duced pressure gave 13.0 g. (70.3%) of aziridinomaleic acid dimethyl ester containing 5% aziridinofumaric acid dimethyl ester as determined by p.m.r. absorption intensities, b.p. 80–82° (0.2 mm.).

Anal. Calcd. for $C_8H_{12}NO_4$: C, 51.80; H, 5.99; N, 7.57. Found: C, 52.14; H, 6.23; N, 7.53.

Substitution of 1:1 benzene–cyclohexane solvent in the procedure gave closely similar results.

B. In Methanol.—A procedure identical with method A was employed in which methanol was substituted for dimethyl sulfoxide. The product was distilled at 80–85° (0.2 mm.) and amounted to 14.0 g. (75.7%) of a semisolid mass which proved to be a mixture of 67% aziridinofuramic acid dimethyl ester and of 33% aziridinomaleic acid dimethyl ester by examination of the p.m.r. spectrum.

An analytical sample of the pure fumarate ester, m.p. 67–70°, was obtained by crystallization from benzene–hexane.

Anal. Calcd. for $C_8H_{12}NO_4$: C, 51.80; H, 5.99; N, 7.57. Found: C, 51.92; H, 5.92; N, 7.45.

Reaction of Aziridine with Ethyl Propiolate. Method A. In Dimethyl Sulfoxide.—To 40 ml. of dimethyl sulfoxide maintained at 25–30° was simultaneously added a solution of 9.80 g. (0.10 mole) of ethyl propiolate in 40 ml. of dimethyl sulfoxide and a solution of 4.30 g. (0.10 mole) of aziridine in dimethyl sulfoxide over a 15-min. interval with magnetic stirring. The reaction solution was stirred for 1.5 hr., diluted with 100 ml. of water, and extracted with three 50-ml. portions of benzene. The benzene extracts were washed with 50 ml. of water, dried (sodium sulfate), decanted, and evaporated *in vacuo*. Distillation of the colorless, mobile residue gave 12.0 g. (85%) of *trans*-aziridinoacrylic acid ethyl ester, b.p. 98–103° (12 mm.). The spectrum possessed only maxima attributable to the *trans* ester.

Anal. Calcd. for $C_7H_{11}NO_2$: C, 59.50; H, 7.85; N, 9.93. Found: C, 59.83; H, 7.63; N, 9.82.

Method B. In Methanol.—The procedure followed was identical with that of method A, with the exception of the substitution of methanol for dimethyl sulfoxide. Distillation of the product provided 10.3 g. (73%), b.p. 89–95° (12 mm.), of a mixture of 58% *cis*-aziridinoacrylic acid ethyl ester and 42% *trans*-aziridinoacrylic acid ethyl ester determined by examination of the p.m.r. spectrum.

Anal. Calcd. for $C_8H_{11}NO_2$: C, 59.50; H, 7.85; N, 9.93. Found: C, 59.78; H, 7.95; H, 10.25.

Equilibration Experiments.—It was determined simply that the esters I and II can be quantitatively recovered unchanged from dimethyl sulfoxide and methanol, respectively, after 10 hr. at room temperature even in the presence of added aziridine. The criteria for judgment rested with the identity of the infrared and p.m.r. spectra of the esters, taken before and after the equilibration experiments.

Likewise, it was found that the ester V was unaffected by pure methanol or methanol containing aziridine after 10 hr. at room temperature. The mixture of IV and V proved to be stable to treatment with either dimethyl sulfoxide or methanol for 10 hr. at room temperature even in the presence of added aziridine.

Acknowledgment.—This work was supported, in part, by Institutional Grant IN-17F from the American Cancer Society to Purdue University.

The Reaction of O^{18}-Labeled Ethanol with Phenols and N,N′-Dicyclohexylcarbodiimide

F. L. Bach

Organic Chemical Research Section, Lederle Laboratories, Division of American Cyanamid Company, Pearl River, New York

Received December 15, 1964

In 1962 Vowinkel[1] reported the synthesis of aryl alkyl ethers from phenols and alcohols using N,N′-dicyclohexylcarbodiimide (DCC) as a condensing agent (see eq. 1). The reaction was carried out in a refluxing, inert solvent and afforded satisfactory yields when primary alcohols were used; however, poor yields were afforded using secondary or tertiary alcohols; *ortho*-substituted phenols also caused a marked decrease in ether formation.

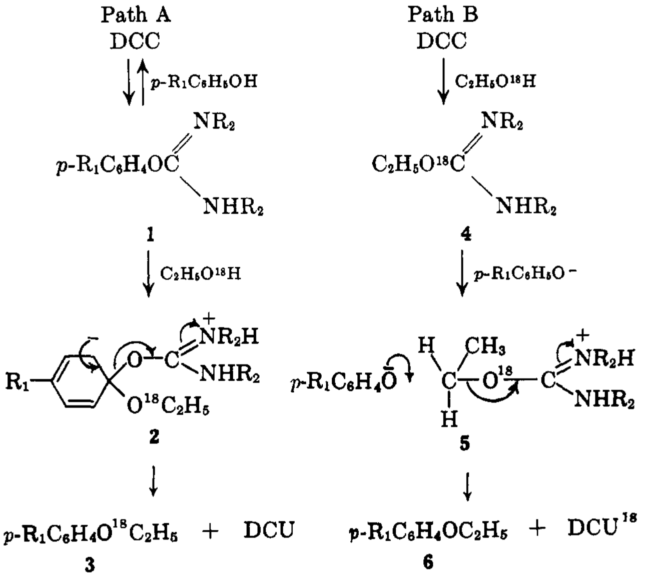
$$\mathrm{ArOH} + \mathrm{ROH} \xrightarrow{\mathrm{DCC}} \mathrm{ArOR} + \mathrm{DCU} \qquad (1)$$

Ar = phenyl or substituted phenyl
R = *n*-alkyls
DCU = N,N′-dicyclohexylurea

In 1963 an improved synthesis of aryl alkyl ethers was described[2] where phenolic substances, primary alcohols, and DCC were heated without solvent in a sealed tube at *ca.* 100° for 24 hr. This modification was repeated in our laboratories and, in every case, excellent yields were afforded (87–92%).

The mechanism proposed by Vowinkel[1] for aryl alkyl ether formation (see path A, Scheme I) in refluxing, inert solvents required the initial formation of a phenol–DCC adduct (**1**) followed by a primary alcohol attack (see **2**). The failure of secondary and tertiary alcohols to participate in this reaction was attributed to nonbonded interaction between the phenyl ring and the attacking branched alcohols. The formation of 2-arylpseudoureas (**1**) from phenols and carbodiimides has been reported[3] and is not questioned. However, there is little analogy for the final step in path A, *i.e.*, nucleophilic attack by a primary alcohol on an aromatic system.

SCHEME I



R_1 = H or NO_2
R_2 = cyclohexyl

An alternate mechanism is therefore outlined in path B (Scheme I) which requires the intermediacy of a 2-alkylpseudourea (**4**). Ordinarily, alcohols are unreactive towards carbodiimides at room temperature; however, high yields are afforded[4] when N,N′-diphenylcarbodiimide and ethanol are heated in a sealed tube (the conditions used in this study). There is also no doubt that owing to increased acidity of phenols the

---

[1] E. Vowinkel, *Chem. Ber.*, **95**, 2997 (1962).

[2] E. Vowinkel, *Angew. Chem., Intern. Ed. Engl.*, [4] **2**, 218 (1963).

[3] M. Busch, G. Blume, and E. Pungs, *J. prakt. Chem.*, [2] **79**, 513 (1909).

[4] F. Lengfeld and J. Stieglitz, *Chem. Ber.*, **27**, 926 (1894).

phenol–DCC adducts (**1**) form faster than the alcohol–DCC adducts (**4**). However, the reversibility of **1**, already described by Vowinkel,[5] would allow a build-up of the 2-alkylpseudourea (**4**) proposed in path B. Once formed **4** would be vulnerable to SN2 attack by phenate ion.[6] The poor yields given by secondary or tertiary alcohols in this system may readily be explained by proposing steric hindrance to SN2 attack in path B (see **5**).

Cogent evidence in favor of one mechanism or the other can be obtained by incorporating ethanol-O^{18} into the phenol–*n*-alcohol–DCC system. As illustrated in Scheme I only "tagged" aryl alkyl ether **3** would result from attack of ethanol-O^{18} on **1** in path A, while only "tagged" DCU (**6**) would result if path B were followed.

Preliminary experiments included the reactions of ethanol-O^{18} with phenol and *p*-nitrophenol using DCC as a condensing agent. *p*-Nitrophenol would be expected to facilitate the mechanism outlined in path A; *viz.*, the "electron-withdrawing" effect of the *p*-nitro group should give additional stability to the transition state[7] resulting from nucleophilic attack by ethanol on the 2-(*p*-nitrophenyl)pseudourea, and the decreased nucleophilicity of the *p*-nitrophenate ion should slow up SN2 attack *via* path B.

One may conclude from the experimental data listed in Table I that aryl alkyl ether formation using DCC as a condensing agent *does not* proceed through path A. Although other mechanisms may be proposed path B seems to explain the results, *i.e.*, *SN2 attack by a phenate ion on a 2-alkylpseudourea intermediate.*

TABLE I

MASS SPECTROMETRIC ANALYSES OF ISOTOPIC PRODUCTS[a,b]

Expt. no.	Compd.	—% of O^{18} predicted by— Path A	Path B	Found
1	Phenetole	1.9[c]	0	0[d]
	DCU	0	1.9[c]	1.8[e]
2	*p*-Nitrophenetole	1.9[c]	0	0[d]
	DCU	0	1.9[c]	1.4[e]

[a] A Consolidated Electrodynamics Corp. mass spectrometer, Model 21-103C, was used to determine O^{18} content. [b] All values reported are maximum values. [c] The ethanol used in this study contained 1.9% O^{18} (maximum value). [d] Trace amounts of O^{18} were not considered significant. [e] Both values are within the limit of experimental error.

Experimental[8]

Purification of Material.—Phenol (U.S.P., Mallinckrodt) and N,N′-dicyclohexylcarbodiimide (American Cyanamid) were used without further purification. *p*-Nitrophenol was obtained by acidifying the dihydrate of sodium *p*-nitrophenate. Two recrystallizations from benzene yielded pure *p*-nitrophenol, m.p. 114–115° (lit.[9] m.p. 113.8°).

General Procedure.—A mixture consisting of 6.6 g. (0.07 mole) of phenol, 14.4 g. (0.07 mole) of N,N′-dicyclohexylcarbodiimide, and 3.4 g. (0.07 mole) of ethanol (1.9% O^{18}) was sealed in a tube and heated to *ca.* 100°. After approximately 72 hr. the quasi-crystalline reaction mass was cooled to room temperature, triturated with three 50-ml. portions of ether, and filtered. The insoluble N,N′-dicyclohexylurea collected in this manner weighed 14.0 g. (91% yield). A sample of the urea derivative recrystallized twice from hot, glacial acetic acid[10] melted at 230–231° (lit.[11] m.p. 229–230°).

An excess of oxalic acid (1.8 g., 0.02 mole) was added to the ethereal filtrate and, after a brief evolution of gas,[12] the solution was decolorized using charcoal, filtered, and concentrated to a yellow oil. Distillation of the crude product using a spinning-band column gave a pure sample of phenetole boiling at 168–169° (765 mm.), lit.[13] b.p. 170° (760 mm.).

The reaction products purified as described above were submitted for mass spectrometric analysis (see Table I).

Acknowledgment.—The author gratefully acknowledges helpful discussions with Drs. V. J. Bauer, E. Cohen, A. S. Kende, and R. Paul and Mr. T. L. Fields. The interpretations of the mass spectrometric analyses by Mrs. R. H. Barritt of the Stamford Research Laboratories, American Cyanamid Company, were invaluable in completing this investigation.

---

(5) E. Vowinkel, *Chem. Ber.*, **96**, 1702 (1963).

(6) Precedents for the proposed SN2 reaction in path B are found in the formation of alkyl halides and N,N′-disubstituted ureas when aqueous, acidic solutions of N,N′-disubstituted 2-alkylpseudoureas are warmed: see F. B. Dains, *J. Am. Chem. Soc.*, **21**, 136 (1899); H. G. Khorana, *Can. J. Chem.*, **32**, 227 (1954).

(7) E. Berliner and L. C. Monack, *J. Am. Chem. Soc.*, **74**, 1574 (1952).

(8) Melting points (determined in a Hershberg apparatus) and boiling points are uncorrected.

(9) N. V. Sidgwick, W. J. Spurrell, and T. E. Davies, *J. Chem. Soc.*, **107**, 1202 (1915).

(10) N,N′-Dicyclohexylurea is insoluble in ordinary organic solvents.

(11) A. Skita and H. Rolfes, *Ber.*, **53B**, 1242 (1920).

(12) Unreacted DCC is decomposed by oxalic acid to give a quantitative yield of DCU, CO_2, and CO.

(13) R. R. Dreisbach and R. A. Martin, *Ind. Eng. Chem.*, **41**, 2875 (1949).

The Nitration of Toluene by Means of Nitric Acid and an Ion-Exchange Resin[1]

OSCAR L. WRIGHT, JOHN TEIPEL, AND DAVID THOENNES

Department of Chemistry, Rockhurst College,
Kansas City, Missouri

Received November 25, 1964

When a dehydrated, sulfonic acid ion-exchange resin, instead of sulfuric acid, is used along with nitric acid to form the nitrating agent in the nitration of toluene, nitration does take place. Decreased *ortho–para* ratios, as low as 0.68, are obtained, indicating that this type of nitrating agent has a large steric effect. In addition to the normal mononitration products, 25–30% of phenylnitromethane is also sometimes produced. Evidence is presented that the nitronium ion is produced, and, when a nonpolar solvent is used, the ions are held as ion pairs on the surface of the resin, creating the steric effect.

The nitration of toluene has been investigated by many investigators, and, although some of the data in the literature appear to be in conflict,[2] the *ortho–para* ratios obtained by most investigators[3] is remarkably consistent at 1.57 ± 0.10. It is presumed from this that the steric effect of the nitrating agent is constant throughout most of the work and that the actual

---

(1) This work was supported in part by Undergraduate Research Participation Grants from the National Science Foundation and from the Kansas City Association of Trusts and Foundations. Thanks is also extended to the Pittsburgh Chemical Co. for permission to publish the portion of the work done in their laboratories.

(2) G. A. Olah and S. J. Kuhn, *J. Am. Chem. Soc.*, **82**, 3684, 3687 (1962); M. I. Usanovich, *et al.*, *Zh. Obshch. Khim.*, **10**, 219, 224, 227, 230 (1940); A. Pictet and E. Khotinsky, *Ber. deut. chem. Ges.*, **40**, 1163 (1907); C. K. Ingold, A. Lapworth, E. Rothstein, and D. Ward, *J. Chem. Soc.*, 1959 (1931).

(3) H. C. Brown and W. H. Bonner, *J. Am. Chem. Soc.*, **76**, 605 (1954); C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 256–269.