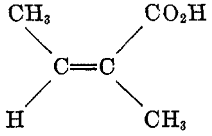
[Contribution from the Chemical Laboratory of the University of California]

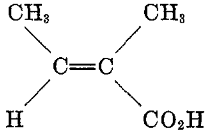
BRANCHED-CHAIN FATTY ACIDS. XXXI. ASSIGNMENT OF GEOMETRIC CONFIGURATION IN THE 2-METHYL-2-ALKENOIC ACIDS[1]

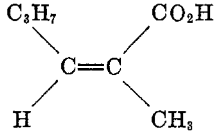
JAMES CASON and MAX J. KALM

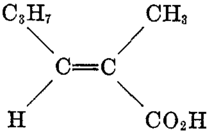
Received July 26, 1954

As a result of the isolation of the physiologically active C_{27}-phthienoic acid from the lipids of the tubercle bacillus (1) and the assignment of a partial structure including the features of a 2-methyl-2-alkenoic acid (2, 3), there has followed an extensive study of the methods of preparation and the properties of such unsaturated acids (3–7). In spite of the considerable synthetic activity in this field, there has not yet been developed a reliable method for assigning geometrical configuration to either the synthetic 2-methyl-2-alkenoic acids or the naturally occurring C_{27}-phthienoic acid. In two recent papers (6, 8), assignments of geometric configuration have been based primarily on correlation of infrared and ultraviolet spectral data with those of angelic and tiglic acids. Although assignment of the *cis* structure to angelic acid (I) and the *trans* structure to tiglic acid (II) is established beyond any reasonable doubt (9), comparison of the spectra of these first members of the series with higher molecular weight compounds seems subject to some uncertainty. The present paper reports the study of an homologous series of 2-methyl-2-alkenoic acids, and of both *cis* and *trans* forms of 2-methyl-2-hexenoic acid (IIIc and IIIt). These studies have, indeed, revealed certain discrepancies in comparisons based on the first members of the series (I and II).


I


II


IIIc


IIIt

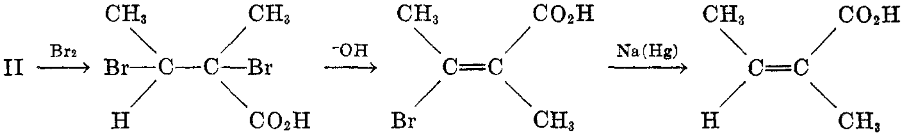
The previous assignments (6, 8) of geometric configuration in the α,β-unsaturated acids have leaned heavily on the exact position of the absorption band due to the carbon, carbon double bond at about 6 μ in the infrared, and on the intensity and position of the ultraviolet absorption band arising from the chromo-

---

[1] This investigation was supported in part by a grant (E-86) from the National Institutes of Health, U. S. Public Health Service.

phore, $-CH{=}\underset{|}{C}-CO_2H$. Since both the ultraviolet and infrared spectra of tiglic and angelic acids differ considerably from the spectra of C_{27}-phthienoic acid and the synthetic 2-methyl-2-alkenoic acids prepared in these laboratories, our first efforts were directed towards preparation of both geometric isomers of one of the higher 2-methyl-2-alkenoic acids.

Myers (10) has been able to isolate *cis*-2-octadecenoic acid from the end product of a series of reactions starting with perhydroxylation of *trans*-2-octadecenoic acid; however, certain of the steps in this series were not stereospecific. When this process was applied to 2-methyl-2-dodecenoic acid, the results were quite unpromising; even the perhydroxylation appeared not to occur stereospecifically. Buckles and Mock (11) have published an entirely stereospecific series for converting tiglic to angelic acid which proceeds through the compounds

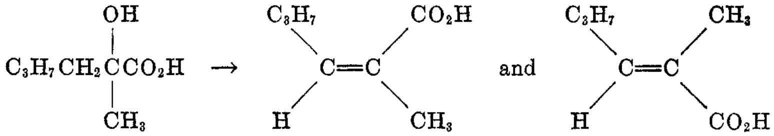


IV V I

represented by formulas IV and V. In our hands, this synthesis of angelic acid could be accomplished readily, but persistent efforts failed to raise the yield in the second step to more than about one-third that reported by the previous workers. Use of potassium *tert*-butoxide for the dehydrohalogenation was of little advantage. When the same sequence was applied to 2-methyl-2-dodecenoic acid, also to 2-methyl-2-eicosenoic acid, none of the isomer of opposite configuration could be isolated. In these instances, the second step was the cause of failure. The acidic product of the reaction appeared to consist largely of a dimeric material containing one atom of bromine, but the product isolated in largest amount was neutral. This neutral material from 2-methyl-2-dodecenoic acid was characterized as 2-bromo-2-dodecene. *trans*-Elimination of carbon dioxide and bromide ion from β-bromoacids and α,β-dibromoacids has been previously observed (9, 12), and the configuration of the hydrocarbon chain would be expected to be opposite to that of the starting acid. Conversion of the bromide to the lithium derivative, followed by carbonation, would give the acid with configuration opposite to that of the starting acid (relationship of II to I); however, no significant yield of acidic material could be secured in this reaction. Very low yields have previously been reported for formation and carbonation of the organolithium compound from vinyl bromides (13). The higher yields secured by Dreiding and Pratt (14) in applying this process to 2-bromo-2-butene may have resulted from the decreased solubility of the lower molecular weight lithium salt resulting from carbonation. This would inhibit further reaction of the salt to give a ketone.

Since synthesis of a pair of geometrical isomers of a higher molecular weight acid has proved so troublesome, an alternative approach has been used. It might be presumed that the spectra of angelic and tiglic acids would differ from the higher homologs because of methyl group interactions in these symmetrical structures; so the next three higher homologs have been synthesized. These acids, containing respectively the ethyl, propyl, and butyl groups attached to the double bond, were prepared by α-bromination and dehydrobromination of the corresponding saturated acids (7). The infrared spectra of these three acids were similar to each other and to higher molecular weight acids (15) prepared by the same method, but were not completely identical. The absorption in the ultraviolet was at a slightly longer wavelength than that of tiglic acid, and with increase in molecular weight there was an increasing extinction coefficient which leveled off at the value observed for the higher acids. It was thus suspected that these acids obtained by dehydrohalogenation were *trans*, and this was verified by determination of the acid dissociation constant of 2-methyl-2-hexenoic acid. This result of the dehydrohalogenation is consistent with expectations, for carboxyl is sterically a larger group than methyl.

Since the spectral properties of the *trans*-2-methyl-2-alkenoic acids appear to be near the limiting value at the molecular weight level of 2-methyl-2-hexenoic acid, the *cis* isomer of this compound was synthesized by the method used by Lucas and Prater (16) to obtain the isomeric 2-methyl-2-pentenoic acids. This synthesis involves pyrolysis of the 2-hydroxy-2-methylhexanoic acid (VI). The *cis* isomer (IIIc) appears to be the primary product of the pyrolysis, for its ratio was increased by conducting the pyrolysis at lower temperatures; however, some *trans* isomer (IIIt) was always obtained. At this molecular weight, the isomeric acids proved to be sufficiently stable to heat to allow their separation by fractional distillation at reduced pressure. The *trans* isomer had the same properties as the sample obtained by dehydrohalogenation. The pure *cis* isomer proved to have an infrared spectrum significantly different from that of the *trans* isomer. The ultraviolet spectrum of the *cis* isomer was somewhat surprising in that the maximum was at essentially the same wavelength (218 mμ) as that for the *trans* isomer (in contrast to angelic and tiglic acids, *cf.* Fig. 1), but the extinction coefficient was much lower. Since this lower extinction coefficient might arise from presence of some spectrally inert material, the *cis* isomer was quantitatively hydrogenated and shown to absorb one equivalent of hydrogen. Also, the equivalent weight and the acid dissociation constant were determined. All criteria supported purity of the *cis* structure.



VI IIIc IIIt

There remained a remote possibility that one of the isomers regarded by us as *cis* and *trans* might be the 2-methylenehexanoic acid (VII). This possibility was eliminated by synthesis of VII by a refinement of the method previously used

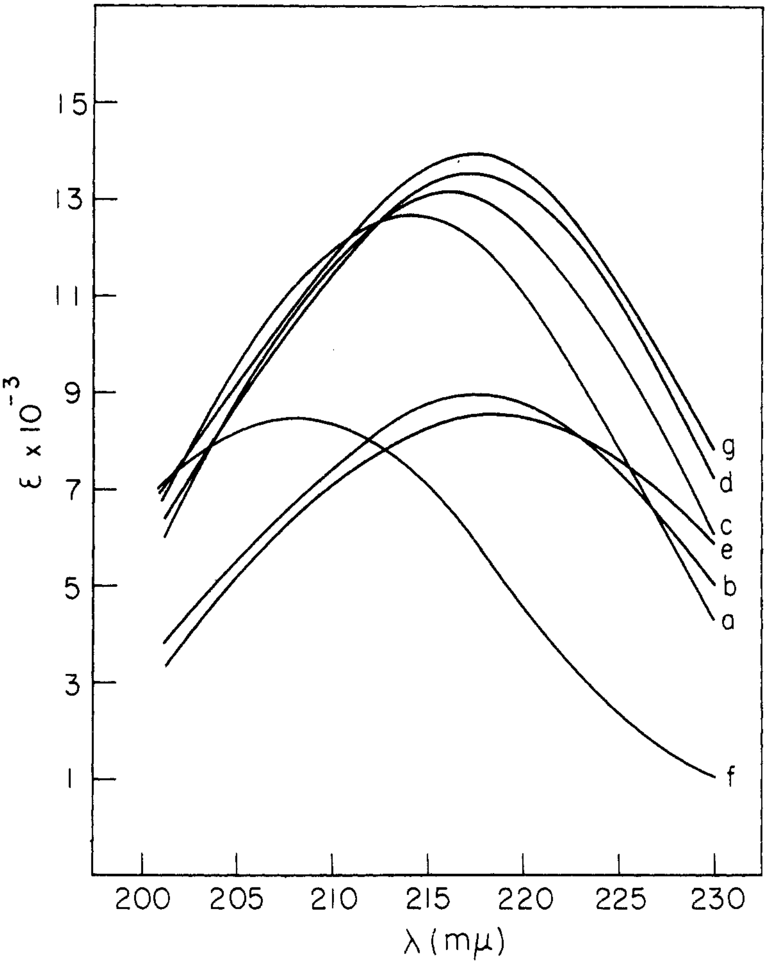
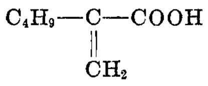


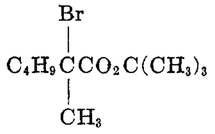
FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF 2-METHYL-2-ALKENOIC ACIDS: (a) Tiglic acid, (b) Angelic acid, (c) *trans*-2-Methyl-2-pentenoic acid, (d) *trans*-2-Methyl-2-hexenoic acid, (e) *cis*-2-Methyl-2-hexenoic acid, (f) 2-Methylenehexanoic acid, (g) *trans*-2-Methyl-2-heptenoic acid.

(4) for securing such structures. This consists of dehydrohalogenation of the bromoester (VIII) with potassium *tert*-butoxide. In the presence of this strong



$$C_4H_9{-}\underset{\underset{CH_2}{\|}}{C}{-}COOH$$

VII



$$C_4H_9\overset{\overset{Br}{|}}{\underset{\underset{CH_3}{|}}{C}}CO_2C(CH_3)_3$$

VIII

base, carbonium ion rearrangement (4) of the initially formed methylene isomer is avoided.

TABLE I

Comparison of the Physical Properties of the Isomeric C_7-Acids

Physical Constant	*trans*-2-Methyl-2-hexenoic Acid	*cis*-2-Methyl-2-hexenoic Acid	2-Methylene-hexanoic Acid
B.P., °C. (10 mm.)	119	110	111
n_D^{25}	1.4602	1.4525	1.4435
pK*	5.13	4.44	4.80
λ_{max}(mμ)	217	218	208.5
ϵ_{max}	13,580	8,780	8,480

* The values for pK appearing in this Table were determined by potentiometric titration, using 0.8–1.0 mg. of acid in 8 ml. of water. The relative values are believed to be reliable and are reproducible, but the absolute values are probably too high by about 0.2 unit. Under these conditions, the pK for 2-methylhexanoic acid was determined as 5.04, and that for *n*-hexanoic acid as 5.05. *n*-Hexanoic acid was sufficiently soluble to permit titration of 0.666 mg. in 2 ml. of 0.01 *M* potassium chloride solution. This procedure gave a value of 4.85, in agreement with the value of 4.83 reported from conductivity measurements [Drucker, *Z. physik. Chem.*, **52**, 641 (1905)].

Physical properties of the three pure isomeric seven-carbon α,β-unsaturated acids are assembled in Table I. The best criterion for identity of the methylene acid is the maximum in the ultraviolet at a shorter wavelength (one less substituent on the double bond). 2-Methylenedodecanoic acid, which has been previously characterized (4), has a similar spectrum. The best criteria, but not the only ones, for identity of the *cis* and *trans* isomers are the acid dissociation constants. The pK values in Table I compare with 4.30 for angelic acid and 5.05 for tiglic acid (17). The ratio of these constants could hardly be influenced significantly by substitution of a larger group for methyl.

The ultraviolet spectra of the methylene acid, the homologous *trans* acids, and the two *cis* acids are shown in Fig. 1. Especially noteworthy is the regular manner in which the spectra of the *trans* acids vary with molecular weight. At a chain length of six or seven carbons, the spectrum becomes the same as those of much higher molecular weight acids. For comparison, the carefully purified, crystalline 2-methyl-2-hexacosenoic acid (5) has an extinction coefficient of 14,000 and λ_{max} at 217 mμ, while for 2-methyl-2-eicosenoic acid (5) the values are 13,500 and 217 mμ. For the two *cis* isomers, it may be noted that increase in molecular weight causes a slight shift of the maximum to longer wavelength, as is the case in the *trans* series; however, the extinction coefficient decreases slightly with increase in molecular weight. Since steric interference between carboxyl and terminal alkyl may be regarded as the cause of the less intense absorption of the *cis* isomer (18), the small decrease in absorption accompanying change from terminal methyl to a larger group may be interpreted as indicating only small steric interference of the substituent beyond the *gamma* position.

In Fig. 2 are assembled the infrared curves of the acids prepared in this work. Although the differences in these curves are not so immediately apparent or quantitatively significant as the differences in ultraviolet spectra, there are cer-

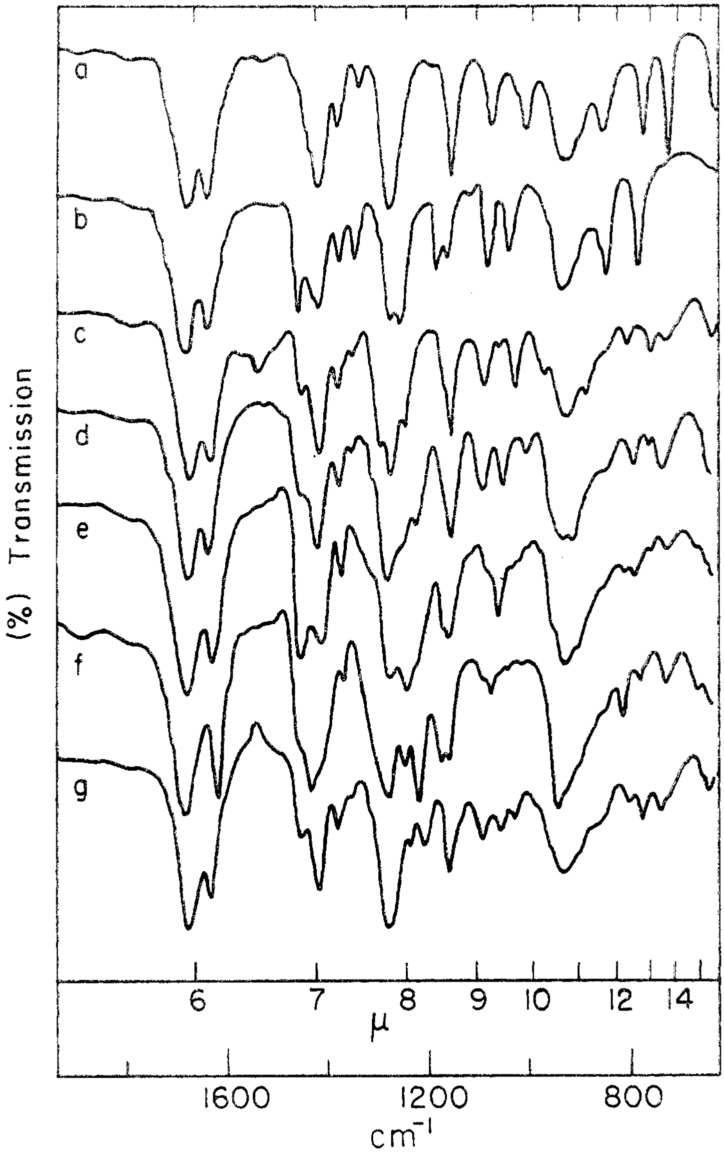


FIG. 2. INFRARED ABSORPTION SPECTRA OF 2-METHYL-2-ALKENOIC ACIDS: (a) Tiglic acid, (b) Angelic acid, (c) *trans*-2-Methyl-2-pentenoic acid, (d) *trans*-2-Methyl-2-hexenoic acid, (e) *cis*-2-Methyl-2-hexenoic acid, (f) 2-Methylenehexanoic acid, (g) *trans*-2-Methyl-2-heptenoic acid.

tain regions of rather clean-cut distinction. In Table II are found the wavelengths of the bands most useful for distinction between the isomeric acids.

For the methylene acid, Freeman (15) has already pointed out that the carbon, carbon stretching band is at a slightly longer wavelength, 6.13 μ, than is the case for any other type of α,β-unsaturated acid. This is confirmed by the present data,

TABLE II

INFRARED ABSORPTION SPECTRA OF THE ISOMERIC C_7-ACIDS; BANDS[a] MOST SUITABLE FOR DIFFERENTIATION OF ISOMERS (in μ)

trans-2-Methyl-2-hexenoic Acid	*cis*-2-Methyl-2-hexenoic Acid	2-Methylenehexanoic Acid
6.09 VS	6.11 VS	6.13 VS
6.85 W	6.84 VS	6.84 Sh
		6.93 VS
7.03 VS	7.04 VS	7.00 Sh
7.76 VS	7.78 VS	7.77 VS
7.95 Sh	8.00 VS	7.95 S
8.15 M	8.12 Sh	8.15 VS
		8.43 S
8.60 S	8.54 S	8.55 S
9.08 M	9.08 Sh	9.06 Sh
		9.2 M
	9.33 S	
9.44 M		9.47 Sh
	9.55 Sh	
9.70 W		
10.7 S	10.55 VS	10.54 VS
10.9 S		

[a] Legend to band intensity abbreviations: VS, Very strong; S, Strong; M, Medium; W, Weak; Sh, Shoulder.

although the *cis* acid is at 6.11 μ, and the *trans* acid at 6.09 μ. When compared with the other isomers, the spectrum of the methylene acid is especially characterized by the very strong, sharp band at 6.93 μ which is not accompanied by other bands as is the case for the 7 μ band in the other isomers. Although all three isomeric acids show some absorption at 8.15 μ, the band for the methylene acid is so much stronger that it is probably of diagnostic value. The double band at 8.43, 8.55 μ is unique for the methylene isomer. In the 9–10 μ region, the spectrum of the methylene isomer is also unique, in that it has a single band at 9.2 μ. The spectrum of the *trans* acid is complicated in this region, while the *cis* isomer has a single well-defined band at 9.33 μ.

For differentiation between the *cis* and *trans* isomers, the 9–10 μ region, just described, is quite useful. The relative complexity of this region is also seen in the curves for *trans* isomers published by Freeman (15), including C_{27}-phthienoic acid. Another region which has been characteristic of all the *trans* isomers is that of the double band at 6.85, 7.03 μ, with the shorter wavelength of the two bands much weaker, sometimes only a shoulder. The *cis* isomers show a marked difference in that the shorter wavelength band is the stronger of the two. There is a second double band of interest for distinction between the *cis* and *trans* isomers, the overlapping carboxyl bands at about 7.8 and 8 μ. Freeman (19) has pointed out that in saturated acids, the second of these bands is always considerably the weaker unless there is present an α-methyl substituent, in which case the second is the stronger. In all of the *trans* α-methyl-α,β-unsaturated acids, as well as the α-methylene acid, the second band proves to be the weaker, but in both the *cis* isomers, the second band is the stronger. Thus, the relative intensities of two pairs of bands are reversed in the *cis* and *trans* isomers.

For this comparison of *cis* and *trans* isomers, the long wavelength unsaturation bands beyond 11 μ have not been considered, for it has been observed (15) that these bands vary considerably with the nature of the substituents on or near the double bond. The consistency of the features discussed for the numerous *trans* acids and for the two *cis* isomers suggests that the comparisons here described may well be general. The greatest differences from these generalizations thus far reported are found in the absorption for 2,5-dimethyl-2-heptadecenoic acid (15). For this compound, established as *trans* by the method of synthesis and its absorption in the ultraviolet (7), the bands at about 6.85 and 7 μ are of equal intensity, and the 9–10 μ region is more simple than for the other *trans* isomers; the double band near 8 μ is quite characteristically that of the *trans* isomers. The 2,4- and 2,5-dimethyl acids prepared by Ställberg-Stenhagen (6) have spectra similar to the 2,5-dimethyl-2-heptadecenoic acid.

In view of the excellent correlation of both the ultraviolet and infrared spectra of C_{27}-phthienoic acid with those of the *trans* acids, as well as the several points of difference with the *cis* acids, it seems safe to conclude that the naturally occurring α,β-unsaturated acid from the tubercle bacillus is the *trans* isomer. This conclusion seems somewhat surprising until it be noted that the hydrocarbon chain in phthienoic acid does have the *cis* configuration, as is usually the case in naturally occurring acids.

It is of interest to re-examine the assignments which have been made using tiglic and angelic acids as standards of comparison. Stenhagen (6) has made tentative assignments of geometry for synthetic 2,4-dimethyl-2-heneicosenoic acid and 2,5-dimethyl-2-heneicosenoic acid. She has concluded that her acids possess the *trans* configuration and the data obtained in the present studies indicate that this assignment is correct. Adams and Van Duuren (8) have also used tiglic and angelic acids as standards of comparison in a series of 2-alkyl-2-butenoic acids derived from various alkaloids, but an examination of their data suggests that the assignments made by these authors are the reverse of those to be deduced from our data.[2]

---

[2] These authors have based the assignment of geometric configuration on both ultraviolet and infrared spectral data. In the infrared, the assignment was based on the intensity and position of the band due to the carbon, carbon double bond, which they reported at 6.06 μ for tiglic acid and at 6.08 μ for angelic acid. We have recorded approximately these same wavelengths for tiglic and angelic acids, but all the higher molecular weight *trans* acids absorb at about the same place as the *cis* angelic acid. Careful measurement of the position of the unsaturation band has given the following values (in μ, with precision of about ±0.005 μ):

angelic	6.090
tiglic	6.064
trans-2-methyl-2-pentenoic	6.094
trans-2-methyl-2-hexenoic	6.094
trans-2-methyl-2-heptenoic	6.105
cis-2-methyl-2-hexenoic	6.113

The isomeric 2-methyl-2-hexenoic acids have also been utilized in a study of the thermodynamic stability of the geometric isomers. Reference has previously been made to the thermodynamic instability of angelic acid (20); and, as previously mentioned, the *trans* isomer obtained in the preparation of *cis*-2-methyl-2-hexenoic acid by pyrolysis of the α-hydroxy acid probably arises through thermal equilibration to the more stable geometric isomer. Temperatures involved were in the range 220–270°. In heating experiments at 210°, it has been found that thermal equilibration of the isomeric 2-methyl-2-hexenoic acids is almost negligible. Heating of the esters for prolonged periods at 260° caused essentially no change in either geometric isomer. This is of considerable interest, for C_{27}-phthienoic acid was isolated by prolonged fractional distillation of its methyl ester at pot temperatures as high as 260°. Furthermore, acids isolated from bacterial lipids in this laboratory have usually been esterified by heating with methanol and sulfuric acid; so stability of the *cis*-2-methyl-2-hexenoic acid to acid esterification was investigated. Esterification for a period of 13 hours under reflux caused no more than 20% equilibration; so a normal period for esterification causes a minor amount of equilibration.

From the above described data concerning stability of the *cis*-2-methyl-2-hexenoic acid, it may be concluded that C_{27}-phthienoic acid has a *trans* configuration in the natural state, for isomerization of the *cis* isomer would not have occurred during any of the procedures used for the isolation.

The *trans*-2-methyl-2-alkenoic acids investigated by Freeman (15) showed this unsaturation band at 6.08 to 6.10 μ, and the *trans* acids reported in the preceding paper (5) showed this band at 6.09 to 6.11 μ. Thus, the *cis* isomer absorbs at a very slightly longer wavelength, but the difference is considerably less than the variation within the *trans* series resulting from minor structural variations. The effect of such a complicated *alpha* substituent as present in the acids investigated by Adams and Van Duuren would be difficult to predict, but it may be tentatively suggested that absorption is at the slightly longer wavelength when the larger groups are on the same side of the double bond (*trans* configuration in these instances). In our spectra (Fig. 2), recorded at a constant molar concentration, there appear to be no significant differences in the intensities of the 6.1 μ band.

In the ultraviolet spectra, these authors concluded that since the *cis* angelic acid has a lower extinction coefficient, the *cis* configuration should be assigned to those acids in their series which have the lower extinction coefficient. Evidence has been presented (18), however, that in hindered structures which tend to decrease the planarity of a conjugated system acting as a chromophore, the molar extinction coefficient will be lowered due to a decrease in the number of vibrational states allowing for electronic transitions. In the compounds studied by Adams and Van Duuren, the α-substituent is a bulky group, larger than carboxyl; therefore steric interference will be greater in the *trans* isomer in which this bulky α-substituent is on the same side as the β-methyl group. One would therefore expect that the *cis* isomer (carboxyl *cis* to β-methyl) should have an extinction coefficient of the same order of magnitude as that of angelic acid (9,000) and that the *trans* isomer (bulky α-group *cis* to methyl) should have a smaller extinction coefficient.

It is the case that one of their isomers has an extinction coefficient very near that of angelic acid and that the other isomer has a still lower extinction coefficient. In this instance, therefore, it is the isomer with higher extinction coefficient that would be expected to be *cis*. This conclusion is consistent with any tentative conclusion that might be reached from the above cited data on the position of the infrared band at about 6.1 μ.

EXPERIMENTAL[3]

2,3-Dihydroxy-2-methyldodecanoic acid was prepared according to the procedure of Myers (10) by allowing 16.6 g. (0.078 mole) of 2-methyl-2-dodecenoic acid to react with 45 ml. of 30% hydrogen peroxide and 113 ml. of glacial acetic acid. After hydrolysis with potassium hydroxide in ethanol the dihydroxy acid was isolated by precipitation with water; recrystallization from acetone yielded 5.0 g. (25.6%) of 2,3-dihydroxy-2-methyldodecanoic acid, m.p. 116.0–117.0°.

Anal. Calc'd for $C_{13}H_{26}O_4$: C, 63.38; H, 10.64; Equiv. wt., 246.3.
Found: C, 62.87; H, 10.37; Equiv. wt., 251.

From the mother liquors there was obtained 2.6 g. (11.3%) of material, m.p. 67–104°.

Anal. Calc'd for $C_{13}H_{26}O_4$: C, 63.38; H, 10.64; Equiv. wt., 246.3.
Found: C, 63.04; H, 10.75; Equiv. wt., 251.

trans-2-Methyl-2-butenoic acid (*tiglic acid,* II) was prepared in 52.8% yield by the procedure described by Buckles and Mock (11), m.p. 65.5–66.5°; literature (11) m.p. 62–64°.

cis-2-Methyl-2-butenoic acid (*angelic acid,* I). Tiglic acid was converted to 2,3-dibromotiglic acid (IV) by the addition of bromine in yields varying between 79 and 90.2%. The dehydrohalogenation was carried out with potassium hydroxide in methanol (11) and with potassium *tert*-butoxide in *tert*-butanol (21). The yields of β-bromoangelic acid (V) varied from 15 to 25% when potassium hydroxide was used, and a 36% yield was obtained with potassium *tert*-butoxide.

Reduction of β-bromoangelic acid with 9% sodium amalgam gave angelic acid (I) in yields varying from 55–69%, m.p. 44.9–46.0°; literature (11) m.p. 44–46°.

Attempted isomerization of 2-methyl-2-dodecenoic acid. 2-Methyl-2-dodecenoic acid, prepared by the procedure described by Cason, Allinger, and Allen (7), was brominated in carbon tetrachloride to yield the dibromoacid. Purification of this liquid acid by distillation was prevented by its instability towards heat. Dehydrohalogenation of the dibromoacid with either potassium hydroxide or potassium *tert*-butoxide gave a mixture of neutral and acidic material which was separated by passage through a four stage Kies extractor containing potassium carbonate in 20% aqueous alcohol.

When the acidic material recovered from the extraction was heated at 190°, neither hydrogen bromide nor carbon dioxide was evolved. Only 20% of this material was soluble in a solution of sodium bicarbonate. Analysis of the bicarbonate-soluble material gave Br, 10.27; Equiv. wt. 403 (theory for 3-bromo-2-methyl-2-dodecenoic acid: Br, 27.44; Equiv. wt., 291.2).

Fractional distillation of the neutral material gave a 20.5% yield of *2-bromo-2-dodecene,* b.p. 95.5–96.0° (3.75 mm.), n_D^{25} 1.4658.

Anal. Calc'd for $C_{12}H_{23}Br$: C, 58.30; H, 9.38; Br, 32.33.
Found: C, 58.23; H, 9.23; Br, 32.22.

Attempted isomerization of 2-methyl-2-eicosenoic acid. The isomerization developed by Buckles and Mock (11) was also applied to 2-methyl-2-eicosenoic acid (5). The product of the dehydrohalogenation was twice passed through a Kies extractor, and after each extraction the acidic material had a low bromine analysis and a high neutral equivalent. Material similar to that obtained from 2-methyl-2-dodecenoic acid is indicated.

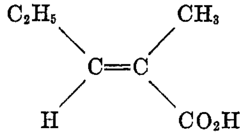
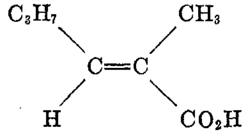
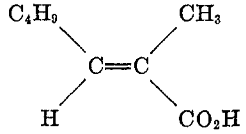
trans-2-Methyl-2-alkenoic acids. The *trans* isomers of 2-methyl-2-pentenoic acid, 2-

---

[3] All melting points are corrected, and all boiling points are uncorrected. Unless otherwise specified, distillations were through a half-meter column with heated jacket and partial reflux head, and containing a tantalum wire spiral of the simple Podbielniak design. Ultraviolet spectra were determined on a Beckman Model DU quartz spectrophotometer, following the precautions previously described (7). Infrared spectra were recorded on a Perkin Elmer Model 21 double beam recording spectrophotometer, using 1 *molar* solutions in carbon tetrachloride and carbon disulfide. Analyses are by the Microanalytical Division, Dept. of Chemistry, Univ. of California.

TABLE III

YIELDS AND PHYSICAL PROPERTIES[a] OF *trans*-2-METHYL-2-ALKENOIC ACIDS

Product	Yield,[b] %	Equiv. Wt. (Calc'd)	B.P., °C. (mm.)	n_D^{25}
	56.7	113.5 (114.1)	Observed 123–125 (29.5) Lit. (16) 106.5 (10)	1.4581 1.4578
	61.1	129.1 (128.2)	Observed 118–119 (11) Lit. (22) 118 (11)	1.4602 1.4581
	67.7	140.5[c] (142.2)	Observed 129.5–131 (11)	1.4605

[a] The b.p. is the range over which the indicated yield was collected. The equiv. wts., indices of refraction, and spectra (Figs. 1 and 2) were determined on samples which were center cuts in a region of constant boiling point. The constant boiling point was secured during the latter half of the distillation, after traces of *cis* or methylene isomer had been removed. [b] Yield based on saturated acid. [c] 2-Methyl-2-heptenoic acid was submitted for carbon and hydrogen analysis. *Anal.* Calc'd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.51; H, 9.65.

methyl-2-hexenoic acid, and 2-methyl-2-heptenoic acid were prepared from the saturated analogs by α-bromination followed by quinoline dehydrohalogenation (7). The saturated acids were prepared *via* alkylation of diethyl methylmalonate. The yields and physical properties of the unsaturated acids are shown in Table III.

cis-2-Methyl-2-hexenoic acid (IIIc). 2-Hexanone, b.p. 125–126°, n_D^{25} 1.4000, prepared in 60% yield by reaction of dibutylcadmium with acetyl chloride, was converted to 2-hydroxy-2-methylhexanoic acid in 66.9% yield by use of the reaction sequence described by Lucas and Prater (16). The hydroxy acid was Claisen-distilled for purification, b.p. 110–120° (1 mm.).

A sample of 35 g. (0.24 mole) of 2-hydroxy-2-methylhexanoic acid was heated for 3 hours at 195–210°, during which time 4.1 g. of ketone and water was distilled through a 2-foot fractionating column. Fractional distillation of the pyrolyzed material yielded 11.4 g. of mixed unsaturated acids, b.p. 104–112° (10 mm.). The residue was once more heated for 1.5 hours at 210–220°, during which time another 0.7 g. of ketone and water distilled. Fractional distillation yielded an additional 11.3 g. of material, b.p. 106–115° (10 mm.). There was a residue of 7 g. at the end of the pyrolysis.

The combined distillates were fractionally distilled through a 4-foot Podbielniak-type column. Of the 20 fractions obtained, fractions 4–13, wt. 12.56 g., had b.p. 111–112° (10 mm.), n_D^{25} 1.4505–1.4533. Since the equivalent weights of these fractions were slightly high, the combined material was passed through a three stage Kies extractor containing potassium hydroxide in 20% aqueous alcohol. Redistillation of the acidic material gave a center constant-boiling fraction of 6.05 g. (19.5%) of *cis*-2-methyl-2-hexenoic acid (IIIc), b.p. 110° (10 mm.), n_D^{25} 1.4523–1.4526, λ_{max} 218 mμ, ϵ_{max} 8,780.

Anal. Calc'd for $C_7H_{12}O_2$: C, 65.59; H, 9.44; Equiv. wt., 128.2.
Found: C, 65.53; H, 9.32; Equiv. wt., 128.9.

An 0.105-g. sample of this acid was hydrogenated in glacial acetic acid over 11 mg. of commercial platinum oxide catalyst at atmospheric pressure and room temperature. The hydrogen uptake, corrected for catalyst, was 21.15 ml. (theory, 21.80 ml.).

2-Methylenehexanoic acid (VII). 2-Methylhexanoic acid was brominated by heating 28.0 g. (0.215 mole) with 60.2 g. (0.22 mole) of phosphorus tribromide and 86.5 g. (0.54 mole) of bromine for 24 hours at 85–90°. After the reaction mixture had been cooled to room temperature, it was poured into a separatory funnel containing 50 g. of ice and 250 ml. of ice-water. The mixture was shaken for 10 minutes with 150 ml. of benzene, then the aqueous phase was extracted with an additional 100 ml. of benzene. Both benzene extracts were washed with a 300-ml. portion of ice-water. Solvent was removed at reduced pressure with a bath temperature of 30–45°. The residue was added to a solution of 21.1 g. (0.54 mole) of potassium metal in 500 ml. of dry *tert*-butanol. The thick suspension was heated under reflux for one hour, then about half the alcohol was distilled. The residue was added to 1000 ml. of water, and the product was extracted with three 400-ml. portions of hexane. The extracts were washed, filtered through anhydrous sodium sulfate, and dried over potassium carbonate. The residue remaining after removal of the solvent was fractionally distilled to yield 26.5 g. (67%) of *tert-butyl 2-methylenehexanoate*, b.p. 85–88° (20 mm.).

Saponification of the ester with alcoholic potassium hydroxide and distillation of the acid through a 4-foot column gave 6.875 g. (25%) of 2-methylenehexanoic acid, b.p. 111–111.5° (10 mm.), n_D^{25} 1.4431–1.4437, λ_{max} 208.5 mμ, ϵ_{max} 8,480.

Anal. Calc'd for $C_7H_{12}O_2$: C, 65.59; H, 9.44; Equiv. wt., 128.2.
Found: C, 65.57; H, 9.76; Equiv. wt., 127.

Methyl trans-2-methyl-2-hexenoate was prepared in 45% yield by heating *trans*-2-methyl-2-hexenoic acid for 2 hours under reflux with 15 mole-equivalents of methanol containing 10% by weight of concentrated sulfuric acid. Distillation yielded methyl *trans*-2-methyl-2-hexenoate, b.p. 81.5–82.0° (30 mm.), n_D^{25} 1.4418–1.4421, λ_{max} 214 mμ, ϵ_{max} 12,380.

Methyl cis-2-methyl-2-hexenoate was prepared in 52.3% yield by heating *cis*-2-methyl-2-hexenoic acid under reflux for 30 minutes with 15 mole-equivalents of methanol containing 10% by weight of concentrated sulfuric acid. The product was purified by distillation in a molecular still, n_D^{25} 1.4332–1.4334, λ_{max} 212 mμ, ϵ_{max} 7,600.

Anal. Calc'd for $C_8H_{14}O_2$: C, 67.57; H, 9.93.
Found: C, 67.70; H, 10.19.

When the *cis* acid was heated under reflux for 13.25 hours with methanol and concentrated sulfuric acid the product obtained had n_D^{25} 1.4344, λ_{max} 213.5 mμ, ϵ_{max} 8,740.

TABLE IV

THERMAL EQUILIBRATION DATA ON ISOMERIC C_7-ACIDS AND -ESTERS

Physical Constant	Before Heating	After Heating	Before Heating	After Heating
	cis-2-Methyl-2-hexenoic acid		*trans*-2-Methyl-2-hexenoic acid	
n_D^{25}	1.4525	1.4522	1.4602	1.4592
Equiv. wt.	128.9	131	129.1	129
λ_{max} (mμ)	218	217	217	218
ϵ_{max}	8,780	9,200	13,580	12,260
	Methyl *cis*-2-methyl-2-hexenoate		Methyl *trans*-2-methyl-2-hexenoate	
n_D^{25}	1.4333	1.4341	1.4420	1.4414
λ_{max} (mμ)	212	214.5	214	214
ϵ_{max}	7,600	7,990	12,380	12,280

Thermal equilibration of cis- and trans-2-methyl-2-hexenoic acids. Approximately 1 g. of each of the isomeric acids was sealed under nitrogen in a heavy-walled Pyrex tube, and the tubes were placed in a furnace at 210° for 17.5 hours. The heated samples were evaporatively distilled before determination of the physical constants shown in Table IV.

Thermal equilibration of methyl cis- and trans-2-methyl-2-hexenoate. Approximately 1 g. of each of the isomeric esters was heated as described for the acids for 17.75 hours at 260°. The heated esters were evaporatively distilled before determination of physical constants (Table IV).

SUMMARY

Assignment of the *trans* configuration to previously synthesized 2-methyl-2-alkenoic acids and to the naturally occurring C_{27}-phthienoic acid has been made possible by comparison of the infrared and ultraviolet spectra of these compounds with *cis*- and *trans*-2-methyl-2-hexenoic acids. The configurations of this isomeric pair have been established. Thermal equilibration studies have shown that the isomeric unsaturated acids are stable at temperatures below 210°, and that their methyl esters are stable at temperatures as high as 260°. It has also been found that equilibration of *cis*-2-methyl-2-hexenoic acid occurs only slowly during acid-catalyzed esterification. From these equilibration studies, it may be concluded that the *trans* C_{27}-phthienoic acid was not formed from the *cis* isomer during isolation, but has the *trans* configuration as it occurs in nature.

BERKELEY 4, CALIF.

REFERENCES

(1) CASON AND SUMRELL, *J. Biol. Chem.*, **192**, 405 (1951).
(2) CASON, FREEMAN, AND SUMRELL, *J. Biol. Chem.*, **192**, 415 (1951).
(3) CASON AND ALLEN, *J. Biol. Chem.*, **205**, 449 (1953).
(4) CASON, ALLINGER, AND WILLIAMS, *J. Org. Chem.*, **18**, 842 (1953).
(5) CASON AND KALM, *J. Org. Chem.*, **19**, 1836 (1954).
(6) STÄLLBERG-STENHAGEN, *Arkiv Kemi*, **6**, 537 (1954).
(7) CASON, ALLINGER, AND ALLEN, *J. Org. Chem.*, **18**, 857 (1953).
(8) ADAMS AND VAN DUUREN, *J. Am. Chem. Soc.*, **75**, 4631 (1953).
(9) CROMBIE, *Quart. Revs.*, **VI-2**, 101 (1952).
(10) MYERS, *J. Am. Chem. Soc.*, **73**, 2100 (1951).
(11) BUCKLES AND MOCK, *J. Org. Chem.*, **15**, 680 (1950).
(12) SHERRILL AND MATLOCK, *J. Am. Chem. Soc.*, **59**, 2134 (1937).
(13) BRAUDE AND TIMMONS, *J. Chem. Soc.*, 2000 (1950).
(14) DREIDING AND PRATT, *J. Am. Chem. Soc.*, **76**, 1902 (1954).
(15) FREEMAN, *J. Am. Chem. Soc.*, **75**, 1859 (1953).
(16) LUCAS AND PRATER, *J. Am. Chem. Soc.*, **59**, 1682 (1937).
(17) HEY, *J. Chem. Soc.*, 2321 (1928).
(18) BRAUDE, *et al.*, *J. Chem. Soc.*, 1890 (1949).
(19) FREEMAN, *J. Am. Chem. Soc.*, **74**, 2523 (1952).
(20) YOUNG, DILLON, AND LUCAS, *J. Am. Chem. Soc.*, **51**, 2528 (1929).
(21) CASON, ALLINGER, AND SUMRELL, *J. Org. Chem.*, **18**, 850 (1953).
(22) HEILBRON, *Dictionary of Organic Compounds*, Vol. III, Oxford University Press, 1953, p. 420.