From 174.0 g (1.0 mol) of dimethyl adipate there was obtained 87.0 g (70% yield) of distilled 3-ethyl-2-cyclopenten-2-ol-1-one of >99% purity according to vpc.

Registry No.—**1b**, 25684-00-8; **2a**, 25684-01-9; **2b**, 25684-02-0; **3**, 80-71-7; **4**, 21835-01-8; Table I—propyl, 25684-04-2; isobutyl, 25684-05-3; benzyl, 25684-06-4.

Acknowledgment.—The author wishes to express his sincere appreciation to Mr. Philip A. Twomey for his competent technical assistance, and to Dr. John J. Beereboom for his interest and many helpful discussions. The author is also indebted to Dr. Charles R. Stephens who suggested the problem.

Diels–Alder Reaction of Acetoxy-1,3-dienes with Dimethyl Acetylenedicarboxylate and Chloromaleic Anhydride. A Synthesis of Benzene Derivatives

JOSEPH WOLINSKY* AND ROBERT B. LOGIN[1]

Department of Chemistry, Purdue University, Lafayette, Indiana 47907

Received January 29, 1970

Acyclic acetoxy-1,3-dienes, generated *in situ* from α,β-unsaturated aldehydes and ketones, undergo the Diels–Alder reaction with dimethyl acetylenedicarboxylate or chloromaleic anhydride to yield phthalic acid derivatives. Cyclic acetoxy-1,3-dienes and dimethyl acetylenedicarboxylate give bicyclo[2.2.2]octadiene derivatives. Heating the bicyclo[2.2.2]octadiene derivatives above 200° yields dimethyl acetoxyphthalates.

Acetoxy-1,3-dienes, preformed[2,3] or generated *in situ*,[4,5] readily participate in the Diels–Alder reaction. This paper describes a convenient one-step synthesis of phthalate derivatives by the reaction of acetoxy-1,3-dienes with dimethyl acetylenedicarboxylate or chloromaleic anhydride. This procedure complements and extends the methods for direct construction of benzene rings developed by Blanc[6] and Hill.[7]

Heating an acyclic α,β-unsaturated aldehyde or ketone in isopropenyl acetate, containing a catalytic amount of *p*-toluenesulfonic acid, with 1.5 equiv of dimethyl acetylenedicarboxylate affords a dimethyl phthalate derivative in good yield. Scheme I shows a pathway for the production of phthalate derivatives and lists representative examples used to demonstrate the scope of this reaction.

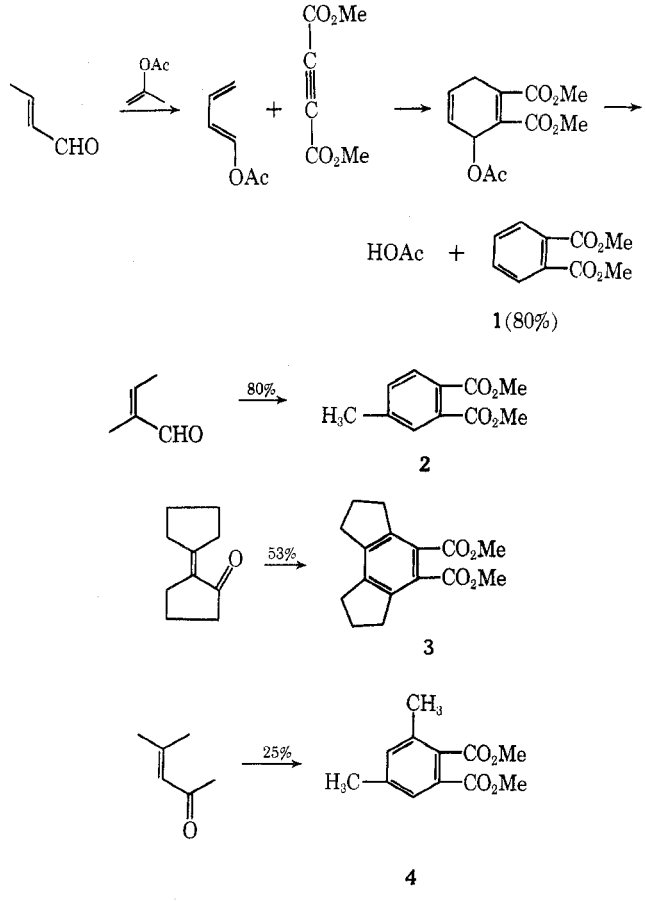
When chloromaleic anhydride is used as the dienophile the corresponding phthalic anhydride derivative is obtained (see Scheme II). The intermediate chloro acetate produced in this reaction must eliminate 1 equiv of acetic acid and hydrogen chloride to give the aromatic system.

Cyclic acetoxy-1,3-dienes were found to undergo the Diels–Alder reaction with dimethyl acetylenedicarboxylate, but not with chloromaleic anhydride. Dimedone gave a white, crystalline adduct **9** whose nmr spectrum exhibited singlets at 0.99, 1.11, 2.08, 2.11, and 3.78 ppm assigned to a *gem*-dimethyl group, two acetate groups, and two methoxy groups, respectively. The methylene group appeared as an AB-type quartet at 1.69 and 2.05 with a coupling constant of 12 Hz, while the bridgehead proton is observed at 3.48 and is coupled (J = 2 Hz) with the vinyl proton at 6.21 ppm.

Hydrolysis of adduct **9** gave keto acetate **10** and keto alcohol **11** which were readily separated by column chromatography. The C-7 methylene group of keto acetate **10** appeared as an AB pattern (J = 12 Hz) in which the upfield signal centered at 1.82 ppm was split into a doublet of doublets *via* long-range coupling (J = 2 Hz) through a "W" arrangement[8] with the endo proton at C-2, whose nmr signal was located at 2.72 ppm.

The structure of keto alcohol **11** was established by its conversion to keto acetate **10** by prolonged heating with acetic anhydride containing a catalytic amount of *p*-toluenesulfonic acid. The unique feature of the nmr

SCHEME I



* Author to whom correspondence should be addressed.

(1) David Ross Fellow, 1968–1969.

(2) H. J. Hagemeyer and D. C. Hull, *Ind. Eng. Chem.*, **41**, 2920 (1949).

(3) W. Flaig, *Justus Liebigs Ann. Chem.*, **568**, 1 (1950).

(4) C. M. Cimarusti and J. Wolinsky, *J. Amer. Chem. Soc.*, **90**, 113 (1968).

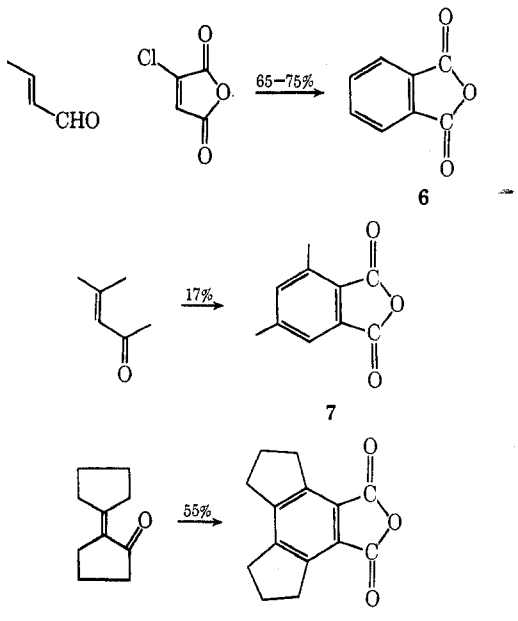
(5) J. Wolinsky and R. Login, *J. Org. Chem.*, **35**, 1986 (1970).

(6) P. Blanc, *Helv. Chim. Acta*, **44**, 1, 607 (1961).

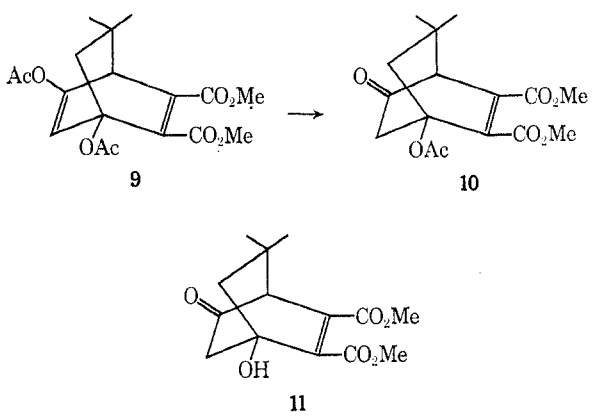
(7) R. K. Hill and R. M. Carlson, *J. Org. Chem.*, **30**, 2414 (1965).

(8) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Elmsford, N. Y., 1969, p 334.

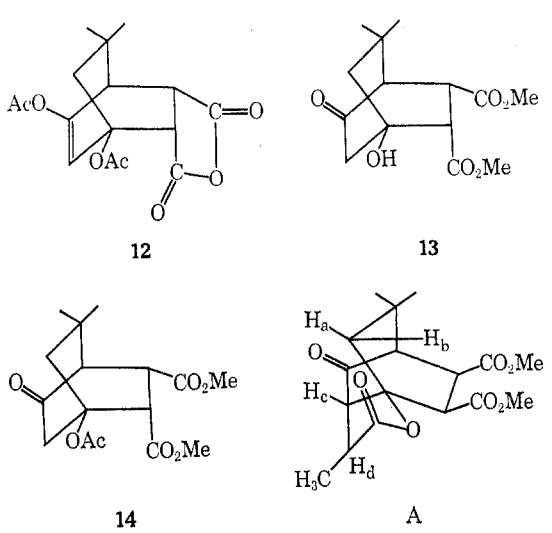
SCHEME II



spectrum of **11** was the appearance of a singlet for the C-7 methylene group at 1.69 ppm, instead of the multiplet shown by keto acetate **10**.



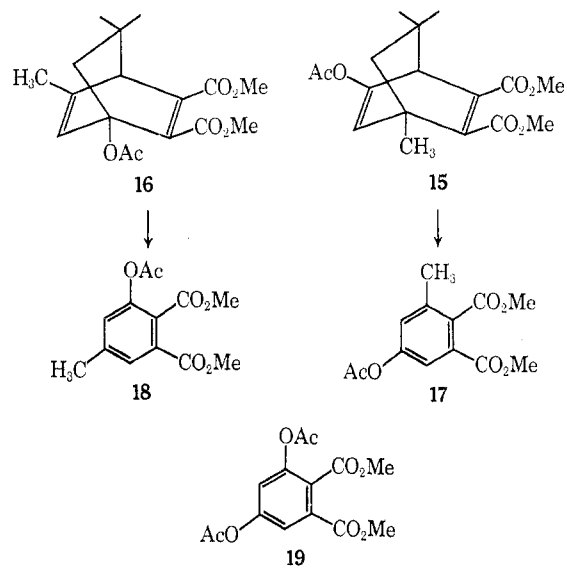
Hydrolysis of **12**[4] with hydrochloric acid in methanol gave the saturated keto alcohol **13** which was transformed into keto acetate **14** on heating with acetic anhydride containing *p*-toluenesulfonic acid. Again



it was found that the C-7 methylene signals of the acetate **14** and alcohol **13** are quite different. Acetate **14** displayed an AB-type doublet in which the high-field signal appeared as a doublet of doublets due to long range "W" type of coupling (J = 1.5 Hz), while the corresponding methylene signal in alcohol **13** appeared as a broad singlet.

A possible explanation for these observations is that the acetate group adopts a preferred conformation in which it is as far as possible from the carbonyl of the neighboring ester group. In this conformation A the protons labeled H_c and H_a are shifted downfield by the anisotropic effect of the carbonyl group, whereas protons H_b and H_d remain in their normal upfield location.

Isophorone reacted with dimethyl acetylenedicarboxylate to give a mixture of adducts **15** and **16** in a ratio of 23:77 on the basis of nmr analysis. Adducts **9** and the mixture of **15** and **16** undergo the Alder–Rickert reaction[9] when heated above 200° to give dimethyl acetoxyphthalate derivative **19** and a mixture of **17** and **18** in quantitative yield.



Experimental Section[10]

Dimethyl Phthalate.—A mixture of 1.82 g of crotonaldehyde, 5.5 g of dimethyl acetylenedicarboxylate, and 25 mg of *p*-toluenesulfonic acid in 30 ml of isopropenyl acetate was refluxed for 54 hr. The volatile reagents were removed under diminished pressure; the residue was added to saturated sodium bicarbonate solution and extracted with ether. The ether solution was washed with saturated salt solution and dried ($MgSO_4$). Distillation afforded 4 g (80%) of dimethyl phthalate, bp 140–145° (10 mm) [lit.[11] bp 137° (6 mm)].

Dimethyl 4-Methylphthalate.—A mixture of 2.02 g of tiglaldehyde and 5.12 g of dimethyl acetylenedicarboxylate was refluxed for 43 hr under the conditions described above and gave 4.0 g (80%) of dimethyl 4-methylphthalate, bp 125–137° (1 mm), $n^{17}D$ 1.5100 (lit.[12] $n^{26}D$ 1.5125).

Dimethyl Dicyclopentanophthalate (3).—The reaction of 2.74 g of 2-cyclopentylidenecyclopentanone with 3.9 g of dimethyl acetylenedicarboxylate, after heating 41 hr, gave on cooling 280 mg of **3**. Work-up of the reaction mixture in the usual manner and column chromatography on neutral alumina and elution with 25% ethyl acetate–hexane gave 2.38 g of **3**. A pure sample

(9) K. Alder and H. F. Rickert, *Justus Liebigs Ann. Chem.*, **524**, 180 (1936).

(10) Boiling and melting points are uncorrected. Microanalyses were performed by Dr. C. S. Yeh and associates.

(11) G. S. Gardner, and J. E. Brewer, *Ind. Eng. Chem.*, **29**, 179 (1937).

(12) A. Eschenmoser and H. Schinz, *Helv. Chim. Acta*, **33**, 171 (1950).

of **3** was obtained by recrystallization from methanol and showed mp 125–126° (lit.[13] mp 127°).

Dimethyl 3,5-Dimethylphthalate (4).—Heating 2.21 g of mesityl oxide with 4.8 g of dimethyl acetylenedicarboxylate under the usual conditions and chromatography of the crude product on neutral alumina gave, on elution with 30% ethyl acetate–hexane, 0.64 g (25%) of phthalate **4**: mp 54–55° (lit.[14] mp 54°); nmr ($CDCl_3$) 2.29 and 2.32 (s, 6, Me–), 3.83 and 3.88 (s, 6, –OMe), 7.2 and 7.6 (s, broad, 2, Ar H). A second fraction of 0.8 g was isolated and exhibited ir ($CHCl_3$) 5.75 and 6.19 μ; nmr ($CDCl_3$) 2.33 (s), 3.5–4.0 (m), 5.0–5.9 (m); tlc indicated a complicated mixture.

Phthalic Anhydride.—A solution of 6.9 g of crotonaldehyde, 13.2 g of chloromaleic anhydride, and 20 mg of *p*-toluenesulfonic acid in 30 ml of isopropenyl acetate was refluxed for 16 hr and yielded on work-up and chromatography on silica gel a 70% yield of phthalic anhydride, mp 129° (lit.[15] mp 127–128°).

3,5-Dimethylphthalic Anhydride (7).—A mixture of 1.67 g of mesityl oxide and 3.4 g of chloromaleic anhydride was refluxed for 60 hr under the usual conditions. The volume of the resulting solution was reduced to ~25 ml and ether was added causing 1.1 g of polymeric material to separate. The ether solution was concentrated and the resulting mixture was chromatographed on 100 g of silica gel. Elution with hexane–ether and recrystallization from hexane gave 0.5 g (17%) of anhydride **7**, mp 115–116° (lit.[16] mp 114.5–115.5°).

3,4,5,6-Dicyclopentanophthalic Anhydride (8).—The reaction of 7.5 g of 2-cyclopentylidenecyclopentanone with 13 g of chloromaleic anhydride under the usual conditions gave, on cooling and addition of ether, 9 g (55%) of solid which was recrystallized from acetic anhydride and showed mp 265–266° (lit.[13] mp 266°).

Dimethyl 1,3-Diacetoxy-8,8-dimethylbicyclo[2.2.2]oct-2,5-diene-5,6-dicarboxylate (9).—A solution of 7.0 g of dimedone and 10 g of dimethyl acetylenedicarboxylate was refluxed for 24 hr in the usual manner and work-up gave 20.4 g of a viscous orange oil. A 2-g portion of this oil was chromatographed on 80 g of silica gel and eluted with hexane–ether–ethyl acetate to give 0.835 g of adduct **9**. Several recrystallizations from hexane gave an analytical sample: mp 96.5–98°; ir ($CHCl_3$) 5.7, 6.05, and 6.15 μ; nmr ($CDCl_3$) 0.99 and 1.11 (s's, 6, CH_3CCH_3), 1.65 and 2.05 (AB-type q, 2, J = 11 Hz, $-CH_2-$), 2.08 and 2.11 (s's, 6, $-OCOCH_3$), 3.48 (d, 1, J = 2 Hz, –CH), 3.78 (s, 6, $-OCH_3$), 6.21 (d, 1, J = 2 Hz, C=C–H); mass spectrum (75 eV) *m/e* (rel intensity), no molecular ion, 310 (9), 279 (14), 268 (57), 237 (14), 226 (85), 195 (47), 194 (100), 136 (42), 69 (52), 57 (22), 56, 55 (24), 43 (96), and 41 (87).

Anal. Calcd for $C_{18}H_{22}O_8$: C, 59.01; H, 6.05. Found: C, 59.19; H, 6.32.

Hydrolysis of Adduct 9.—A solution of 1 g of adduct **9** in 40 ml of 50% aqueous methanol containing 10 ml of 0.1 *N* hydrochloric acid was refluxed for 2 hr. The mixture was poured into salt solution and extracted with ether. The ether extracts were dried ($MgSO_4$) and evaporated to give 900 mg of an oil. The oil was chromatographed on 75 g of silica gel. Elution with 10% ether–hexane gave 0.36 g of keto acetate **10** which was recrystallized from benzene–hexane and displayed mp 106–108°; ir ($CHCl_3$) 5.75 and 6.05 μ; nmr ($CDCl_3$) 1.02 and 1.15 (s's, 6, CH_3CCH_3), 2.04 (s, 3, $OCHCH_3$), 1.82 (d, of d, 1, J = 12 Hz and J = 2 Hz, C^7-H), 2.35 (d, 1, J = 12 Hz, C^7-H), 2.72 (d, 1, J = 2 Hz, C^2-H), 2.78 (s, 1, –CH), 3.32 (s, 1, C^4-H), 3.78 and 3.80 (s's, 6, $-OCH_3$); mass spectrum (75 eV) *m/e* (rel intensity) 293 (22) (p − 31), 264 (52), 250 (53), 249 (79), 235 (83), 219 (26), 217 (90), 208 (81), 206 (39), 203 (39), 194 (39), 193 (60), 175 (27), 91 (25), and 43 (100).

Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.41; H, 6.22.

Further elution of the chromatography column gave 0.41 g (50%) of keto alcohol **11** which crystallized after standing for several months. An analytical sample was obtained by recrystallization from ethyl acetate–hexane and showed mp 78–79°; ir ($CHCl_3$) 5.8 and 6.12 μ; nmr ($CDCl_3$) 1.0 and 1.11 (s's, 6, $-CCH_3$), 1.69 (s, 2, $-C^7$-H_2), 2.33 (s, 2, $-C^2$-H_2), 3.31 (s, 1, $-C^4$-H), 3.78 and 3.85 (s's, 6, $-OCH_3$); mass spectrum (75 eV) *m/e* (rel intensity) 282 (4), 264 (8), 251 (20), 249 (28), 240 (63), 235 (53), 209 (80), 208 (100), 194 (41), 193 (64).

Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.70; H, 6.21.

When 10 g of adduct **9** was refluxed for 48 hr in 100 ml of methanol containing 2 ml of concentrated hydrochloric acid there was obtained 7.4 g (100%) of an oil identical with keto alcohol **11**. This oil also crystallized on prolonged standing. A 2.4 g sample of keto alcohol **11** was refluxed for 72 hr in 30 ml of acetic anhydride containing 100 mg of *p*-toluenesulfonic acid. On work-up an oil was obtained which gradually crystallized. Recrystallization from benzene–hexane (Norit) gave 2.5 g of keto acetate **10**, mp 106–108°.

Dimethyl 1-Hydroxy-8,8-dimethylbicyclo[2.2.2]octan-3-one-5,6-dicarboxylate (13).—A solution of 2.85 g of adduct **12**[4] in 50 ml of methanol containing 2 ml of concentrated hydrochloric acid was refluxed for 20 hr. Water (30 ml) was added and the solution heated another 5 hr. Work-up gave 1.60 g of **13** which was recrystallized from ethyl acetate–hexane and showed mp 105–107°; nmr ($CDCl_3$) 1.0 and 1.21 (s's, 6, CH_3CCH_3), 1.05 (d, 2, $-C^7$-H_2), 2.01 and 2.32 (d of d, 1, J = 19 Hz, J = 2 Hz, exo-C^2-H), 2.1 (d, 1, J = 3 Hz, $-C^4$-H), 2.89 and 3.09 (d of d, 1, J = 12 Hz, C^6-H), 3.0 and 3.32 (d, 1, J = 19 Hz, endo-C^2-H), 3.49 (d, 1, J = 3 Hz, $-C^5$-H), 3.59 and 3.61 (s's, 6, $-OCH_3$), and 4.42 ppm (s, 1, –OH); mass spectrum (75 eV) *m/e* (rel intensity) 284 (37), 253 (44), 224 (16), 221 (25), 169 (60), 145 (45), 140 (87), 125 (100), 113 (69), 95 (38), 83 (40), 81 (29), and 69 (33).

Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 709. Found: C, 59.00; H, 6.85.

Dimethyl 1-Acetoxy-8,8-dimethylbicyclo[2.2.2]octan-3-one-5,6-dicarboxylate (14).—A solution of 600 mg of **13** in 20 ml of acetic anhydride containing 10 mg of *p*-toluenesulfonic acid was refluxed for 24 hr and after cooling was added to 50 ml of saturated sodium bicarbonate solution. The resulting mixture was extracted with ether. The ether solution was dried and evaporated to give 600 mg of **14** which was recrystallized from hexane and showed mp 116–118°. This sample of acetate **14** did not depress the melting point of an authentic sample of **14**.[4]

Dimethyl 1-Acetoxy-3,8,8-trimethylbicyclo[2.2.2]octa-2,5-diene-5,6-dicarboxylate (16) and Dimethyl 3-Acetoxy-1,8,8-trimethylbicyclo[2.2.2]octa-2,5-diene-5,6-dicarboxylate (15).—The reaction of 9.4 g of isophorone and 14.7 g of dimethyl acetylenedicarboxylate conducted for 48 hr in the usual manner gave 28.1 g of an orange oil. Column chromatography failed to separate **15** and **16** which were indicated to be present in a 77:23 ratio by nmr analysis: ir ($CHCl_3$) 5.8, 6.02, 6.15; nmr ($CDCl_3$) 0.95, 1.02, and 1.05 (s's, CH_3), 1.84 (d, J = 1.8 Hz, $C=CCH_3$), 2.07 and 2.10 (s's, $OCOCH_3$), 3.71 (s, $-OCH_3$), 5.72 (d, J = 2 Hz, C=CH), and 6.0 (m, –C=CH).

Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 62.95; H, 6.89.

Heating a sample of this mixture above 200° gave a quantitative yield of a mixture of **17** and **18**: ir ($CHCl_3$) 5.61 and 5.75 μ; nmr ($CDCl_3$) 2.23, 2.26, 2.33, and 2.8 (s's, $-OCOCH_3$, CH_3Ar), 3.85 and 3.9 (s, $-OCH_3$), 7.17 and 7.58 (m, Ar H); mass spectrum (75 eV) *m/e* (rel intensity) 266 (11), 235 (18), 225 (11), 224 (84), 193 (74), 192 (100), 162 (18), 134 (68), 133 (13).

Anal. Calcd for $C_{13}H_{14}O_6$: C, 58.64; H, 5.30. Found: C, 58.41; H, 5.02.

Dimethyl 3,5-Diacetoxphthalate (19).—Heating a sample of adduct **9** above 200° gave a quantitative yield of phthalate **19**: mp 77.5–80.5°; ir ($CHCl_3$) 5.62 and 5.75 μ; nmr ($CDCl_3$) 2.25 and 2.28 (s's, 6, $OCOCH_3$), 3.88 and 3.90 (s's, 6, $-OCH_3$), 7.22 and 7.62 (AB q, J = 2 Hz, Ar H). The mass spectrum of **19** was essentially identical with that of adduct **9**.

Anal. Calcd for $C_{14}H_{14}O_8$: C, 54.20; H, 4.55. Found: C, 54.45; H, 4.82.

Registry No.—**9**, 25864-63-5; **10**, 25864-64-6; **11**, 25864-65-7; **13**, 25864-66-8; **15**, 25864-67-9; **16**, 25864-68-0; **17**, 25864-69-1; **18**, 25864-70-4; **19**, 25907-95-3; dimethyl acetylenedicarboxylate, 762-42-5; chloromaleic anhydride, 96-02-6.

(13) D. S. Greidinger and D. Ginsburg, *J. Org. Chem.*, **22**, 1406 (1957).
(14) K. Alder, R. Munders, W. Krane, and P. Wirtz, *Justus Liebigs Ann. Chem.*, **627**, 59 (1959).
(15) L. Carius, *ibid.*, **148**, 62 (1868).
(16) H. Pines and R. H. Kozlonski, *J. Amer. Chem. Soc.*, **78**, 3776 (1956).