of the genuine sample. A similar reaction but with ethanol (2 equiv), added 30 min after the Li, gave the same result. A reaction with excess Li (36 equiv) and *tert*-butyl alcohol (26 equiv, initially present) gave an oil whose nmr spectrum ($CDCl_3$) showed vinyl protons at δ 5.4, 5.7 but no aromatic absorption; *i.e.*, the phenyl rings were reduced to cyclohexyl groups. Reaction of **14c,d** at −78° (Dry Ice–acetone bath) with Li (2 equiv) and methanol (initially present) gave phenyl benzyl ketone (33%) and no stilbenes.[37]

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[37] This cleavage of a vinyl phosphate to the enolate of phenyl benzyl ketone, which is then protonated by methanol, is related to other cleavage reactions of enol phosphorylated species which are currently under investigation in our laboratory.[30a]

Registry No.—**11**, 1021-45-0; **12a**, 10409-51-5; **12b**, 10409-50-4; **14a**, 10409-53-7; **14b**, 10409-52-6; **14c**, 31327-09-0; **14d**, 31327-10-3; **15**, 4452-32-8; **22**, 31327-12-5; **24**, 31327-13-6; **28a**, 31327-14-7; **28b**, 31327-15-8; **31a**, 31327-16-9; **31b**, 31327-17-0; **32a**, 31327-18-1; **32b**, 31428-82-7; **36**, 31327-21-6; **37**, 30758-41-9; **38**, 31327-19-2; **39**, 31327-22-7; **40**, 5954-28-9; **41**, 1733-53-5; **42**, 31327-25-0; **43**, 30842-23-0; **44**, 31327-27-2.

Acknowledgment.—We are indebted to Professors Grace Borowitz, Bernard Miller, and Koji Nakanishi for stimulating discussions.

α-Anions. IV. Positional and Stereochemical Isomerization of 2- and 3-Unsaturated Carboxylic Acid Dianions[1a]

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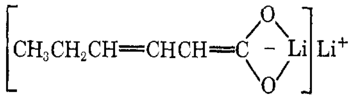
Received April 23, 1971

The stable dianions (carbanions of carboxylate salts) of the geometric isomers of 2- and 3-hexenoic acids were prepared and the nature of the carbanions was determined by deuteration and alkylation. Each of the four geometric anions, *i.e.*, *cis*- and *trans*-2-hexenoate dianions and *cis*- and *trans*-3-hexenoate dianions, on reprotonation gave 3-hexenoic acid exclusively. The results suggest the carbanion species of the 3-alkenoic acid salts to be more stable than the carbanion species of the 2-alkenoic acid salts. The geometric transformations that evolved provided further insights into the nature of the isomerizations. *trans*-2-Hexenoic acid gave a mixture of the cis-3 isomer (67%) and trans-3 isomer (33%), whereas *cis*-2-hexenoic acid gave the trans-3 isomer exclusively. The dianions from *cis*- and *trans*-3-hexenoic acids showed no indication of either positional or geometric isomerization since reprotonation regenerated the acids unchanged. A mechanistic scheme is described in terms of a polarized dianion of the following structure to explain these phenomena.



$$\left[CH_3CH_2CH{=}CHCH{=}C\begin{smallmatrix}O\\ \diagup\diagdown\\ \\ \diagdown\diagup\\ O\end{smallmatrix}\!\!-Li\right]Li^+$$

The isomeric 3-olefinic acids I and 2-olefinic acids II, have been reported by Linstead and Noble[2] to equilibrate (eq 1) in the pure state and in organic solvents,

$$\underset{\text{I}}{RCH{=}CHCH_2COOH} \rightleftarrows \underset{\text{II}}{RCH_2CH{=}CHCOOH} \qquad (1)$$

water, and alkaline solutions. The acids were induced to isomerize at elevated temperatures (100–200°), and the rates were greatly accelerated at these temperatures by alkali. The 2-olefinic isomer II was produced in the equilibrium as the thermodynamically favored acid, *i.e.*, the proportions of 2-olefinic to 3-olefinic were 70:30 for the *n*-hexenoic and *n*-pentenoic acids and 98:2 for *n*-butenoic acid.

In a continuation of our studies on the chemistry of α-metalated carboxylic acids (RCHLiCOOLi),[3–5] we have examined the carbanions derived by reaction of lithium diisopropylamide with isomeric 2- and 3-alkenoic acids. Crotonic acid produced a dianion that on quenching with hydrochloric acid yielded 3-butenoic acid quantitatively and exclusively. This unexpected shift of the conjugated double bond into the β,γ position is counter to the results reported for the thermodynamic equilibrium of the isomeric acid pair for which α,β-alkenoic acid predominates.[6] Since butenoic acid isomers provide limited stereochemical information, the longer chain 2- and 3-hexenoic acids were chosen for a more detailed investigation of the transformation.

The dianions of cis and trans isomers of 2- and 3-hexenoic acids were prepared by reaction of the individual geometric isomers with lithium diisopropylamide in tetrahydrofuran (THF) solution at 0°; the solution was then quickly warmed to room temperature and allowed to stir for 30 min.[3,5] The dianions were quenched with dilute hydrochloric acid and the recovered acids, after their conversion to methyl esters with diazomethane, were examined by glpc for determinations of geometric and positional isomerization. The *trans*-2-hexenoic acid (III) gave a mixture of 67% *cis*-3-hexenoic acid (IV) and 33% *trans*-3-hexenoic acid (V) in a combined yield of 98% (eq 2).[7] Prolonged heating (4 hr) of this dianion mixture at 45–50° induced no change in its isomeric composition. Similar treatment of the *cis*-2-hexenoic acid (VI) gave *trans*-3-hexenoic acid (V) exclusively (eq 3). The complete isomeriza-

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[1] (a) Presented at the 161st National Meeting of the American Chemical Society, Los Angeles, Calif., March 28–April 2, 1971. (b) Eastern Marketing and Nutrition Research Division, Agricultural Research Service, U. S. Department of Agriculture.

[2] R. P. Linstead and E. G. Noble, *J. Chem. Soc.*, 610 (1934).

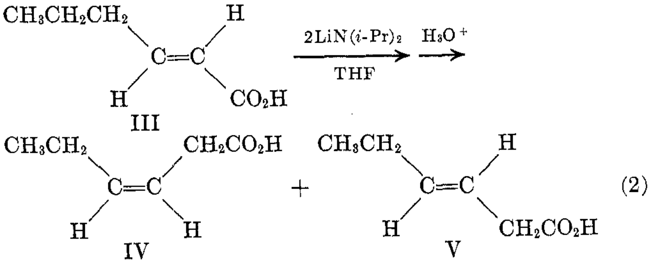
[3] P. E. Pfeffer and L. S. Silbert, *J. Org. Chem.*, **35**, 262 (1970).

[4] P. E. Pfeffer and L. S. Silbert, *Tetrahedron Lett.*, 699 (1970).

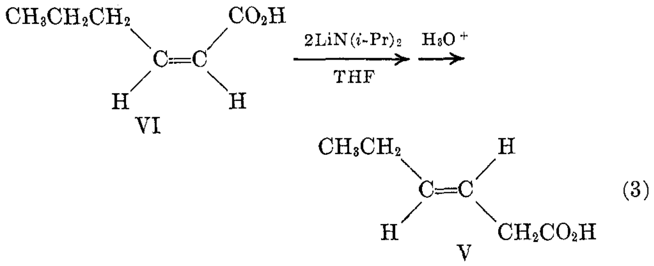
[5] P. E. Pfeffer, L. S. Silbert, and J. M. Chirinko, Jr., *J. Org. Chem.*, in press.

[6] A photochemical transformation of crotonic acid to 3-butenoic acid has previously been reported to occur in 59% yield after prolonged irradiation and equilibration of crotonic and isocrotonic acids: P. J. Kropp and H. J. Krauss, *ibid.*, **32**, 3222 (1967).

[7] A cis,trans mixture of α,β-unsaturated acids has been reported to isomerize photochemically to their β,γ isomers composed of a cis/trans ratio of 0.5: R. R. Rando and W. von E. Doering, *ibid.*, **33**, 1671 (1968).



III IV V (2)



VI V (3)

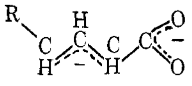
tion of 2-hexenoic acid isomers to 3-hexenoic acid isomers reflects the relative stability of the carbanions of the latter acids as the thermodynamically more stable forms. Further demonstration of this relationship is provided by the observation that *trans*-3-hexenoic acid (V) and *cis*-3-hexenoic acid (IV) are metalated to the stable *trans*-3-hexenoate dianion (Va) and *cis*-3-hexenoate dianion (IVa), respectively, with no indication of isomerization to the 2 isomers nor change in stereochemical purity (eq 4). Deuterium oxide quenching of the dianions ob-

$$CH_3CH_2CH{=}CHCH_2COOH \xrightarrow[\text{THF}]{2LiN(CH_3)_2} CH_3CH_2CH{=}CH\bar{C}HCOO^- \quad (4)$$

IV, cis acid
V, trans acid

IVa, cis dianion
Va, trans dianion

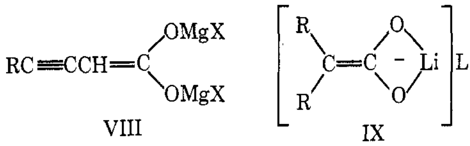
tained from each of the four isomers quantitatively introduced one deuterium atom at the α position. These results suggested that the negative charge of the carbanion involves only the α-carbon position without its participation in delocalization as expected for a resonance hybrid of the allylic anion of structure VII.



VII

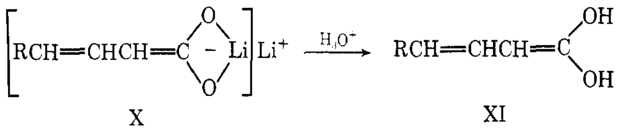
Alkylation with CH_3I of the dianion derived from each isomer gave exclusive substitution at the 2-carbon position. In the case of *trans*-2-hexenoic acid, there were obtained the two monomethylated products, *cis*-2-methyl-3-hexenoic acid (57%) and *trans*-2-methyl-3-hexenoic acid (29%) and the dimethylated product mixture of the cis and trans forms of 2,2-dimethyl-3-hexenoic acid (14%). The ratio of *cis*- and *trans*-monomethylated product is in accord with the ratio observed for the carbanions prior to alkylation. *cis*-2-Hexenoate dianion is methylated to a mixture of *trans*-2-methyl-3-hexenoic acid (85%) and 2,2-dimethyl-3-hexenoic acid (15%) (geometric configuration not determined). Chain methylation of *cis*-3-hexenoate and *trans*-3-hexenoate dianions resulted in formation of their respective cis and trans isomers of 2-methyl-3-hexenoic acid with no evidence of any stereochemical change.

Ivanoff, *et al.*,[8] have acquired spectral evidence for the organomagnesium salts of 3-acetylenic acids which they depicted as a conjugated triple-double bond structure (VIII) and Creger[9] has suggested a similar delocalized "aci-carboxylate" (IX)[10] which he termed an



VIII IX

"ate" structure, for the metalated species of saturated acids. A corresponding alkene "aci-carboxylate" (X) representing the dianion intermediate common to both 2- and 3-hexenoic acids may assist in explaining the



X XI

stability of the dianion as well as the resulting products obtained after protonation.[11] Since reprotonation gives rise only to 3-hexenoic acids, this is interpreted as indicating little conjugative interaction between the π bond at C_3–C_4 and the strongly polarized π bond at C_1–C_2. Reprotonation of X would be effected at the carboxylate grouping to generate the enol form of the acid (XI) that would prototropically shift only to the α carbon.[11a]

The stereochemical transformations of reactions 2 and 3 are relevant for their geometric differences, since both geometric isomers arise only from *trans*-2-hexenoic acid (reaction 2) in the course of the positional shift. *cis*-Allylic anions are reported to be the more stable thermodynamic anion species for the isomerization of terminal olefins to internal olefins.[12,13] Also, the specific base-catalyzed isomerization of simple olefins *via* the intermediate carbanions has been accorded an explanation by Kloosterziel and Van Drunen.[14] In terms of their concept for trans-to-cis isomerizations the *cis*-alkylallylic anions are more stable than the trans isomers; for cis-to-trans isomerizations, an all-cis conformation in the anion intermediate is prevented by steric hindrance. Although their interpretations serve as an explanation for simply constituted olefins, they are inadequate for rationalizing the results observed for the more complicated structures of our polar substituted olefinic systems. For example, application of the simple allylic concept to the isomerization of *trans*-2-hexenoate

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[8] D. Ivanoff, B. Jordanov, and B. Blagoev, *Naturwissenschaften*, **51**, 286 (1964).

[9] P. L. Creger, *J. Amer. Chem. Soc.*, **89**, 2500 (1967).

[10] The designation "aci-carboxylate" indicates that the dianion structure is the salt of the enol form of the parent acid. This enolization corresponds to the nitro-aci-nitro relationship.

[11] Efforts to characterize these unsaturated dianions by nmr analysis were unsuccessful because of the high degrees of aggregation. The molecular weight averages determined by ultracentrifugation were in the range of 8000–30,000. The tetrahydrofuran solutions exhibited goth a Tyndall effect and fluorescence.

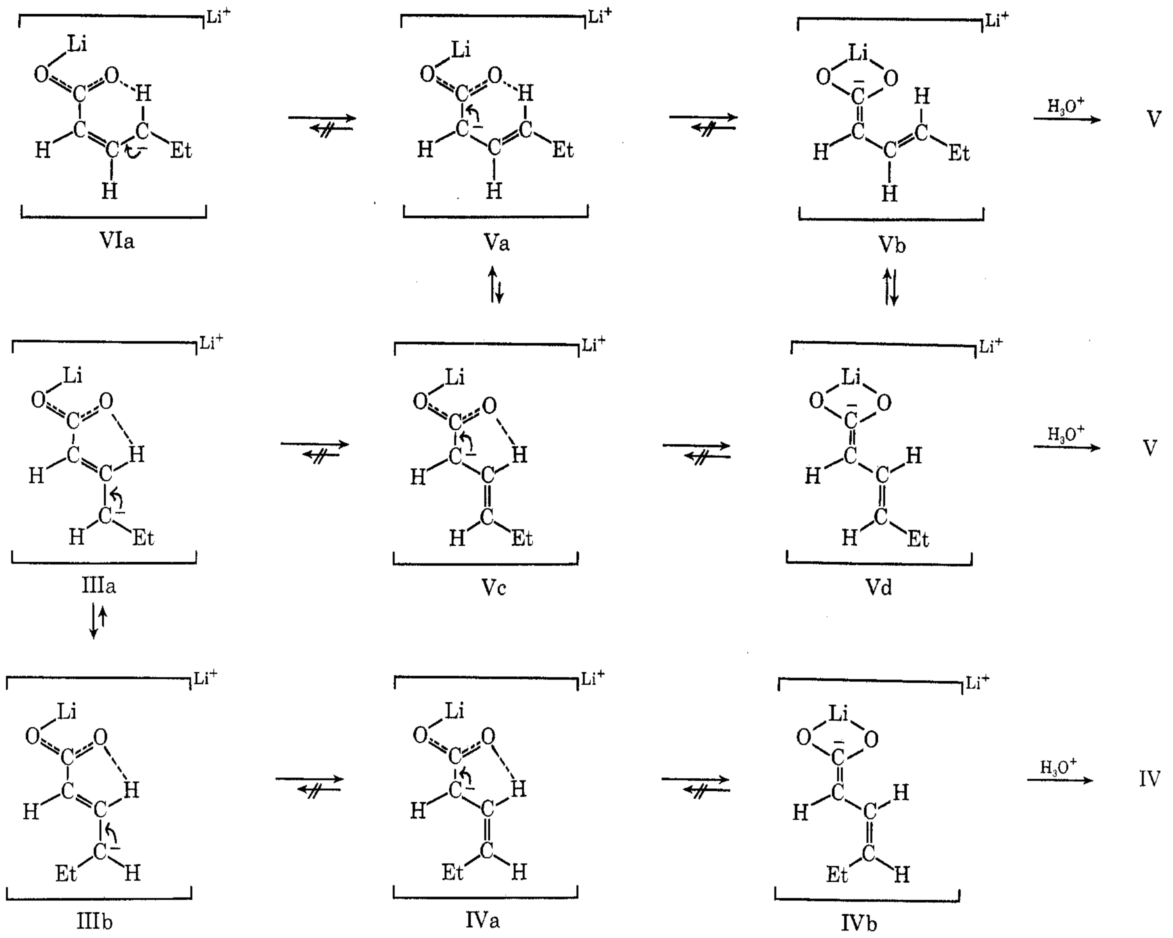
[11a] Note Added in Proof.—Since submission of this paper a recent investigation into the nature of the dianion derived from 2-methyl-3-phenylpropionic acid using nmr has indicated the structure to be consistent with the enolic form, $\overset{PhCH_2}{\underset{CH_3}{}}{>}C{=}C{<}\overset{OLi}{\underset{OLi}{}}$ (P. L. Creger, private communication). In a recent study, Y. N. Kuo, F. Chen, and C. Ainsworth, *Chem. Commun.*, 136 (1971), trapping of the dianions derived from various carboxylic acids with trimethylsilyl chloride gave rise to ketene bis-silyl acetals, $R_1R_2C{=}C(OSiMe_3)_2$, thus substantiating the localization of charge on oxygen.

[12] S. Bank, A. Schriesheim, and C. A. Rowe, Jr., *J. Amer. Chem. Soc.*, **87**, 3244 (1965).

[13] S. Bank, *ibid.*, **87**, 3245 (1965).

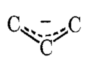
[14] H. Kloosterziel and J. A. A. Van Drunen, *Recl. Trav. Chim. Pays-Bas*, **89**, 37 (1970).

SCHEME I



dianion leads to the conclusion that only *cis*-3-hexenoic acid should be the expected product whereas 67% cis and 33% trans isomers of 3-hexenoic acid are in fact obtained. In addition, if the 2-hexenoate and 3-hexenoate dianions were freely interacting through common allylic anion species, a change in the stereochemistry would be anticipated whereas none is observed. A proposed sequence of transformations for each isomer is depicted in Scheme I.

The salient features underlining the proposed scheme take into account the following generalizations: (a) prior to carbanion formation, the electronegative carboxylate group may stabilize specific conformations by formation of hydrogen bonded five-membered and six-membered quasi rings for which the six-membered rings are more stable; (b) after carbanion formation, the "aci-carboxylate" structure stabilizes the anion by formation of a polarized olefin; (c) unsaturated carbanions that are capable of conjugation with the aci form are stabilized by charge distribution onto the electronegative group;[15] and (d) the resonant allylic anion structure (XII) serves inadequately as a representation of the incipient allylic anion owing to formation of a stable "aci-carboxylate."



XII

trans-3-Hexenoate (Va) and *cis*-2-hexenoate (VIa) salts may each maintain the six-membered quasi ring during proton abstraction and anion migration without undergoing conformational changes. The *trans*-3-hexenoate dianion (Va) would shift directly to the trans-ene aci-carboxylate (Vb) whereas the *cis*-2-hexenoate isomer (VIa) would transiently pass through the *trans*-3-hexenoate (Va) stage in formation of Vb and thereby protonate to the same product, trans-3-hexenoic acid (V).

cis-3-Hexenoate dianion (IVa) may exist in only one stable quasi-ring structure, a five-membered ring that would consequently pass directly to the cis-ene aci-carboxylate (IVb) that reprotonates to *cis*-3-hexenoic acid (IV) exclusively.

trans-2-Hexenoate dianion may form two quasi-five-membered ring conformations (IIIa and IIIb), the relative amounts of each being dependent upon their respective stabilities; of the two conformations, IIIb (cis,-trans) and IIIa (trans,trans), the latter is reported to be the less stable type in the corresponding unsubstituted olefinic system.[14] Conformational isomer IIIb would proceed through the cis-3 stage IVa to the cis-ene aci-carboxylate (IVb) in formation of *cis*-3-hexenoic acid (IV) (67%). The other conformer (IIIa) would pass through the *trans*-3-enoate stage (Vc) to produce the trans-ene aci-carboxylate (Vd) that finally reprotonates to *trans*-3-hexenoic acid (V) (33%).

Experimental Section

Reagents.—Tetrahydrofuran was dried over sodium and distilled from a ketyl solution (sodium and benzophenone). Diisopropylamine was distilled from calcium hydride prior to use.

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(15) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press New York, N. Y., 1965, p 205.

n-Butyllithium was purchased from Foote Mineral Co.[16] in 1.6 *M* hexane solution.

trans-2-Hexenoic and *trans*-3-hexenoic acids were obtained commercially, the former recrystallized and the latter distilled to $99+\%$ purity. *cis*-2-Hexenoic acid was prepared by the method of Rappe and Adeström.[17] *cis*-3-Hexenoic acid was prepared by the rearrangement of *trans*-2-hexenoic acid using lithium diisopropylamide (see below).

Equipment.—All nmr spectra were recorded on a JEOLCO C-60 spectrometer in CCl_4. All shifts are reported relative to tetramethylsilane. Ir spectra were recorded on a Perkin-Elmer IR-457 spectrometer.

Anionic Rearrangement of Hexenoic Acids.—Anhydrous THF (20 ml) and diisopropylamine (1.7 g, 0.0174 mol) were added to a dry, nitrogen-flushed flask and maintained under a nitrogen atmosphere throughout the reaction. *n*-Butyllithium in hexane (8.45 ml of 1.6 *M*, 0.0176 mol) was added to the magnetically stirred solution followed by addition of hexenoic acid (1.0 g, 0.00875 mol), each added at a controlled rate for maintaining the temperature below 0°. The solution was stirred for 30 min at room temperature, quenched with 10% HCl, and extracted with petroleum ether (bp 30–60°). The extracts were dried, the solvent was evaporated, and the mixtures of acids were converted to methyl esters with ethereal diazomethane. The products were analyzed by glpc (4-ft column, 10% $AgNO_3$–ethylene glycol) at 65° column temperature. The four methyl hexenoate isomers were readily separated at their indicated retention times: methyl *cis*-2-hexenoate (3.5 min), methyl *trans*-2-hexenoate (4 min), methyl *trans*-3-hexenoate (16 min), and methyl *cis*-3-hexenoate (32 min). These esters were subsequently trapped for their complete spectral analysis and comparison with authentic samples.

The hexenoic anion solutions prepared as above were quenched with D_2O (20 ml) and acidified with dilute HCl. The acids were extracted and the solutions dried and evaporated. The extent of deuterium incorporation in the 2 position was determined by nmr and the total deuterium content confirmed by mass spectral analysis.

Alkylations of Anions with Methyl Iodide.—Alkylation was carried out by the addition of methyl iodide (1.5 mol per mole of acid). The alkylations were complete within 90 min. Washings and isolation of products were the same as described above. The acids were converted to methyl esters with diazomethane and analyzed by glpc (4-ft column, $AgNO_3$–ethylene glycol). These esters were trapped and fully characterized with the exception of the isomeric methyl 2,2-dimethyl-3-hexenoates (cis and trans).

Spectral Data.—Spectral data for *trans*-2-, *trans*-3-, *cis*-2-, and *cis*-3-hexenoic acids and methyl esters have been documented.[17,18]

Methyl *cis*-2-methyl-3-hexenoate: nmr (CCl_4) δ 5.30 (m, 2, olefinic), 3.55 (s, 3, OCH_3), 3.22 (d, 1, α CH), 2.02 (m, 2, allylic CH_2), 1.15 (d, 3, CH_3), 0.95 (t, 3, CH_3); ir (CCl_4) 1740 cm^{-1} (C=O), no bands in 970-cm^{-1} region; mass spectrum (70 eV) *m/e* 142.

Methyl *trans*-2-methyl-3-hexenoate: nmr (CCl_4) δ 5.40 (m, 2, olefinic), 3.59 (s, 3, OCH_3), 2.95 (m, 1, α CH), 2.05 (m, 2, allylic CH_2), 1.15 (d, 3, CH_3), 0.98 (t, 3, CH_3); ir (CCl_4) 1740 (C=O), 968 cm^{-1} (trans double bond); mass spectrum (70 eV) *m/e* 142.

Isomeric mixture (cis and trans) of methyl 2,2-dimethyl-3-hexenoate: nmr (CCl_4) δ 5.4 (m, 2, olefinic), 3.55 (s, 3, OCH_3), 2.05 (m, 2, allylic CH_2), 1.2 (s, 6, CH_3), 1.0 (t, 3, CH_3); ir (CCl_4) 1740 (C=O), 968 cm^{-1} (trans double bond); mass spectrum (70 eV) *m/e* 156.

Registry No.—Methyl *cis*-2-methyl-3-hexenoate, 31599-11-8; methyl *trans*-2-methyl-3-hexenoate, 31599-12-9; methyl *cis*-2,2-dimethyl-3-hexenoate, 31599-13-0; methyl *trans*-2,2-dimethyl-3-hexenoate, 31599-14-1; *cis*-2-hexenoate dianion, 31599-17-4; *trans*-2-hexenoate dianion, 31599-18-5; *cis*-3-hexenoate dianion, 31599-15-2; *trans*-3-hexenoate dianion, 31599-16-3.

Acknowledgment.—The authors are grateful to Thomas F. Kumosinski for the ultracentrifuge determination of the dianion aggregates and to C. J. Dooley for the mass spectral analyses.

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[16] Reference to a particular manufactured product does not constitute a recommendation by the U. S. Department of Agriculture over similar products not mentioned.

[17] C. Rappe and R. Adeström, *Acta Chem. Scand.*, **19**, 383 (1965).

[18] A. F. Mabrouk, H. J. Dutton, and J. C. Cowan, *J. Amer. Oil Chem. Soc.*, **41**, 153 (1964); (b) E. N. Frankel, E. Selke, and C. A. Glass, *J. Amer. Chem. Soc.*, **90**, 2446, (1968).

Elements of Stereoisomerism and Prostereoisomerism[1]

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The elements of stereoisomerism, such as centers of stereoisomerism, which are used to specify the differences between stereoisomers can be tested for chirality by two reflection tests. These tests allow one to determine (a) whether the description of the configuration of an element requires reference to a chiral object, and (b) whether the element can or cannot contribute to the chirality of a molecular model. Definitions of the various chiral (*e.g.*, chiral centers) and achiral elements are proposed which are based on both reflection tests. Additional steric elements must be defined if all atoms and groups within a molecule that can be distinguished by chemical or physical tests are also to be distinguished in chemical discourse. These are named elements of prostereoisomerism and are defined by relating them to the corresponding elements of stereoisomerism. Prochiral centers constitute an important class of such elements. The prochirality concept is also applied to achiral configurations.

In developing the sequence rule procedure for specifying molecular chirality, Cahn, Ingold, and Prelog used as their steric elements the center, axis, and plane and on occasion the conformational helix.[2] They considered two types of the center, axis, and plane (the chiral and the pseudoasymmetric) but did not provide an explicit definition of these categories. Following this approach one of us[3] introduced the concept of prochiral elements and defined these by relating them to the cor-

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[1] (a) Supported in part by Grants AM 9105 and K6-AM-14367 from the National Institutes of Health (H. H.), and GB 12428 from the National Science Foundation (K. R. H.). (b) The study was undertaken as a result of discussions by the Panel on Stereonomenclature of the Office of Biochemical Nomenclature, National Academy of Sciences–National Research Council (current panel membership: S. Englard, K. R. Hanson, H. Hirschmann, S. J. Kiehl, and G. J. Schroepfer, Jr.; corresponding members: D. Arigoni and W. Klyne) and its predecessor, the NAS–NRC Subcommittee on Biochemical Nomenclature. Our preliminary conclusions were presented at a IUPAC–IUB meeting at the Ciba Foundation in London (1968) and in greater detail at a Table Ronde Roussel in Paris (1970).

[2] R. S. Cahn, C. K. Ingold and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, **5**, 385, 511 (1966).

[3] K. R. Hanson, *J. Amer. Chem. Soc.*, **88**, 2731 (1966).