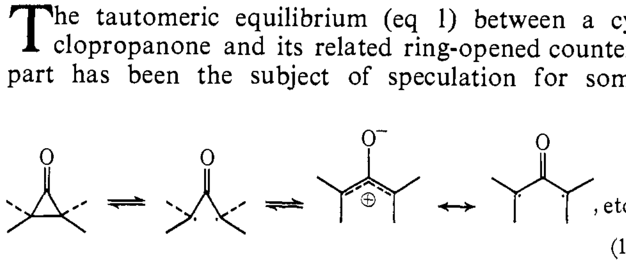
Cyclopropanones. XVII. Kinetics of the Cycloaddition Reaction of Cyclopropanones with 1,3-Dienes[1a]

Simon S. Edelson[1b] and Nicholas J. Turro[1c]

Contribution from the Chemistry Department, Columbia University, New York, New York 10027. *Received October 22, 1969*

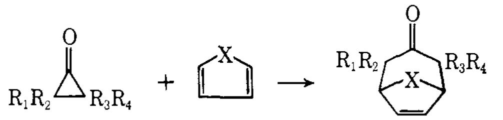
Abstract: The kinetics of the 4 + 3 → 7 cycloaddition reactions of cyclopropanone **1** and some alkylcyclopropanones **2**, **3**, **4**, and **5** with furan and 1,3-cyclopentadiene have been studied. The reaction appears to be first order in cyclopropanone and diene. Relative reactivities of cyclopropanones toward a common diene and other considerations suggest that a ring-opened tautomer is a reactive intermediate in these reactions. Attempts to study the kinetics of the 2 + 3 → 5 cycloaddition of cyclopropanones and reactive carbonyl compounds were frustrated by a slow rate of cycloaddition and the occurrence of competing reactions which destroyed the cyclopropanones.

The tautomeric equilibrium (eq 1) between a cyclopropanone and its related ring-opened counterpart has been the subject of speculation for some years.[1-11] In order to determine if such an equilibrium actually occurs and, if it does, to elucidate the nature of the species involved, cyclopropanones were treated with dienes and species of the types X=Y and X=Y=Z in an attempt to trap the reactive ring-opened intermediate. The latter two types were both dipolar and neutral. Results of these studies have been reported elsewhere.[12-19]



(1)

We now report the results of a kinetic study of the cycloaddition reactions (eq 2) of cyclopropanone (**1**), methycyclopropanone (**2**), 2,2-dimethylcyclopropanone (**3**), trimethylcyclopropanone (**4**), and tetramethylcyclopropanone (**5**).



(2)

1, $R_1 = R_2 = R_3 = R_4 = H; X = O$
2, $R_1 = CH_3; R_2 = R_3 = R_4 = H; X = CH_2$
3, $R_1 = R_2 = CH_3; R_3 = R_4 = H$
4, $R_1 = R_2 = R_3 = CH_3; R = H$
5, $R_1 = R_2 = R_3 = R_4 = CH_3$

Results and Discussion

The absolute kinetics of the reaction of **3** with furan were determined. The initial reaction rates at 0° were evaluated over a 14-fold change in the furan concentration and an approximately 15% change in the concentration of **3** (Experimental Section). The change in rate with the change in concentration indicated that—within experimental error—the reaction is first order in both **3** and furan. A second-order rate constant was derived by dividing the initial rates by the initial concentrations of reactants, yielding a value of $k = 0.00151 \pm 0.00016\ M^{-1}\ \text{min}^{-1}$. A similar but much less extensive study of the reaction of **3** with cyclopentadiene indicated that $k = 0.0045\ M^{-1}\ \text{min}^{-1}$ for that reaction.

Various competitive reactions were run to determine the relative reactivities of the different cyclopropanones toward furan (Table I). Similarly, the relative reactivities of furan and other dienes with **3** were determined. Cyclopentadiene was found to react with **3** approximately three times faster than furan. This is in good agreement with the absolute rate constants described above. 2-Methylfuran reacted with **3** approximately 1.25 times faster than furan. Furan reacted with **3** approximately 2.7 times faster than 2-carbomethoxyfuran.

Table I. Relative Rates of Cycloaddition[13] of Cyclopropanones to Furan

Cyclopropane	k_{rel}
1	$<10^{-4}$
2	$\sim 1^{a}$
3	1
4	$>10^{2}$
5	$\sim$1–2

[a] This value was previously reported[13] to be ~0.1. Reinvestigation has shown that this earlier value was in error.

---

[1] (a) Paper XVI in this series: N. J. Turro and R. B. Gagosian, *J. Amer. Chem. Soc.*, **92**, 2036 (1970). The authors thank the Air Force Office of Scientific Research (Grant No. AFOSR-68-1381) for their support of this work. We also thank the Upjohn Company for a generous gift; (b) National Science Foundation Predoctoral Fellow, 1966–1969; (c) Alfred P. Sloan Fellow.

[2] A. S. Kende, *Org. Reactions*, **11**, 261 (1960).

[3] R. B. Loftfield, *J. Amer. Chem. Soc.*, **72**, 632 (1950); **73**, 4707 (1951).

[4] J. G. Aston and J. D. Newkirk, *ibid.*, **73**, 3900 (1951).

[5] J. G. Burr, Jr., and M. J. S. Dewar, *J. Chem. Soc.*, 1201 (1954).

[6] G. Stork and I. J. Borowitz, *J. Amer. Chem. Soc.*, **82**, 4307 (1960).

[7] H. O. House and W. F. Gilmore, *ibid.*, **83**, 3980 (1961).

[8] A. W. Fort, *ibid.*, **84**, 4979 (1962).

[9] (a) R. C. Cookson and M. J. Nye, *Proc. Chem. Soc.*, 129 (1963); (b) R. C. Cookson, M. J. Nye, and G. Subrahmanyam, *J. Chem. Soc. C*, 473 (1967).

[10] R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 1475 (1968).

[11] J. M. Pochan, J. E. Baldwin, and W. H. Flygare, *ibid.*, **90**, 1072 (1968); **91**, 1896 (1969).

[12] N. J. Turro, W. B. Hammond, and P. A. Leermakers, *ibid.*, **87**, 2774 (1965).

[13] See N. J. Turro, S. S. Edelson, J. R. Williams, T. R. Darling, and W. B. Hammond, *ibid.*, **91**, 2283 (1969), and references therein.

[14] N. J. Turro, *Accounts Chem. Res.*, **2**, 25 (1969).

[15] W. B. Hammond and N. J. Turro, *J. Amer. Chem. Soc.*, **88**, 2880 (1966).

[16] N. J. Turro and W. B. Hammond, *Tetrahedron*, 6017 (1968).

[17] N. J. Turro, S. S. Edelson, J. R. Williams, and T. R. Darling, *J. Amer. Chem. Soc.* **90**, 1926 (1968).

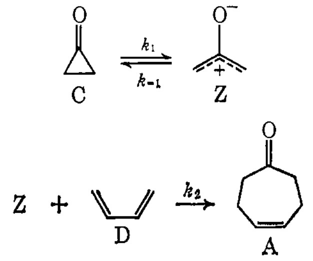
[18] N. J. Turro and J. R. Williams, *Tetrahedron Lett.*, 321 (1969).

[19] N. J. Turro and S. S. Edelson, *J. Amer. Chem. Soc.*, **90**, 4499 (1968).

Discussion and Conclusions

If the reaction sequence shown in Chart I is followed,

Chart I



one can derive the following rate law using the standard steady-state assumptions

$$\frac{dA}{dt} = \frac{k_1k_2CD}{k_{-1} + k_2D}$$

There are two limiting cases. When $k_2D \gg k_{-1}$ the rate law becomes

$$\frac{dA}{dt} = k_1C$$

In other words, when the formation of the intermediate is rate determining, the diene concentration drops out of the rate law. When $k_{-1} \gg k_2D$, the rate law becomes

$$\frac{dA}{dt} = \frac{k_1}{k_{-1}}k_2CD = k'CD$$

In other words, when the second step is slow enough to allow rapid equilibration between the intermediate and the starting compound, it becomes impossible to detect the intermediate by kinetic methods alone. When $k_{-1} \sim k_2D$, the rate law will show fractional order in diene. Unfortunately, the reaction turns out to be first order in both cyclopropanone and furan (within experimental error). Thus, our kinetics provide no answer to the question about an intermediate. It may be possible, however, to either (a) find dienes which react fast enough with cyclopropanones to allow the rates of the equilibration step in Chart I to be comparable with the rate of addition or (b) construct cyclopropanones which are much more reactive than those studied to date.

A parallel with the kinetics of ring opening of cyclopropyl cations[11–22] and the relative rates of reaction of the various cyclopropanones listed in Table I with furan provide some evidence of zwitterionic character in the cycloaddition transition state. Schleyer[21] and coworkers have studied the acetolysis of various cyclopropyl tosylates. Their results are shown in Table II. This reaction is thought to involve concerted loss of the tosyl group and opening of the cyclopropane ring to allyl cation.[21,22] One can see that conflicting steric and electronic effects operate in this series. Increasing substitution increases the (electronic) stability of the allyl cation. However, in those cases where at least one methyl group is required to rotate inward, the steric strain introduced by such a rotation more than makes up for the stabilizing inductive electronic effect of the methyl group. We were unable to detect any cycloaddition reaction in the case of cyclopropanone. Methylcyclopropanone is much more reactive than cyclopropanone. 2,2-Dimethylcyclopropanone reacts at about the same rate as **2**. Trimethylcyclopropanone shows a large increase in reactivity over **3** while tetramethylcyclopropanone reacts at approximately the same rate as **3**.

Table II. Acetolysis of Cyclopropyl Tosylates

	k_{rel} 100°	k_{rel} 150°
Cyclopropyl tosylate	1.0	1.0
2-*cis*-3-*cis*-Dimethyl		4.0
2-*trans*-3-*trans*-Dimethyl	41,000	18,000
2-*cis*-3-*trans*-Dimethyl	490	260
2,2-Dimethyl	470	330
2,2-3-*cis*-Trimethyl		80
2,2-3-*trans*-Trimethyl	48,000	
2,2,3,3-Tetramethyl	8,050	5,500
2-*trans*-Methyl	70 (est)[a]	

[a] Reference 22.

Several factors must be considered in rationalizing these results. First, increased substitution on the cyclopropanone decreases the bond dissociation energy of the back bond. An idea of the effect can be found from Table III which lists the carbon–carbon bond dissociation energies for various substituted ethanes. The effect should be of even greater magnitude with cyclopropanones because of the eclipsing interactions which occur when substituents are placed on the ring. Thus, one could say that increasing substitution of the three-membered ring increases the rate of reaction simply because it weakens the back bond and makes it more likely to react.

Table III. Bond Dissociation Energies of Substituted Ethanes[a]

	kcal/mol
CH_3–CH_3	88
CH_3–CH_2CH_3	85
CH_3–$CH(CH_3)_2$	84
CH_3–$C(CH_3)_3$	80
Et–$CH(CH_3)_2$	80
$(CH_3)_2CH$–$CH(CH_3)_2$	77.5

[a] S. W. Benson, "Thermochemical Kinetics," John Wiley & Sons, Inc., New York, N. Y., 1968, p 215.

One can consider the possibility of the concerted cycloaddition of the closed form of cyclopropanone in this light. Since the electron density of cyclopropane bonds is in the plane of the ring and away from the ring[23] (I), one would expect attack from the rear of the molecule (II).

Examination of Dreiding models indicates that increasing methyl substitution on the cyclopropanone increases the steric hindrance to attack from the rear. But, the magnitude of this effect would be expected to increase in a continuous manner; however, there does not seem to be a large reactivity difference between **2**

---

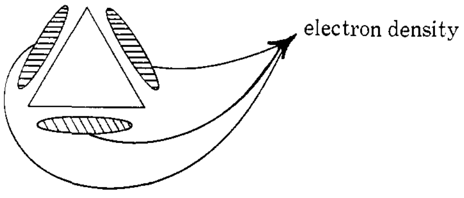
(20) W. J. Linn, *J. Amer. Chem. Soc.*, **87**, 3665 (1965); R. Huisgen and F. Meitzsch, *Angew. Chem. Intern. Ed. Engl.*, **3**, 83 (1964).

(21) (a) P. V. R. Schleyer, G. W. V. Dine, U. Schollkopf, and J. Paust, *ibid.*, **88**, 2868 (1966); (b) C. H. DePuy, L. G. Schnack, and J. W. Hausser, *ibid.*, **88**, 3343 (1966).

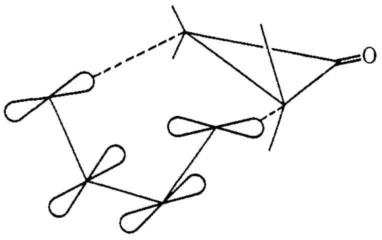
(22) P. v. R. Schleyer, Twentieth National Organic Chemistry Symposium of the American Chemical Society, Burlington, Vt., 1967.

(23) J. March, "Advanced Organic Chemistry: Reactions, Mechanisms and Structure," McGraw-Hill Book Co., Inc., New York, N. Y., 1968, p 119.

and **3**. Furthermore, it is hard to explain the drastic difference in reactivity between **4** and **5**, on the basis of a concerted attack by diene on the ring-closed cyclopropanone. The relative reactivities indicate that the methyls on **3** and **5** have a larger steric effect than the methyls on **2** and **4**. If the cyclopropanone approaches planarity in the transition state for cycloaddition, an effect is quite understandable. One can see that the latter model for reaction predicts a break in the reactivity scale which should occur only at the points where the number of methyl groups being rotated inward increases (*i.e.*, with **3** and **5**).



I



II

Attempts were made to study the kinetics of the 2 + 3 → 5 cycloaddition reaction of **3** with chloral.[13] Unfortunately, decomposition products complicated several methods which were employed to analyze for adduct formation. It appears that this reaction is generally slower than the 4 + 3 → 7 reactions with dienes.

Conclusion

These facts would seem to imply that the cyclopropanone portion of the transition state for the cycloaddition is analogous in some respects to the cyclopropyl cation. In other words, the cyclopropanone has probably assumed a large degree of zwitterionic character in the transition state for cycloaddition. However, it has not been established with complete certainty whether the reaction starts with the cyclopropanone as the zwitterion or the closed form. Experiments directed toward answering the latter question are now in progress.

Experimental Section

Infrared spectra were taken on a Perkin-Elmer 137 spectrometer. Nuclear magnetic resonance spectra were taken on a Varian A-60 or A-60 A analytical high-resolution nmr spectrometer. Vpc analyses were performed on an Aerograph Model A90P or Model 1200 gas chromatograph. The following liquid phases were used: 1,2,3-tris(2-cyanoethoxy)propane (*βββ*); Carbowax 20M (CWX 20M); SE 30; UC-W98. Chromosorb P (Chrom P), acid washed, dimethyldichlorosilane treated Chromosorb W (a/w DMCS Chrom W), and acid washed, dimethyldichlorosilane treated Chromosorb G (a/w DMCS Chrom G) were used as solid supports. All commercial chemicals used were reagent quality.

Kinetic Study of the 2,2-Dimethylcyclopropanone (3)–Furan Reaction. In a typical experiment, 1 ml of a 2,2-dimethylcyclopropanone–CH_2Cl_2 solution was mixed with 10 μl of acetophenone (0.085 mmol; internal standard) in a test tube sealed with a serum cap. The test tube was cooled to 0° and a measured amount of furan was added with a syringe. The temperature was maintained at 0° with an ice–water bath and aliquots were withdrawn periodically and analyzed by vpc (6 ft × 1/8 in., 5% SE 30, DMCS a/w, 60–80 Chrom G, 100°, 30 cc of He/min). The adduct concentration was then plotted as a function of time and the rate constant was derived from the slope of the initial "straight-line" portion of the curve. This portion usually contained a minimum of three points and the extent of product formation was usually less than 5% although, in a few cases, it was as high as 8 or 9%.

In several cases, a smaller amount of 2,2-dimethylcyclopropanone–CH_2Cl_2 solution was diluted to 1 ml with CH_2Cl_2 or CH_3CN and the acetophenone was added to this more dilute solution. The remainder of the reaction was run exactly as described above. The results are listed in Table IV.

Table IV

3 concn $(M)^a$	Furan concn $(M)^a$	Solvent	Δ adduct/Δ*t* ($\Delta A/\Delta t$) $\times 10^5\ M$ min^{-1}	$k^b \times 10^3$ M^{-1} min^{-1}
0.139	0.136	CH_2Cl_2	2.94	1.55
0.131	0.136	CH_2Cl_2	2.84	1.60
0.131	0.136	CH_2Cl_2	2.47	1.39
0.138	0.270	CH_2Cl_2	5.15	1.38
0.130	0.270	CH_2Cl_2	5.8	1.65
0.130	0.270	CH_2Cl_2	5.6	1.60
0.135	0.530	CH_2Cl_2	9.79	1.37
0.128	0.530	CH_2Cl_2	9.46	1.39
0.128	0.530	CH_2Cl_2	10.5	1.55
0.130	1.02	CH_2Cl_2	18.7	1.41
0.123	1.02	CH_2Cl_2	18.8	1.49
0.123	1.02	CH_2Cl_2	19.3	1.54
0.121	1.9	CH_2Cl_2	44.0	1.91
0.115	1.9	CH_2Cl_2	28.4	1.30
0.0689	0.270	1/2 CH_2Cl_2	1.02	0.549
0.0651	1.02	1/2 CH_3CN	3.61	0.544
0.0618	1.02	1/2 CH_3CN	3.31	0.526
0.064	0.530	CH_2Cl_2	3.47	1.03
0.064	0.530	CH_2Cl_2	3.42	1.00
0.032	0.530	CH_2Cl_2	1.15	0.68
	Cyclopentadiene concn^a			
0.139	0.119	CH_2Cl_2	7.97	4.82
0.137	0.234	CH_2Cl_2	13.8	4.30
0.134	0.458	CH_2Cl_2	28.8	4.69

[a] These molarities are based on the approximation that the volume of the solution equals the sum of the volumes of the reactants. [b] *k* is derived by assuming that the reaction is first order in both **3** and diene and then dividing $\Delta A/\Delta t$ by the initial concentrations of both.

Several approximations are inherent in this method. First of all, no account is taken of the time between withdrawal of an aliquot and its analysis. During this time, the aliquot would warm up to some extent. This period was kept as small as possible. It was assumed that injection into the vpc quenched the reaction. Since the vaporization of the sample greatly increased its volume and greatly decreased the concentration of reactants, this assumption is not unreasonable. It was assumed that the volume of the solution equaled the sum of the volumes of the reactants. This should not introduce a large error.

Kinetic Study of the 2,2-Dimethylcyclopropanone (3)–Cyclopentadiene Reaction. This was run in the same manner as the furan reaction. The following changes were made: (1) *n*-tetradecane (10 μl; 0.0385 mmol) was used as the internal standard; (2) the vpc conditions were 10 ft × 1/8 in., 5% CWX 20M, 30 cc of He/min, 160°. The results are listed in Table IV.

Treatment of 1 with Acetyl Chloride or Acetic Anhydride. One-half milliliter portions of cyclopropanone in CH_2Cl_2 (~0.275 mmol of I) were mixed with 100 μl of acetyl chloride (1.42 mmol) or with 100 μl of acetic anhydride (1.06 mmol). The solutions were left at room temperature and nmr analysis indicated that in those solutions with acetyl chloride the cyclopropanone had a half-life of ~24 hr while it decomposed in several hours in those solutions with acetic anhydride. Cyclopropanone in solutions without acetyl chloride or acetic anhydride decomposed in minutes at room temperature.

Treatment of 1 with Furan. A CH_2Cl_2 solution (5 ml) of cyclopropanone (~2.75 mmol) was mixed with furan (13 ml, ~180 mmol) and acetyl chloride (1 ml, ~14.2 mmol) and the mixture was left at room temperature. After 3 days, no adduct could be detected by nmr, ir, or vpc (6 ft × $^1/_8$ in., 10%, UC-W98, 30 cc of He/min, 120°). Under similar conditions, **3** reacted quantitatively in less than 20 min. This implies that **24** reacts at least 10^4 times faster.

Treatment of 3 with Furan in the Presence of Acetyl Chloride. A CH_2Cl_2 solution (0.5 ml) of 2,2-dimethylcyclopropanone (0.14 mmol) was mixed with acetyl chloride (0.1 ml, 1.42 mmol) and furan (~0.5 ml, ~7 mmol) and the mixture was left at room temperature. At the same time, another mixture in which the acetyl chloride was replaced with an equivalent amount (0.1 ml) of CH_2Cl_2 was made up and left at room temperature. Vpc analysis (6 ft × $^1/_8$ in., 10%, UC-W98, 30 cc of He/min, 120°) indicated that the yield of adduct in the first mixture was $^1/_2$ the yield of adduct in the second.

Treatment of a Mixture of 2 and 3 with Furan. A CH_2Cl_2 solution (250 μl) of 2,2-dimethylcyclopropanone (0.07 mmol) was mixed with a CH_2Cl_2 solution (250 μl) of methylcyclopropanone (~0.125 mmol) and a CH_2Cl_2 solution (200 μl) of furan (~0.84 mmol) was added to the above mixture. The resulting solution was left at room temperature and aliquots were removed periodically for vpc analysis (6 ft × $^1/_8$ in., 10% UC-W98, 30 cc of He/min, 120°). This indicated that the rates of adduct formation were approximately equal for both cyclopropanones.

Treatment of Furan with a Mixture of 3 and 4. A CH_2Cl_2 solution (250 μl) of trimethylcyclopropanone (~0.01 mmol) was combined with a CH_2Cl_2 solution (250 μl) of 2,2-dimethylcyclopropanone (0.07 mmol) and a CH_2Cl_2 solution (5 μl) of furan (0.007 mmol) was added to the mixture which was left at room temperature. Aliquots were removed periodically for vpc analysis (6 ft × $^1/_8$ in., 10%, UC-W98, 80–100 support, 30 cc of He/min, 140°) which indicated that the trimethylcyclopropanone reacted at least 100 times faster than the 2,2-dimethylcyclopropanone. Excess furan was then added to the reaction mixture. Further vpc analysis then indicated that the concentration of the dimethylcyclopropanone adduct had surpassed that of the trimethylcyclopropanone adduct. This indicated that the initial result was not due to the decomposition of the dimethylcyclopropane.

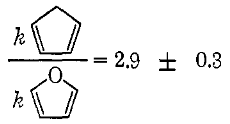
Treatment of Furan with a Mixture of 3 and 5. A solution (250 μl) of tetramethylcyclopropanone (0.04 mmol) in CH_2Cl_2 was mixed with a solution (250 μl) of 2,2-dimethylcyclopropanone (0.07 mmol) in CH_2Cl_2. Furan (100 μl, 1.41 mmol) was added and the resulting mixture was left at room temperature. Aliquots were removed periodically over a period of 2 hr and analyzed by vpc (6 ft × $^1/_8$ in., 10%, UC-W98, 80–100 support, 30 cc of He/min, 140°). The results are shown in Table V. These results imply that the tetramethylcyclopropanone reacts with furan at a rate similar to that of 2,2-dimethylcyclopropanone. It is possible that the rate is slightly faster, maybe by as much as a factor of 2.

Table V

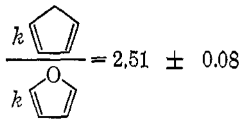
Sample	Time	Ratio [3 adduct]:[5 adduct]
A	5 min	1.05
B	25 min	1.28
C	50 min	1.37
D	1 hr 10 min	1.51
E	1 hr 40 min	1.73
F	20 hr	2.1

Treatment of 3 with a Mixture of Furan and 2-Methylfuran. In each of 4 test tubes were placed 0.5 ml of a 2.09 *M* CH_2Cl_2 solution of **3**, 0.90 ml of 2-methylfuran (10 mmol), and 0.72 ml of furan (10 mmol). After being cooled to 77°K, evacuated, degassed once, and sealed, the tubes were heated at 40–50° for 48 hr. Vpc analysis (5 ft × $^1/_4$ in., 25% ββ'β, Chrom P, 158°, 60 cc of He/min) then indicated that the 2-methylfuran reacted about 1.25 times as fast as furan with **3**.

Treatment of 3 with a Mixture of Furan and Cyclopentadiene. A. A mixture of 50 μl of a CH_2Cl_2 solution of **3** (0.1045 mmol), 82.5 μl of cyclopentadiene (1 mmol), and 72 μl of furan (1 mmol) was left at room temperature in a sealed (serum cap) tube for 3 days. Vpc analysis (5 ft × $^3/_8$ in., 22% CWX 20M, Chrom P, 233°, 120 cc of He/min) indicated that



B. Cyclopentadiene (0.825 ml, 10 mmol), 0.72 ml of furan (10 mmol), and 0.104 ml cyclohexanone (1 mmol, internal standard) were mixed in a test tube and the tube was sealed with a serum cap. After cooling the tube to −78°, 0.5 ml of a CH_2Cl_2 solution of **3** (1.05 mmol) was added and the tube was allowed to warm to room temperature. Aliquots were taken every 10 min and analyzed by vpc (5 ft × $^3/_8$ in., 22% CXW 20M, Chrom P, 220°, He 60 cc/min). This indicated that



Treatment of 3 with a Mixture of Furan and 2-Carbomethoxyfuran. A CH_2Cl_2 solution (0.25 ml) of 2,2-dimethylcyclopropanone (0.4 mmol) was added to a mixture of furan (9.335 ml, 4.67 mmol) and 2-carbomethoxyfuran (0.5 ml, 4.67 mmol). The resulting mixture was left at room temperature overnight, after which vpc analysis (6 ft × $^1/_8$ in., 5% SE 30, a/w DMCS, 60–80 Chrom G, 30 cc of He/min, 125°) indicated that the ratio of 2-carbomethoxyfuran adducts to furan adduct was 0.37.