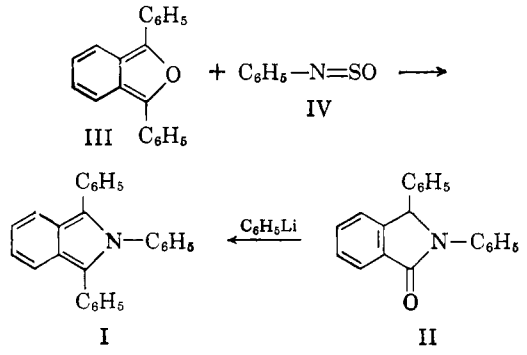
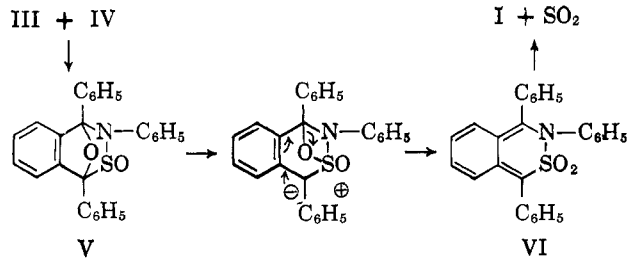
unchanged. Since Diels–Alder reactions can be greatly accelerated by Lewis acid catalysts,[4] the addition of III to IV was attempted in refluxing benzene in the presence of boron trifluoride etherate. Under these conditions, after thirteen hours heating, there was isolated directly 1,2,3-triphenylisoindole in 78% yield. The isoindole I was obtained also in 46% yield when compounds III and IV were heated together without a solvent at 84° for thirty-six hours.



The exact mechanism of the conversion of furan III to isoindole I is somewhat obscure. We propose that the normal Diels–Alder adduct (V) is first formed. Rearrangement of adduct V, as illustrated, could lead to an *o*-quinoid δ-sultam (VI), which then collapses to 1,2,3-triphenylisoindole by thermal extrusion of sulfur dioxide. The loss of sulfur dioxide in this manner from both unsaturated δ-sultones and unsaturated δ-sultams has ample analogy.[5,6]



Experimental

Reaction of 1,3-Diphenylisobenzofuran (III) with Thionylaniline (IV). A. In the Presence of Boron Trifluoride.—Boron trifluoride etherate (3.0 ml.) was added to a solution of furan III (1.00 g., 4.1 mmoles) and thionylaniline[7] (0.62 g., 4.4 mmoles) in benzene (50 ml.). After refluxing for 13 hr., the brown reaction solution was washed well with water (two 150-ml. lots), dried over magnesium sulfate, and evaporated. The dark residue was dissolved in benzene (10 ml.) and chromatographed on Woelm neutral alumina (grade II, 60 g.). The column was eluted with benzene (250 ml.), and the eluate was evaporated to yield isoindole I, which was crystallized from ethanol as fine pale yellow needles (1.10 g., 78%), m.p. 234–235° (lit.[1] m.p. 234.5°). The infrared and ultraviolet spectra of this material corresponded exactly to the reported spectral data[1] for compound I.

Anal. Calcd. for $C_{26}H_{19}N$: C, 90.40; H, 5.54; N, 4.06. Found: C, 90.48; H, 5.36; N, 4.22.

B. Reaction of III and IV in the Absence of Catalyst.—The reaction described before was repeated a number of times with minor variations in the absence of boron trifluoride; furan III was recovered in all cases in at least 80% yield. The variations included the use of refluxing toluene in place of benzene as solvent, increasing the heating time to 36 hr. and using a 4-equiv. excess of thionylaniline. Isoindole I was formed in moderate yield, however, in the following reaction in which solvent was omitted.

A mixture of furan III (1.00 g., 4.1 mmoles) and thionylaniline (2.0 ml., 17.7 mmoles) was heated for 36 hr. at 84° (water bath) in a test tube fitted with a loose cotton plug. The resulting brown mass was dissolved in benzene (20 ml.), and the solution was diluted with ethanol (80 ml.). The solution was concentrated by boiling to 35 ml. and allowed to cool, when isoindole I (0.650 g., 46%), m.p. 233°, separated as pale yellow needles.

Acknowledgment.—We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(4) P. Yates and P. Eaton, *J. Am. Chem. Soc.*, **82**, 4436 (1960).

(5) Th. Morel and P. E. Verkade, *Rec. trav. chim.*, **70**, 35 (1951), and earlier references cited therein.

(6) B. Helferich and W. Klebert, *Ann.*, **657**, 79 (1962).

(7) A. Michaelis and R. Herz, *Ber.*, **23**, 3481 (1890).

Acetylenic Amines. VI. Amides of Secondary Acetylenic Amines

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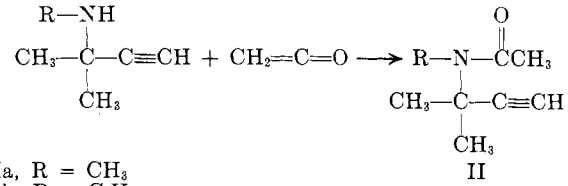
The availability[1,2] of many substituted propargylamines and the notable activity of some of these as hypotensive agents[3a,b] suggested the preparation of assorted derivatives. The preparation and reactions of some of the amides derived from secondary propargylamines (I) are discussed in this paper.



Ia, R = CH_3
b, R = C_2H_5
c, R = $CH(CH_3)_2$
d, R = $C(CH_3)_3$

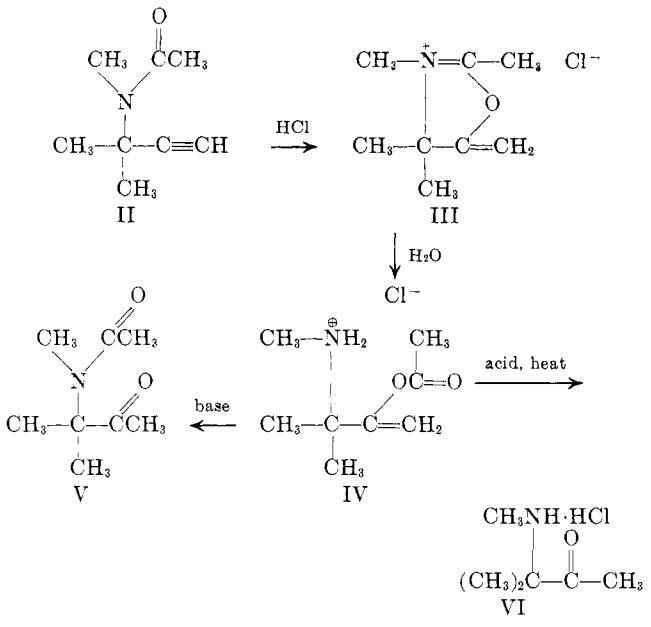
When the N-methyl-1,1-dimethylpropargylamine (Ia) was dissolved in dry ether and treated with ketene, the desired amide (IIa) was obtained and could be isolated by distillation. Similar products were obtained with Ib and Ic, but no derivative of Id could be obtained even after a twelve-hour treatment with ketene. It was found that these amides could be prepared by the usual treatment with acetic anhydride followed by treatment with water, if the water solutions were made basic. However, when solutions of these amides in dilute hydrochloric acid were neutralized, the acetylenic amides (II) were not recovered and, instead, the keto amides (V) were isolated.

Treatment of the amide II in dry ether with anhydrous hydrogen chloride gave a solid material III. Elemental analyses indicated only the addition of hydrogen chloride. The infrared spectrum showed the absence of both the acetylene C—H absorption band at 3.05 μ and the carbonyl absorption at 6.2 μ. However, two new bands in the 6-μ region were present;

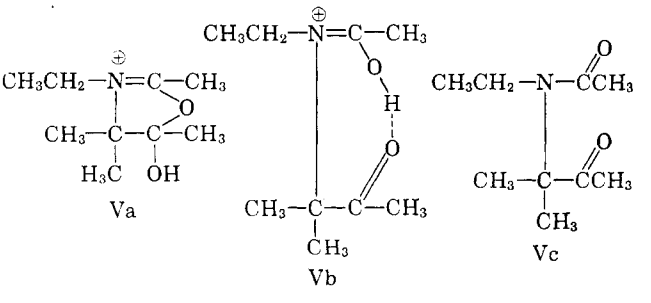
(1) (a) G. F. Hennion and R. S. Hanzel, *J. Am. Chem. Soc.*, **82**, 4908 (1960); (b) N. R. Easton, R. D. Dillard, W. J. Doran, M. Livezey, and D. E. Morrison, *J. Org. Chem.*, **26**, 3772 (1961).

(2) C. Ainsworth and N. R. Easton, *ibid.*, **26**, 3776 (1961).

(3) (a) Abstracts 46–50, 138th National Meeting of the American Chemical Society, New York, N. Y., September, 1960; (b) C. W. Ryan, N. R. Easton, R. D. Dillard, and F. G. Henderson, *J. Med. Pharm. Chem.*, **5**, 780 (1962).



one of these was at 6.02 μ and the other at 5.88 μ. These were indicative of C=C and C=N groups. On this basis structure III was assigned to this compound. III was rather unstable especially in the presence of moisture. Recrystallization from wet solvents converted III to a new compound (IV). This material retained the infrared band at 6.02 μ, but not the one at 5.88 μ. New bands at 5.65 μ and 6.33 μ are attributed to carbonyl and to NH_2. From this information this material was assigned structure IV. When IV was made basic an O → N acyl shift took place, and the keto amide (V) was produced. This compound showed infrared bands at 5.85 μ and 6.12 μ. Heating an acid solution of IV gave the amino ketone (VI). The keto amide (V) also was soluble in dilute hydrochloric acid and formed a hydrochloride in ether. The infrared spectrum of the hydrochloride showed that the two peaks at 5.85 μ and 6.12 μ had disappeared; a new band at 5.97 μ and a shoulder at about 3 μ were present. The band at 5.97 could be assigned best to a $C{=}\overset{\oplus}{N}$ linkage. The structures of the type Va and Vb are considered the best possibilities.



Since the hydrochloride of the N-methyl derivative (V) was very slightly soluble in chloroform and the hydrochloride of the N-ethyl compound (Vc) quite soluble, this latter homolog was used in the n.m.r. studies.

The n.m.r.[4] of the free base (Vc) shows a quartet centered at 210 c.p.s. (2H) ($N{-}CH_2{-}$) and single peaks (3H) at 127 c.p.s. and at 123 c.p.s. ($2C\overset{O}{\overset{\|}{C}}CH_3$). The remaining protons are grouped further upfield between 70 c.p.s. and 100 c.p.s. However, in the hydrochloride, the quartet shifted, to 241 c.p.s. and the single peaks to 163.2 c.p.s. and 111 c.p.s. Structure Va would be favored by these shifts, since the quartet would be expected to move downfield when the nitrogen becomes positive. The methyl shift downfield could be explained by the change from $\overset{O}{\overset{\|}{C}}{-}CH_3$ to $N{=}C{-}CH_3$. The upfield shift of the other methyl could be explained by the change from $\overset{O}{\overset{\|}{C}}{-}CH_3$ to $\overset{O}{\overset{/}{C}}{-}CH_3$. A dilution study was run to determine the effect of concentration upon the chemical shift of the hydroxyl group. The effect is shown in Table I.

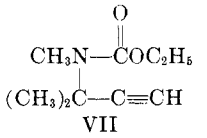
TABLE I

EFFECT OF CONCENTRATION UPON CHEMICAL SHIFT OF THE HYDROXYL GROUP

Concn., mg./0.35 cc.	77	14	10	3.4
Chemical shift, c.p.s.	490	457	436	356

These data showing a move upfield with dilution would favor external hydrogen bonding as in Va rather than internal hydrogen bonding as in Vb.

In an extension of this reaction to other amides, it was found that the benzamido derivative reacted in the same manner as did the acetyl compound. The formamido analog, however, formed a hydrochloride which appeared from the infrared spectrum to be merely the salt of the acetylenic amide. Confirmation of this was obtained when neutralization of a solution of the salt gave the original formamide. Heating the formamide in dilute hydrochloric acid gave only a small amount of hydration of the triple bond, together with hydrolysis, so that the major product was the acetylenic amine accompanied by a small amount of the amino ketone. Treatment of the acetylenic amine under the same conditions did not give any of the keto amine. The urethan (VII), however, was not soluble in dilute hydrochloric acid, nor did it form a hydrochloride in ether with dry hydrogen chloride.



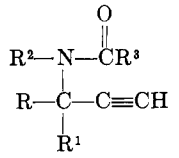
A sequence of reactions has been reported[5] for the solvolysis of *trans*-2-benzamidocyclohexyl *p*-toluene sulfonate in which the intermediate, 2-phenyl-4,5-tetramethyleneoxazoline tosylate, was converted to the benzoate of 2-aminocyclohexanol tosylate and hence to the 2-benzamidocyclohexanol. It also has been shown[6] that the bromination of 3-benzamidopropene gives 2-

(4) The machine used was the Varian Associates Model HR 60, 60 Mc. Deuteriochloroform was used as the solvent and tetramethylsilane as the internal reference.

(5) S. Winstein and R. Boschan, *J. Am. Chem. Soc.*, **72**, 4669 (1950).

(6) L. Goodman and S. Winstein, *ibid.*, **79**, 4788 (1957).

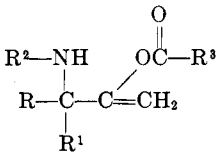
TABLE II



Amides

R	R¹	R²	R³	M.p. or b.p., °C. (mm.)	Analyses: Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Formula
—$(CH_2)_5$—		C_2H_5	CH_3	72–74	74.56	74.81	9.91	9.92	$C_{12}H_{19}NO$
$(CH_3)_2CH$	H	CH_3	CH_3	95–97 (10)	70.55	70.98	9.87	10.08	$C_9H_{15}NO$
C_6H_5	CH_3	C_2H_5	CH_3	156–162 (10)	78.10	77.90	7.96	8.18	$C_{14}H_{17}NO$
CH_3	CH_3	CH_3	C_6H_5	38–40	77.58	77.69	7.51	7.57	$C_{13}H_{15}NO$
CH_3	CH_3	CH_3	H	70 (4)	67.17	67.32	8.86	8.61	$C_7H_{11}NO$
CH_3	CH_3	CH_3	OC_2H_5	56 (4)	63.88	63.80	8.94	8.98	$C_9H_{15}NO_2$
CH_3	CH_3	CH_3	OCH_3	48 (4)	61.91	62.15	8.44	8.40	$C_8H_{13}NO_2$
CH_3	CH_3	CH_3	CH_3	39–41	69.03	68.73	9.41	9.25	$C_9H_{13}NO$
CH_3	CH_3	C_2H_5	CH_3	30–31	70.55	70.46	9.87	9.97	$C_9H_{15}NO$
CH_3	C_2H_5	C_2H_5	CH_3	64 (0.08)	71.81	71.15	10.25	9.98	$C_{10}H_{17}NO$
C_2H_5	C_2H_5	C_2H_5	CH_3	50–52	72.88	72.74	10.57	10.42	$C_{11}H_{19}NO$

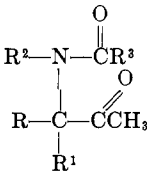
TABLE III



·HCl Enol acetates

R	R¹	R²	R³	M.p., °C.	Empirical formula	Analyses: Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
CH_3	CH_3	CH_3	CH_3	125–126	$C_8H_{10}ClNO_2$	49.61	49.95	8.33	8.27
CH_3	CH_3	CH_3	C_6H_5	132–134	$C_{13}H_{18}ClNO_2$	61.05	60.69	7.09	6.79
CH_3	C_2H_5	C_2H_5	CH_3	120–121	$C_{10}H_{20}ClNO_2$	54.17	54.23	9.09	9.23

TABLE IV



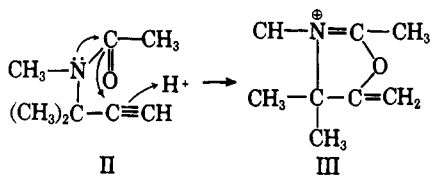
Keto amides

R	R¹	R²	R³	M.p. or b.p., °C. (mm.)	Analyses: Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Empirical formula
CH_3	CH_3	CH_3	CH_3	52–54	61.12	61.22	9.62	9.87	$C_9H_{15}NO_2$
CH_3	CH_3	CH_3	C_6H_5	48–50	71.20	71.53	7.82	8.08	$C_{13}H_{17}NO_2$
CH_3	C_2H_5	C_2H_5	CH_3	104 (0.75)	64.82	64.86	10.34	10.07	$C_{10}H_{19}NO_2$
C_2H_5	C_2H_5	C_2H_5	CH_3	72–74	66.29	66.79	10.62	10.62	$C_{11}H_{21}NO_2$
CH_3	C_2H_5	$(CH_3)CH$	CH_3	90 (0.06)	[a]	[a]			$C_{11}H_{21}NO_2$

[a] Calcd. for nitrogen: 7.03. Found: 6.88.

phenyl-5-bromomethyl-2-oxazolinium bromide, which on neutralization gives 2-phenyl-5-bromomethyl-2-oxazoline and on refluxing in aqueous medium gives 3-bromo-2-benzoyloxypropylamine hydrobromide.

Since these reactions follow very closely those we have observed (II → III → IV → V), it would appear that the present findings constitute an extension of the neighboring group reaction to include the triple bond and that the mechanism of the conversion of II to III may be pictured in the following manner.



II III

Experimental

Preparation of Amides. (1) **Acetic Anhydride Method.**—A mixture of the amine (30 g.) and acetic anhydride (20 ml.) was stirred and warmed in a water bath until the temperature reached 45°. An exothermic reaction occurred, and the temperature of the mixture was maintained at 45–50° until the reaction had subsided. (If the temperature rose above 50°, considerable darkening occurred.) The mixture was poured onto ice and made basic with sodium hydroxide. It was extracted with ether and the ether solution dried and concentrated. The residue was distilled at reduced pressure, or if a solid, recrystallized from methylcyclohexane or low boiling petroleum ether. Yields were from 40–80%.

(2) **Ketene Method.**—The amine was dissolved in ether, and ketene was bubbled through the solution for 4 hr. The mixture was concentrated at reduced pressure and then distilled.

Preparation of the Urethanes.—To a solution of 0.2 mole of the alkyl chlorocarbonate in 50 ml. of anhydrous ether, there was added, slowly with stirring, a solution of 0.2 mole of the amine

in 50 ml. of anhydrous ether. The mixture was stirred for 3 hr. and worked up in the usual manner. See Table II.

2,3,4,4-Tetramethyl-5-methylene-2-oxazolinium Chloride (III).—Dry hydrogen chloride was bubbled into a solution of N-methyl-N-acetyl-3-methyl-1-butyne-3-amine in ether. The solid which formed was filtered and recrystallized from a mixture of dry ethyl acetate and dry isopropyl alcohol, m.p. 191–193°.

Anal. Calcd. for $C_8H_{14}ClNO$: C, 54.70; H, 8.03. Found: C, 54.76; H, 8.10.

3,4-Diethyl-2,4-dimethyl-5-methylene-2-oxazolinium Bromide.—This compound had m.p. 196–198°.

Anal. Calcd. for $C_{10}H_{18}BrNO$: C, 48.39; H, 7.31. Found: C, 48.33; H, 7.29.

Due to the rapid reaction with water these compounds were difficult to purify; hence only a few were obtained in an analytically pure state.

Preparation of the Enol Esters (IV).—The amide hydrochlorides were suspended in acetone, and a small amount of water was added until the salt went into solution. The mixture was concentrated at reduced pressure, and the residue was recrystallized from a mixture of acetone and ethyl acetate. See Table III.

Preparation of the Keto Amides (V).—The oxazolinium salt was dissolved in water, and the solution was made basic with sodium hydroxide. The mixture was extracted with ether, and the ether solution was dried and concentrated. The residue was recrystallized from methylcyclohexane or a mixture of ether–petroleum ether or was distilled at reduced pressure. See Table IV.

N-Formyl-N-methyl-1,1-dimethylpropargylamine.—To 29.1 g. (0.3 mole) of the amine there was added slowly, with stirring, a mixture of 25 g. (0.6 mole) of formic acid and 51 g. (0.5 mole) of acetic anhydride. The temperature of the solution was kept below 65° by cooling with ice. After all of the anhydride solution had been added, the reaction mixture was poured onto ice, and the resulting solution was made basic with sodium hydroxide. The mixture was extracted with ether and the ether solution was dried over magnesium sulfate and concentrated. The residue was distilled at reduced pressure. See Table II.

N-Ethyl-3-acetamido-3-methyl-2-pentanone Hydrochloride.—To a solution of N-ethyl-3-acetamido-3-methyl-2-pentanone in ether dry hydrogen chloride was added. The solid was filtered and recrystallized from methylethyl ketone, m.p. 93–95°.

Anal. Calcd. for $C_{10}H_{20}ClNO$: Cl, 15.99. Found: Cl, 15.89.

N-Isopropyl-3-acetamido-3-methyl-2-pentanone hydrochloride was prepared in the same manner, m.p. 170–172°.

Anal. Calcd. for $C_{11}H_{22}ClNO_2$: Cl, 15.04. Found: Cl, 14.69.

3-Methylamino-3-methyl-2-butanone.—A solution of 20 g. of N-acetyl-N-1,1-trimethylpropargylamine, 100 ml. of water, and 25 ml. of concentrated hydrochloric acid was refluxed for 3 hr. The solution was cooled, made basic with a 50% solution of sodium hydroxide, and saturated with potassium carbonate. The layers were separated and the water layer extracted twice with 50-ml. portions of ether. The organic layers were combined, dried over magnesium sulfate, and distilled. The yield was 14.6 g. (89%), b.p. 84–85° (82 mm.).

Anal. Calcd. for $C_6H_{13}NO$: C, 62.57; H, 11.38. Found: C, 62.42; H, 11.26.

Acknowledgment.—The microanalyses were performed by Messrs. William Brown, Howard Hunter, George Maciak, and Alfred Brown. Many of the starting materials were prepared by Dr. Dwight Morrison and Mr. Lawrence White. The infrared spectra were obtained by Mrs. Doris Stephens and Miss Martha Hoffmann. The authors wish to thank especially Messrs. Paul Landis and Donald Woolf, Jr., for their invaluable services in interpreting and compiling the infrared and n.m.r. data. The authors also express their sincere appreciation to Dr. George Hennion for his many helpful suggestions and much appreciated encouragement.

Solvent Effects on the Claisen Rearrangement of β-Methylallyl Phenyl Ether

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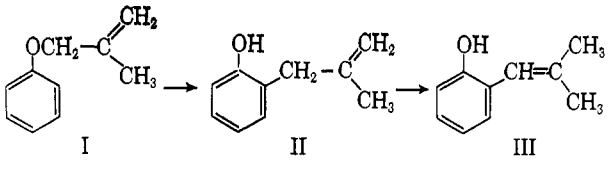
Received March 11, 1963

The need for highly purified samples of variously substituted *o*-allyl- and *o*-propenylphenols, in connection with a study of intramolecular hydrogen bonding, has led to the employment of gas–liquid chromatography both for the isolation as well as for the verification of homogeneity of various synthetic samples. A previously studied compound,[1] *o*-(β-methylallyl)phenol (II), was found, by analysis upon an ethylene glycol succinate chromatographic column, to contain a sizeable per cent of a faster moving component; this was readily identified as the isomeric *o*-isobutenylphenol (III).



I II III

TABLE I

PRODUCT DISTRIBUTION IN THE CLAISEN REARRANGEMENT OF β-METHYLALLYL PHENYL ETHER (I)

No.	Solvent	Solvent b.p., °C.	Reaction temp. °C.	At 5% of unchanged starting material: Elapsed time, Hr.	% II	% III	% IV
1	None	...	205–216	3.3	53	12	26
2	Nitrobenzene	211	200–206	4.2	73	11	10
3	2,6-Xylenol	212	198–199	3.5	6	10	73
4	2,6-Xylidine	217	212–215	3.7	8	44	32
5	N,N-Dimethyl-*m*-toluidine	211	208–216	3.5	81	4	1
6	Tributylamine	214	205–215	7.8	85	3	2
7	*p*-Tolunitrile	217	208–218	3.0	80	9	6
8	Dodecane	215	203–210	5.5	76	9	10

TABLE II

EFFECTS OF VARIOUS TERTIARY AROMATIC AMINES AS SOLVENTS IN THE CLAISEN REARRANGEMENT OF β-METHYLALLYL PHENYL ETHER

Solvent	Solvent b.p., °C.	Reaction temp., °C.	At 5% of unchanged starting material: Elapsed time, hr.	% II	% III	% IV
N,N-Dimethyl-*o*-toluidine	184	188–200	10	81	3	1
N,N-Dimethylaniline	193	199–205	4.8	90	2	1
N,N-Dimethyl-*m*-toluidine	212	208–216	3.5	81	4	1
N,N-Diethylaniline	216	207–218	2.8	86	4	2
N,N-Diethyl-*p*-toluidine	229	214–225	1.9	87	3	2

(1) A. W. Baker and A. T. Shulgin, *J. Am. Chem. Soc.*, **81**, 4524 (1959).