Cyclobutenone Derivatives from Ethoxyacetylene[1]

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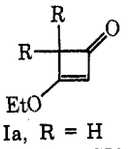
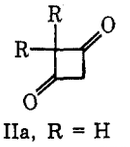
Cycloaddition reactions of ketenes to ethoxyacetylene have been investigated as routes to cyclobutenone derivatives. Ketenes are either used directly or formed *in situ* from the corresponding acid chlorides. 1,3-Cyclobutanedione prepared in this manner has been converted to a series of 3-substituted derivatives by reaction with a variety of nucleophiles, either directly or through the monoenol ether.

In earlier communications we have described the preparation of cyclobutenone ethers from ethoxyacetylene and ketenes, a reaction first observed by Arens and coworkers.[2] Our studies[3,4] have involved the preparation of ketenes *in situ* by the dehydrohalogenation of acid chlorides and have also included the preparation of the parent compounds in this series, 3-ethoxy-2-cyclobutenone (Ia) and 1,3-cyclobutanedione (IIa).



Ia, R = H
b, R = CH_3

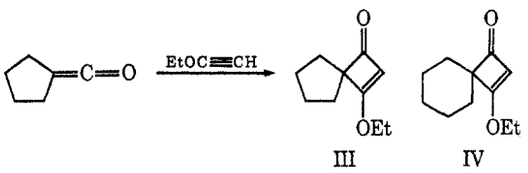


IIa, R = H
b, R = CH_3

We now report applications of this cycloaddition reaction to the preparation of derivatives in this series, as well as further transformations of I and II which may serve as useful methods for the formation of 3-substituted 2-cyclobutenones. Related work on dialkylketenes,[5,6] on the addition of ketenes to ynamines,[7-9] and on the preparation of the parent compound, 2-cyclobutenone,[10] has been reported in recent years.

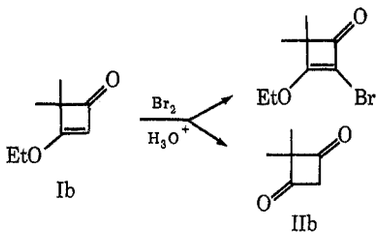
When ketene is passed through a cold solution of ethoxyacetylene in methylene chloride, formation of Ia takes place slowly. The product, mp 26–27° (30%), exhibits strong absorption in the infrared at 1760 and 1580 cm^{-1}; its nmr spectrum includes singlets at τ 5.12 and 6.89 due to the vinyl and methylene ring protons, respectively, of the cyclobutenone system. Generation of dimethylketene *in situ* from isobutyryl chloride in the presence of ethoxyacetylene yields Ib (66%). The cyclobutenone structure is shown by absorptions at 1750 and 1575 cm^{-1} in the infrared, an ultraviolet spectrum almost identical with that of Ia, and a nmr spectrum exhibiting singlets at τ 5.27 and 8.81, areas 1:6, as well as absorption due to the ethyl protons.

The cycloaddition of ketenes to ethoxyacetylene also provides a novel entry into the spiro[3.4]octane and spiro[3.5]nonane systems. Thus, tetramethyleneketene generated from cyclopentanecarboxylic acid chloride with trimethylamine gives III (27%), while in a similar fashion IV may be obtained from cyclohexanecarboxylic acid chloride (65%). Both compounds are thermally unstable, and both give ultraviolet and infrared spectra typical of the cyclobutenone system.



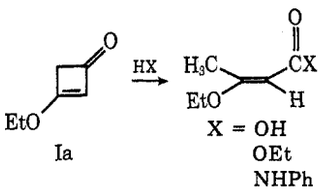
III IV

A solution of Ib in carbon tetrachloride instantly decolorizes bromine and then slowly evolves hydrogen bromide to give 2-bromo-3-ethoxy-4,4-dimethyl-2-cyclobutenone. The position of the bromine is confirmed by the nmr spectrum, which shows a quartet at τ 5.31, a triplet at 8.50, and a singlet at 8.77 with relative areas of 2:3:6. This assignment is also in keeping with the fact that 3-hydroxy-2,4-dimethylcyclobutenone undergoes a similar bromination.[11,12]



Ib IIb

While compound Ia undergoes ring-opening reactions with water, ethanol, and aniline, Ib appears to be more resistant to ring cleavage. When stirred overnight with moist ether, Ia gives a poor yield of β-ethoxycrotonic acid as the only isolable product. Similarly, with hot ethanol, the ethyl ester of β-ethoxycrotonic acid is formed, and with aniline at room temperature a crystalline product is produced, the infrared and nmr spectra of which are consistent with those expected for the anilide of β-ethoxycrotonic acid.



Ia X = OH, OEt, NHPh

On the other hand, when Ib is treated with warm, dilute acid, hydrolysis to IIb occurs. More vigorous heating with aqueous acid[3] or base results in degrada-

(1) This investigation was supported in part by U. S. Public Health Service Research Grant GM-07874 from the National Institutes of Health.

(2) J. F. Arens, "Advances in Organic Chemistry, Methods and Results," Vol. 2, Interscience, New York, N. Y., 1960, p 117.

(3) H. H. Wasserman and E. Dehmlow, *Tetrahedron Lett.*, 1031 (1962).

(4) H. H. Wasserman and E. V. Dehmlow, *J. Amer. Chem. Soc.*, **84**, 3786 (1962).

(5) R. H. Hasek, P. G. Gott, and J. C. Martin, *J. Org. Chem.*, **29**, 2510 (1964).

(6) R. B. Johns and A. B. Kriegler, *Aust. J. Chem.*, **17**, 765 (1964).

(7) M. E. Kuehne and P. J. Sheeran, *J. Org. Chem.*, **33**, 4406 (1968).

(8) W. E. Truce, R. H. Barry, and P. S. Bailey, Jr., *Tetrahedron Lett.*, 5651 (1968).

(9) M. Delaunois and L. Ghosez, *Angew. Chem., Int. Ed. Engl.*, **8**, 72 (1969).

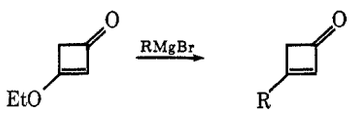
(10) J. B. Sieja, *J. Amer. Chem. Soc.*, **93**, 2481 (1971).

(11) D. G. Farnum, M. A. T. Heybey, and B. Webster, *ibid.*, **86**, 673 (1964).

(12) R. B. Woodward and G. Small, Jr., *ibid.*, **72**, 1297 (1950).

tion to methyl isopropyl ketone. In contrast to the reaction of Ia with aniline, Hasek, Gott, and Martin report[5] that the dimethyl derivative Ib reacts with ammonium hydroxide to give 3-amino-4,4-dimethyl-2-cyclobutenone and with piperidine to give the corresponding 3-piperidino derivative.[5] Thus it appears that Ib is less subject to ring-opening reactions than is Ia.

Considering the above results, it was surprising to observe that phenylmagnesium bromide and *n*-butylmagnesium bromide readily add to Ia in a conjugate manner with elimination of ethoxide ion to give 3-phenyl-2-cyclobutenone (V)[13] and 3-(1-butyl)-2-cyclobutenone (VI). The above results now make it possible



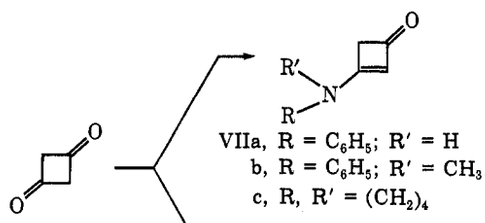
V, R = C_6H_5
VI, R = n-C_4H_9

in theory to vary alkyl substituents at each position of the cyclobutenone ring. Thus, substitution at the 2 position can be controlled by varying the acetylene used,[14] substituents at the 4 position may be changed by varying the ketene,[3-5] and substitution at the 3 position may be accomplished *via* the Grignard reaction. Using sodium methoxide in methanol, substitution at the 3 position proceeds further to give 3,3-dimethoxycyclobutanone.

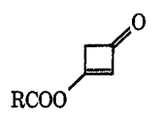
The hydrolysis of Ia may be controlled to give the dione IIa (64%), by using cold ether previously shaken with concentrated hydrochloric acid. Under these conditions hydrolysis takes place almost immediately. Formation of IIa also takes place slowly when Ia is allowed to stand in a moist atmosphere at −10°. As reported for related compounds,[6,11] both IIa and IIb are highly acidic with pK_a's of 3.0 and 2.65, respectively. The ultraviolet spectra of IIa and IIb are similar to each other and to those of Ia and Ib, indicating that in dilute ethanol solutions IIa and IIb exist nearly completely in the enolic form. It was noted[5] that IIb exists mainly in the enol form in polar solvents, while in chloroform solutions the diketone form predominates. The same is true of IIa. The nmr spectrum of IIa in chloroform or acetonitrile solutions shows a singlet at τ 6.14, while in dimethyl sulfoxide three singlets at −0.25, 5.28, and 6.90 are observed. The infrared spectrum of IIa in chloroform shows only very weak bands attributable to the enolic form. Previous work suggests that the presence of a 2-methyl group stabilizes the enolic form, since both 2-methyl-[6] and 2,4-dimethylcyclobutane-1,3-dione[11] appear to exist in the enolic form in chloroform solutions (as shown by their infrared spectra). The mass spectrum of IIa is similar to those reported for other ketene dimers,[15] showing a parent peak (*m/e* 84) and peaks at *M*/2, M − 28, and M − 56 which are 6, 100, 1, and 7% of the base peak, respectively.

(13) S. L. Manatt, M. Vogel, D. Knutson, and J. D. Roberts, *J. Amer. Chem Soc.*, **86**, 2465 (1964).
(14) B. Rosebeek and J. F. Arens, *Rec. Trav. Chim. Pays-Bas*, **81**, 549 (1962).
(15) N. J. Turro, D. C. Neckers, P. A. Leermakers, D. Seldner, and P. D'Angelo, *J. Amer. Chem. Soc.*, **87**, 4097 (1965).

The formation of 3-amino-2-cyclobutenones (VII) takes place when equimolar amounts of amine and IIa are combined in methylene chloride solution at room temperature.



VIIa, R = C_6H_5; R' = H
b, R = C_6H_5; R' = CH_3
c, R, R' = $(CH_2)_4$



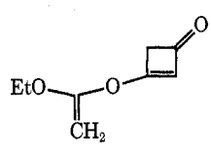
VIIIa, R = CH_3
b, R = C_6H_5

As noted for 3-piperidino-4,4-dimethyl-2-cyclobutenone,[5] compounds VIIa–c are amide-like, showing carbonyl frequencies in the infrared at 1730–1740 cm^{-1}. The nmr absorption peaks of the α protons on the pyrrolidine ring of VIIc are at τ 6.5 as compared to those in pyrrolidine itself at 7.26.

Reactions which reflect the enolic character of IIa include acylation and the addition of IIa to ethoxyacetylene. When ketene is bubbled through a solution of IIa in methylene chloride, the enol acetate VIIIa is formed. Assignment of structure is based on the nmr spectrum, which shows three singlets at τ 4.54, 6.68, and 7.65, areas 1:2:3. Upon exposure to moisture the product readily reverts to IIa. In the infrared there are anhydride-like carbonyl absorptions at 1795 and 1770 cm^{-1}. The analogous enol acetate of acetylacetone exhibits absorption at 1762 cm^{-1} for the vinyl ester carbonyl.[16] In the olefinic region of the infrared there is the expected absorption at 1565 cm^{-1} and a second (medium intensity) absorption at 1590 cm^{-1}.

The enol benzoate, VIIIb, can be prepared (39%) using equimolar quantities of 1-ethoxyvinyl benzoate[17] and IIa. It shows carbonyl absorption at 1760 cm^{-1} with a shoulder at 1770 cm^{-1}.

When cyclobutanedione (IIa) is treated with ethoxyacetylene in the presence of mercuric acetate in methylene chloride solution, IX is formed, although it is too



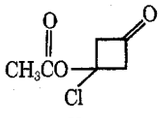
IX

unstable to permit isolation in pure form. The infrared spectrum exhibits carbonyl absorption at 1765 cm^{-1} and olefinic absorption at 1670 and 1580 cm^{-1} in methylene chloride solution. The nmr spectrum in chloroform shows singlets at τ 5.03 and 6.60 due to the vinyl and methylene ring protons, respectively, a triplet at 8.67 due to the methyl group, and a complex absorption (four protons) around 6.1 which is a combination of the methylene quartet centered at 6.06 (J = 7 Hz) and the doublet absorptions of the terminal

(16) R. Filler and S. M. Naqvi, *Tetrahedron*, **19**, 879 (1963).
(17) H. H. Wasserman and P. S. Wharton, *J. Amer. Chem. Soc.*, **82**, 661 (1960).

methylene protons at 6.12 and 6.32 (J = 4 Hz). Phenylmagnesium bromide undergoes reaction with IX to give V, but the reaction is not as clean as the preparation from Ia. Amines also react with IX to give VII. Here, the reaction of IX with pyrrolidine yields VIIc in much higher yield (89%) than in the comparable reaction with IIa (52%), although, in general, the combination of amines with IIa gives better results. Acids also react with IX to give VIII but, again, yields are poorer and products are less pure than in the methods described above.

In an attempt to prepare VIIIa by another method, IIa was dissolved in acetyl chloride and the solution was concentrated *in vacuo*. The liquid residue contained chlorine, and upon standing in the cold decomposed slowly to VIIIa. The process could be reversed by bubbling hydrogen chloride through a solution of VIIIa in benzene.



X

Structure X is proposed for the unstable product. Although the chlorine in X is reactive, *i.e.*, the compound reacts with sodium iodide in acetone and eliminates hydrogen chloride slowly upon standing, it is not as reactive as would be expected of a halogen β to a ketone carbonyl and α to an oxygen. For instance, X can be refluxed in ether or distilled *in vacuo* without significant decomposition. The infrared spectrum of X exhibits carbonyl absorption at 1805 and 1785 cm^{-1}. (Note high absorption at 1773 cm^{-1} for α-bromoethyl acetate.[18]) There is no absorption in the olefinic region. The nmr spectrum of X shows only two sharp singlets at τ 6.24 and 7.86, areas 4:3. The equivalence of the four ring protons is somewhat surprising and indicates a similar shielding effect by the chloro and acetate groups.

Experimental Section[19]

3-Ethoxy-2-cyclobutenone (Ia).—Ketene was bubbled through a stirred solution containing 40 g of ethoxyacetylene in 75 ml of methylene chloride cooled in an ice bath. The progress of the reaction could be followed by watching the disappearance of the carbon–carbon triple bond absorption at 2155 cm^{-1} in the infrared and the appearance of the carbon–oxygen and carbon–carbon double bond absorptions of the product. After 8–10 hr, some ethoxyacetylene still remained, but additional reaction time did not increase the yield and resulted in the formation of dark-colored side products. The volatile materials were removed under reduced pressure, leaving a dark liquid residue which solidified at −20°. This material was dissolved in 40 ml of 50:50 ether–petroleum ether (bp 30–60°), and the product was allowed to crystallize at −50° for 24 hr. Filtration in the cold gave 20 g (31%) of Ia, mp 22–25°. An analytical sample from ether–pentane melted at 26–27.5°: λ_{max} (anhydrous ethanol) 233 mμ (ε 12,450); ν (CCl_4) 1760, 1580 cm^{-1}; nmr (CCl_4) τ 5.12 (s), 5.74 (q), 6.89 (s), and 8.55 (t), areas 1:2:2:3.

Anal. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19; OC_2H_5, 40.19. Found: C, 64.03; H, 7.21; OC_2H_5, 38.11.

A solution of 250 mg of Ia in 10 ml of moist ether was stirred for 24 hr at room temperature. Concentration of the solution under reduced pressure left moist crystals which were recrystallized from acetonitrile to give 60 mg (21%) of β-ethoxycrotonic acid, mp 141.5–142° (lit.[20] mp 140°). A mixture melting point with an authentic sample was undepressed. In absolute alcohol Ia did not deteriorate appreciably in 24 hr at room temperature. After 4.5 hr of heating at 60°, however, ethyl β-ethoxycrotonate was formed almost quantitatively. The infrared spectrum was superimposable on that of an authentic sample.

β-Ethoxycrotonic Acid Anilide.—A solution of 224 mg (0.002 mol) of Ia and 186 mg (0.002 mol) of aniline in 10 ml of benzene was allowed to stand at room temperature in a nitrogen atmosphere for 4 days. Concentration of the solution under reduced pressure left a liquid residue, which solidified when stored in the refrigerator under nitrogen. Recrystallization from carbon tetrachloride gave 380 mg (93%) of white crystals: mp 108–110°; ν ($CHCl_3$) 3440, 3330 (broad), 1670, 1610, 1595 cm^{-1}; nmr ($CDCl_3$) τ 2.7 (m), 4.93 (s), 6.20 (q), 7.64 (s), 8.65 (t), areas 5:1:2:3:3.

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.83. Found: C, 70.06; H, 7.25; N, 7.00.

3-Ethoxy-4,4-dimethyl-2-cyclobutenone (Ib).—A solution of 6.7 g of triethylamine in 20 ml of anhydrous ether was added over a period of 45 min to a stirred solution of 6.7 g of isobutyryl chloride, 6.6 g of ethoxyacetylene, and a trace of mercuric acetate[21] in 150 ml of anhydrous ether cooled below 0°. Precipitation of the amine salt started immediately. After 1 week at room temperature, filtration gave 90–98% of the theoretical amount of triethylamine hydrochloride. The filtrate was concentrated under reduced pressure and the residual oil was distilled *in vacuo*, giving 5.1 g (66%) of Ib, bp 78–82° (9 mm). A center fraction was redistilled for analysis: bp 90–92° (26 mm); λ_{max} (95% ethanol) 233 mμ (ε 12,700); ν (CCl_4) 1750, 1575 cm^{-1}; nmr (CCl_4) τ 5.27 (s), 5.78 (q), 8.53 (t), and 8.81 (s), areas 1:2:3:6.

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.35; H, 8.69.

2-Bromo-3-ethoxy-4,4-dimethyl-2-cyclobutenone.—A solution of 0.275 ml of bromine in 5 ml of carbon tetrachloride was added slowly to a cooled solution of 0.75 g of Ib in 15 ml of carbon tetrachloride. The bromine was decolorized instantaneously, and after 15 min a slow evolution of hydrogen bromide began. After warming on a water bath for 1 hr, the solvent was distilled, and most of the residual oil was soluble in a hexane–benzene mixture. This solution was chromatographed on activity II alumina using hexane as the eluent and the resulting material was distilled *in vacuo*. Direct distillation of the residual oil did not remove all of the impurities. The analytical material boiled at 96–98° (25 mm): λ_{max} (95% ethanol) 249 mμ (ε 9950); ν (CCl_4) 1780, 1600 cm^{-1}; nmr (CCl_4) τ 5.31 (q), 8.50 (t), 8.77 (s), areas 2:3:6.

Anal. Calcd for $C_8H_{11}BrO_2$: C, 43.86; H, 5.06; Br, 36.48. Found: C, 43.54; H, 4.94; Br, 36.41.

1-Keto-3-ethoxyspiro[3.4]oct-2-ene (III).—A solution of 6.3 g of cyclopentanecarboxylic acid chloride, 11 g of ethoxyacetylene, and 7.5 ml of triethylamine in absolute ether was stirred at 5° for 14 days, after which 5.85 g (89.7%) of triethylamine hydrochloride had precipitated. The filtered solution was concentrated *in vacuo*, and the residual brown oil was taken up in hexane. This solution was stirred for 20 min with alumina containing 8% of water to destroy any excess acid chloride. The solution was then shaken with dilute potassium hydroxide solution, stirred with fresh alumina (8% water), and concentrated *in vacuo*, leaving 2.17 g (27.5%) of almost pure Ic. An analytical sample was obtained by chromatography followed by molecular distillation. The material was chromatographed on activity II alumina. Elution with hexane and 2–5% ether gave a trace of impurities. Hexane containing 20% ether gave Ic, which was distilled in a molecular still: λ_{max} 234.5 mμ (ε 11,250); ν 1755, 1570 cm^{-1}. The compound is thermolabile and decomposes upon distillation at aspirator vacuum.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.25; H, 8.64.

1-Keto-3-ethoxyspiro[3.5]non-2-ene (IV).—A solution of 15.6 g of cyclohexanecarboxylic acid chloride, 21 g of ethoxyacetylene, and 15 ml of triethylamine was stored at 5° for 3 weeks, after which 13.7 g (94%) of triethylamine hydrochloride precipitated. The filtered solution was concentrated *in vacuo*, leaving 12.5 g of almost pure IV as an oil: λ_{max} 236 mμ (ε 8850);

(18) E. Buckley and E. Whittle, *Can. J. Chem.*, **40**, 1611 (1962).

(19) Infrared spectra were recorded using a Perkin-Elmer 421 spectrophotometer, and nmr spectra using a Varian Associates A-60 nmr spectrometer with TMS as an internal standard.

(20) M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky, E. A. Smith, and W. E. Vaughan, *J. Amer. Chem. Soc.*, **60**, 440 (1938).

(21) The presence or absence of mercuric ions does not seem to influence the reaction.

ν 1755, 1575 cm^{-1}. The compound decomposes upon distillation at aspirator vacuum. A center cut from molecular distillation under high vacuum was analyzed.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.36; H, 9.28.

Cyclobutane-1,3-dione (IIa).—3-Ethoxy-2-cyclobutenone (Ia) (4.6 g, 0.041 mol) was dissolved in 125 ml of cold ether which had previously been shaken with cold, concentrated hydrochloric acid. Concentration of the solution under reduced pressure left a semisolid residue, which was recrystallized from acetonitrile and washed with cold ether to give 1.0 g of crystals. The mother liquor yielded another 0.6 g. An additional 0.6 g was obtained by adding a drop of concentrated hydrochloric acid to the mother liquor and concentrating *in vacuo*. The total yield was 2.2 g (64%) of nearly white crystals. An additional crystallization from acetonitrile gave pure white crystals of IIa: mp 119–120° with exothermic decomposition; λ_{max} (absolute ethanol) 237 mμ (ϵ 11,800); ν ($CHCl_3$)[22] 1755, 1570 cm^{-1} (weak); nmr ($CDCl_3$) τ 6.14 (s); nmr (DMSO) τ −0.25 (s), 5.28 (s), 6.90 (s). The material decomposes upon standing at room temperature and more slowly when stored at −15°.

Anal. Calcd for $C_4H_4O_2$: C, 57.14; H, 4.80. Found: C, 57.01; H, 5.10.

2,2-Dimethylcyclobutane-1,3-dione (IIb).—A solution of 1.6 g of Ib in 6 ml of water, 4 ml of ethanol, and 2 ml of concentrated hydrochloric acid was heated at 80° for 1 hr. The cooled solution was extracted with methylene chloride, the extracts were dried over anhydrous sodium sulfate, and the solvent was removed *in vacuo*. The resulting semisolid mass on treatment with pentane gave 0.65 g (51%) of long crystal rods. The remaining oil consisted largely of unreacted starting material. After recrystallization from ether–petroleum ether, the material had mp 129–130°; λ_{max} (95% ethanol) 241 mμ (ϵ 14,100); ν ($CHCl_3$) 1750, 1575 cm^{-1} (weak).

Anal. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.04; H, 7.24.

A vigorous reaction took place between IIb and diazomethane in ether. Removal of the volatile materials and molecular distillation of the residue gave 3-methoxy-4,4-dimethyl-2-cyclobutenone, ν 1745, 1575 cm^{-1}.

Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.25; H, 8.13.

A solution of 80 mg of IIb in 10% aqueous alcoholic sodium hydroxide was heated for 2 hr on a steam bath and acidified with hydrochloric acid. After warming for an additional 1 hr, 2,4-dinitrophenylhydrazine reagent was added and the 2,4-dinitrophenylhydrazone of methyl isopropyl ketone precipitated from the solution. After two recrystallizations from ethanol the melting point was 118–118.5° and the mixture melting point with an authentic sample was undepressed.

3-Phenyl-2-cyclobutenone (V).—To a cooled solution of 0.80 g (0.0072 mol) of Ia in 15 ml of ether was added 5.5 ml of an ether solution of phenylmagnesium bromide (0.0013 mol/ml). The resulting mixture was allowed to come to room temperature for 15 min and was then poured into 7% hydrochloric acid. The ether layer was removed and the aqueous layer was extracted twice with ether. The combined ether extracts were dried over anhydrous sodium sulfate and concentrated *in vacuo* leaving a semisolid residue with a cinnamon-like odor. This was recrystallized twice from ether at −78° and the resulting material was sublimed at 40–44° (1 mm), giving 0.55 g (53%) of white crystals, mp 51–52°. Infrared and nmr spectral properties were identical with those reported by Roberts,[13] except that the small cross-ring coupling reported in the nmr was not observed on our instrument.

Anal. Calcd for $C_{10}H_8O$: C, 83.31; H, 5.59. Found: C, 83.48; H, 5.82.

3-(1-Butyl)-2-cyclobutenone (VI).—To a cooled solution of 2.24 g (0.02 mol) of Ia in 25 ml of ether was added 14 ml of a solution of *n*-butylmagnesium bromide (0.0014 mol/ml). The resulting mixture was allowed to come to room temperature for 15 min and was then poured into 7% hydrochloric acid. The ether layer was removed and the aqueous layer was extracted twice with ether. The combined ether extracts were dried over anhydrous sodium sulfate and concentrated *in vacuo*, leaving an oil which was distilled *in vacuo*, giving 1.6 g (65%) of product: bp 35–60° (1 mm); ν (CCl_4) 1765, 1580 cm^{-1}; nmr (CCl_4) τ 4.13 (m), 6.92 (m), 7.42 (t, broad), 8.85, (m), 9.07 (m), areas 1:2:2:4:3.

Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 76.91; H, 9.83.

3,3-Dimethoxycyclobutanone.—A solution of 5.2 g (0.046 mol) of Ia in 10 ml of methanol was added to a solution of 1.0 g (0.044 g-atom) of sodium in 50 ml of methanol cooled in an ice bath. The resulting solution was allowed to come to room temperature over 15 min, and saturated salt solution was added followed by enough water to redissolve the precipitated salt. The solution was extracted with eight 30-ml portions of ether. The combined ether extracts were concentrated *in vacuo* to about 50 ml, dried over anhydrous sodium sulfate, and further concentrated to give 3.0 g (49%) of crude 3,3-dimethoxycyclobutanone as an oil. Chromatography of 1.5 g of this material on 25 g of methanol-deactivated silica gel eluted with ether–hexane (1:6) gave 1.0 g of pure material in the early fractions: ν (CCl_4) 1790 cm^{-1}; nmr (CCl_4) τ 6.78 (s), 6.97 (s), areas 3:2. Later fractions appeared to be contaminated with 3-methoxycyclobutenone.

Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.10; H, 7.56.

3-Anilino-2-cyclobutenone (VIIa).—A solution of 168 mg (0.002 mol) of IIa and 186 mg (0.002 mol) of aniline in 10 ml of methylene chloride was allowed to stand at room temperature for 8 days. Concentration of the solution under reduced pressure left a solid residue which was recrystallized from benzene to give 330 mg (98%) of VIIa: mp 136–137° dec; ν ($CHCl_3$) 1730, 1600, 1560 cm^{-1}; nmr ($CDCl_3$) τ 2.7 (m), 4.77 (s), 6.62 (s), areas 5:1:2.

Anal. Calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.24; H, 5.51; N, 8.68.

3-(*N*-Methylanilino)-2-cyclobutenone (VIIb).—A solution of 168 mg (0.002 mol) of IIa and 214 mg (0.002 mol) of *N*-methylaniline in 10 ml of methylene chloride was allowed to stand at room temperature for 8 days. Concentration of the solution under reduced pressure left an oil which was taken up in ether. Upon cooling, 280 mg (78%) of crystalline VIIb was deposited: mp 87–88°; nmr ($CDCl_3$) τ 2.70 (s), 4.67 (s), 6.57 (s), 6.90 (s), areas 5:1:3:2; ν ($CHCl_3$) 1735, 1555 cm^{-1}.

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.09. Found: C, 76.47; H, 6.62; N, 7.98.

3-Pyrrolidino-2-cyclobutenone (VIIc). A. From Cyclobutane-1,3-dione (IIa).—A solution of 168 mg (0.002 mol) of IIa and 142 mg (0.002 mol) of pyrrolidine in 15 ml of methylene chloride was allowed to stand at room temperature for 48 hr. Concentration of the solution under reduced pressure left a liquid residue which was triturated with two 10-ml portions of ether. Removal of the ether left 140 g (52%) of light yellow crystals, mp 40–41°. An analytical sample from ether–hexane melted at 41.5–42°: ν ($CHCl_3$) 1740, 1590 cm^{-1}; nmr ($CDCl_3$) τ 5.47 (s), 6.50 (m), 6.67 (s), 7.90 (m), areas 1:4:2:4.

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.89; H, 8.25; N, 9.97.

B. From the 1-Ethoxyvinyl Enol Ether of Cyclobutane-1,3-dione (IX).—A solution of 168 mg (0.002 mol) of IIa, 160 mg (0.0023 mol) of ethoxyacetylene, and 5 mg of mercuric acetate in 10 ml of methylene chloride was allowed to stand at room temperature for 4 hr. A solution of 142 mg (0.002 mol) of pyrrolidine in 3 ml of methylene chloride was added to the resulting light yellow solution. The reaction was mildly exothermic. After standing at room temperature for 2 hr, the solvent was removed under reduced pressure, and the resulting oil was triturated with ether. Removal of the ether left 240 mg (89%) of light yellow crystals, mp 40–42°.

The Enol Acetate of IIa, VIIIa.—Ketene was bubbled for 2 hr through a solution of 0.60 g of IIa in 50 ml of methylene chloride cooled in an ice–salt bath. Concentration of the solution under reduced pressure left 0.85 g (95%) of almost pure VIIIa as a liquid which solidified in the refrigerator. Two recrystallizations from anhydrous ether at −78° gave 0.60 g (67%) of VIIIa: mp 29–31°; ν (CCl_4) 1795, 1770, 1590, 1565 cm^{-1}; nmr (CCl_4) τ 4.54 (s), 6.68 (s), 7.65 (s), areas 1:2:3. The compound is extremely sensitive to moisture, as is VIIIb, characterized below.

Anal. Calcd for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.28; H, 4.80.

The Enol Benzoate of IIa, VIIIb.—To a solution of 380 mg (0.002 mol) of 1-ethoxyvinyl benzoate[18] in 10 ml of methylene chloride was added 168 mg (0.002 mol) of IIa. The solution was allowed to stand in the refrigerator for 5 days and concentrated

(22) For assignments of bands in the infrared and Raman spectra see F. A. Miller, K. E. Kiviat, and I. Matsubara, *Spectrochim. Acta, Part A*, **24**, 1523 (1968).

under reduced pressure. The resulting semicrystalline residue was partially soluble in dry hexane. Cooling of the hexane gave 150 mg (39%) of white crystals: mp 65–68°; ν (CCl_4) 1770 (shoulder), 1760, 1590, 1565 cm^{-1}; nmr (CCl_4) τ 1.97 (m), 2.37 (m), 4.53 (s), 6.70 (s), areas 2:3:1:2.

Anal. Calcd for $C_{11}H_8O_3$: C, 70.21; H, 4.29. Found: C, 70.13; H, 4.34.

The 1-Ethoxyvinyl Enol Ether of IIa, IX.—A solution of 84 mg (0.001 mol) of IIa, 105 mg (0.0013 mol) of ethoxyacetylene, and 5 mg of mercuric acetate in 10 ml of methylene chloride was allowed to stand at room temperature for 5 hr. An infrared spectrum of the solution exhibited absorption at 1760, 1672, and 1578 cm^{-1}. In the nmr spectrum of the solution there is a vinyl ring proton peak at τ 5.03 (s) and ring methylene protons at 6.60 (s); the two terminal vinyl protons are superimposed on the methylene resonance of the ethoxy group at about τ 6.1. When the solvent was removed from the solution, the residue reacted violently with water to give IIa and ethyl acetate.

3-Acetoxy-3-chlorocyclobutanone (X).—A solution of 1.0 g of IIa in 25 ml of acetyl chloride was allowed to stand at room temperature for 2 hr. The excess acetyl chloride was removed under reduced pressure and the residue was distilled *in vacuo*, giving 1.36 g (73%) of X: bp 51–52° (17 mm); ν (CCl_4) 1805, 1785 cm^{-1}; nmr (CCl_4) τ 6.24 (s), 7.86 (s), areas 4:3.

A sample stored at −15° in a sealed tube decomposed to a 50:50 mixture of X and VIIIa after 2 weeks. A sample distilled at aspirator vacuum gave a distillate which was 87% VIIIa. Treatment of 2 drops of X with alcoholic silver nitrate gave an immediate precipitate of silver chloride. When X was treated with sodium iodide in acetone, sodium chloride precipitated upon warming.

When hydrogen chloride was bubbled through a solution of VIIIa in dry benzene, large quantities of X could be detected in the product by infrared and nmr spectroscopy.

Registry No.—Ia, 4683-54-9; Ib, 4313-48-8; IIa, 15506-53-3; IIb, 3183-44-6; III, 38425-45-5; IV, 10576-21-3; V, 38425-47-7; VI, 38425-48-8; VIIa, 38425-49-9; VIIb, 38425-50-2; VIIc, 38425-51-3; VIIIa, 38425-52-4; VIIIb, 38425-53-5; X, 38425-54-6; ketene, 463-51-4; ethoxyacetylene, 927-80-0; aniline, 62-53-3; β-ethoxycrotonic acid anilide, 38425-55-7; isobutyryl chloride, 79-30-1; 2-bromoethoxy-4,4-dimethyl-2-cyclobutenone, 38425-56-8; cyclopentanecarboxylic acid chloride, 4524-93-0; diazomethane, 334-88-3; 3-methoxy-4,4-dimethyl-2-cyclobutenone, 15517-68-7; phenyl bromide, 108-86-1; butyl bromide, 109-65-9; 3,3-dimethoxycyclobutanone, 38425-58-0; pyrrolidine, 123-75-1; 1-ethoxyvinyl benzoate, 38425-59-1.

Base-Induced Cyclizations of Alkyl-Substituted Propargyloxyethanols[1]

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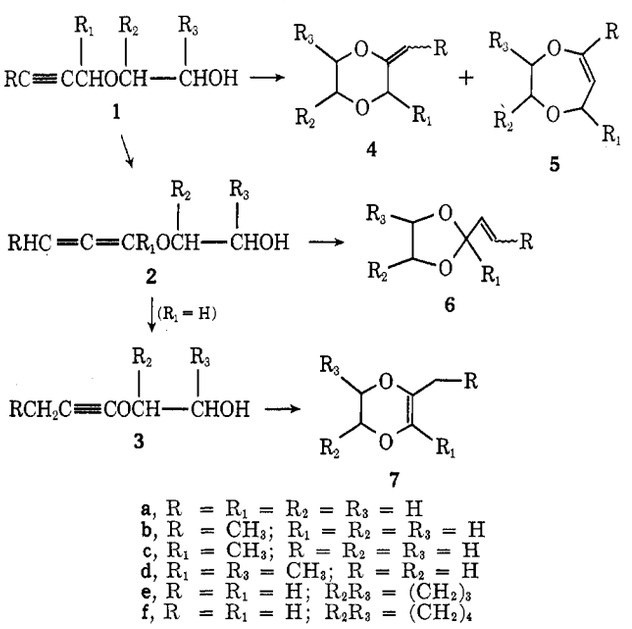
Cyclization reactions of alkyl-substituted propargyloxyethanols **1a–1f** induced by potassium hydroxide in water, dimethyl sulfoxide (DMSO), and *tert*-butyl alcohol were studied. Products obtained included the corresponding 2-methylene-1,4-dioxanes, 3,6-dioxacycloheptenes, 2-vinyl-1,3-dioxolanes, and 2-methyl-1,4-dioxenes. The mechanism proposed to account for base-induced cyclizations of propargyloxyethanol (ref 2) required modification to include two alternative pathways to the 2-methyl-1,4-dioxenes: cyclization of the allenyloxyethanol formed by prototropic rearrangement of the propargyloxyethanol, and, in DMSO only, base-induced rearrangement of the corresponding 2-methylene-1,4-dioxane.

The course of hydroxide-induced cyclization of propargyloxyethanol (**1a**) is strikingly dependent on reaction conditions.[2] In water, the main products are 2-methylene-1,4-dioxane (**4a**) and 3,6-dioxacycloheptene (**5a**); in the aprotic solvents decalin, dimethyl sulfoxide (DMSO), and triglyme, the main products are 2-vinyl-1,3-dioxolane (**6a**) and 2-methyl-1,4-dioxene (**7a**). A mechanism (Scheme I) that accounted for the dependence of product composition on solvent was proposed for the formation of **4a–7a**.[2] Formation of **4a** and **5a** was explained as occurring by intramolecular nucleophilic addition of alkoxide to the internal and terminal acetylenic carbons of **1a**, and the main pathways to **6a** and **7a**, respectively, were pictured as cyclizations of allenyloxyethanol (**2a**) and 1-propynyloxyethanol (**3a**), the products of successive prototropic rearrangements of **1a**.

Faure and Descotes,[3] who cyclized **1a** and six alkyl- and aryl-substituted propargyloxyethanols by treatment with potassium hydroxide in the diol corresponding to the substituted propargyloxyethanol, proposed other mechanisms for dioxene and dioxolane formation. They found that 1-(3-butyn-2-yloxy)-2-propanol (**1d**), the only propargyloxyethanol they examined that could not give a dioxene by the route shown in Scheme I, gave 2,3,5-trimethyl-1,4-dioxene (**7d**) as the major product; the only other product detected was 2-methylene-3,6-dimethyl-1,4-dioxane (**4d**). As **4d** and their other 2-methylene-1,4-dioxanes slowly isomerized to the

SCHEME I



a, R = R_1 = R_2 = R_3 = H
b, R = CH_3; R_1 = R_2 = R_3 = H
c, R_1 = CH_3; R = R_2 = R_3 = H
d, R_1 = R_3 = CH_3; R = R_2 = H
e, R = R_1 = H; R_2R_3 = $(CH_2)_3$
f, R = R_1 = H; R_2R_3 = $(CH_2)_4$

(1) Taken from the Ph.D. Thesis of J. G. Maroski, University of California, Davis, 1971.

(2) A. T. Bottini, F. P. Corson, and E. F. Böttner, *J. Org. Chem.*, **30**, 2988 (1965).

(3) R. Faure and G. Descotes, *Bull. Soc. Chim. Fr.*, 1569 (1966).