Catalytic Ethynylation of Ketones[1]

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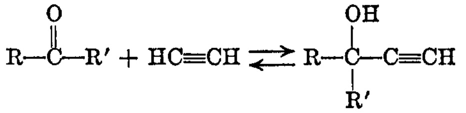
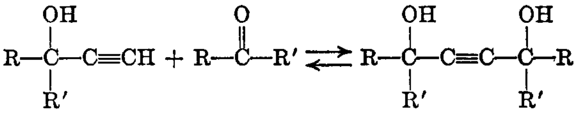
An improved catalytic method for the ethynylation of ketones which involves the use of an alkali-metal acetylide, alkoxide, or hydroxide catalyst in an anhydrous nonacidic medium has been developed. At room temperature, tertiary ethynylcarbinols were produced almost exclusively in high yields; only small amounts of acetylenic glycol or other by-products were formed. Under the conditions employed, the ethynylation of aliphatic ketones was found to be operationally irreversible. The rates of ethynylation of cyclohexanone and of acetone were measured in *N*-methylpyrrolidone in the temperature range 0–40° under atmospheric pressure. The data were interpreted in terms of an irreversible nucleophilic addition of acetylide anion to ketone.

The addition of acetylene to ketones in the presence of a basic condensing agent to give ethynylcarbinols (equation 1) and acetylenic glycols (equation 2) has been studied extensively since the turn of the century.[2]



$$R-\overset{\overset{O}{\|}}{C}-R' + HC\equiv CH \rightleftarrows R-\underset{\underset{R'}{|}}{\overset{\overset{OH}{|}}{C}}-C\equiv CH \quad (1)$$



$$R-\underset{\underset{R'}{|}}{\overset{\overset{OH}{|}}{C}}-C\equiv CH + R-\overset{\overset{O}{\|}}{C}-R' \rightleftarrows R-\underset{\underset{R'}{|}}{\overset{\overset{OH}{|}}{C}}-C\equiv C-\underset{\underset{R'}{|}}{\overset{\overset{OH}{|}}{C}}-R \quad (2)$$

The reversibility of these reactions was investigated recently by Chodkiewicz[3] who examined some of the factors relating to the equilibria, particularly for aromatic ketones. All of the early work and many more recent publications[3,4] relating to the ethynylation of ketones have dealt with the use of at least stoichiometric quantities of a basic condensing agent.

A truly catalytic synthesis was discovered first by Reppe[5] who employed aqueous or alcoholic base at elevated temperatures under pressure. The use of a strongly basic ion exchange resin catalyst under similar experimental conditions was disclosed by Whitfield.[6] Very recently, Nedwick and Watanabe of this laboratory patented a continuous, condensed phase, high pressure, high temperature process for the catalytic ethynylation of cyclohexanone and its homologs.[7]

Results and Discussion

This publication concerns a procedure for the catalytic ethynylation of ketones under very mild conditions. Alkali-metal acetylides (prepared *in situ* from the alkali metals), alkoxides, or hydroxides were employed as catalysts (*ca.* 5 mole % based on ketone) in anhydrous nonacidic media to achieve rapid ethynylation at room temperature. Tertiary ethynylcarbinols were produced almost exclusively; only small amounts of acetylenic glycols or other by-products were formed. The effects of temperature and solvent and the variations of ketone and catalyst were investigated in batch experiments under pressure (400–500 p.s.i.g.). Kinetic data for the catalytic ethynylation of cyclohexanone and acetone in *N*-methylpyrrolidone were obtained in the temperature range 0–40° under acetylene at atmospheric pressure.

Batch Experiments under Pressure.—The data shown in Table I for cyclohexanone indicate that

TABLE I

EFFECT OF TEMPERATURE ON THE BASE-CATALYZED ETHYNYLATION OF CYCLOHEXANONE

Experiment No.[a]	Time, Hr.	T, °C.	Conversion to Carbinol, %[b]	Conversion to Glycol, %[b,c]	Recovered Ketone, %
1	3.0	81	40.8	27.2	. . .
2	1.7	57	49.5	4.5	19.1
3	1.2	24–32[e]	46.8	1	29.6
4[d]	5.5	24–40[e]	81.2	6.0	. . .

[a] Reaction charge: 100 g. of *N*-methylpyrrolidone, 0.76 mole of cyclohexanone, 0.043 g.-atom of sodium. [b] Based on ketone. [c] The glycol, bis(1-hydroxycyclohexyl)acetylene, was isolated from the distillation residue and recrystallized from carbon tetrachloride, m.p. 107–109°. [d] For this experiment, 0.65 mole of cyclohexanone was employed. [e] Ambient temperature.

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[1] Presented before the 138th Meeting of the American Chemical Society, New York, N. Y., September, 1960.

[2] A. W. Johnson, "Acetylenic Compounds," Vol. I, Edward Arnold & Co., London, 1946, pp. 11–16; R. A. Raphael, "Acetylenic Compounds in Organic Synthesis," Academic Press Inc., New York, 1955, pp. 10–15; J. A. Nieuwland and R. R. Vogt, "The Chemistry of Acetylene," Reinhold Publishing Corp., New York, 1945, pp. 81–88.

[3] W. Chodkiewicz, *Ann. Chim.* (Paris), **2**, 819 (1957).

[4] O. Pesta and F. Ebel, U. S. Patent 2,302,345 (1942); N. Robert, W. Chodkiewicz, and P. Cadiot, *Compt. rend.*, **252**, 526 (1956); J. Colonge, R. Falcotet, and R. Gaumont, *Bull. soc. chim. France*, No. 2, 211 (1958); E. F. Smith, U. S. Patent 2,385,548 (1945); Rheinpreussen A.-G. fur Bergbau und Chemie, British Patent 783,417 (1957); J. Zeltner and M. Genas, German Patent 862,005 and 882,701 (1953); R. F. Kleinschmidt and S. H. Pitts, Jr., U. S. Patent 2,858,344 (1958); R. N. Lacey and H. Jowitt, U. S. Patent 2,904,596 (1959); T. F. Rutledge, U. S. Patent 2,910,510 (1959); S. Chodroff and M. Dunkel, U. S. Patent 2,919,281 (1959); T. Herbertz, *Ber.*, **92**, 541 (1959); H. Pasedach and M. Seefelder, German Patent 1,081,883 (1960); E. Tamate and S. Kinoshita, *Kôgyô Kagaku Zasshi*, **60**, 729 (1959), *Chem. Abst.*, **53**, 11206 (1959).

[5] W. Reppe, *Ann.*, **596**, 30 (1955).

[6] G. H. Whitfield, U. S. Patent 2,826,614 (1958); British Patent 735,118 (1955).

[7] J. J. Nedwick and W. H. Watanabe, U. S. Patent 2,973,390 (1961).

TABLE II

EFFECT OF SOLVENT ON THE BASE-CATALYZED ETHYNYLATION OF CYCLOHEXANONE

Experiment No.[a]	Solvent[b]	Time, Hr.	T, °C.[c]	Conversion to Carbinol, %	Recovered Ketone, %
3	*N*-Methylpyrrolidone	1.2	24–32	46.8	29.6
5	*N*-Methylpyrrolidone[d]	1.6	24–30	1–3	90
6	*N*,*N*-Dimethylformamide	1.5	22–29	42.5	40.5
7	Dimethyl sulfoxide	1.5	27–36	71.6	19.3
8	1,2-Dimethoxyethane	1.5	23–37	42.4	51.4
9	Tetrahydrofuran	1.5	18–28	28	48.7
10	Benzene	1.5	20–22	12.9	78.1
11[e]	Methanol	1.5	19–22	0.9	90
12	Isopropyl alcohol	1.5	17–21	8.0	69.7
13	*t*-Butyl alcohol	1.5	21–27	30	51.8
14	Tetraethylene glycol dimethyl ether	1.2[f]	21–25	54	33.8
15	Pyridine	1.5	18–24	>28.5[g]	27.8
16	Diethyl ether	1.5	21–25	17.9	60.4

[a] Reaction charge: 100 g. of solvent, 0.76 mole of cyclohexanone, 0.043 g.-atom of sodium. [b] The solvents were carefully purified by distillation. In all cases the water content was less than 0.07 wt. % (analysis with Karl Fischer reagent). [c] Ambient temperature. [d] Only 25 g. of solvent was employed. [e] For this experiment, 0.064 g.-atom of sodium was used. [f] The mixture was stirred for 1.2 hr. and then was allowed to remain under acetylene (300–500 p.s.i.g.) for 2 days before carbonation. [g] The product mixture was flash-distilled to a pot temperature of 98° at 5–10 mm. Consequently, much of the product remained with the residue.

TABLE III

VARIATION OF KETONE

Experiment No.[a]	Ketone[b]	Time, Hr.	T, °C.[c]	Conversion to Carbinol, %	Recovered Ketone, %
3	Cyclohexanone	1.2	24–32	46.8	29.6
17	Acetone	1.1	22–40	41.5	38.4
18[d]	Acetone	20	25–36	72.5	*ca.* 15
19	Ethyl methyl ketone	1.9	24–34	47.2	47.5
20	Diethyl ketone	1.6	23–37	71.9	14.7
21[e]	*di-n*-Butyl ketone	1.8	24–33	56.5	29.1
22	Methyl vinyl ketone	1.4	23–27	0	0[f]
23	Mesityl oxide	1.1	26–43	0	*ca.* 30[g]
24	Acetophenone	1.9	27–32	13.5	77.3
25[h]	Acetophenone	3.0	21–26	29.5	...
26[i]	Benzophenone	3.0	23–26	25.3	...

[a] Reaction charge: 100 g. of *N*-methylpyrrolidone, 0.76 mole of ketone, 0.043 g.-atom of sodium. [b] Anhydrous ketone. [c] Ambient temperature. [d] 0.69-Mole sample of ketone employed. [e] 0.61-Mole sample of ketone employed. [f] A solid polymer with a coconut-like odor was formed. [g] Mainly high-boiling condensation products and water were obtained. [h] Reaction charge: 100 g. of dimethyl sulfoxide, 0.76 mole of ketone, 0.052 g.-atom of sodium. [i] Reaction charge: 100 g. of dimethyl sulfoxide, 0.55 mole of ketone, 0.052 g.-atom of sodium.

at room temperature acetylenic glycol formation was extremely slow. As the temperature of the reaction was raised, the rate of glycol formation increased. The temperature was not controlled for the experiments conducted at room temperature. In each instance when a significant amount of ethynylation occurred an initial brief exotherm was noted.

It was surprising to find that a large variety of solvents could be employed successfully for the reaction (Table II). Even relatively nonpolar solvents such as benzene and diethyl ether afforded homogeneous reaction mixtures and significant conversions of ketone to carbinol. The highest conversions were obtained, as expected, in the better acetylene solvents; dimethyl sulfoxide was particularly effective.[8] Apparently, almost any anhydrous nonacidic organic solvent may be used, with the exception of primary and perhaps secondary alcohols. If too little solvent was employed (experiment no. 5), the reaction did not take place readily, presumably owing to precipitation of the active catalyst. This suggests that the ketone itself does not function as a satisfactory reaction solvent.

Ketones which are not exceedingly sensitive to base under the mild conditions of the reaction underwent ethynylation smoothly (Table III). With the aliphatic ketones, high conversions to ethynylcarbinol (40–70%) were achieved during a reaction period of 1–2 hours. Under comparable experimental conditions much lower conversions were observed with the aromatic ketones. The base sensitive ketones, methyl vinyl ketone and mesityl oxide, underwent self-condensation in preference to ethynylation.

Sodium and potassium, as well as sodium methoxide, were employed successfully in catalytic amounts (generally 5 mole % based on ketone) to

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(8) During the preparation of this paper our attention was directed to two very recent patents by J. H. Blumenthal (Canadian Patent 623,966, July 18, 1961, and U. S. Patent 2,996,522, August 15, 1961) which claim a process for the base-catalyzed ethynylation of ketones in ethylenediamine or liquid organic sulfoxide media under mild experimental conditions.

TABLE IV

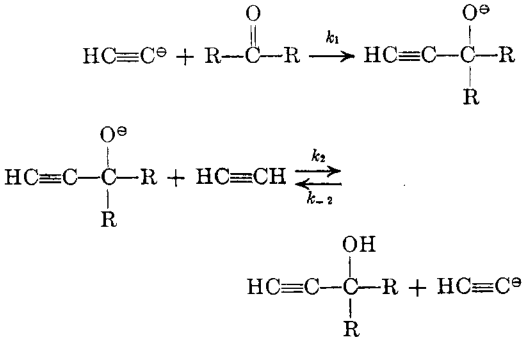
VARIATION OF CATALYST

Experiment No.[a]	Catalyst	Moles of Catalyst	Time, Hr.	T, °C[b]	Conversion to Carbinol, %	Recovered Ketone, %
3	Na[c]	0.043	1.2	24–32	46.8	29.6
27	Na[c]	0.022	1.5	24–33	51.8	43.5
28	K[c]	0.041	1.5	16–26	53.1	31.5
29	$NaOCH_3$[d]	0.044	1.6	27–34	54.2	25.7
30	NaOH[e]	0.043	1.6	30–35	46.4	...
31	KOH[e]	0.043	1.6	29–40	66.3	...
32	Li[c,f]	0.073	1.5	18–22	0	*ca.* 100
33	Li/CH_3OH[f]	0.044	1.5	16–20	0	*ca.* 100
34	n-C_4H_9Li[g]	0.042	1.5	12–17	0	*ca.* 100

[a] Reaction charge: 100 g. of *N*-methylpyrrolidone, 0.76 mole of cyclohexanone. [b] Ambient temperature. [c] Pea-sized chunks. [d] Mathieson sodium methoxide used. [e] Crushed reagent grade material. [f] Some unchanged metallic lithium was recovered. [g] Reaction charge: 22 ml. of 1.9 *M* *n*-butyllithium (in petroleum ether), 68 g. of cyclohexanone, 90 g. of *N*-methylpyrrolidone.

promote the reaction. The reaction mixtures, heterogeneous at the outset, became homogeneous when acetylene was introduced, apparently as a result of alkali-metal acetylide formation and subsequent reaction. Contrary to our earlier report,[9] both sodium hydroxide and potassium hydroxide were found to be effective ethynylation catalysts[8] (experiment no. 30 and 31). Metallic lithium, lithium methoxide, and *n*-butyllithium failed to serve as catalysts under the conditions employed. The data are summarized in Table IV.

Kinetic Experiments at Atmospheric Pressure.—Under the mild conditions employed, the ethynylation of aliphatic ketones was shown by experiment to be operationally irreversible. When cyclohexanone was treated with acetylene in the presence of catalyst for a long period of time, the theoretical amount of acetylene was absorbed. For many of the kinetic experiments the quantity of acetylene which reacted corresponded to a high degree of conversion (>80%). That essentially all of the acetylene absorbed (except for solubility) was converted to ethynylcarbinol was demonstrated experimentally by isolation. Furthermore, 1-ethynylcyclohexanol did not undergo observable cleavage on treatment with catalyst solution at room temperature. The data obtained for the ethynylation of acetone and cyclohexanone under pressure also suggest irreversibility rather than equilibrium (see Table I, experiment no. 3 and 4 and Table III, experiment no. 17 and 18).



$$HC{\equiv}C^{\ominus} + R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}R \xrightarrow{k_1} HC{\equiv}C{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle O^{\ominus}}{|}}{C}}{-}R$$

$$HC{\equiv}C{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle O^{\ominus}}{|}}{C}}{-}R + HC{\equiv}CH \underset{k_{-2}}{\overset{k_2}{\rightleftarrows}} HC{\equiv}C{-}\underset{\underset{\displaystyle R}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}{-}R + HC{\equiv}C^{\ominus} \qquad (4)$$

In view of these considerations, the preceding reaction scheme was formulated. If it is assumed that (a) $[HC{\equiv}CH]$ = constant (constant acetylene pressure) and (b) $d\,[HC{\equiv}C{-}\overset{\overset{\displaystyle O^{\ominus}}{|}}{C}R_2]/dt = 0$ (steady state with respect to the product anion), then the following rate expression may be derived.

$$[C_0]\left(\log \frac{[C_0]}{[C_0] - [P]}\right) - \left(1 - \frac{k_1}{k_{-2}}\right)\frac{[P]}{2.3} = \frac{k_1K[A][H]t}{2.3} \qquad (5)$$

or

$$f[P] = \frac{k_1K[A][H]t}{2.3} \qquad (5a)$$

where, $K = k_2/k_{-2}$, $[C_0]$ = original ketone concentration, $[H]$ = acetylene concentration, $[P]$ = product concentration at time t, $[A]$ = concentration of product anion.

The validity of the steady state assumption bears further amplification. If the second step of the reaction (equation 4) is an equilibrium, one might take exception to the assumption that $d[A]/dt = 0$ after a short induction period, for both the acetylide concentration $[N]$, and the alkoxide concentration, $[A]$, clearly depend upon the concentration of the product, $[P]$, which is constantly changing. Accordingly, a further assumption is necessary; namely; $k_{-2}[P][N] >> k_2[A][H]$. Because an acetylenic hydrogen is considerably less acidic than a hydroxyl hydrogen, it is not unreasonable to expect that the equilibrium between alkoxide and acetylene to give carbinol and acetylide would be very unfavorable. Thus, after a short induction period, the alkoxide concentration, $[A]$, would be almost numerically equivalent to the catalyst concentration at the start, and the concentration of the active catalyst, $[N]$, would be extremely small. As $[P]$ increases, $[N]$ should decrease according to the following expression

$$[N] = \frac{k_2[A][H]}{k_1[C] + k_{-2}[P]}$$

where $[C]$ is the concentration of ketone.

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[9] Norman Shachat, Abstracts of the 138th Meeting of the American Chemical Society, New York, N. Y., September, 1960, p. 75P.

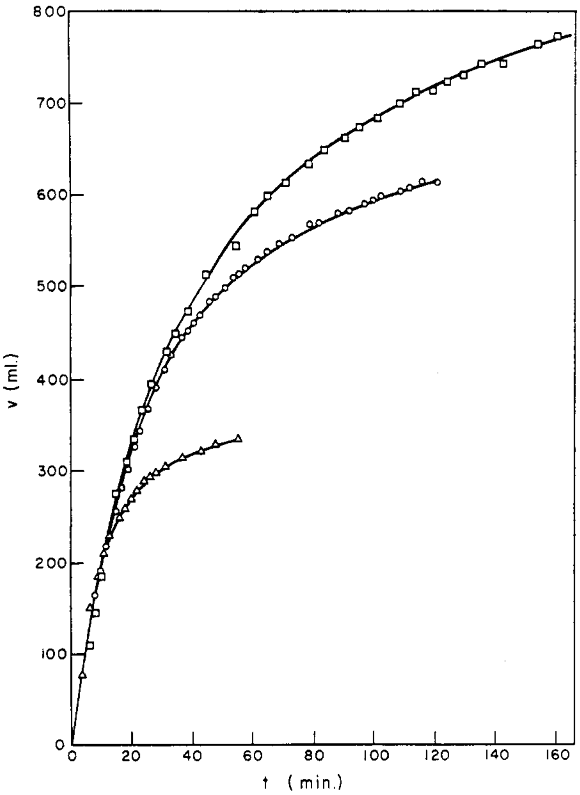


Fig. 1.—Typical plots of acetylene absorption *vs.* time for catalytic ethynylation of cyclohexanone: △—experiment no. 35; ○—experiment no. 38; □—experiment no. 41

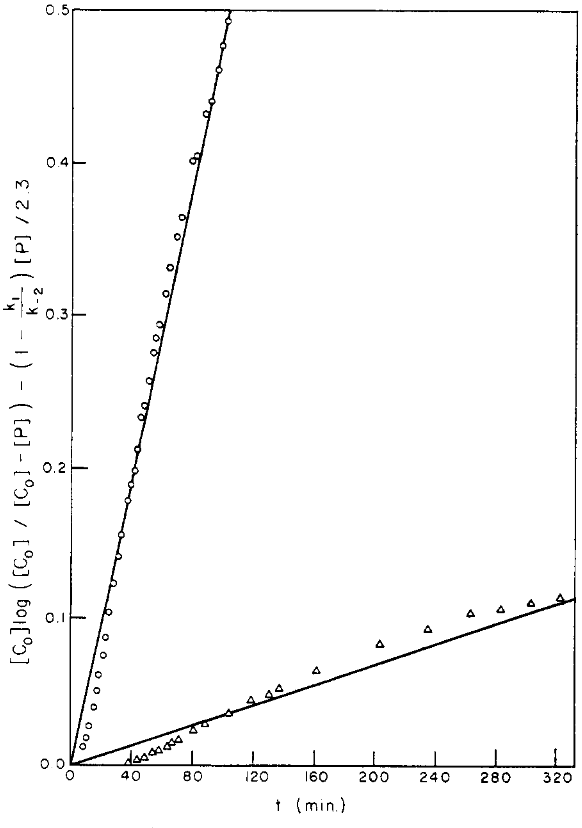


Fig. 2.—Typical plots of $f[P]$ *vs.* time: ○—experiment no. 38; △—experiment no. 44

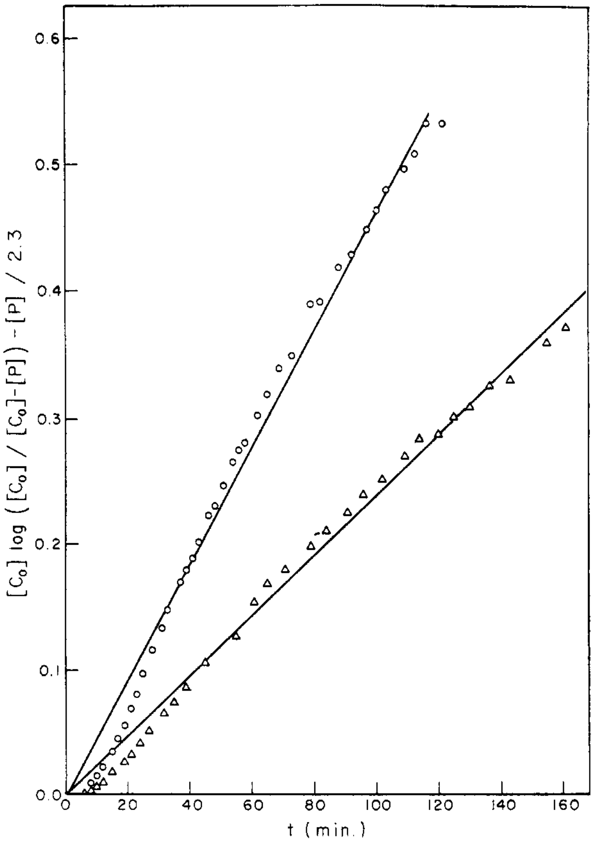


Fig. 3.—Typical plots of $f'[P]$ *vs.* time: ○—experiment no. 38; △—experiment no. 41

If, as anticipated, $k_1 << k_{-2}$, then $(1-k_1/k_{-2}) \approx 1$ and equation 4 may be written in the simplified form designated equation 6

$$[C_0]\left(\log\frac{[C_0]}{[C_0]-[P]}\right)-\frac{[P]}{2.3}=\frac{k_1K[A][H]t}{2.3} \quad (6)$$

or

$$f'[P]=\frac{k_1K[A][H]t}{2.3} \quad (6a)$$

Equations 5 and 6 predict a linear relationship between $f'[P]$ (or $f[P]$) and t, with a slope directly proportional to k_1, K, the initial catalyst concentration and the acetylene concentration.

The course of the reaction was followed by measuring the absorption of acetylene at one atmosphere (Fig. 1). The product concentration was calculated from the quantity of acetylene absorbed, corrected for solubility effects. All of the data was analyzed in terms of equation 6. For several experiments, the values of $1-k_1/k_{-2}$ and $k_1K[A][H]/2.3$ given by equation 5 were calculated, and the best linear slopes calculated by the method of least squares of plots of $f[P]$ against t were compared with those obtained from plots of $f'[P]$ against t. The data, presented in Table V, confirm the assumption that $k_1 < < k_2$ and also indicate fair agreement between the values of $k_1K[A][H]/2.3$ given by equations 5 and 6, particularly for the experiments carried to a high degree of conversion.

TABLE V

EFFECT OF $[C_0]$ ON THE RATE OF ETHYNYLATION OF CYCLOHEXANONE IN N-METHYLPYRROLIDONE

Experiment No.[a]	[Cat.] (M)[b]	$[C_0]$ (M)	$(k_1K[A][H]/2.3) \times 10^3$ by Equation 6 (moles/min.)	$(k_1K[A][H]/2.3) \times 10^3$ by Equation 5 (moles/min.)	$1 - k_1/k_{-1}$
35[c]	0.173	0.79	10.2 ± 0.2[g]	11.1 ± 0.5[g]	0.90 ± 0.06[g]
36[c]	0.071	0.81	4.05 ± 0.08	....	....
37[c]	0.076	0.78	5.25 ± 0.17	....	....
38[d]	0.158	1.50	4.65 ± 0.05	4.80 ± 0.016	0.97 ± 0.03
39[d]	0.158	1.47	4.42 ± 0.06	....	....
40[e]	0.146	2.07	2.55 ± 0.06	....	....
41[e]	0.146	2.08	2.39 ± 0.03	2.45 ± 0.10	0.99 ± 0.02
42[f]	0.136	2.71	1.07 ± 0.04	....	....
43[f]	0.136	2.82	0.91 ± 0.04	0.50 ± 0.02	1.08 ± 0.01
44[f]	0.127	3.20	0.48 ± 0.01	0.34 ± 0.01	1.06 ± 0.01

[a] $T = 20.0°$, $[H] = 1$ atm. [b] Catalyst prepared from sodium and acetylene in N-methylpyrrolidone. [c] Conducted to 90–96% conversion. [d] Conducted to 78–88% conversion. [e] Conducted to 55–65% conversion. [f] Conducted to 40–49% conversion. [g] Calculated standard deviations.

Some typical plots of $f[P]$ *vs.* t and $f'[P]$ *vs.* t are illustrated in Figures 2 and 3, respectively. Although the calculated standard deviations from linearity in all cases were small suggesting that the plots could be approximated by straight lines, it can be seen by visual examination that the experimental points afforded S-shaped curves, consistently dipping below the straight line at low values of $f[P]$ and $f'[P]$ and rising above the line at the higher values. The more serious derivations, those which occurred generally at the early stages of the reaction, may have been due to errors in the experimental method. The rate of product formation was followed experimentally by measuring rate of acetylene absorption. Solubility corrections were made assuming instantaneous establishment of equilibrium between the gas and liquid phases; however, it is known that such processes are diffusion controlled and do not occur instantaneously. If the rate of product formation at the beginning of the experiment was somewhat greater than the rate of acetylene absorption, the calculated value of $[P]$ would be less than the actual concentration of product in the mixture. Undoubtedly, the small exotherm of short duration which was observed on addition of the ketone contributed to this error. In addition, it should be noted that at low degrees of conversion, the functions $f[P]$ and $f'[P]$ represent a very small difference between two small numbers.

As previously mentioned, if after a short induction period $[A] =$ [Cat.] then the slope of a plot of $f'[P]$ against t should be directly proportional to the initial catalyst concentration. The experimental data for a few experiments in which only the catalyst concentration was significantly varied (Table V, experiments no. 35–37; Table VI, experiment no. 47–49), tend to substantiate this relationship moderately well.

TABLE VI

EFFECT OF TEMPERATURE ON THE BASE-CATALYZED ETHYNYLATION OF CYCLOHEXANONE

Experiment No.[a]	T, °C.	[Cat.] (M)[d]	$(k_1K[A][H]/2.3) \times 10^3$ (mole/min.)
45[b]	0.6	0.064	0.28 ± 0.02[e]
46[c]	9.7	0.060	0.71 ± 0.03
47[c]	20.0	0.064	2.02 ± 0.05
48[c]	20.0	0.029	0.89 ± 0.02
49[c]	20.1	0.027	0.96 ± 0.01
50[c]	30.3	0.027	1.95 ± 0.05
51[c]	31.0	0.062	3.07 ± 0.19
52[c]	35.5	0.027	2.12 ± 0.07
53[c]	41.5	0.027	4.07 ± 0.16

[a] $[C_0] = 0.89$ M, $[H] = 1$ atm. [b] Conducted to 55–65% conversion. [c] Conducted to 78–88% conversion. [d] Catalyst prepared from equimolar quantities of sodium methoxide and 1-ethynylcyclohexanol in N-methylpyrrolidone. [e] Calculated standard deviations.

The effect of temperature on the rate of ethynylation of cyclohexanone in the temperature range 0–40° in N-methylpyrrolidone was determined (Table VI). The values of the slope, $k_1K[A][H]/2.3$, at each temperature were calculated for a constant $[A]$, assuming slope α [Cat.]. An Arrhenius plot (Figure 4) afforded a straight line of slope $= -3.0 \pm 0.2 \times 10^3$ from which the activation energy for the over-all process was calculated:

$$E_a = RT^2 \frac{\mathrm{d} \ln k_1K}{\mathrm{d}T} = 2.3 \times R \times - (\text{slope}) \times 10^3 = 13.8\,\text{kcal}$$

It was rather surprising to find that as the initial ketone concentration, $[C_0]$, was increased, the rate dropped markedly in roughly logarithmic fashion (Table V). The slopes given by equation 6 were calculated for a constant catalyst concentration (assuming slope α [Cat.]) and plotted against $[C_0]$ in Figure 5. This effect may have been due in part to the decrease in the degree of conversion to which the experiments were carried as $[C_0]$ was increased. The regularity and magnitude of the decrease in rate suggest, however, that perhaps marked solvent effects are operative. In the extreme cases, the concentration of N-methylpyrrolidone was varied from 9 to 6.6 M, and the ketone concentration, from 0.8 to 3.2 M. Many recent publications[3,10] have dealt with the marked accelerating effect on

(10) H. E. Zaugg, B. W. Harrom, and S. Borgwardt, *J. Am. Chem. Soc.*, 2895 (1960); T. P. Johnston, L. B. Holum, and J. A. Montgomery, *J. Am. Chem. Soc.*, **80**, 6265 (1958); W. E. Truce and R. F. Heine, *J. Am. Chem. Soc.*, **78**, 6034 (1956); H. E. Zaugg, *et al.*, Abstracts of the 138th Meeting of the American Chemical Society, New York, September, 1960, p. 9 P.

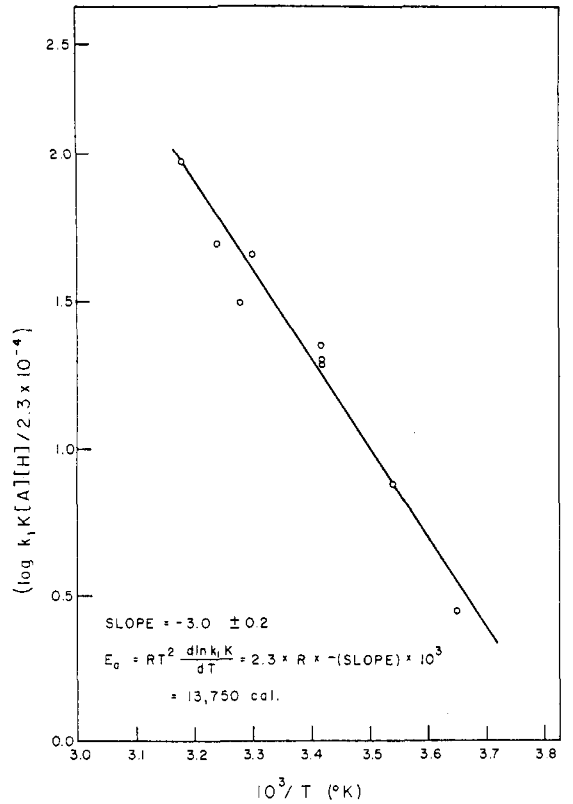


Fig. 4.—Arrhenius plot for the catalytic ethynylation of cyclohexanone in *N*-methylpyrrolidone: $[C_0] = 0.89\ M$; $[\text{Cat.}] = 0.064\ M$

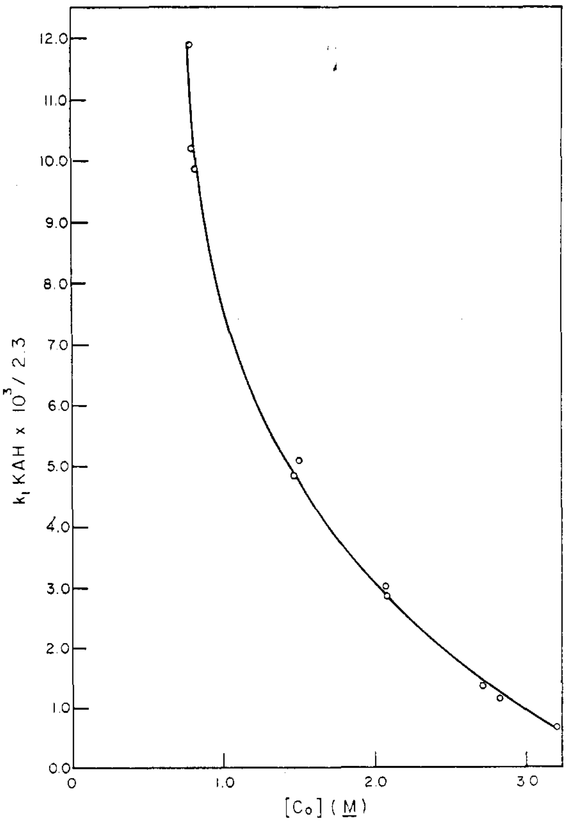
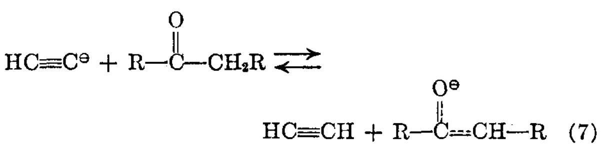


Fig. 5.—Effect of $[C_0]$ on the rate of ethynylation of cyclohexanone: $[\text{Cat.}] = 0.173\ M$

the rate of certain ionic reactions of polar additives, such as *N*-methylpyrrolidone, dimethylsulfoxide, etc. It seems reasonable to suspect, therefore, that the solvent plays an active role in the reaction mechanism, presumably as solvator for the anionic species.

An alternative explanation for the decrease in rate with an increase in $[C_0]$ may be found in enolate formation (equation 7). An increase in ketone concentration would tend to shift the equilibrium to the right and thereby decrease the concentration of the active acetylide catalyst.



$$HC{\equiv}C^{\ominus} + R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_2R \rightleftharpoons HC{\equiv}CH + R{-}\overset{\overset{\displaystyle O^{\ominus}}{|}}{C}{=}CH{-}R \quad (7)$$

The decelerating effect of small amounts of methanol on the rate of ethynylation of cyclohexanone is clearly demonstrated by the data in Table VII. The mode of deactivation by methanol or any proton donor (water, isopropyl alcohol, etc.) most likely involves removal of acetylide in accordance with the following equilibrium.

$$CH_3OH + NaC{\equiv}CH \rightleftharpoons CH_3ONa + HC{\equiv}CH \quad (8)$$

This suggests that the catalyst solution prepared from the alkali-metal and acetylene should be more active than that prepared from the alkali-metal alkoxide and the ethynylcarbinol. A comparison of rates, corrected to the same experimental conditions by means of Figure 5 and the assumption, slope $\alpha[\text{Cat.}]$, is shown in Table VIII.

Table VII

Effect of Methanol on the Base-Catalyzed Ethynylation of Cyclohexanone[a,b]

$[CH_3OH]$ (*M*)	Conversion, %, after 30 Min.
0.000	14.7
0.064	7.9
0.096	6.9
0.160	4.1
0.320	*ca.* 1.1

[a] $[C_0] = 1.58\ M$, $[\text{Cat.}] = 0.064\ M$ in *N*-methylpyrrolidone. [b] Catalyst prepared from sodium and acetylene.

Table VIII

Comparison of Catalyst Systems[a]

Catalyst System[b]	$(k_1K[A][B]/2.3) \times 10^3$ (moles/min.)
Na + HC≡CH	8.85
$NaOCH_3$ + 1-ethynylcyclohexanol	5.39

[a] $[C_0] = 0.89\ M$, $[\text{Cat.}] = 0.173\ M$, $T = 20.0°$. [b] In *N*-methylpyrrolidone.

The modest amount of experimental data relating to the rate of ethynylation of acetone in *N*-methylpyrrolidone is given in Table IX. Unfortunately, the conditions for the acetone experiments were not the same as those used for the cyclohexanone reactions. A crude comparison, made by extrapolation of the data for cyclohexanone to the conditions employed for the acetone ethynylations (by means of Figure 5 and the assumption slope α [Cat.]), suggests that at 20°, the rate of ethynylation of cyclohexanone is approximately five times the rate of ethynylation of acetone.

TABLE IX

RATES OF ETHYNYLATION OF ACETONE IN *N*-METHYLPYRROLIDONE

Experiment No.[a]	T, °C.	[Cat.] (*M*)	$(k_1K[A][H]/2.3) \times 10^3$ (mole/min.)
54[b]	20.0	0.054	0.20 ± 0.00[d]
55[c]	20.0	0.074	0.29 ± 0.01
56[b]	30.3	0.058	0.44 ± 0.01
57[c]	30.3	0.074	0.55 ± 0.01

[a] $[C_0] = 1.35\ M$, [H] = 1 atm. [b] Conducted to 40–49% conversion. [c] Conducted to 55–65% conversion. [d] Calculated standard deviations.

Experimental

Batch Experiments under Pressure.—The following detailed description of a single experiment (experiment no. 27) will serve to illustrate the method.

A mixture of 100 g. of freshly distilled, anhydrous *N*-methylpyrrolidone, 0.5 g. (0.022 g.-atom) of metallic sodium, and 75.0 g. (0.76 mole) of anhydrous cyclohexanone was treated with acetylene at 400–500 p.s.i. g. for 1.5 hr. at ambient temperature (24–33°) in a magnetically stirred autoclave. Acetylene was passed in periodically to maintain the pressure. Reaction was stopped by the introduction of carbon dioxide gas under additional pressure to neutralize the catalyst. Three grams of glacial acetic acid was added to the reaction mixture which had gained 16 g. during the reaction. The solution on distillation to a maximum pot temperature of 140° at 1.2 mm. afforded a colorless distillate (172.1 g.) and an almost colorless, solid, water-soluble residue (7.1 g.). A vapor phase chromatogram of the distillate exhibited only three significant peaks, those due to cyclohexanone, 1-ethynylcyclohexanol, and *N*-methylpyrrolidone. The solution, degassed of acetylene, was analyzed for acetylenic hydrogen by the method of Barnes and Molinini[11] and showed 2.30 meq./g. or a total of 0.396 equivalents of 1-ethynylcyclohexanol. This represented a conversion of 51.8% based on cyclohexanone. The recovered ketone, estimated by vapor phase chromatography, amounted to 32.6 g. or 43.5%; it could be removed from the solution by fractional distillation. The product could be separated from the solvent by adding water to the mixture, extracting the product from the aqueous solution with ether, and distilling the ether solution.

Kinetic Experiments at Atmospheric Pressure.—The rate data were obtained from experiments conducted in a quantitative gas absorption apparatus consisting of a reaction flask equipped with a thermometer, a magnetic stirrer, an orifice sealed with a rubber membrane, and an opening which led to a mercury manometer and to a 1-l. calibrated gas reservoir. A given quantity of catalyst solution; prepared either by treating a mixture of sodium and *N*-methylpyrrolidone with acetylene under pressure at room temperature or by adding equal molar amounts of sodium methoxide and an ethynylcarbinol to *N*-methylpyrrolidone, was saturated with acetylene at the reaction temperature in the reaction flask. An accurately weighed quantity of ketone was then introduced with a syringe through the rubber membrane. While the temperature of the reaction mixture and the pressure of acetylene above the mixture were kept constant, the absorption of acetylene was followed.

Freshly distilled, anhydrous *N*-methylpyrrolidone and ketone were employed in all cases. The strong base strength of the catalyst solution was determined by potentiometric titration of an aliquot of the solution before each experiment. All of the experiments were carried out under one atmosphere of acetylene. Before each experiment the system was tested for leaks and thoroughly flushed with acetylene. The details of a typical experiment (experiment no. 38) follow.

A catalyst solution was prepared by treating a mixture of 150 ml. of *N*-methylpyrrolidone and 1.5 g. of sodium with acetylene at room temperature under 25–30 atm. pressure in a magnetically stirred autoclave. The red solution was decanted from a small amount of a colorless solid (insoluble sodium acetylide), diluted with an additional 50 ml. of *N*-methylpyrrolidone, and stored in a sealed bottle under dry nitrogen. An analysis of the solution showed that it contained 0.19 meq./ml. of strong base.

A portion of the solution (20.0 ml.) was saturated with acetylene at 20.0° in the reaction flask. In a separate experiment the amount of acetylene absorbed by 20.0 ml. of the catalyst solution at 20.0° was determined to be 780 ml. (gas temperature in reservoir, 25° = 298.1°K). Throughout the experiment the gas in the reservoir remained at 25 ± 1°. To the saturated catalyst solution was added 3.90 g. (0.0398 mole) of cyclohexanone from a calibrated syringe. A slight brief exotherm was noted on addition of the ketone which required about 30 sec. The end of addition was recorded as zero time. The volume of acetylene absorbed (*v*) was measured at short time intervals for 121 min. A plot of *v vs. t* is shown in Figure 1.

In separate experiments it was found that 1-ethynylcyclohexanol degases a saturated solution of acetylene in *N*-methylpyrrolidone to the extent of 0.45% of the original acetylene concentration per millimole of carbinol; on the other hand, when cyclohexanone was added to *N*-methylpyrrolidone saturated with acetylene at 20.0°, 13.7 ml. of acetylene gas (at 25°) was absorbed per milliliter of ketone. The degassing factor was relatively constant in the temperature range 0–40°, and was found to be numerically the same for 3-methyl-1-butyn-3-ol. The solubility of acetylene in the ketone was found to vary with temperature and the structure of the ketone; accordingly, at each reaction temperature the solubility had to be determined for the particular ketone employed.

The product concentration, $[P]$, was calculated from the volume of acetylene absorbed by means of the ideal gas law, taking into account the correction factors described in the previous paragraph. The volume of the reaction mixture was assumed to be the volume of catalyst solution employed plus the volume of ketone added. When catalyst was prepared from sodium metal, as above, $[C_0]$ was calculated as the difference between the amount of ketone added and the total amount of catalyst in solution. On the other hand, when catalyst was prepared from sodium methoxide and ethynylcarbinol, $[C_0]$ was calculated simply from the amount of ketone added. The function $[C_0] \log ([C_0]/[C_0] - [P]) - P/2.3$ was plotted against t and the slope of the best straight line was determined by the method of least squares (Figure 3). Similarly, the best values for $1 - k_1/k_{-2}$ and the slope of $[C_0] \log ([C_0]/[C_0] - [P]) - (1 - k_1/k_{-2})\ [P]/2.3$ *vs.* t were determined from the same data (Table V).

All of the calculations were performed with a Bendix G-15D computer.

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[11] L. J. Barnes, Jr., and L. J. Molinini, *Anal. Chem.*, **27**, 1025 (1955).