

acrylonitrile and 372 g. (3.00 moles of amine) of 25% aqueous methylamine. The yield was 110 g. (65.5%), b.p. 37° (4 mm.).

4-(2'-Cyanoethyl)-amino-3-penten-2-one (I). The method of Cromwell and coworkers³ was employed using 13.5 g. (0.19 mole) of β -aminopropionitrile and 20.0 g. (0.20 mole) of acetylacetone. The yield was 28 g., m.p. 89.5–90° (lit.,³ 89.5–90°), after three recrystallizations from benzene-petroleum ether (3:1).

4-Amino-3-penten-2-one (II). The method of Combes and Combes¹⁷ was applied using 10.0 g. (0.1 mole) of acetylacetone and anhydrous ammonia. The product crystallized on standing and was purified by distillation at reduced pressure. The yield was 8.3 g., m.p. 43° (lit.,¹⁶ 43°).

4-N-(2'-Cyanoethyl)-methylamino-3-penten-2-one (III). The method of Cromwell and coworkers³ was employed using 20.0 g. (0.20 mole) of acetylacetone and 17.0 g. (0.20 mole) of β -methylaminopropionitrile. The yield was 32.5 g. The product was recrystallized three times from benzene-petroleum ether, and gave m.p. 69–70° (lit.,³ 69–70°).

Ferric chloride studies. Solutions for the spectroscopic study were prepared by the addition of excess ketone to a

small volume of 1% ethanolic ferric chloride solution. The solutions were measured in a 1 cm. cell against ethanol as the reference solvent.

The ferric chloride tests in chloroform solution were carried out according to the method of Soloway and Wilen.¹⁸

Measurements in the visible and ultraviolet region. The Cary Spectrophotometer (Model 11) was used for measurements in these regions. Spectra were measured on solutions (against the solvent as reference).

Measurements in the infrared region. The samples were measured as solids dispersed in potassium bromide pellets (against a pure potassium bromide pellet as reference) or milled in "Halocarbon Oil"¹⁹ (against the pure oil as reference). The samples were also studied in solution in carbon tetrachloride, against carbon tetrachloride as reference. A Beckman IR-3 spectrophotometer was used for the measurements. Lithium fluoride and sodium chloride optics were used for studies in the 3 μ and 6 μ regions, respectively.

Photochemical isomerization. The solutions contained in a 1 cm. quartz cell were exposed to ultraviolet radiation from a General Electric AH-4 mercury arc without the glass envelope. To prevent excessive heating of the sample, a water filled cell was placed between the source and the sample cell. For irradiation with the 313 m μ mercury line, a Pyrex glass filter was used to cut off radiation lines below 300 m μ . No filter was used for irradiation with the 254–265 m μ mercury lines.

NATICK, MASS.

(18) S. Soloway and S. H. Wilen, *Anal. Chem.*, **24**, 979 (1952).

(19) "Halocarbon Oil" is a blend of completely halogenated chlorofluorocarbons and was obtained from the Halocarbon Products Corp., Hackensack, N. J.

TABLE III

ULTRAVIOLET ABSORPTION BANDS OF THE AMINO KETONES IN VARIOUS MEDIA (m μ)

Compound	95% EtOH	Iso-octane	H ₂ O	0.1N KOH
I	308	298	310	311
II	300	286	300	301
III	306	289	313	313

(17) A. Combes and C. Combes, *Bull. Soc. Chim.*, (3) **7**, 779 (1892).

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, BUTLER UNIVERSITY]

Use of Anion Exchange Resins in the Synthesis of Benzyl Ethers of Phenols

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Benzyl ether formation of a number of phenols can be effected by treating the phenolate of a strongly basic anion exchange resin with an ethanol solution of benzyl chloride. The conventional column and batch techniques are used. Eleven benzyl ethers have been prepared and their identification shown.

Benzyl ethers of phenols are usually synthesized by coupling an alkali phenolate and benzyl halide in an appropriate solvent with the aid of heat. This report presents a method for carrying out the synthesis at room temperature by the use of the phenolates of strongly basic anion exchange resins. The resins used are based on polystyrene and contain quaternary ammonium groups.

The method consists of absorbing the phenol on the resin.² The phenol-absorbed resin is then treated

with an ethanol solution of benzyl chloride by the conventional column or batch techniques employed in ion exchange resin technology. Generally a pure product may be obtained on a single crystallization of the residue from evaporation of the eluate or filtrate.

The method is particularly applicable to the synthesis of benzyl ethers of monohydric phenols. The dihydric phenols, hydroquinone and resorcinol, yield, in the case of hydroquinone, a mixture of both mono and dibenzyl ethers; in the case of resorcinol, the dibenzyl ether only.

The phenol benzyl ethers prepared by both column and batch techniques are summarized in Table I. The yields are based upon the amount of the phenol converted to the benzyl ether.

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(2) The reaction also occurs if the phenol is dissolved in the ethanol with the benzyl chloride. Subsequent separation of the benzyl ether is simplified and the yield improved if absorption of the phenol on the resin is carried out first.

TABLE I
BENZYL ETHERS PREPARED FROM BENZYL CHLORIDE AND PHENOLS WITH ANION EXCHANGE RESINS

Benzyl Ether	Resin	Yield, %		M.P., °C.	M.P., °C. (lit.)	Analyses ^a	
		Column techn.	Batch techn.			Calcd.	Found
Phenol	A ^b	57	62	39-39.5 ^c	39 ⁶ 40 ⁷		
	D ^d	66	— ^e				
Chlorothymol	A	74	83	54.5-55	55 ¹⁰	C 74.30	74.21
						H 6.97	7.01
Thymol	A	90	81	Oil ^f			
Guaiacol	A	66	63	57.5-58.5 ^g	57.5-58.5 ¹⁶		
	D	63	— ^e				
Eugenol	A	72	79	27-27.5	30-31 ¹⁷	C 80.24	80.83
						H 7.13	7.64
p-Bromophenol	A	55	38	63-64	64 ⁸	Br 30.38	30.4
p-Nitrophenol	A	20	23	106-106.5	106 ¹⁸	C 68.11	68.40
						H 4.84	4.83
Alpha Naphthol	A	52	52	77-77.5	77-77.5 ¹⁹	C 87.15	87.23
						H 6.02	6.49
Beta Naphthol	A	43	53	99.5-100	99 ²⁰ 100 ²¹	C 87.15	87.92
						H 6.02	6.37
Hydroquinone	A	Mono 9	14	121-121.5 ^h	121-122 ¹⁴		
		Di 10	27	128.5-129	128-129 ¹³ 130 ¹³	C 82.73	82.82
Resorcinol	A	Mono — ⁱ	— ⁱ			H 6.25	6.66
		Di — ^j	16	73-74	73-74 ¹⁴	C 82.73	83.06
						H 6.25	6.45

^a Carried out by Drs. Weiler and Strauss, Oxford, England, and by the Microanalytical Laboratory, Organic Chemistry Division, Eli Lilly & Co., Indianapolis. ^b Refers to Amberlite IRA-400. ^c B.p. 285-286° uncorr.; lit.⁸ b.p. 286-287° uncorr. ^d Refers to Dowex 1-X4. ^e Not carried out. ^f B.p. 169-170° (7 mm.), n_D^{20} 1.5553; lit.¹⁶ b.p. 169-170° (7 mm.), n_D^{20} 1.5556. ^g n_D^{20} 1.5737; lit.¹⁶ n_D^{25} 1.5780. ^h Mixture melting point with authentic sample showed no depression. ⁱ Attempts to isolate monobenzyl ether were unsuccessful. ^j Attempts to isolate dibenzyl ether were unsuccessful.

EXPERIMENTAL

Resin preparation. Amberlite IRA-400^a and Dowex 1-X4^a as supplied commercially (20-50 mesh) were converted to their hydroxyl form by the usual column technique with 5% aqueous sodium hydroxide (4 to 5 times the volume of resin). The resins were rinsed with distilled water until the washings were neutral, and then with absolute methanol. The residual methanol was removed by passing a current of carbon dioxide-free air through the column of resin.

Absorption of the phenol on the resin. The quantity of resin employed for each benzyl ether synthesis was based upon the absorption capacity of the air-dried resin as determined by the method of Kunin and Myers.⁴ About 15 to 20% excess resin was used to absorb the phenol. A general procedure was followed: The phenol (0.05 mole) was dissolved in 250 to 300 ml. distilled water or, if necessary, in dilute sodium hydroxide solution and passed through the resin in a column 20 mm. in diameter. The resin column was first rinsed with distilled water until the washings were neutral, then with two 75-ml. portions of ethanol.

Benzyl ether formation of monohydric phenols. The preparation of phenyl benzyl ether illustrates the synthesis of the benzyl ethers by the column technique.

A column 20 mm. in diameter packed with 35 g. of Dowex 1-X4 upon which 4.7 g. (0.05 mole) of Phenol U.S.P. had been absorbed was eluted with 400 ml. of ethanol containing 16.4 g. (0.13 mole) of benzyl chloride. The rate of flow was 1 ml. per minute. The column was then rinsed with 150 ml. of ethanol. Evaporation to dryness of the combined eluate and rinse yielded 6.10 g. (66%) of phenyl benzyl ether, m.p.

38-38.5°. The product on a single crystallization from ethanol melted at 39-39.5°; lit.^{6,7} m.p. 39°, 40°. The b.p. was 285-286° uncorr.; lit.⁸ b.p. 286-287° uncorr.

The preparation of chlorothymol benzyl ether illustrates the synthesis of the benzyl ethers by the batch technique.

Twenty-five grams of Amberlite IRA-400 upon which 9.23 g. (0.05 mole) of chlorothymol had been absorbed was placed in a 500-ml. ground glass-stoppered erlenmeyer flask. Three hundred milliliters of ethanol and 9.5 g. (0.075 mole) of benzyl chloride were then added. The mixture was mechanically agitated for 72 hr. At the end of this period the resin was filtered off and washed on the filter with 150 ml. ethanol.⁹ Evaporation to dryness of the combined filtrate and washings yielded 11.74 g. of white crystals melting at 52.5-53.5°. The product crystallized once from ethanol yielded 10.9 g. (83%) of chlorothymol benzyl ether melting at 54.5-55°; lit.¹⁰ m.p. 55°.

Anal. Calcd. for C₁₇H₁₉ClO: C, 74.30; H, 6.97. Found: C, 74.21; H, 7.01.

Benzyl ether formation of dihydric phenols. The preparation of the benzyl ethers of hydroquinone and resorcinol paralleled the column and batch operations described for the synthesis of phenyl benzyl ether and chlorothymol benzyl ether; except that the quantities of benzyl chloride were increased¹¹ and the quantity of resin (for the batch opera-

(6) S. G. Powell and R. Adams, *J. Am. Chem. Soc.*, **42**, 656 (1920).

(7) C. A. Bischoff and A. von Hedenström, *Ber.*, **35**, 3434 (1902).

(8) F. Sintenis, *Ann.*, **161**, 337 (1872).

(9) Ether was found to be more satisfactory for washing the resin on the filter in subsequent experiments with other phenols.

(10) B. Jones, *J. Chem. Soc.*, 364 (1941).

(11) For the column technique, 16.4 g. (0.13 mole) of benzyl chloride in 400 ml. of ethanol was used; for the batch technique, 9.4 g. (0.075 mole) in 300 ml. of ethanol.

(3) Analytical grade manufactured by Rohm & Haas Co., Philadelphia, Pa.

(4) Supplied through the courtesy of Dow Chemical Co., Midland, Mich.

(5) R. Kunin and R. J. Myers, *Ion Exchange Resins*, John Wiley and Sons, Inc., New York, 1950, p. 150.

tion only) approximately doubled. The eluates and filtrates from the column and batch operations, respectively, required further processing to separate the mixtures of the mono and dibenzyl ethers formed.

Hydroquinone dibenzyl ether. The separation of the dibenzyl ether of hydroquinone was accomplished by treating the residues from evaporation of the eluate and filtrate with 0.1N sodium hydroxide solution and extracting the resulting alkaline-aqueous mixtures with several portions of ether. Evaporation of these ether extractives, first washed free of alkali, yielded hydroquinone dibenzyl ether which when crystallized once from ethanol melted at 128.5–129°; lit.^{12,13} m.p. 128–129°, 130°. Yield: column technique, 1.6 g. (10%); batch technique, 4 g. (27%).

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.82; H, 6.66.

Hydroquinone monobenzyl ether. The alkaline-aqueous portions from which the hydroquinone dibenzyl ether was removed were acidified with diluted hydrochloric acid and extracted with ether. These ether extractives washed free of acid and evaporated to dryness left crystalline residues. Crystallization of the residues from diluted ethanol yielded hydroquinone monobenzyl ether, m.p. 121–121.5°; lit.¹⁴ m.p. 121–122°. A mixture melting point with an authentic sample of Hydroquinone monobenzyl ether showed no depression. Yield: column technique, 0.96 g. (9%); batch technique, 1.46 g. (14%).

(12) A. Colson, *Bull. soc. chim.*, **3**, 347 (1889).

(13) H. Schiff and G. Pellizzari, *Ann.*, **221**, 369 (1883).

(14) J. Druvey, *Bull. soc. chim.*, **5**, 1740 (1935).

Resorcinol dibenzyl ether. Although both column and batch techniques were applied to the preparation of this ether, only the latter technique yielded the compound. The monobenzyl ether of resorcinol could not be obtained by either the column or the batch techniques.

The isolation of the resorcinol dibenzyl ether was accomplished in the same manner as described for the isolation of the dibenzyl ether of hydroquinone. The yield was 2.35 g. (16%), m.p. 73–74°; lit.¹⁴ m.p. 73–74°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 83.06; H, 6.45.

Experiments are being continued to ascertain whether any ethers of phenols other than benzyl can be prepared by the method herein described; and similarly, whether any benzyl or alkyl groups can replace non-carboxylic hydrogens on other types of compounds.

INDIANAPOLIS, IND.

(15) F. Caujolle, C. Franck, and L. Girard, *Compt. rend.* **218**, 572 (1944).

(16) I. M. Heilbron, *Dictionary of Organic Compounds*, Oxford University Press, New York, 1946, Vol. II, p. 136.

(17) T. F. West, *J. Chem. Soc.*, 490 (1945).

(18) G. Kumpf, *Ann.*, **224**, 123 (1884).

(19) V. H. Dermer and O. C. Dermer, *J. Org. Chem.*, **3**, 291 (1938).

(20) W. Staedel, *Ber.*, **14**, 899 (1881).

(21) HLA, BAW, *Quart. J. Indian Chem. Soc.*, **3**, 101 (1926); *Chem. Abstr.*, **20**, 3695 (1926).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, AIN SHAMS UNIVERSITY]

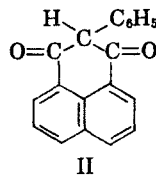
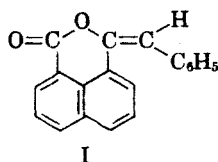
Comparative Study between Phthalides and Naphthalides. II¹

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In addition to the β -diketone (II), 3-benzalnapthalide (I) was isolated from the product of interaction of naphthalic anhydride and phenylacetic acid. Infrared curves for the naphthalide (I) and the phthalide (VI) together with the β -diketones (II), (III) and (IV) are discussed.

Recently, Aly, Awad, and Islam,¹ investigated the condensation of naphthalic anhydride with phenylacetic acid in the presence of sodium acetate, and obtained a product (m.p. 214°) to which they assigned the benzalnapthalide structure (I).



Cesaris² obtained from the same condensation a product which possessed no ketonic properties and to which he gave β -diketone structure (II). He claimed that in contrast to ortho-anhydrides such as phthalic anhydride, which gives only the

phthalide, naphthalic anhydride gives directly the β -diketone (II).

In the light of the above controversial results, we decided to reinvestigate the whole problem in more detail.

We have now isolated from the reaction mixture of the above Perkin condensation, two products. The main product is orange in color, m.p. 214°, and is fairly soluble in cold dilute sodium hydroxide and dilute sodium carbonate solutions. Infrared measurements of this compound (Fig. 1) show a clear carbonyl stretching frequency (1570 cm^{-1}) in the normal carbonyl group region (the carbonyl stretching frequency for β -diketones is 1640–1540 cm^{-1}).³ Similar carbonyl stretching frequencies are present in the infrared curves of the two β -diketones, III⁴ (Fig. 2) and IV¹ (Fig. 3), being 1620

(1) Compare Comparative Study between Phthalides and Naphthalides, O. M. Aly, W. I. Awad, and A. M. Islam, *J. Org. Chem.*, **22**, 517 (1957).

(2) M. Cesaris, *Gazz. chim. ital.*, **42**, II, 453.

(3) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Methuen, London, 1957, p. 114.

(4) G. Errera, *Gazz. chim. ital.*, **41**, I, 190.