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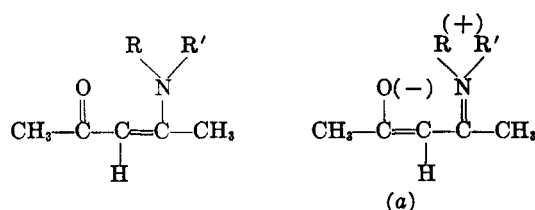
A Study of β -Amino- α,β -unsaturated Ketones¹

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A study of the N—H stretching bands of 4-(2'-cyanoethyl)amino-3-penten-2-one (I) and 4-amino-3-penten-2-one (II) in the 3 μ region of the infrared spectrum is described. Evidence is provided for the presence of intramolecular hydrogen bonds in these compounds in both the solid and solution phases. The existence of II in polymeric aggregates, held together by intermolecular hydrogen bonding is also shown. These conclusions are confirmed by measurements in the 6 μ region, and the assignment of a band to N—H deformation is made. The spectroscopic data support the enamine (IV) structure for these compounds rather than the imine (V) structure. Photochemical isomerization studies of I and 4-*N*-(2'-cyanoethyl)methylamino-3-penten-2-one (III) provide evidence for both *cis* and *trans* isomers of these compounds. The results of a spectroscopic investigation of the positive ferric chloride test given by I and II in ethanol suggest that these compounds form complexes with ferric chloride prior to their hydrolysis to acetylacetone. Positive ferric chloride tests are reported for I and II in chloroform.

An infrared absorption study of β -amino- α,β -unsaturated ketones was carried out by Cromwell, Miller, and co-workers.³ These investigators found the C=O band at unusually long wave lengths and attributed this to an appreciable contribution of the ionic resonance form (a) to the ground state. The fact that the displacement of the C=O band



I, R = H, R' = CH₂CH₂C≡N
 II, R = R' = H
 III, R = CH₃, R' = CH₂CH₂C≡N

was greatest in those compounds where R or R' = H suggested the presence of intramolecular hydrogen bonds. Their study was devoted mainly to a consideration of the absorption bands in the 6 μ region of the spectra of the amino ketones measured as solids. The work reported here was concerned, in part, with an investigation of the N—H stretching bands of I and II in the 3 μ region, in order to obtain additional information concerning the nature of the hydrogen bonding which occurs in the solid and solution states. In order to obtain additional data, measurements on I, II, and III in solution and as solids were made in the 6 μ region.

Associated with the hydrogen bonding problem is that of the geometry of the β -amino- α,β -unsaturated ketones. Chelation would tend to stabilize compounds I and II in the configuration in which

the functional groups are *cis* with respect to one another. However, the existence of these compounds in the *trans* modification is possible and might be observed under the proper conditions. In the case of III, steric factors would be expected to be of importance in determining the relative stability of the two isomers. In this work, direct evidence for these *cis* and *trans* isomers was sought by photochemical studies.

When compounds I, II, and III are treated with 1% ethanolic ferric chloride, a red color is immediately formed.³ This color might be due solely to the ferric chloride-acetylacetone complex. Acetylacetone is readily formed by the hydrolysis of the β -amino- α,β -unsaturated ketones under acidic conditions. However, the instantaneity of the color formation might signify initial complex formation between the amino-ketones and ferric chloride. It was decided, therefore, to investigate the color reaction spectroscopically.

RESULTS AND DISCUSSION

Infrared absorption spectra. The spectrum of compound I in carbon tetrachloride solution showed a band at 3.16 μ (with a shoulder at 3.11 μ). The intensity of this band did not change on dilution, indicating that the absorption band is due to the vibration of the N—H group engaged in an intramolecular hydrogen bond with the carbonyl oxygen. This assignment is further substantiated by the observation that no band attributable to free N—H was formed on dilution. The internal hydrogen bond persists in the solid state, as shown by the presence of an absorption band at 3.16 μ in the spectrum of the solid. Previous workers did not detect this band.⁴

(1) Presented before the Division of Organic Chemistry at the 131st Meeting of the American Chemical Society, Miami, Fla., April 1957.

(2) Present address: U. S. Army Research & Development Liaison Group, Rheingau Allee 2, Frankfurt a/Main, Germany.

(3) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace, *J. Am. Chem. Soc.*, **71**, 3337 (1949).

(4) Cromwell, *et al.*, *cf.* ref. (3), attributed the failure to observe the N—H stretching frequency to a shift of this band to slightly longer wave lengths (near 3.4 μ) where it would be obscured by the C—H stretching frequencies of "Nujol."

The spectrum of II in carbon tetrachloride showed several bands in the N—H stretching region. Two of these bands (2.86 μ and 2.96 μ) were strongly affected by dilution, as shown in Fig. 1.

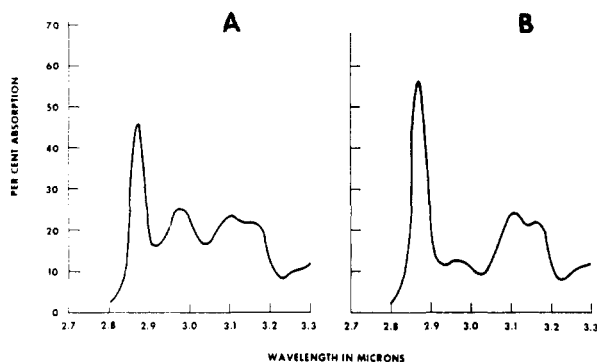


Fig. 1. Curve A represents the infrared absorption spectrum in the 3 μ region of a dilute solution of II in CCl_4 , measured in a 0.5 mm. cell. Curve B is the spectrum observed after the solution was diluted to $1/4$ its original concentration and measured in a 2.0 mm. cell

The band at 2.86 μ which showed an intensity increase on dilution is attributed to free N—H. The 2.96 μ band, which on dilution showed a decrease in intensity, is due to intermolecularly bonded N—H. The doublet at 3.09 and 3.15 μ showed no intensity change, and is assigned to intramolecularly bonded N—H. In the spectrum of II in the solid phase two absorption bands were found, one at 2.98 μ and the other at 3.14 μ . The 2.98 μ band corresponds to the 2.96 μ band in the solution spectrum, and is due to intermolecularly bonded N—H. The absence of an absorption band at shorter wave lengths, attributable to free N—H, indicates that association through intermolecular hydrogen bonding is complete in the solid state. The band at 3.14 μ is attributed to intramolecularly bonded N—H. Band assignments in the 3 μ region are listed in Table I.

TABLE I
INFRARED BAND ASSIGNMENTS IN THE 3 μ REGION

Compound	State	N—H		
		Free (μ)	Inter- molecu- larly Bonded (μ)	Intra- molecu- larly Bonded (μ)
I	Solid	^a	^a	3.16 (3.11) ^b
	Solution	^a	^a	3.16 (3.11)
II	Solid	^a	2.98	3.14
	Solution	2.86	2.96	3.09, 3.15

^a No absorption band. ^b Shoulders on the main absorption band are indicated in parentheses.

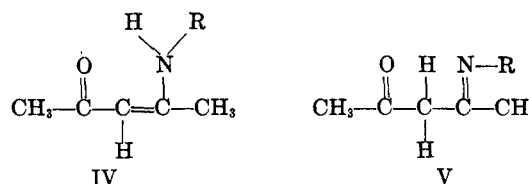
In agreement with the evidence of Cromwell and co-workers,^{3,5-7} the present spectroscopic data sup-

(5) N. H. Cromwell and W. R. Watson, *J. Org. Chem.*, **14**, 411 (1949).

(6) N. H. Cromwell and R. S. Johnson, *J. Am. Chem. Soc.*, **65**, 2481 (1943).

(7) N. H. Cromwell and R. S. Johnson, *J. Am. Chem. Soc.*, **65**, 316 (1943).

port the enamine (IV) structure for the compounds investigated, rather than the imine (V) structure.



The imine structure was recently proposed by Edwards and Petrow⁸ for the condensation products of *o*-, *m*- and *p*-chloroaniline with acetylacetone. If I possessed the imine structure, then the spectrum of I would not show an N—H band.

The carbonyl absorption band of I and III in carbon tetrachloride appeared at 6.18 μ and 6.04 μ respectively. On dilution the carbonyl band did not show a wave length or intensity change in either case. This observation provides additional support for a chelate structure for I, and also agrees with the expected behavior of III, where there is no N—H available for the formation of intermolecular hydrogen bonds.

The spectra in the 6 μ region of II in carbon tetrachloride and in the solid state are shown in Fig. 2.

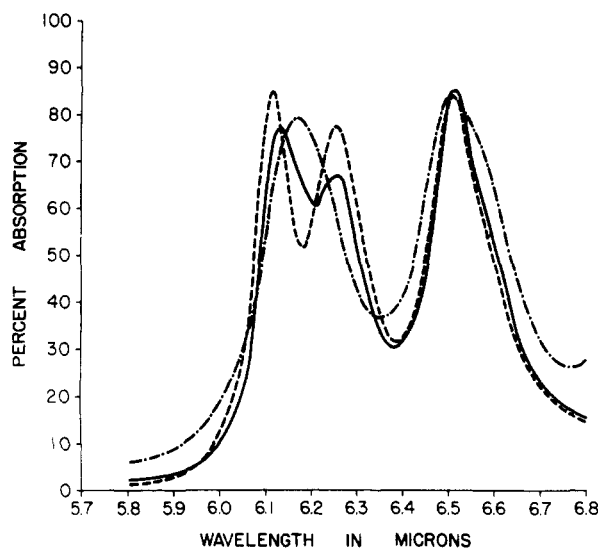


Fig. 2. The infrared absorption spectra of II in the 6 μ region: (—) CCl_4 solution measured in a 0.1 mm. cell; (---) solution diluted to $1/5$ its initial concentration and measured in a 0.5 mm. cell; (-·-·-) solid dispersed in a KBr pellet

In the spectrum of the solid a strong, broad band was found at 6.17 μ . This absorption, however, was resolved into two strong bands in the solution spectra. In the more concentrated solution the carbonyl band appeared at 6.13 μ and the second band at 6.26 μ . On dilution the carbonyl band was found at 6.12 μ , and showed a marked intensity increase. This behavior is attributed to the dissociation of

(8) W. G. H. Edwards and V. Petrow, *J. Chem. Soc.*, 2853 (1954).

intermolecular hydrogen bonds. The intensity increase also shown by the 6.26 μ band on dilution suggests its assignment to an N—H deformation vibration. The 6.26 μ band is found within the wave-length range observed for primary amines.⁹ In the spectrum of the solid the broad band at 6.17 μ results from the overlapping of the carbonyl band shifted to longer wave lengths and the N—H band shifted to shorter wave lengths. It was found, when solid and solution samples of comparable concentrations were measured, that the area under the 6.17 μ band in the spectrum of the solid agreed within 4% with the total area under the 6.13 μ and 6.26 μ bands in the solution spectrum. Shifts of the carbonyl stretching and N—H deformation bands in opposite directions upon changes of state result from the formation or dissociation of intermolecular hydrogen bonds, and have been reported for amides.¹⁰ In the spectrum of the more concentrated solution a significant contribution from the 6.17 μ band was observed on the long wavelength side of the C=O absorption.

A strong band at 6.30 μ appeared in both the solution and solid spectra of I. This absorption is found within the wave-length range observed for the N—H deformation band of secondary amines.⁹ Normally this band is weak, but it appears as a medium to strong band in secondary amides.^{10,11} Compound I, as well as II and III, is a vinylog of an amide, and this may account for the enhanced intensity of the N—H deformation band. Failure to observe a wave-length shift of this band upon a phase change can be attributed to the fact that I is not associated through hydrogen bonding.

In the solid and solution spectra of the tertiary amine (III) there was no absorption corresponding to the bands assigned to N—H deformation in the

spectra of I and II. Band assignments in the 6 μ region are listed in Table II.

In a recent infrared study of II in the liquid phase a carbonyl band was reported at 5.88 μ .¹² This was interpreted as evidence for structure V (R = H) in a non-hydrogen bonded configuration. In the present investigation no evidence for this structural assignment was found in either the solution or solid phase. The 5.88 μ band was also missing from the solid spectrum of the analogous compound, 4-amino-3-methyl-3-penten-2-one, studied by Cromwell.³

Photochemical isomerization and decomposition. It has been shown for other conjugated, unsaturated compounds that irradiation of their solutions with light of a wave length corresponding approximately to the wave length of their absorption band, results in some geometrical isomerization.¹³ Reversal of the reaction occurs when the solution is allowed to stand after the exciting radiation is removed.

In Fig. 3, the curve of highest absorption intensity represents the ultraviolet spectrum of an iso-octane solution of I prior to irradiation. When the

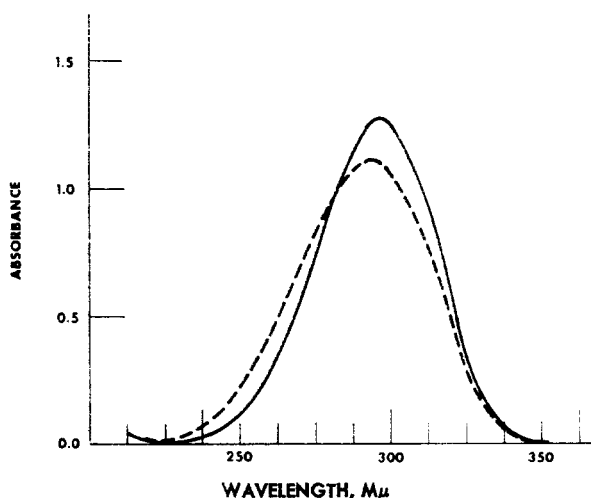


Fig. 3. The ultraviolet absorption spectra of I in iso-octane before irradiation with the 313 $m\mu$ line from a mercury arc (—) and after irradiation for six minutes (---). The original curve (— · —) is obtained when the solution is allowed to stand for 35 minutes in the dark, after irradiation

solution was irradiated for 6 minutes with the 313 $m\mu$ line from a medium pressure mercury arc, partial conversion to the less stable isomer occurred, as shown by the decrease in the intensity of absorption and the shift of the band to shorter wave lengths. The original spectrum was again observed when the solution was allowed to stand in darkness for 35 minutes at room temperature. Since the infrared data provide evidence for chelation, the

TABLE II

INFRARED BANDS IN THE 6 μ REGION

Compound	State	C=O	N—H	$(\mu)^a$
		Stretching (μ)	Deformation (μ)	
I	Solution	6.18	6.30	6.62
	Solid ^b	6.20	6.30	6.59
II	Solution	6.13 ^c	6.26	6.52
	Solid ^b	6.17 ^d	6.17 ^d	6.50
III	Solution	6.04	e	6.44
	Solid ^b	6.11	e	6.51

^a See ref. (3) for a discussion of the origin of this band.

^b Samples were dispersed in potassium bromide pellets.

^c In more dilute solution the band was found at 6.12 μ .

^d Results from the overlapping of the C=O and N—H bands. ^e No absorption band.

(9) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley & Sons, New York, 1954, p. 212.

(10) R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, 1248 (1947).

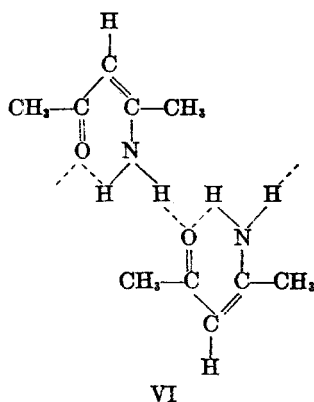
(11) *The Chemistry of Penicillin*, Princeton University Press, Princeton, N. J., 1949, p. 389.

(12) H. F. Holtzclaw, Jr., J. P. Collman, and R. M. Aire, *J. Am. Chem. Soc.*, 80, 1100 (1958).

(13) G. M. Wyman, *Chem. Revs.*, 55, 625 (1955).

more stable isomer is that in which the carbonyl and amino groups are *cis*.

Compound II decomposed under the conditions employed (irradiation with the 254–265 $m\mu$ mercury lines) as shown by the irreversibility of the spectral changes. No evidence was obtained for the existence of geometrical isomers. However, it can be inferred from the infrared data that the more stable structure is that in which both the carbonyl and amino groups lie on the same side of the molecule. The hydrogen bonding and geometrical arrangement in this molecule may be represented by structure VI. This structure also indicates the existence of II in polymeric aggregates.



A reversible spectral change, similar to that observed with compound I, was noted when an iso-octane solution of III was irradiated with the 313 $m\mu$ mercury line for 4 minutes. In the *cis* configuration (similar to VI) this compound could not be coplanar, due to overcrowding introduced by the bulky groups on the nitrogen atom. Consequently, it is probable that the more stable isomer is the one in which the functional groups are in a *trans* configuration with respect to one another.

Ferric chloride test. The visible absorption spectra of I, II, and III in 1% ethanolic ferric chloride were measured. In the spectra of I and II an initial absorption band was observed which gradually shifted to shorter wave lengths, and became more intense as the compounds hydrolyzed to give finally the 434 $m\mu$ band of the iron-acetylacetonate complex. For compound I these absorption changes are shown in Fig. 4. The initial absorption band may be attributed to complex formation between the β -amino- α,β -unsaturated ketones and ferric chloride. The nature of this complex must be speculative at this time. However, complex formation may signify that I and II exist to a slight extent in the enol (VII) structure in ethanol, although the enamine (IV) structure apparently predominates in the solid phase and in the non-polar solvent, carbon tetrachloride. Removal of the enol by complex formation would rapidly shift a keto-enol equilibrium toward the formation of more enol.¹⁴

(14) A. Hantzsch, *Ber.*, **43**, 3049 (1910).

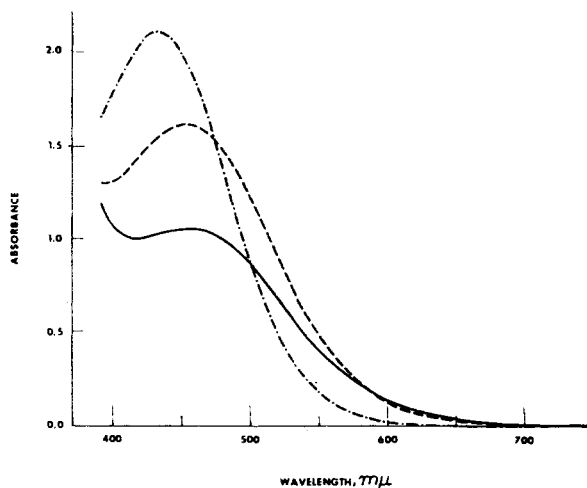
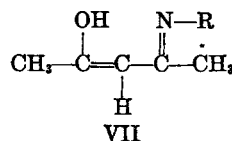


Fig. 4. The visible absorption spectra of I in ethanolic FeCl_3 . Initial absorption (—); absorption after 15 minutes (---); absorption after 35 minutes, when the change was complete (-·-·-)



No change was observed in the initial absorption spectrum of III. The absorption band at 434 $m\mu$ due to the iron-acetylacetonate complex was found immediately. For this compound the positive ferric chloride test results solely from its rapid hydrolysis to acetylacetonate under the experimental conditions.

Chloroform solutions of compounds I and II immediately produced a pink color when treated with a few drops of chloroform solution of anhydrous ferric chloride. The color change may be attributed to complex formation between ferric chloride and the amino ketones. Compounds I and II may possibly exist to a small extent in the enol form in chloroform.

No immediate color change occurred when III was treated in the same way. On standing, however, the chloroform solution gradually became yellow. In this compound there is no enolizable hydrogen. The yellow color probably results from the gradual formation of a ferric chloride complex of a decomposition product of III.

EXPERIMENTAL

β -Aminopropionitrile. The procedure of Buc, Ford, and Wise¹⁵ was employed using 1950 ml. (30 moles) of concentrated ammonium hydroxide and 396 ml. (6 moles) of acrylonitrile. The yield was 100 g. (23%), b.p. 46–48° (4 mm.). The picrate had m.p. 178° (lit.,¹⁶ 178°).

β -Methylaminopropionitrile. The procedure of Whitmore and co-workers¹⁶ was employed using 106 g. (2.00 moles) of

(15) S. R. Buc, J. H. Ford, and E. C. Wise, *J. Am. Chem. Soc.*, **67**, 92 (1945).

(16) F. C. Whitmore, H. S. Mosher, R. R. Adams, R. B. Taylor, E. C. Chapin, C. Weisel, and W. Yanko, *J. Am. Chem. Soc.*, **66**, 725 (1944).

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 mullied 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.