***N*-Methyl-*N*-[4-(*N*,*N*-dimethylamino)-2-methylbenzyl]-*N*′,*N*′-dimethyl-4,4′-diamino-2,2′-dimethyldiphenylmethane (19)**: $^1$H NMR ($CCl_4$) δ 2.11 (s, 6 H, $ArCH_3$), 2.17 (s, 3 H, $ArCH_3$), 2.74 (s, 3 H, $NCH_3$), 2.77, 2.79 (2 s, 12 H, $NCH_3$), 3.56 (s, 2 H, $ArCH_2Ar$), 4.17 (s, 2 H, $NCH_2Ar$), 6.10–6.90 (m, 9 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 3000–2800 (s), 1620 (vs), 1515 (vs), 1480 (m), 1450 (m), 1350 (s), 805 (s), 780 (w), 760 (w), 705 (vw), 695 (vw) cm$^{-1}$; mol wt of $C_{28}H_{37}N_3$, 415.62; mass spectrum (70 eV), *m*/*e* 415, 400, 354, 340, 281, 252, 148, 134.

***N*,*N*,*N*′-Trimethyl-4,4′-diamino-2,2′-dimethyldiphenylmethane (20)**: $^1$H NMR ($CCl_4$) δ 2.05, 2.09 (2 s, 6 H, $ArCH_3$), 2.67 (s, 3 H, $NCH_3$), 2.75 (s, 6 H, $NCH_3$), 3.15 (s, 1 H, NH), 3.57 (s, 2 H, $ArCH_2Ar$), 6.05–6.65 (m, 6 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 3400 (s), 3000–2800 (vs), 1615 (vs), 1510 (vs), 1445 (s), 1348 (s), 1328 (s), 800 (s), 775 (m), 700 (w) cm$^{-1}$; mol wt of $C_{18}H_{24}N_2$, 268.39; mass spectrum (70 eV), *m*/*e* 268, 253, 148, 134, 133, 119, 118, 105, 104.

***N*,*N*,*N*′,*N*′-Tetramethyl-4,4′-diamino-2,2′-dimethyldiphenylmethyl Chloride (21).** This compound was identified by comparison with an authentic sample (spectrum over the visible range). As the authentic sample, a dye obtained by photochemical oxidation of *N*,*N*,*N*′,*N*′-tetramethyl-4,4′-diamino-2,2′-dimethyldiphenylmethane in $CH_2Cl_2$ and in $CHCl_3$–acetonitrile and $CCl_4$–acetonitrile mixtures was used.

**C. Products of *N*,*N*-dimethyl-*o*-toluidine. *N*-Methyl-*N*-(β-trichloroethyl)-*o*-toluidine (22)**: $^1$H NMR ($CCl_4$) δ 2.32 (s, 3 H, $ArCH_3$), 2.96 (s, 3 H, $NCH_3$), 4.0 (s, 2 H, $NCH_2$), 6.95–7.30 (m, 4 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 2960 (s), 2940 (vs), 2860 (s), 1605 (w), 1495 (m), 1350 (m), 810 (m), 795 (s), 765 (s), 720 (s) cm$^{-1}$; mol wt of $C_{10}H_{12}NCl_3$, 252.57; mass spectrum (70 eV), *m*/*e* molecular ions 257, 255, 253, and 252, other ions 220, 218, 216, 134, 120, and 91.

***N*-Methyl-*N*-(β-dichloroethyl)-*o*-toluidine (23)**: $^1$H NMR ($CCl_4$) δ 2.20 (s, 3 H, $ArCH_3$), 2.71 (s, 3 H, $NCH_3$), 3.49 (d, *J* = 6.5 Hz, 2 H, $NCH_2$), 5.44 (t, *J* = 6.5 Hz, 1 H, CH), 6.70–7.15 (m, 4 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 2990–2805 (s), 1605 (s), 1500 (vs), 1455 (s), 1425 (s), 1380 (w), 1350 (m), 800 (m), 790 (s), 775 (s), 730 (s) cm$^{-1}$; mol wt of $C_{10}H_{13}NCl_2$, 218.12; mass spectrum (70 eV), *m*/*e* molecular ions 221, 219, and 217, other ions 184, 182, 134, 120, 119, and 91.

***N*-Methyl-*N*-[4-(*N*,*N*-dimethylamino)-3-methylbenzyl]-*o*-toluidine (24)**: white crystalline solid; $^1$H NMR ($CCl_4$) δ 2.20, 2.30 (2 s, 6 H, $ArCH_3$), 2.48 (s, 3 H, $NCH_3$), 2.58 (s, 6 H, $NCH_3$), 3.85 (s, 2 H, $NCH_2$), 6.84–7.18 (m, 7 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 3070 (w), 3030 (m), 2990–2800 (s), 1615 (w), 1605 (s), 1510 (vs), 1500 (vs), 1460 (s), 1445 (m), 1430 (w), 1380 (w), 1360 (s), 1315 (s), 765 (s), 730 (s) cm$^{-1}$; mol wt of $C_{18}H_{24}N_2$, 268.40; mass spectrum (70 eV), *m*/*e* 268, 148, 134, 132, 118, 105, 104, 91.

***N*-Methyl-*o*-toluidine (25).** This compound was identified by comparison with an authentic sample ($R_f$ and $^1$H NMR and IR spectra).

***N*,*N*,*N*′,*N*′-Tetramethyl-4,4′-diamino-3,3′-dimethyldiphenylmethane (26)**: $^1$H NMR ($CCl_4$) δ 2.10 (s, 6 H, $ArCH_3$), 2.76 (s, 12 H, $NCH_3$), 3.66 (s, 2 H, $CH_2$), 6.15–6.95 (m, 6 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 2980–2860 (s), 1615 (s), 1500 (s), 1470 (m), 1460 (m), 1380 (m), 1320 (vw), 775 (m), 760 (m), 730 (m) cm$^{-1}$; mol wt of $C_{19}H_{26}N_2$, 282.43; mass spectrum (70 eV), *m*/*e* 282, 267, 148, 134, 119.

***N*-Methyl-2,4-bis[4-(*N*-methylamino)-3-methylbenzyl]-6-methylaniline (27)**: $^1$H NMR ($CCl_4$) δ 1.98 (s, 9 H, $ArCH_3$), 2.75 (s, 9 H, $NCH_3$), 3.80 (s, 3 H, NH), 4.19 (s, 4 H, $CH_2$), 6.25–7.15 (m, 8 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 3430 (s), 2980–2825 (s), 1625 (vs), 1525 (vs), 1475 (m), 1455 (s), 1375 (s), 1325 (s), 815 (s) cm$^{-1}$; mol wt of $C_{26}H_{33}N_3$, 387.57; mass spectrum (70 eV), *m*/*e* 387.

***N*,*N*′-Dimethyl-4,4′-diamino-3,3′-dimethyldiphenylmethane (28)**: white crystalline solid; $^1$H NMR ($CCl_4$) δ 1.90 (s, 6 H, $ArCH_3$), 2.71 (s, 6 H, $NCH_3$), 3.10 (s, 2 H, NH), 3.60 (s, 2 H, $CH_2$), 6.22–6.90 (m, 6 H, aromatic protons); IR (film) $\tilde{\nu}_{max}$ 3440 (vs), 3075 (m), 3045 (m), 3005 (s), 2980 (s), 2910 (vs), 2815 (s), 1620 (vs), 1520 (vs), 1470 (s), 1450 (m), 1435 (m), 1415 (m), 1380 (m), 1335 (s), 1320 (s), 820 (s), 805 (s), 775 (w), 750 (m) cm$^{-1}$; mol wt of $C_{17}H_{22}N_2$, 254.38; mass spectrum (70 eV), *m*/*e* 254, 239, 224, 134, 120, 119, 105.

Trichloromethane (**29**), hexachloroethane (**30**) and dichloromethane (**31**) were identified as described previously.[2,6]

**Acknowledgment.** Our thanks are due to Barbara Poplawska, M.Sc., for her assistance during measurements of quantum yields of hydrogen chloride. This work was supported in part by the Institute of Organic Chemistry of the Polish Academy of Sciences (interdisciplinary problem no. I.12).

**Registry No.** **1**, 71050-19-6; **2**, 71050-20-9; **3**, 30724-66-4; **4**, 23970-61-8; **5**, 7137-79-3; **6**, 7137-82-8; **7**, 71050-21-0; **8**, 64794-20-3; **9**, 623-08-5; **10**, 71050-22-1; **11**, 71050-23-2; **12**, 71050-24-3; **13**, 71050-25-4; **14**, 71050-26-5; **15**, 71050-27-6; **16**, 71050-28-7; **17**, 696-44-6; **18**, 71050-29-8; **19**, 71050-30-1; **20**, 71050-31-2; **21**, 71050-32-3; **22**, 71050-33-4; **23**, 71050-34-5; **24**, 71050-35-6; **25**, 611-21-2; **26**, 40761-68-0; **27**, 71050-36-7; **28**, 6370-28-1; **29**, 67-66-3; **30**, 67-72-1; **31**, 75-09-2; $CCl_4$, 56-23-5; DMpT, 99-97-8; DMmT, 121-72-2; DMoT, 609-72-3.

# Stereochemistry of Ene Reactions of Glyoxylate Esters

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The stereochemistry of the thermal and catalytic ene reactions of methyl glyoxylate is examined. With *cis*-2-butene at 200 °C, a 54% yield of a 7.4:1 mixture of endo–exo adducts is obtained. With cyclohexene and ferric chloride catalyst, a 4.4:1 mixture of endo–exo adducts is obtained. Trisubstituted alkenes give very little selectivity. The intramolecular ene reaction of prenyl glyoxylate proceeds at 90 °C, giving a 1:1 mixture of *cis*- and *trans*-3-isopropenyl-2-hydroxybutyrolactones.

The ene reaction, like the related Diels–Alder reaction, can proceed through an endo or exo transition state. Unlike the Diels–Alder reaction, very little is known about the stereochemistry of intermolecular ene reactions. β-Pinene has been investigated with a wide variety of enophiles,[1,2] and Gill has recently shown that Lewis acids can drastically influence the stereochemistry of the ene reaction of β-pinene with chloral.[2c] Ene reactions with 1,2-disubstituted or trisubstituted alkenes produce two adjacent chiral centers. If one diastereomer is highly

(1) For a review see H. M. R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 8, 556 (1969).

(2) (a) R. K. Hill, J. W. Morgan, R. V. Shetty, and M. E. Synerholm, *J. Am. Chem. Soc.*, **96**, 4201 (1974); (b) H. K. Spencer and R. K. Hill, *J. Org. Chem.*, **40**, 217 (1975); (c) G. B. Gill and B. Wallace, *J. Chem. Soc., Chem. Commun.*, 382 (1977); (d) R. T. Arnold and J. S. Showell, *J. Am. Chem. Soc.*, **79**, 419 (1957).

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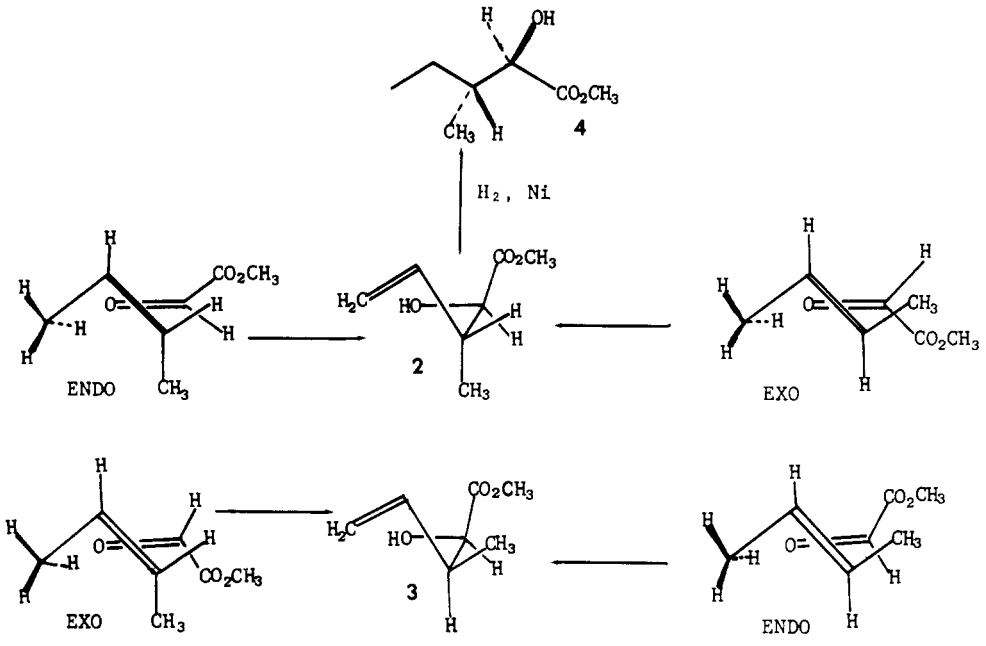



**Figure 1.** Stereochemistry of thermal ene reactions of 2-butenes with methyl glyoxylate.

favored, these reactions will be useful in synthesis. However, with the exception of Berson's pioneering work with 2-butenes and cyclopentene using maleic anhydride as an enophile,[3] the stereochemistry of these ene reactions is not known. Since glyoxylate esters undergo thermal ene reactions at 150 °C and Lewis acid catalyzed ene reactions at 25 °C[4] and the resulting adducts are useful synthetic intermediates, we chose to investigate the stereochemistry of these ene reactions.

The thermal reaction of methyl glyoxylate (1) with *cis*-2-butene (60 h at 200 °C) gives a 7.4:1 mixture of epimeric methyl 2-hydroxy-3-methyl-4-pentenoates (**2** and **3**) in 54% yield. The minor isomer, **3**, was identified by comparison to an authentic sample prepared by addition of (trimethylsilyl)acetylide to ethyl *trans*-2,3-oxidobutanoate followed by desilylation and semihydrogenation.[5] The major isomer, **2**, was identified by hydrogenation over Raney nickel to give (±)-methyl isoleucate (**4**) whose spectra were identical with those of an authentic sample. This constitutes an efficient highly stereoselective synthesis of isoleucic acid, a component of the antibiotic depsipeptide monamycin.[6] The reported ene reaction of methyl toluenesulfonyliminoacetate with *cis*-2-butene[7] may provide a stereoselective route to isoleucine if the endo–exo ratio is similar to that obtained with **1**.

The major isomer (**2**) results from an endo transition state while the minor isomer (**3**) results from the exo transition state (see Figure 1). The inherent preference for an endo transition state and steric repulsion between

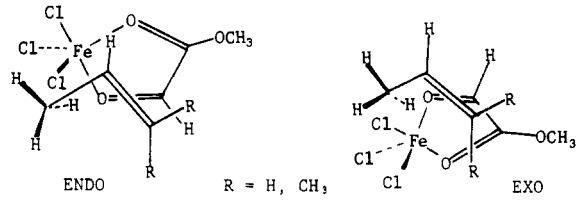



**Figure 2.** Transition states for the ferric chloride catalyzed ene reaction of methyl glyoxylate with 2-butenes.

the carbomethoxy group and the methyl group in the exo transition state result in a large preference for the formation of **2** from *cis*-2-butene. *trans*-2-Butene and **1** at 150 °C give a 0.57:1 mixture of **2** and **3** in 20% yield. In this case steric repulsion between the methyl and carbomethoxy groups is present in the endo transition state, resulting in much lower selectivity for the endo isomer **3** (see Figure 1). These results are similar to Berson's results with maleic anhydride and 2-butenes.[3] *cis*-2-Butene gives a 4:1 endo–exo mixture, while *trans*-2-butene gives a 1.22:1 endo–exo mixture.

The Lewis acid catalyzed reactions of **1** with 2-butenes give quite different results. Treatment of *cis*-2-butene with **1** and 1 equiv of ferric chloride at 25 °C in methylene chloride gives a 31% yield of a 1.4:1 mixture of **2** and **3** and a 20% yield of a 1:1 mixture of epimeric methyl 4-chloro-2-hydroxy-3-methylpentanoates (**5** and **6**).[8] Under these conditions, *trans*-2-butene gives a 36% yield of a 1.45:1 mixture of **2** and **3** and a 22% yield of a 4.05:1.55:1:2.4 mixture of chlorides **7**, **5**, **6**, and **8**. In both catalytic cases considerably more of the exo ene adduct is formed than in the thermal reactions. This may be due to the nature of the chelated ferric chloride–**1** complex. Examination of models shows that the chlorides of this complex appear to interact with the butene in the endo transition states (see Figure 2). The chlorides **5**–**8** are derived from a two-step reaction. Chlorides **5** and **6**, which are stereospecifically obtained from *cis*-2-butene, are probably epimers at C-2 since condensation of *cis*- or *trans*-2-butene with paraformaldehyde and hydrogen chloride at 65 °C gives predominantly trans addition of

(3) J. A. Berson, R. G. Wahl, and H. D. Perlmutter, *J. Am. Chem. Soc.*, 88, 187 (1966).

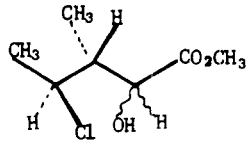
(4) (a) E. I. Klimova and Y. A. Arbuzov, *Dokl. Chem. (Engl. Transl.)*, 167, 419 (1966); (b) E. I. Klimova, E. G. Treshchova, and Y. A. Arbuzov, *ibid.*, 180, 504 (1968); (c) E. I. Klimova and Y. A. Arbuzov, *ibid.*, 173, 386 (1967); (d) E. I. Klimova and Y. A. Arbuzov, *J. Org. Chem. USSR (Engl. Transl.)*, 4, 1726 (1968); (e) E. I. Klimova, N. D., Antonova, and Y. A. Arbuzov, *ibid.*, 5, 1312 (1969); (f) O. Achmatowicz, Jr., and B. Szechner, *J. Org. Chem.*, 37, 964 (1972).

(5) We thank Professor Paul Bartlett of the University of California, Berkeley, for providing spectra of authentic samples of *erythro*- and *threo*-ethyl 2-hydroxy-3-methyl-4-pentenoates. See also P. A. Bartlett and J. Myerson, *J. Am. Chem. Soc.*, 100, 3950 (1978).

(6) C. H. Hassall in "Some Recent Developments in the Chemistry of Natural Products", S. Rangaswami and N. V. Subba Rao, Eds., Prentice-Hall of India, New Delhi, 1972, pp 146–152.

(7) O. Achmatowicz, Jr., and M. Pietraszkiewicz, *J. Chem. Soc., Chem. Commun.*, 484 (1976).

(8) Formation of chlorides has been noted in the aluminum chloride catalyzed reactions of chloral with 2-butenes. See G. B. Gill, S. J. Parrott, and B. Wallace, *J. Chem. Soc., Chem. Commun.*, 655 (1978).



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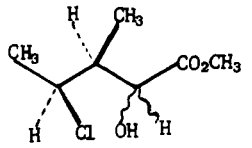
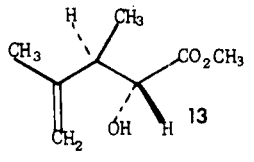


7,8

hydroxymethyl and chloride to the double bond.[9] Similarly **7** and **8**, obtained preferentially from *trans*-2-butene, are also probably epimeric at C-2. Although complete proton NMR data are available, ambiguities in conformation do not allow the assignment of configuration to **5**–**8**.

The thermal ene reaction of **1** with cyclohexene at 150 °C proceeds poorly, giving a 5% yield of an 8.3:1 mixture of epimeric methyl α-hydroxy-2-cyclohexen-1-ylacetates (**9** and **10**). With ferric chloride an 80% yield of a 4.4:1 chromatographically separable mixture of **9** and **10** is obtained. Arbuzov and co-workers have reported a similar result without characterizing the minor isomer or determining the stereochemistry.[4d] Hydrolysis of **9** and **10** followed by iodolactonization leads to more rigid structures which can be assigned the stereochemistry shown from $J_{Ha,Hb}$ = 6.5 Hz for the major isomer **11** and $J_{Ha,Hb}$ = 9.6 Hz for the minor isomer **12**.[10,11] Thus the major isomer **9** results from an endo transition state. Cyclohexene differs from *cis*-2-butene in that the endo transition state is still favored with ferric chloride catalysis because of steric interaction in the exo transition state between the ring protons and ferric chloride (see Figure 3).

The trisubstituted alkenes 2-methyl-2-butene and 1-methylcyclohexene give good yields of mixtures of ene adducts under thermal or catalytic conditions. 2-Methyl-2-butene and **1** at 150 °C give a 1.72:1 mixture of **13** and **14** in 30% yield. Under catalytic conditions a 78% yield of a 1.08:1 mixture of **13** and **14** is obtained. The structures of **13** and **14** are very tentatively assigned by comparison of GC retention times and NMR data with **2** and **3**. 1-Methylcyclohexene and **1** at 150 °C give a 41% yield of a 1:1 mixture of **15** and **16**, each as a 3:2 mixture



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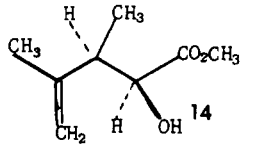

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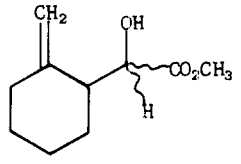

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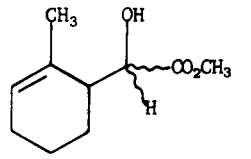

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of isomers as determined by NMR and GC. Treatment of this mixture with ferric chloride in methylene chloride converts **15** to **16**. With ferric chloride, 1-methylcyclohexene gives a 1.26:1 mixture of the isomers of **16** in 66% yield.

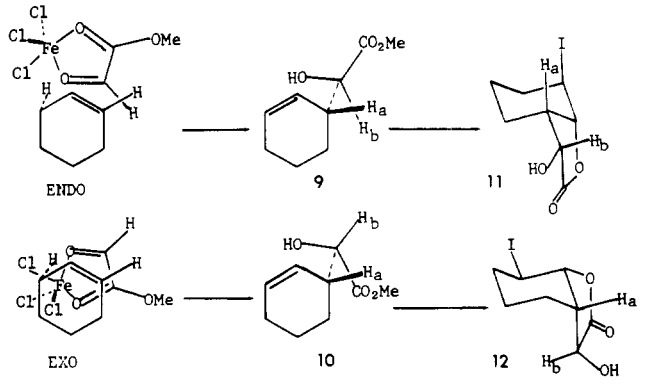
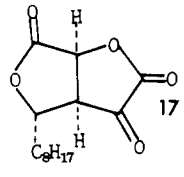


Figure 3. Ferric chloride catalyzed reaction of cyclohexene with methyl glyoxylate.

As a route to α-hydroxy lactones such as avenaciolide (**17**), the intramolecular ene reactions of allylic glyoxylates were investigated. Crotyl glyoxylate (**18**) was easily prepared by oxidation of dicrotyl tartrate with periodate. The tartrate was easily prepared from tartaric acid, crotyl alcohol, and acid. Prenyl tartrate could not be prepared, so prenyl glyoxylate (**19**) was synthesized via the method of Jurczak and Zamojski.[12] Prenyl bromoacetate is converted to the nitrate with silver nitrate and to the hydrated glyoxylate by treatment with sodium acetate in $Me_2SO$. Stirring with phosphorus pentoxide gives **19**.

Both prenyl and crotyl glyoxylates are unstable, decomposing in the presence of Lewis acids or on distillation. Crotyl glyoxylate decomposes at 150 °C without undergoing the desired ene reaction.[13] Prenyl glyoxylate reacts slowly at 90 °C, giving a 30% yield of a 1:1 mixture of ene adducts **20** and **21** after 60 h. The stereochemistry is



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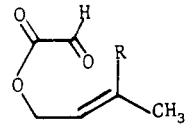
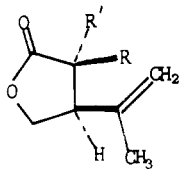


18 R = H
19 R = $CH_3$



20 R = H, R' = OH
21 R = OH, R' = H

assigned on the basis of NMR data. For the trans adduct **20**, $J_{Ha,Hb}$ = 10.2 Hz, while for the cis adduct **21**, $J_{Ha,Hb}$ = 7.8 Hz. These values are typical for 2,3-disubstituted butyrolactones.[11] The formation of isomeric mixtures has been noted in similar ene reactions.[14]

The ene reactions of *cis*-1,2-disubstituted alkenes give good yields of ene adducts under thermal or catalytic conditions with good endo selectivity which should be of value for control of stereochemistry in acyclic systems.

## Experimental Section

IR spectra were obtained on a Perkin-Elmer 283 spectrometer. NMR spectra were taken on a Varian A-60 or Perkin-Elmer R32 spectrometer. $^{13}C$ NMR spectra were recorded with a Varian

(9) P. R. Stapp and D. S. Weinberg, *J. Org. Chem.*, **34**, 3592 (1969).
(10) We thank Professor Bartlett[5] for providing us with spectra, prior to publication, of the corresponding lactones in which the acetoxy group has been replaced by a methyl. These lactones have very similar coupling constants to those of **11** and **12**.
(11) For studies on lactone stereochemistry from NMR data see (a) R. N. Johnson, J. B. Lowry, and N. V. Riggs, *Tetrahedron Lett.*, 5113 (1967); (b) D. Savastianoff and M. Pfau, *Bull. Soc. Chim. Fr.*, 4162 (1967); (c) J. A. Altman, H. Gilboa, and D. Ben-Ishai, *Tetrahedron*, **33**, 3173 (1977); (d) S. A. M. Tayyeb Hussain, W. D. Ollis, C. Smith, and J. F. Stoddart, *J. Chem. Soc., Perkin Trans. 1*, 1480 (1975).
(12) J. Jurczak and A. Zamojski, *Rocz. Chem.*, **44**, 2257 (1970).
(13) The marked instability of allyl pyruvate has been noted: R. Louw and E. C. Kooyman, *Recl. Trav. Chim. Pays-Bas*, **86**, 1041 (1967).
(14) W. Oppolzer and V. Snieckus, *Angew. Chem., Int. Ed. Engl.*, **17**, 476 (1978).

XL-100 spectrometer. Microanalyses were performed by Galbraith Laboratories. Methylene chloride was purified by distillation from calcium hydride. Anhydrous ferric chloride was used without further purification. All gas chromatographic analyses were performed on a 10% XF-1150 column on Chromosorb W.

**Methyl glyoxylate (1)** was prepared by the procedure of Kelly[15] by oxidation of (+)-dimethyl tartrate with periodate in ether. Distillation of the crude product from $P_2O_5$ gave monomeric methyl glyoxylate which polymerized on standing. Freshly distilled or stored 1 gave identical yields in ene reactions.

**Thermal Ene Reactions with Methyl Glyoxylate. General Procedure.** Methyl glyoxylate (880 mg, 10 mmol), alkene (20 mmol), and pyridine (10 μL) were dissolved in 15 mL of benzene and sealed in Pyrex tubes. After the indicated reaction time the solvent was evaporated.

**Thermal Reaction with *cis*-2-Butene.** Reaction for 24 h at 150 °C gave recovered 1, a mixture of 2 and 3, and methyl dimethoxyacetate. Chromatography on silica with 4:1 hexane–ethyl acetate as eluant gave 0.42 g (29%) of a 7.7:1 mixture of the acetates of 2 and 3 contaminated with <5% of methyl dimethoxyacetate. Elution with ether gave 0.33 g (37%) of recovered 1. Pure samples of 2 and 3 were prepared by preparative GC. The data for 2 are as follows: NMR ($CDCl_3$) δ 5.5–6.1 (1 H, m), 5.2–5.0 (2 H, m), 4.13 (1 H, d, $J$ = 3.5 Hz), 3.77 (3 H, s), 2.50 (1 H, m), 1.18 (3 H, d, $J$ = 7 Hz); IR ($CCl_4$) 3540, 3080, 1735, 1645, 915 $cm^{-1}$; GC $t_R$ = 14.75 min (100 °C). The data for 3 are as follows: NMR ($CDCl_3$) δ 5.6–6.2 (1 H, m), 5.0–5.2 (2 H, m), 4.20 (1 H, d, $J$ = 5 Hz), 3.80 (3 H, s), 2.65 (1 H, m), 1.05 (3 H, d, $J$ = 7 Hz); IR ($CCl_4$) 3540, 3080, 1735, 1645, 915 $cm^{-1}$; GC $t_R$ = 16.50 min (100 °C). Anal. Calcd for $C_7H_{12}O_3$ (mixture of 2 and 3): C, 58.31; H, 8.39. Found: C, 58.07; H, 8.19.

Reaction of 500 mg of 1 with 750 mg of *cis*-2-butene in 2 mL of benzene for 60 h at 200 °C gave, after chromatography, 441 mg (54%) of a 7.4:1 mixture of 2 and 3.

**Thermal Reaction with *trans*-2-Butene.** Reaction and purification as described for *cis*-2-butene gave 0.29 g (20%) of a 0.57:1 mixture of 2 and 3 contaminated with <5% of methyl dimethoxyacetate and 0.37 g (42%) of recovered 1.

**Thermal Reaction with Cyclohexene.** Reaction for 24 h at 150 °C resulted in a ≤5% yield of an 8.32:1 mixture of 9 and 10 as determined by GC. Longer times and/or higher temperatures gave no better results.

**Thermal Reaction with 2-Methyl-2-butene.** Reaction for 24 h at 150 °C followed by distillation at 60–65 °C (0.6 mm) gave 0.47 g (30%) of a 1.72:1 mixture of 13 and 14. The data for 13 are as follows: NMR ($CCl_4$) δ 4.75 (2 H, m), 4.05 (1 H, d, $J$ = 5 Hz), 3.75 (3 H, s), 2.57 (1 H, m), 1.72 (3 H, br s), 1.16 (3 H, d, $J$ = 6.5 Hz); IR ($CCl_4$) 3540, 3080, 1740, 1642, 895 $cm^{-1}$; GC $t_R$ = 21.5 min (100 °C). The data for 14 are as follows: NMR ($CCl_4$) δ 4.75 (2 H, m), 4.08 (1 H, d, $J$ = 3.7 Hz), 3.75 (3 H, s), 2.57 (1 H, m), 1.78 (3 H, br s), 1.02 (3 H, d, $J$ = 6.5 Hz); IR ($CCl_4$) 3540, 3080, 1740, 1642, 895 $cm^{-1}$; GC $t_R$ = 22.5 min (100 °C). The structures of 13 and 14 are tentatively assigned by analogy to 2 and 3 on the basis of relative GC retention times and the NMR chemical shift of the low-field methine and high-field methyl groups.

**Thermal Reaction with 1-Methylcyclohexene.** Reaction for 24 h at 150 °C followed by distillation at 76–82 °C (0.5 mm) gave 0.75 g (41%) of a ca. 3:3:2:2 mixture of four isomers, **15a**, **16a**, **15b**, and **16b**, as determined by GC; $t_R$ = 17.0, 18.3, 19.5, and 20.5 min at 150 °C. Treatment of this mixture with a catalytic amount of ferric chloride in methylene chloride converted 15 to 16. GC analysis showed peaks only at 18.3 and 20.5 min in a ratio of 3:2. The GC and NMR spectra of this mixture were similar to those obtained from the catalytic reaction. The spectral data for 15 determined from the mixture are as follows: NMR ($CDCl_3$) δ 4.70 (2 H, m), 4.3 (1 H, m), 3.75 (3 H, s), 2.4 (3 H, m), 1.5–2.0 (6 H, m).

**General Procedure for the Catalyzed Reactions.** A variety of Lewis acids including stannic chloride, titanium tetrachloride, zinc bromide, aluminum chloride, and titanium tetrachloride–tetrabutyltitanate mixtures were investigated. Ferric chloride gave the best results. To a mixture of 0.88 g (10 mmol) of methyl glyoxylate and 1.62 g (10 mmol) of anhydrous ferric chloride in 15 mL of anhydrous methylene chloride was added dropwise with stirring 20 mmol of alkene. The mixture was stirred overnight, poured into 50 mL of water, and extracted three times with 10 mL of ether. The combined organic layers were washed twice with water, dried over magnesium sulfate, and concentrated.

***cis*-2-Butene.** Distillation of the residue gave 0.45 g (31%) of a 1.4:1 mixture of 2 and 3, bp 38–42 °C (0.5 mm), followed by 0.35 g (20%) of a 1:1 mixture of 5 and 6, bp 62–65 °C (0.5 mm). Chlorides 5 and 6 were purified by preparative GC. The spectral data for 5 are as follows: NMR ($CDCl_4$) δ 4.75 (1 H, d, $J$ = 2.5 Hz), 4.15 (1 H, dq, $J$ = 9.5 and 7 Hz), 3.82 (3 H, s), 2.80 (1 H, s, OH), 2.20 (1 H, m), 1.50 (3 H, d, $J$ = 7 Hz), 0.89 (3 H, d, $J$ = 7 Hz); IR ($CCl_4$) 3540, 1735, 675 $cm^{-1}$; GC $t_R$ = 13.0 min (150 °C); MS $m/e$ 180 ($M^+$). The spectral data for 6 are as follows: NMR ($CCl_4$) δ 4.25 (1 H, d, $J$ = 8 Hz), 4.25 (1 H, dq, $J$ = 4 and 7 Hz), 3.82 (3 H, s), 2.85 (1 H, s, OH), 2.25 (1 H, m), 1.52 (3 H, d, $J$ = 7 Hz), 1.05 (3 H, d, $J$ = 7 Hz); IR 3540, 1735, 720, 675 $cm^{-1}$; GC $t_R$ = 14.5 min (150 °C); MS $m/e$ 180 ($M^+$). Anal. Calcd for $C_7H_{13}ClO_3$ (mixture of 5 and 6): C, 46.54; H, 7.25; Cl, 19.63. Found: C, 46.83; H, 7.53; Cl, 19.21.

***trans*-2-Butene.** Distillation of the crude product gave 0.50 g (36%) of a 1.4:1 mixture of 2 and 3, bp 38–42 °C (0.5 mm), and 0.4 g (22%) of a 4.05:1.55:1:2.4 mixture of 7, 5, 6, and 8, bp 62–65 °C (0.5 mm). The major isomers 7 and 8 were isolated by preparative GC. The spectral data for 7 are as follows: NMR ($CCl_4$) δ 4.10 (1 H, d, $J$ = 4 Hz), 4.10 (1 H, dq, $J$ = 5 and 7 Hz), 3.85 (3 H, s), 2.82 (1 H, s, OH), 2.20 (1 H, m), 1.62 (3 H, d, $J$ = 7 Hz), 1.05 (3 H, d, $J$ = 7 Hz); GC $t_R$ = 11.5 min (150 °C). The spectral data for 8 are as follows: NMR ($CCl_4$) δ 4.45 (1 H, dq, $J$ = 4 and 7 Hz), 4.00 (1 H, d, $J$ = 7 Hz), 3.75 (3 H, s), 2.55 (1 H, s, OH), 2.40 (1 H, m), 1.50 (3 H, d, $J$ = 7 Hz), 1.00 (3 H, d, $J$ = 7 Hz); GC $t_R$ = 18.75 min (150 °C).

**Cyclohexene.** Distillation of the crude product gave 1.36 g (80%) of a 4.4:1 mixture of **9**:**10**, bp 78–80 °C (0.7 mm). Chromatography of the distillate on silica with 4:1 hexane–ethyl acetate as eluant gave 1.0 g of 9, 0.15 g of pure 10, and mixed fractions. The spectral data for 9 are as follows: GC $t_R$ = 16.0 min (150 °C); NMR ($CDCl_3$) δ 5.4–5.8 (2 H, m), 3.98 (1 H, d, $J$ = 4.4 Hz), 3.75 (3 H, s), 2.45 (3 H, m), 2.0–1.3 (4 H, m); IR ($CCl_4$) 3540, 3020, 1735, 1650 $cm^{-1}$; MS $m/e$ 170 ($M^+$). The spectral data for 10 are as follows: GC $t_R$ = 18.5 min (150 °C); NMR ($CDCl_3$) δ 5.35–5.8 (2 H, m), 4.06 (1 H, d, $J$ = 4 Hz), 3.75 (3 H, s), 2.50 (3 H, m), 2.05–1.4 (4 H, m); MS $m/e$ 170 ($M^+$). Anal. Calcd for $C_9H_{14}O_3$ (mixture of 9 and 10): C, 63.38; H, 8.46. Found: C, 63.51; H, 8.29.

**2-Methyl-2-Butene.** Distillation of the crude product gave 1.23 g (78%) of a 1.08:1 mixture of 13 and 14, bp 60–65 °C (0.6 mm).

**1-Methylcyclohexene.** Distillation of the residual gave 1.20 g (66%) of a 1.26:1 mixture of the isomers of 16, bp 76–82 °C (0.5 mm). The isomers **16a** and **16b** were separated by preparative GC. The spectral data for **16a** are as follows: NMR ($CCl_4$) δ 5.50 (1 H, m), 4.40 (1 H, d, $J$ = 2.5 Hz), 3.75 (3 H, s), 2.40 (3 H, m), 2.10–1.30 (7 H, m); IR ($CCl_4$) 3542, 3040, 1735, 893 $cm^{-1}$; GC $t_R$ = 18.25 min (150 °C). The spectral data for **16b** are as follows: NMR ($CCl_4$) δ 5.45 (1 H, m), 4.20 (1 H, d, $J$ = 3.2 Hz), 3.75 (3 H, s), 2.55 (3 H, m), 2.10–1.5 (7 H, m); GC $t_R$ = 20.5 min (150 °C).

**Stereochemistry of 2 and 3.** The 1.4:1 mixture of 2 and 3 (100 mg, 0.69 mmol) obtained from *trans*-2-butene with ferric chloride was dissolved in 2 mL of ethanol containing 100 mg of potassium carbonate, and the mixture was stirred 16 h at 25 °C. The solution was filtered and concentrated, yielding 86 mg (80%) of a 1.4:1 mixture of **2a** and **3a** (the ethyl esters corresponding to 2 and 3). Preparative GC gave pure samples of **2a** and **3a**. The data for **2a** are as follows: NMR ($CCl_4$) δ 5.75 (1 H, m), 5.10 (2 H, m), 4.25 (2 H, q, $J$ = 7 Hz), 4.10 (1 H, d, $J$ = 3.5 Hz), 2.70 (2 H, m, CH and OH), 1.30 (3 H, t, $J$ = 7 Hz), 1.18 (3 H, d, $J$ = 7 Hz). The data for **3a** are as follows: NMR ($CCl_4$) δ 4.12 (1 H, d, $J$ = 5 Hz), 1.05 (3 H, d, $J$ = 7 Hz). The remaining signals are the same as for **2a**. The spectrum of **3a** is identical with the spectrum of an authentic sample prepared from addition of (trimethylsilyl)ethynyllithium to ethyl *trans*-2,3-oxidobutanoate followed by desilylation and partial hydrogenation.[5]

**Synthesis of Methyl Isoleucate.** A 7.4:1 mixture of 2 and 3 (50 mg) was stirred with 10 mg of W2 Raney nickel in 3 mL

(15) T. R. Kelly, T. E. Schmidt, and J. C. Haggerty, *Synthesis*, 544 (1972).

of methanol under 1 atm of hydrogen for 2 h at 25 °C. Filtration gave 35 mg (69%) of a 7.84:1 mixture of methyl isoleucate and methyl alloisoleucate. The major isomer was identical by chromatographic and NMR spectral comparisons with an authentic sample prepared from commercially available isoleucic acid.

**Iodolactonization of the Major Isomer 9.** A solution of methyl ester **9** (500 mg, 2.95 mmol) and sodium hydroxide (240 mg, 6 mmol) in 5 mL of water was stirred for 3 h, neutralized with dry ice, and cooled to 0 °C. A solution of iodine (780 mg, 3 mmol) and potassium iodide (500 mg, 3 mmol) dissolved in 5 mL of water was added dropwise. The reaction mixture was stirred for 14 h at 25 °C. Extraction with ether, which was washed with sodium bisulfite solution and brine, gave, after evaporation of the ether, 540 mg (60%) of iodolactone **11**: NMR ($CCl_4$) $\delta$ 4.65 (3 H, m), 3.00 (1 H, m), 1.5–2.05 (6 H, m). Since the desired coupling constants could not be determined, 520 mg of **11** was acetylated in 10 mL of pyridine with 1.5 mL of acetic anhydride. After being stirred for 16 h, the mixture was poured into water and extracted with ether. The ether solution was washed with cupric sulfate solution and with water and dried. Evaporation of the solvent gave 509 mg (85%) of the acetate: NMR ($CCl_4$) $\delta$ 5.56 (1 H, d, $J$ = 6.5 Hz), 4.80 (2 H, br s), 3.15 (1 H, m), 2.18 (3 H, s), 2.2–1.5 (6 H, m).

**Iodolactonization of the Minor Isomer 10.** Methyl ester **10** (150 mg) was converted as described above to 162 mg (65%) of iodolactone **12**: NMR ($CCl_4$) $\delta$ 4.74 (1 H, dd, $J$ = 8 and 6.4 Hz), 4.39 (1 H, d, $J$ = 9.6 Hz), 4.00 (1 H, m), 2.60 (1 H, m), 1.3–2.2 (6 H, m). Acetylation of 150 mg of **12** gave 154 mg (78%) of the acetate: NMR ($CCl_4$) $\delta$ 5.40 (1 H, d, $J$ = 10 Hz), 4.70 (1 H, dd, $J$ = 8 and 6.5 Hz), 4.10 (1 H, m), 2.70 (1 H, m), 2.12 (3 H, s), 1.5–2.2 (6 H, m).

**Synthesis of Crotyl Glyoxylate.** (+)-Tartaric acid (45 g, 300 mmol), crotyl alcohol (64.8 g, 900 mmol), and *p*-toluenesulfonic acid (100 mg) were heated at 110 °C until all of the tartaric acid dissolved. The mixture was cooled, diluted with 100 mL of ether, and washed with sodium bicarbonate solution and water. The organic layer was dried with magnesium sulfate and concentrated in vacuo to give dicrotyl tartrate, which was dissolved in 500 mL of ether and treated with paraperiodic acid (68.4 g, 300 mmol). Reaction and workup as described in the synthesis of **1**[15] gave 44 g (82%) of crotyl glyoxylate which decomposed on attempted distillation.

**Synthesis of 3-Methyl-2-butenyl Glyoxylate.** This compound was synthesized in 20% overall yield by the procedure of Jurczak and Zamojski.[12] 3-Methyl-2-butenol (50 g, 0.35 mol) and triethylamine (40 mL) in 50 mL of methylene chloride was added dropwise to a stirred solution of 72.2 g (0.36 mol) of bromoacetyl bromide in 100 mL of methylene chloride at 0 °C during the course of 6 h. Water (500 mL) was added, and the solution was extracted with three portions of ether which were washed with 5% hydrochloric acid, dried, and evaporated. Distillation gave 39 g [54%, bp 63–66 °C (0.5 mm)] of the bromoacetate.

The bromoacetate (39 g, 0.19 mol) was dissolved in 150 mL of acetonitrile and mixed with 64.6 g (0.38 mol) of silver nitrate dissolved in 150 mL of acetonitrile. After 120 h the precipitate was filtered, the solvent was evaporated, and the residue was dissolved in ether. The solution was washed with water, dried, and concentrated in vacuo. The crude nitrate was dissolved in 300 mL of $Me_2SO$. A suspension of sodium acetate trihydrate (25.8 g, 0.19 mol) was added with stirring. After 30 min the reaction was poured into 2 L of brine and exhaustively extracted with ether, which was washed with water, dried, and evaporated to give 9 g (30%) of 3-methyl-2-butenyl glyoxylate dihydrate. Distillation led to decomposition. Treatment with 5 g of phosphorus pentoxide in 50 mL of ether followed by filtration and concentration gave 7.2 g of the anhydrous glyoxylate.

**Thermal Ene Reaction of 3-Methyl-2-butenyl Glyoxylate.** Methylbutenyl glyoxylate (1.42 g, 10 mmol) was dissolved in 15 mL of benzene and heated 60 h at 90 °C in a sealed tube. The solvent was evaporated. Distillation of the residue led to 0.57 g (40%) of a 75% pure 1:1 mixture of **20** and **21**, bp 105–110 °C (0.8 mm). Purification of 500 mg of the mixture on silica with 1:1 hexane–ethyl acetate as eluant gave 150 mg of pure trans-substituted lactone **20** followed by 150 mg of pure cis-substituted lactone **21**. The spectral data for **20** are as follows: $^1$H NMR ($CDCl_3$) $\delta$ 4.93 (2 H, m), 4.45 (1 H, d, $J$ = 10.2 Hz), 4.40 (1 H, dd, $J$ = 9.5 and 9 Hz), 4.00 (1 H, dd, $J$ = 10.4 and 9.5 Hz), 3.10 (1 H, ddd, $J$ = 10.2, 9, and 10.4 Hz), 1.80 (3 H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 177.4 (s), 139.4 (s), 113.4 (t), 70.3 (d), 67.6 (t), 49.8 (d), 20.0 (q). The spectral data for **21** are as follows: $^1$H NMR ($CDCl_3$) $\delta$ 4.95 (1 H, br s), 4.82 (1 H, br s), 4.65 (1 H, d, $J$ = 7.8 Hz), 4.40 (1 H, dd, $J$ = 9.4 and 5.5 Hz), 4.30 (1 H, dd, $J$ = 9.4 and 3 Hz), 3.25 (1 H, ddd, $J$ = 7.8, 5.5, and 3 Hz), 1.75 (3 H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 177.4 (s), 140.5 (s), 114.2 (t), 69.4 (t), 68.5 (d), 46.7 (d), 21.0 (q).

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**Registry No.** 1, 922-68-9; **2**, 71215-25-3; **2a**, 71215-26-4; **3**, 71215-27-5; **3a**, 71249-94-0; **4**, 71242-64-3; **5**, 71215-28-6; **6**, 71242-61-0; **7**, 71242-62-1; **8**, 71242-63-2; **9**, 71215-29-7; **10**, 71215-30-0; **11**, 71215-31-1; **11** acetate, 71215-32-2; **12**, 71215-33-3; **12** acetate, 71215-34-4; **13**, 71215-35-5; **14**, 71215-36-6; **15a**, 71215-37-7; **15b**, 71215-38-8; **16a**, 71215-39-9; **16b**, 71215-40-2; **18**, 71242-99-4; **19**, 71243-00-0; **20**, 71215-41-3; **21**, 71215-42-4; *cis*-2-butene, 590-18-1; *trans*-2-butene, 624-64-6; cyclohexene, 110-83-8; 2-methyl-2-butene, 513-35-9; 1-methylcyclohexene, 591-49-1; methyl alloisoleucate, 71242-65-4; (+)-tartaric acid, 87-69-4; crotyl alcohol, 6117-91-5; 3-methyl-2-butenol, 556-82-1; bromoacetyl bromide, 598-21-0; 3-methyl-2-butenol bromoacetate, 71215-43-5.