Acid Dehydration of 10.—A 10-mg sample of **10** was heated with 0.2 ml of 4 *M* acetic acid in triglyme. The solution was diluted with benzene and washed repeatedly with water. The organic layers were concentrated to dryness under reduced pressure to yield an 11-mg residue, which was shown by glc and nmr to be a mixture of **10** and **11**, approximately 1:1, slightly contaminated by triglyme.

Conversion of 9-Deuterio-7 to 9-Deuterio-10.—An 11-mg sample of 9-deuterio-**7** was heated under nitrogen with 0.1 ml of triglyme at 240° for 30 min. The solution was diluted with benzene and hexane and chilled. The precipitate amounted to 3.3 mg. The filtrates were washed repeatedly with water and concentrated to dryness under reduced pressure. The residue was crystallized from benzene to provide 4.3 mg of 9-deuterio-**10**, mp 148–151°. The nmr spectrum was identical to that of **10**, but lacked the aromatic proton absorption. Collection of 420 spectra and integration by cut and weigh showed that ~5% of this possessed an aromatic proton, δ 8.5 ppm; mass spectrum *m/e* 276 (3), 275 (22), 274 (100), 273 (32), 272 (19), 259 (30), 256 (22), 241 (19), 218 (48), 216 (38), 162 (60).

Interaction of 8 and 10.—A mixture of 73 mg of **8** and 76 mg of **10** was heated under nitrogen at 280° for 5 min. The product was taken up in benzene and filtered to recover 45 mg of **8**. The benzene solution was concentrated to dryness to leave 103 mg. Analysis by nmr and glc showed the following composition: **9**, 29%; **10**, 54%; **12**, 12%. When heating was continued 70 min, recovery of **8** amounted to 17%; the composition of the benzene soluble portion was **9**, 46%; **10**, 15%; **11**, 6%; **12**, 34%.

Interaction of 9,9-Deuterio-8 and 10.—A sample of dideuterioparaformaldehyde (0.32 g) was converted to the dimedone derivative[14] (2.5 g), of which 0.5 g was heated with 5 ml of ammonia in a steam bath overnight to provide 0.38 g of dideuterio-**8**. This material was recrystallized from ethanol. A recrystallized sample (20 mg) was mixed with an equal weight of **10** and heated in a sealed tube under nitrogen at 284° for 75 min. The material was suspended in benzene, filtered, and the filtrate concentrated to dryness (32 mg). Glc showed **9**, 43%; **10**, 13%; **11**, 17%; **12**, 28%. Mass spectra: 9-deuterio-**9**, *m/e* 273 (8), 272 (31), 271 (5), 216 (100), 215 (12); **10**, identical with that of pure material; **11**, identical with pure material, except for *m/e* 256 (19) and 241 (38); 1-deuterio-**12** and 1,9-dideuterio-**12**, 260 (24), 259 (72), 258 (72), 244 (45), 243 (45), 204 (42), 203 (100), 202 (95).

This material was chromatographed on a thick plate eluting by 1:1 hexane–ether. The slowest moving band provided **10**, with nmr identical with that of known material; the next band provided 9-deuterio-**9** with nmr identical with known material, but lacking the aromatic proton; the fastest moving band provided a 1:1 mixture of **11** and 9-deuterio-**12** with the nmr δ 7.88 ppm (relative strength 0.6), 7.76 (0.9), 6.25 (d, 1.0), and 5.75 (d, 1.0). Intensities were determined by cut and weigh of the spectrum obtained by accumulating 225 spectra.

Interaction of 8 and 11.—A mixture of 1.2 mg of **11** and 1.5 mg of **8** was heated under nitrogen at 280° for 18 min. Glc analysis of the volatile components of the mixture showed **9**:**11**:**12** in the approximate ratio 8:4:3.

Registry No.—**7**, 27448-28-8; **7** methyl ester, 35619-79-5; **8**, 2645-77-4; **9**, 27361-25-7; **10**, 35619-82-0; **10** acetate, 35619-83-1; **11**, 27447-99-0; **12**, 27361-27-9; **16**, 35619-86-4; **17**, 35619-87-5; **22**, 35619-88-6; **23**, 35619-89-7; bis(1,3-dioxocyclohexyl-2)acetic acid, 35619-90-0.

Asymmetric Induction in the Thermal Reactions of Allylic Alcohols with *N,N*-Dimethylacetamide Dimethyl Acetal and Triethyl Orthoacetate[1]

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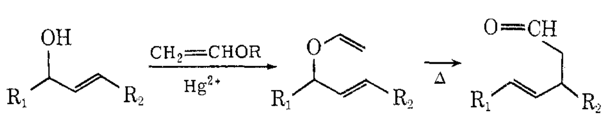
Optically active *trans*-3-penten-2-ol was used as the substrate for Claisen-type reactions with *N,N*-dimethylacetamide dimethyl acetal and triethyl orthoacetate. The products, the *N,N*-dimethyl amide and ethyl ester, respectively, of 3-methyl-4-hexenoic acid, were formed in greater than 90% optical purity and with inversion of configuration. The magnitude of asymmetric induction observed makes these reactions particularly useful for the stereospecific introduction of a carbon–carbon bond at an asymmetric center.

Stimulated by recent practical modifications,[2] the Claisen rearrangement of allyl vinyl ethers (eq 1) has seen increasing use in synthesis. A characteristic feature of the reaction, responsible in large measure for its success, is the high degree of stereospecificity which extends to the creation of asymmetric centers in high optical yield as well as to the production of predominantly trans double bonds.[3]



(1)

Of a number of variants of the Claisen rearrangement, two have proven particularly valuable for practical synthetic application in attaching a two-carbon chain because, in contrast to the original procedure, they can be carried out directly on an allylic alcohol without the need to isolate a vinyl ether intermediate. They are (a) the reaction of an allylic alcohol with *N,N*-dimethylacetamide dimethyl acetal (I) or its equivalent, 1-methoxy-1-dimethylaminoethylene (II), a reaction discovered by Meerwein[4] and systematized by Eschenmoser and coworkers[5] and which provides a one-step route to unsaturated amides (eq 2); and (b) the acid-catalyzed thermal reaction of allylic alcohols with triethyl orthoacetate (III), recently reported by

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[1] This research was supported by grants from the National Science Foundation (GP-9094 and GP-28056X), to whom the authors express their appreciation.

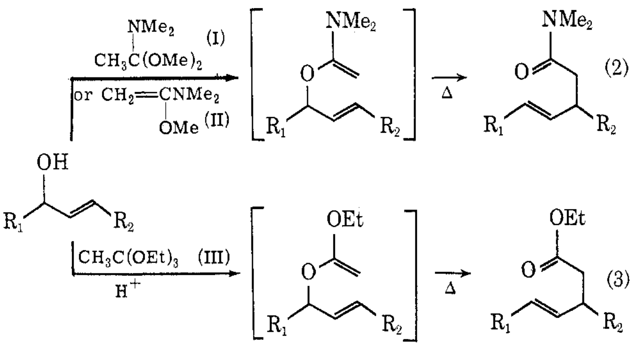
[2] (a) A. F. Thomas and M. Ozainne, *J. Chem. Soc. C*, 220 (1970), and references cited therein; (b) W. S. Johnson, T. J. Brocksom, P. Loew, D. H. Rich, L. Werthemann, R. A. Arnold, T. T. Li, and D. J. Faulkner, *J. Amer. Chem. Soc.*, **92**, 4463 (1970); (c) G. Büchi and J. E. Powell, Jr., *ibid.*, **89**, 4559 (1967); **92**, 3126 (1970).

[3] (a) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, N. J., 1971, p 375, and references cited therein; (b) A. Jefferson and F. Scheinmann, *Quart. Rev., Chem. Soc.*, **22**, 391 (1968), and references cited therein.

[4] H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Justus Liebigs Ann. Chem.*, **641**, 1 (1961).

[5] A. E. Wick, D. Felix, K. Steen, and A. Eschenmoser, *Helv. Chim. Acta*, **47**, 2425 (1964); D. Felix, K. Gschwend-Steen, A. E. Wick, and A. Eschenmoser, *ibid.*, **52**, 1030 (1969).

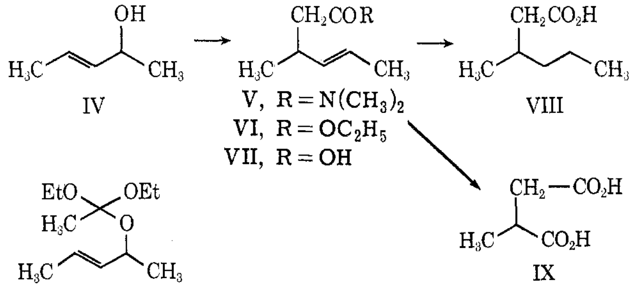
Johnson and coworkers,[6] which leads directly to the corresponding ethyl ester (eq 3).



Both of these variations allow the easy, high-yield addition of an acetic acid unit to the γ carbon of an allylic alcohol, and both have already found extensive application in the synthesis of natural products.[7]

It has been reported[6,7] that both reactions lead almost exclusively to products in which the new double bond is trans, and we were led to investigate whether this striking geometrical specificity was paralleled by comparable optical stereospecificity. We now report that both rearrangements, when applied to an optically active alcohol, proceed in optical yields greater than 90%, and consequently provide valuable methods of forming new carbon–carbon bonds at an asymmetric center with high stereospecificity.

Treatment of *trans*-3-penten-2-ol (IV) with a mixture of I and II in refluxing xylene for 17 hr afforded an amide in 80% yield. The nmr spectrum (see Experimental Section) confirmed its structure as *N*,*N*,3-trimethyl-4-hexenamide (V). Similarly, heating IV with 7 equiv of triethyl orthoacetate containing a trace of propionic acid at 180° for 22 hr while ethanol was removed through a long Vigreux column yielded, on fractionation, ester VI in 68% yield. Alkaline hydrolysis of V or VI gave 3-methyl-4-hexenoic acid (VII). Compounds V, VI, and VII all appeared as single peaks on glc analysis and, from the strong infrared absorption at 950–970 cm^{-1}, are apparently >98% trans isomers. Hydrogenation of VII gave the known 3-methylhexanoic acid (VIII), while ozonolysis furnished methylsuccinic acid (IX).



IV

V, $R = N(CH_3)_2$
VI, $R = OC_2H_5$
VII, $R = OH$

VIII

IX

X

When optically active *trans*-3-penten-2-ol was used in these reactions, both the amide V and ester VI formed were optically active. Alcohol IV, $[\alpha]^{25}D$ −13.2°, afforded amide V, $[\alpha]D$ −15.7°, while dextrorotatory IV, $[\alpha]^{25}D$ +8.52°, yielded levorotatory VI, hydrolyzed to acid VII, $[\alpha]^{25}D$ −13.6°.

To assess the direction and magnitude of asymmetric induction, it was necessary to determine the absolute configuration and optical purity of acid VII. The racemic acid was partially resolved with quinine, giving a salt of mp 138–139°, $[\alpha]^{25}D$ −82.1° ($CHCl_3$), after three recrystallizations from chloroform–acetone. Regeneration of the acid with dilute HCl gave material with $[\alpha]^{25}D$ +33.8°. Ozonolysis of this dextrorotatory acid yielded methylsuccinic acid of $[\alpha]^{25}D$ −14.1°. Since the maximum rotation reported[8] for methylsuccinic acid is 16.5°, the ozonolysis product and its precusor are 85.4% optically pure, and the maximum rotation of VII is calculated to be 39.6°. Moreover, since levorotatory methylsuccinic acid has been conclusively established[9] as the *R* enantiomer, dextrorotatory VII is the *R* enantiomer.

These conclusions about maximum rotation and absolute configuration of VII were independently checked by hydrogenating a sample of VII, $[\alpha]^{25}D$ +22.5°, to 3-methylhexanoic acid (VIII), $[\alpha]^{24}D$ +1.63°. Based on the maximum reported rotation[10] of VIII of 2.5° and its reported configuration as L-(−), the maximum rotation of VII is calculated to be 34.5° and its configuration *R*-(+), in agreement with the conclusions derived from ozonolysis.

The absolute configuration of the starting allylic alcohol, (*S*)-(−)-*trans*-3-penten-2-ol, has been determined both by ozonolysis[11] to the levorotatory zinc salt of (*S*)-(+)-lactic acid and by hydrogenation[11,12] to (*S*)-(+)-2-pentanol. As Goering and Kimoto[13] have emphasized, the optical purity is best based on the phthalate, with a maximum rotation of 38° ($CHCl_3$) established by isotope dilution,[14] since the rotation of the allylic alcohol itself is not accurately reproducible. Using these values, the optical purities calculated for the starting alcohol and rearrangement products are shown in Table I.

Both reactions produce rearrangement products of inverted configuration and in optical yields of 90% or greater.[15] Inversion of configuration is the conse-

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[6] W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. T. Li, D. J. Faulkner, and M. R. Petersen, *J. Amer. Chem. Soc.*, **92**, 741 (1970).

[7] H. Muxfeldt, R. S. Schneider, and J. B. Mooberry, *J. Amer. Chem. Soc.*, **88**, 3670 (1966); D. F. Morrow, T. P. Culbertson, and R. M. Hofer, *J. Org. Chem.*, **32**, 361 (1967); W. Sucrow, *Angew. Chem.*, **80**, 626 (1968); W. Sucrow, *Tetrahedron Lett.*, 4725 (1970); F. E. Ziegler and J. G. Sweeny, *ibid.*, 1097 (1969); F. E. Ziegler and G. B. Bennett, *J. Amer. Chem. Soc.*, **93**, 5930 (1971); I. J. Bolton, R. G. Harrison, and B. Lythgoe, *Chem. Commun.*, 1512 (1970); R. G. Harrison and B. Lythgoe, *ibid.*, 1513 (1970); D. H. Miles and W. S. Johnson, Abstracts of Papers, 23rd Southeastern Regional Meeting of the American Chemical Society, Nashville, Tenn., Nov 4–5, 1971, p 43.

[8] A. Fredga, *Ark. Kemi, Mineral. Geol.*, **15B**, No. 23, 1 (1942), reported $[\alpha]^{20}D$ +16.5° (*c* 4.352, ethanol). R. Adams and D. Fles, *J. Amer. Chem. Soc.*, **81**, 4946 (1959), reported $[\alpha]^{26}D$ +15.9° (*c* 1.36, ethanol) for optically pure methylsuccinic acid.

[9] J. A. Mills and W. Klyne in "Progress in Stereochemistry," Vol. 1, W. Klyne, Ed., Academic Press, New York, N. Y., 1954, pp 188, 202, 203.

[10] I. A. Holliday and N. Polgar, *J. Chem. Soc.*, 2934 (1957).

[11] P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **81**, 703 (1929).

[12] H. W. J. Hills, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 576 (1936).

[13] H. L. Goering and W. I. Kimoto, *J. Amer. Chem. Soc.*, **87**, 1748 (1965).

[14] H. L. Goering, M. M. Pombo, and K. D. McMichael, *ibid.*, **85**, 965 (1963).

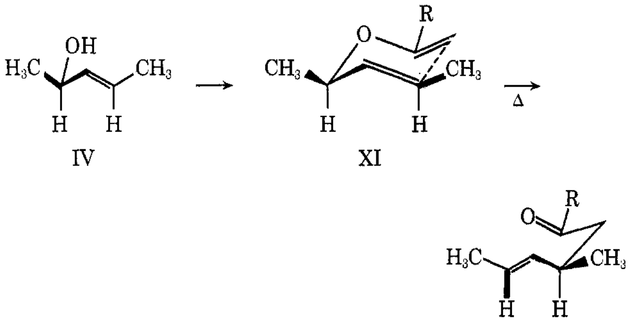
[15] Some uncertainty results in calculating optical yields since different values for the maximum rotation of the starting alcohol IV are obtained depending on whether the phthalate or saturated alcohol is used as the standard, different values for the maximum rotation of the acid VII are obtained depending on whether the ozonolysis product or hydrogenation product is used as the standard, and different maximum rotations have been reported for methylsuccinic acid. In each case we have chosen the more conservative value, so that our yields of 90% are a minimum and may be as much as 5–6% higher.

TABLE I

Starting alcohol			Rotation of product			
Rotation of phthalate	Rotation of alcohol	Optical purity, %	V	VII	Optical purity,[d] %	Optical yield, %
+37.3° (*c* 5.2, ether)	−13.2° (*c* 2.5, $CHCl_3$)	63.2[a]	+15.7° (*c* 3.1, $CHCl_3$)	+22.5° (*c* 1.6, $CHCl_3$)	56.9	90.0
	−7.35° (*c* 1.6, $CHCl_3$)	35.2[b]	+9.90° (*c* 4.7, $CHCl_3$)	+12.6° (*c* 0.77, $CHCl_3$)	31.9	90.6
−14.5° (*c* 1.24, $CHCl_3$)	+8.52° (*c* 7, $CHCl_3$)	38.2[c]		−13.6° (*c* 28, $CHCl_3$)	34.4	90.1

[a] Based on phthalate calculated to have maximum rotation of 59.0° in ether. [b] Based on above optical rotation of alcohol. [c] Based on maximum rotation[14] of phthalate of 38° in chloroform. [d] Based on maximum rotation of VII of 39.6° (see text).

quence of reaction *via* a transition state conformation (XI), resembling chair cyclohexane with all substituents equatorial, characteristic of Claisen and Cope rearrangements in unconstrained molecules;[3,16] the generation of a trans double bond in the product is, of course, a simultaneous consequence of this transition-state geometry.[3] The magnitude of the asymmetric induction, which parallels (as it should) the geometric stereospecificity, is higher in these two reactions than in most simple Claisen rearrangements, and approaches that observed[16a] in the Cope rearrangement of 3-methyl-3-phenyl-1,5-heptadiene. It has already been pointed out[6,17] that the high stereoselectivity in the formation of trans double bonds can be attributed to nonbonded interactions between the group R in XI and other substituents in the transition states leading to cis product, and this also accounts for the high optical specificity in the generation of a new asymmetric center.



The unusual magnitude of asymmetric induction in these modifications of the Claisen rearrangement makes them particularly suitable for stereospecific synthesis. Beginning with optically active allylic alcohols, compounds readily available by resolution or by asymmetric reduction,[18] it is possible to form a new carbon–carbon bond at an asymmetric center in almost quantitative optical yield and in a predictable absolute orientation. Even the simple examples reported here illustrate the power of this approach: an earlier attempt to prepare 3-methyl-4-hexenoic acid by malonic ester synthesis with optically active 2-chloro-3-pentene led to totally racemized product,[19] in contrast to the 90% optical yields reported here.

Experimental Section

Melting points were determined on a Thomas-Hoover oil immersion apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 237B spectrophotometer. Nuclear magnetic resonance spectra were obtained on a Varian HA-100 spectrometer by Mr. Courtney Pape; chemical shifts are recroded as δ units, using tetramethylsilane as an internal reference. Elemental analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

3-Penten-2-ol.—Racemic 3-penten-2-ol, bp 45–47° (25 mm), was prepared in 60% yield by the reaction[20] of methylmagnesium iodide with crotonaldehyde, and converted to the phthalate, mp 90–91°. Resolution was effected[12] through the brucine salt, which was recrystallized four times from chloroform–acetone. The phthalate was regenerated by stirring the brucine salt in ice-cold 3 *M* hydrochloric acid, extracting with ether, concentrating the dried extracts, and recrystallizing the residue from ether–pentane. The product of a typical resolution had mp 83–84°, $[\alpha]^{25}_{\mathrm{D}}$ +39.2° (*c* 5.6, ether), +38.9° (*c* 6.6, ethanol), +25.2° (*c* 2.6, $CHCl_3$).[21] Optically active alcohol was obtained by lithium aluminum hydride reduction of the phthalate as recommended by Goering.[14] In a typical run, phthalate of $[\alpha]^{25}_{\mathrm{D}}$ +37.3° (*c* 5.2, ether) was reduced to alcohol with $[\alpha]_{\mathrm{D}}$ −13.2° (*c* 1.78, $CHCl_3$), −7.23° (*c* 4.3, ether), bp 45° (30 mm).

Hydrogenation of 3-Penten-2-ol.—An ether solution of 2.8 g of 3-penten-2-ol, $[\alpha]^{25}_{\mathrm{D}}$ +8.35° (*c* 2.5, $CHCl_3$), was hydrogenated over Adams catalyst (220 mg) at atmospheric pressure. After the catalyst was filtered, distillation gave 2.2 g of 2-pentanol, bp 47° (25 mm), $[\alpha]^{25}_{\mathrm{D}}$ −6.37° (*c* 2.3, $CHCl_3$), −5.32° (neat, 1 dm). The product was homogeneous by vpc and had an infrared spectrum identical with that of authentic material.

In another run, 3-penten-2-ol, $[\alpha]^{25}_{\mathrm{D}}$ −13.2° (*c* 2.5, $CHCl_3$), was reduced to 2-pentanol, $[\alpha]^{25}_{\mathrm{D}}$ +10.7° (*c* 1.8, $CHCl_3$).

Based on the maximum reported[22] rotation of 2-pentanol of 13.9° (neat), 2-pentanol with $[\alpha]^{25}_{\mathrm{D}}$ −5.32° (neat) is 38.3% optically pure. The maximum rotation calculated for 3-penten-2-ol from this experiment is 21.8°.

Reaction with *N*,*N*-Dimethylacetamide Dimethyl Acetal. A.—A solution of 4.3 g of *trans*-3-penten-2-ol and 13 g of a mixture[5,23] of *N*,*N*-dimethylacetamide dimethyl acetal and 1-methoxy-1-dimethylaminoethylene in 70 ml of dry xylene was refluxed for 17 hr and then fractionated. Amide V was collected at 110–150° (20 mm): yield 6.1 g (80%); ir (neat) 1655, 1260, 1120, 950 cm^{-1}; nmr ($CDCl_3$) δ 0.98 (3 H, d, J = 6 Hz), 1.58 (3 H, d, J = 5.5 Hz), 2.21 (2 H, m), 2.63 (1 H, m), 2.83 (3 H, s), 2.97 (3 H, s), 5.40 (2 H, m).

Anal. Calcd for $C_{19}H_{17}NO$: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.76, 69.83; H, 10.98, 11.03; N, 9.06, 8.90.

B.—*trans*-3-Penten-2-ol, $[\alpha]^{25}_{\mathrm{D}}$ −13.2° (*c* 2.5, $CHCl_3$), 0.43 g, when treated under the same conditions with 2.0 g of a mixture of I and II in 20 ml of xylene, gave V, $[\alpha]^{25}_{\mathrm{D}}$ +15.7° (*c* 3.1, $CHCl_3$).

C.—*trans*-3-Penten-2-ol, $[\alpha]^{25}_{\mathrm{D}}$ −7.35° (*c* 1.6, $CHCl_3$), treated as in B, gave V, $[\alpha]^{25}_{\mathrm{D}}$ +9.90° (*c* 4.7, $CHCl_3$).

Hydrolysis of Amide V. A.—Amide V, 550 mg, $[\alpha]_{\mathrm{D}}$ +15.7°,

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(16) (a) R. K. Hill and N. W. Gilman, *Chem. Commun.*, 619 (1967); (b) R. K. Hill and N. W. Gilman, *Tetrahedron Lett.*, 1421 (1967).

(17) C. L. Perrin and D. J. Faulkner, *Tetrahedron Lett.*, 2783 (1969).

(18) See ref 3a, Chapter 5, for an excellent survey.

(19) E. Bergmann, *Helv. Chim. Acta*, **20**, 590 (1937).

(20) E. R. Coburn, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 696.

(21) In contrast to the report[13,14] that the phthalate has essentially the same rotation in ether as in chloroform, we consistently observed the magnitude of the rotation in ether to be 1.5 that of the rotation in chloroform.

(22) D. H. Brauns, *J. Res. Nat. Bur. Stand.*, **31**, 83 (1943).

(23) H. Bredereck, F. Effenberger, and G. Simchen, *Angew. Chem.*, **73**, 493 (1961); *Chem. Ber.*, **96**, 1350 (1963).

was heated in a solution of 4 g of sodium hydroxide in 30 ml of water at 100–110° for 8 hr. After cooling, the solution was washed with ether, acidified with hydrochloric acid, and extracted with ether. The ether extracts were washed with water, dried, and distilled to yield 3-methyl-4-hexenoic acid[24] (VII): bp 160° (bath) (25 mm); yield 330 mg (73%); $[\alpha]^{25}\mathrm{D}$ +22.5° (*c* 1.6, $CHCl_3$). The infrared spectrum was identical with that of the acid from hydrolysis of ester VI.

B.—Hydrolysis of a sample of V, 120 mg, $[\alpha]^{25}\mathrm{D}$ +9.9°, under similar conditions gave acid VII: bp 140° (bath) (18 mm) $[\alpha]^{25}\mathrm{D}$ +12.6° (*c* 0.77, $CHCl_3$); yield 90 mg (90%); nmr δ 1.03 (3 H, d, $J = 6.5$ Hz), 1.62 (3 H, d, $J = 5$ Hz), 2.29 (2 H, m), 2.60 (1 H, m), 5.41 (2 H, m), 11.2 (1 H, s).

Reaction with Ethyl Orthoacetate.—A mixture of 17 g of racemic *trans*-3-penten-2-ol, 225 g of ethyl orthoacetate, and 1.0 g of propionic acid was refluxed vigorously (bath temperature 180°) for 22 hr, then fractionally distilled. The product VI (21 g, 68%) was collected at 85–90° (20 mm); vpc analysis (on 20% SDC 710, at 150°, flow rate 40 ml/min) showed a single peak. The compound was identified as VI by chemical and spectroscopic evidence: ir (neat) 1735, 1180, 3040, 970 cm^{-1}; nmr (CCl_4) δ 1.03 (3 H, d, $J = 6$ Hz), 1.25 (3 H, t, $J = 7$ Hz) 1.65 (3 H, d, $J = 5$ Hz), 2.26 (2 H, d), 2.55 (1 H, m), 4.17 (2 H, q, $J = 7$ Hz), 5.48 (2 H, m).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.25; H, 10.47.

In a similar run under milder conditions, the reagents were heated at 140° (bath temperature) for 18 hr while ethanol was continuously removed by fractionation through a long Vigreux column. The product collected at 87–95° (40 mm) showed two main peaks on vpc analysis. Pure samples of the two major components were collected by preparative vpc. The more volatile was identical with VI, while the second was assigned the structure X: ir 3040, 1230, 1192, 1160, 1060. 970 cm^{-1}; nmr δ 1.18 (6 H, t, $J = 7$ Hz), 1.23 (3 H, d, $J = 7$ Hz), 1.45 (3 H, s), 1.68 (3 H, d, $J = 5$ Hz), 3.6 (4 H, q, $J = 7$ Hz), 4.4 (1 H, m), 6.62 (2 H, m).

Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.31; H, 10.96. Found: C, 65.10; H, 11.12.

Hydrolysis.—A solution of 21 g of VI in 90 ml of ethanol was treated with 30 g of sodium hydroxide in 90 ml of water and refluxed for 30 min. After acidification the mixture was extracted with ether. Distillation of the dried extracts furnished 13.5 g (80%) of 3-methyl-4-hexenoic acid (VII), bp 129° (15 mm). The infrared spectrum was identical with that of the acid obtained by hydrolysis of amide V.

Anal. Calcd for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.38; H, 9.31.

Reaction of (+)-IV with Ethyl Orthoacetate.—A mixture of *trans*-3-penten-2-ol, $[\alpha]^{25}\mathrm{D}$ +8.52° (*c* 7, $CHCl_3$), prepared by hydrolysis of acid phthalate of $[\alpha]^{25}\mathrm{D}$ −14.5° (*c* 1.24, $CHCl_3$), together with 26 g of ethyl orthoacetate and 0.5 g of propionic acid was heated at 145° for 40 hr. Because of difficulty in cleanly separating the product from excess orthoacetate by distillation, the reaction mixture was heated with 5 ml of 10 *M* NaOH and 20 ml of methanol for 2 hr, then distributed between water and ether. The alkaline layer was acidified with hydrochloric acid and extracted with ether several times. The combined extracts were washed with saturated ammonium chloride solution, dried, and distilled, affording 1.75 g (60%) of acid VII, bp 127–130° (37 mm), $[\alpha]^{25}\mathrm{D}$ −13.6° (*c* 28, $CHCl_3$). The ir and nmr spectra were identical with those of racemic material.

Resolution of 3-Methyl-4-hexenoic Acid. A. With Brucine. A mixture of 6.4 g of the racemic acid and 23.3 g of brucine tetrahydrate was dissolved in 80 ml of hot 9:1 acetone–methanol and allowed to crystallize. The first crop, yield 6.31 g, mp 89–92°, $[\alpha]^{24}\mathrm{D}$ −50.7° (c 2.5, $CHCl_3$), was recrystallized three more times from the same solvent pair to give 3.0 g of salt with mp 93–94°, $[\alpha]^{24}\mathrm{D}$ −48.9° (*c* 4.1, $CHCl_3$).

The acid was regenerated by dissolving the salt in dilute hydrochloric acid and extracting with ether. Distillation gave 0.55 g, bp 160° (bath) (2.5 mm), $[\alpha]^{25}\mathrm{D}$ −13.6° (*c* 1.9, $CHCl_3$).

B. With Quinine.—A warm solution of 5.12 g of the racemic acid and 12.97 g of anhydrous quinine in 50 ml of 1:2 chloroform–acetone was diluted with 100 ml of ether and allowed to crystallize. The first crop, yield 6.98 g, mp 131–133°, $[\alpha]^{24}\mathrm{D}$ −100.7° (*c* 1.05, $CHCl_3$), was recrystallized three more times from chloroform–acetone to afford salt with mp 138–139°, $[\alpha]^{24}\mathrm{D}$ −82.1° (*c* 1.9, $CHCl_3$).

Regeneration of the acid was again effected by dissolving the salt in dilute hydrochloric acid and extracting with ether. Distillation gave 0.63 g of acid, bp 100–105° (bath) (0.3 mm), $[\alpha]^{25}\mathrm{D}$ 33.8°, $[\alpha]^{25}_{578}$ +35.1°, $[\alpha]^{25}_{546}$ +40.2°, $[\alpha]^{25}_{436}$ +71.3° (*c* 1.89, $CHCl_3$).

Ozonolysis of 3-Methyl-4-hexenoic Acid.—A stream of ozonized oxygen (3% in ozone) was bubbled through a solution of 220 mg of 3-methyl-4-hexenoic acid, $[\alpha]^{25}\mathrm{D}$ +33.8° (*c* 1.89, $CHCl_3$), in 25 ml of ethyl acetate at −75° for 4 min, until the solution became blue. The solvent was removed at reduced pressure at room temperature and the residue was treated with a mixture of 10 ml of 10% aqueous sodium carbonate and 6 ml of 30% hydrogen peroxide at 70–80° for 3 hr. After cooling, the solution was acidified with concentrated hydrochloric acid, saturated with sodium chloride, and extracted with ether. Removal of the solvent left a crystalline residue (128 mg) of methylsuccinic acid, mp 108–110°, $[\alpha]^{25}\mathrm{D}$ −14.1° (*c* 1.27, ethanol).

Hydrogenation of 3-Methyl-4-hexenoic Acid.—A solution of 70 mg of 3-methyl-4-hexenoic acid, $[\alpha]^{25}\mathrm{D}$ +22.5° (*c* 1.6, $CHCl_3$), in 35 ml of ethanol was hydrogenated at atmospheric pressure over platinum black for 12 hr. After filtration of the catalyst, the filtrate was concentrated and distilled to afford 60 mg of 3-methylhexanoic acid, bp 150° (bath) (25 mm), $[\alpha]^{25}\mathrm{D}$ +1.63° (*c* 0.67, benzene).

Registry No.—I, 18871-66-4; III, 78-39-7; (+)-IV, 35666-69-4; (−)-IV, 926-58-9; (+)-V, 35666-71-8; (±)-VI, 35666-72-9; (±)-VII, 35666-73-0; (+)-VII, 35666-74-1; (−)-VII, 35666-75-2; (−)-VII brucine salt, 35666-76-3; (+)-VII quinine salt, 35737-20-3; (+)-VIII, 35666-77-4; (±)-X, 35666-78-5.

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[24] A. W. Burgstahler, *J. Amer. Chem. Soc.*, **82**, 4681 (1960).