p. 144–150° at 0.1 mm.

Anal. Calcd. for $C_{12}H_{19}NO$: C, 74.5; H, 9.9; N, 7.2. Found: C, 74.2; H, 9.9; N, 7.1.

Reduction of II to Hexahydrojulolidine.—To a solution of 1.2 g. of powdered lithium aluminum hydride in 40 ml. of dry tetrahydrofuran was added 6.1 g. of II in 20 ml. of tetrahydrofuran. The reaction was refluxed 4 hr. and then treated first with ethyl acetate and finally with water to destroy the unused hydride. The mixture was filtered, the gelatinous precipitate was washed well with tetrahydrofuran, and the filtrate and washings were combined and dried over sodium sulfate. Removal of solvent and distillation gave 3.6 g. (72%) of hexahydrojulolidine, b.p. 110–120° at 5 mm.

Three grams of this product was chromatographed following the procedure of Bohlmann[7] to give 1.5 g. of III, picrate m.p. 225–226°, and 1.0 g. of IV, picrate m.p. 186–187°.

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[7] F. Bohlmann and C. Arndt, *Chem. Ber.*, **91**, 2167 (1958).

Preparation of Quinol Ethers

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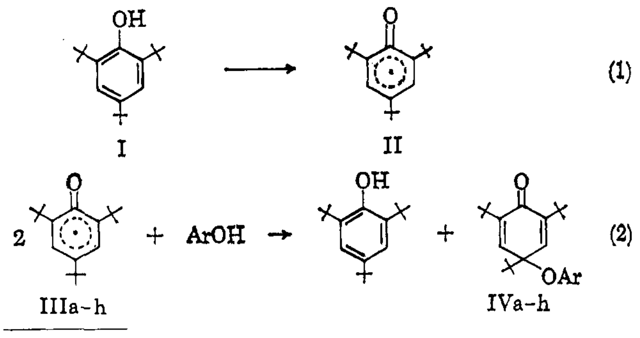
Chemical reactions of radicals obtained by oxidation of sterically hindered phenols such as 2,4,6-tri-*t*-butylphenol (I) have been widely studied during recent years.[1-3] An interesting result was reported by Müller, Ley and Schlechte, who found that 2 moles of 2,4,6-tri-*t*-butylphenoxyl (II) react with 1 mole of a phenol (III) to form 1 mole of 2,4,6-tri-*t*-butylphenol (I) and 1 mole of a 4-quinol ether (IV)[4] (reactions 1 and 2). For preparative use this reaction has the disadvantage that the quinol ether is often difficult to separate from the simultaneously formed I. Reoxidation of I to II with potassium ferricyanide in this reaction has been practiced, but this procedure is very tedious.[4,5]



Another method of preparing quinol ethers of this type is the reaction of 4-bromo-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one with alkali phenolates.[4] The reaction can be carried out in an organic solvent; however, separate preparation of the starting materials from the phenols is required.

Our interest in oxidations with active manganese dioxide[6] has now led to a very convenient method for the preparation of quinol ethers. We observed that 2,4,6-tri-*t*-butylphenol (I) in benzene solution in contact with active manganese dioxide instantly forms the blue solution of 2,4,6-tri-*t*-butylphenoxyl (II) in apparently high yield. Successive additions of 1 mole of a phenol (IIIa–h) per mole of 2,4,6-tri-*t*-butylphenol (I) to the MnO_2-containing radical solution leads to irreversible discharge of the blue color. Since the 2,4,6-tri-*t*-butylphenol formed in the reaction is immediately reoxidized by the manganese dioxide present, the isolation of the quinol ether is no longer difficult. Filtration and evaporation of the solvent give the quinol ethers (IVa–h) in excellent yield and high state of purity. We have used this method to prepare quinol ethers previously not reported (see Table I), including the reaction product of 2,4,6-tri-*t*-butylphenoxyl with the unsubstituted phenoxy radical.

Table I

Ar in III and IV	Quinolid bands in IV (cm.$^{-1}$)
a, Phenyl	1645, 1665[a]
b, 2,4,6-Trichlorophenyl	1645, 1666[b]
c, Pentachlorophenyl	1642, 1664[b]
d, 4-Phenylmercaptophenyl	1645, 1665[b]
e, 4-Methoxyphenyl	1636, 1662[b]
f, 4-Benzoyloxyphenyl	1640, 1662[b]
g, 4-Benzyloxyphenyl	1640, 1662[b]
h, 4-Phenoxyphenyl	1645, 1665[a]

[a] Liquid film. [b] In potassium bromide.

The infrared spectra (see Table I) of all quinol ethers prepared exhibit double peaks at about 6 μ, typical for compounds with quinolid structure.[4]

Compared with known procedures for quinol ether formation, this new method appears to be the most convenient, since the starting materials are easily available, the reaction is carried out in an organic solvent, and the procedure does not involve any separation problems.

When we extended the reaction of phenols with active manganese dioxide to the cooxidation of 4-bromo-2,6-di-*t*-butylphenol (V) and pentachlorophenol (reaction 3), we isolated in excellent yield the aromatic quinone ketal VII, 4,4-bis(pentachlorophenoxy)-2,6-di-*t*-butyl-2,5-cyclohexadiene-1-one. Its structure is confirmed by analytical data (see Experimental), its infrared spectrum (bands at 1655 and 1680 cm.$^{-1}$, in KBr), and its conversion into pentachlorophenol and 2,6-di-*t*-butyl-benzoquinone-1,4 by treatment with boiling 96% ethanol.

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[1] E. Müller, A. Riecker, and K. Scheffler, *Ann. Chem.*, **645**, 92 (1961), and previous papers.

[2] C. D. Cook and N. D. Gilmour, *J. Org. Chem.*, **25**, 1429 (1960), and previous papers.

[3] For a recent review, see H. Musso, *Angew. Chem.*, **75**, 965 (1963).

[4] E. Müller, K. Ley, and G. Schlechte, *Chem. Ber.*, **90**, 2660 (1957).

[5] T. Matsuura and H. J. Cahnmann, *J. Am. Chem. Soc.*, **82**, 2055 (1960).

[6] E. Adler and H.-D. Becker, *Acta Chem. Scand.*, **15**, 849 (1961); H.-D. Becker, *ibid.*, **15**, 683 (1961); **16**, 78 (1962).