The mechanism predicts that the isomerization reaction should be of first order with respect to ester and of second order with respect to amine. The kinetic studies reported in this communication show that this is found to be true. Since a proton is necessary for association with the carbonyl oxygen, tertiary amines would not be expected to have any catalytic effect. Such has been found to be the case. According to the mechanism stronger bases, because of their ability to readily donate a pair of electrons, might be expected to be better catalysts for isomerization. Work with different amines has shown that, although other effects are involved, there is a correlation between basic strength and catalytic ability.

The proposed mechanism is applicable to the isomerization of esters of all $\alpha$–$\beta$ unsaturated acids. It is also applicable to the amine-catalyzed isomerization of $\alpha$–$\beta$ unsaturated acids. However, in this case the protons would be supplied by the substituted ammonium ions formed by the reaction of the acid with the amine. Thus, even tertiary amines should be catalysts for the isomerization of $\alpha$-$\beta$ unsaturated acids. The reported catalysis of the isomerization of maleic acid to fumaric acid by pyridine[2] is thus readily explained.

## Summary

A mechanism has been proposed for the amine catalyzed isomerization of diethyl maleate. Experimental evidence in support of the mechanism has been presented. The applicability of the mechanism to the isomerization of all $\alpha$–$\beta$ unsaturated esters and acids has been discussed.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

# The Reduction of Multiple Carbon–Carbon Bonds. III. Further Studies on the Preparation of Olefins from Acetylenes[1,2]

BY KENNETH N. CAMPBELL AND LAWRENCE T. EBY

The preparation of the pure *trans* isomers of 3-hexene, 3-octene, 4-octene and 5-decene by reduction of the corresponding dialkylacetylenes with sodium in liquid ammonia, and the preparation of the *cis* isomers by catalytic hydrogenation of the acetylenes in the presence of Raney nickel were described in a previous paper.[3] In the present paper data are also recorded for the *cis* and *trans* isomers of 2-hexene and 2-octene, thus completing the series of the *cis* and *trans* isomers of all the straight chain hexenes and octenes.

Since the reduction of dialkylacetylenes with sodium in liquid ammonia led to olefins of a high degree of purity, uncontaminated by any saturated compound, and easily freed from traces of unreduced acetylene, the method was tried with monoalkylacetylenes. It was found to proceed smoothly and gave good yields of 1-alkenes. This method is superior to catalytic hydrogenation of alkylacetylenes for the preparation of such olefins. Lebedev and his co-workers[4] have shown that terminally unsaturated olefins hydrogenate more rapidly than symmetrically disubstituted ethylenes, and Campbell and O'Connor[5] found that in the catalytic hydrogenation of monoalkylacetylenes there is much less change in velocity at half-reduction than with the dialkylacetylenes. In using catalytic methods with monoalkylacetylenes it is, therefore, harder to stop precisely at the olefin stage, and the olefin obtained may contain traces of saturated hydrocarbon which are hard to remove by fractional distillation. When the sodium–liquid ammonia method is used, however, there is no danger of contaminating the olefin with saturated hydrocarbon, since olefins are not attacked under these conditions.[6] This was confirmed in the present work by treating 1-heptene and the *cis* and *trans* isomers of 5-decene with sodium in liquid ammonia; in every case the olefin was recovered unchanged.

The data in Table I indicate that the 1-alkenes prepared by sodium reduction are purer than those prepared by catalytic hydrogenation. The ones from sodium reduction show the higher freezing points and lower boiling points and densities.

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[1] Paper II, THIS JOURNAL, 63, 216 (1941).

[2] Paper XLIII on substituted acetylenes and their derivatives; previous paper, THIS JOURNAL, 63, 1151 (1941). The material in this paper was presented before the Organic Division at the St. Louis meeting of the American Chemical Society, April, 1941.

[3] Campbell and Eby, *ibid.*, 63, 216 (1941).

[4] Lebedev, Koblinsky and Yakubchik, *J. Chem. Soc.*, 127, 417 (1925).

[5] Campbell and O'Connor, THIS JOURNAL, 61, 2897 (1939).

[6] Lebeau and Picon, *Compt. rend.*, 159, 70 (1914).

TABLE I

| Compound | F. p., °C. | B. p.,[a] °C. | Press., mm. | $d^{20}_4$ | $n^{20}_D$ | $n^{20}_C$ | $n^{20}_F$ | $n^{20}_{G'}$ | $n^{20}_F - n^{20}_C$ | *MR*D obs. | *MR*D[d] calcd. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1-Hexene (H)[b] | −145 | 63.65 | 743 | 0.67520 | 1.38675 | 1.38448 | 1.39323 | 1.39665 | 0.00784 | 28.954 | 29.441 |
| 1-Hexene (Na)[b] | −141 | 63.15 | 750 | .67337 | 1.38758 | 1.38524 | 1.39336 | 1.39771 | .00812 | 29.464 | |
| *cis*-2-Hexene | −146 | 68.25 | 749 | .68449 | 1.39538 | 1.39296 | 1.40139 | 1.40592 | .00843 | 29.502 | |
| *trans*-2-Hexene | −133.5 | 67.55 | 750 | .67802 | 1.39348 | 1.39104 | 1.39956 | 1.40420 | .00847 | 29.657 | |
| *cis*-3-Hexene | −135 | 66.8–6.9 | 741 | .67964 | 1.39338 | 1.39093 | 1.39951 | 1.40416 | .00858 | 29.579 | |
| *trans*-3-Hexene | −113 | 67.4–7.6 | 741 | .67788 | 1.39377 | 1.39128 | 1.39991 | 1.40460 | .00863 | 29.682 | |
| 1-Heptene (H) | −125 | 93.0 | 737 | .70096 | 1.39842 | 1.39610 | 1.40404 | 1.40831 | .00794 | 33.836 | 34.059 |
| 1-Heptene (Na) | −120 | 92.8 | 749 | .69680 | 1.39910 | 1.39675 | 1.40492 | 1.40931 | .00817 | 34.090 | |
| 1-Octene (H) | −106 | 121.15 | 742 | .71695 | 1.40765 | 1.40531 | 1.41347 | 1.41780 | .00816 | 38.582 | 38.677 |
| 1-Octene (Na) | −102 | 120.75 | 742 | .71553 | 1.40815 | 1.40577 | 1.41407 | 1.41848 | .00830 | 38.700 | |
| *cis*-2-Octene | −104 | 124.6 | 750 | .72287 | 1.41391 | 1.41146 | 1.41994 | 1.42453 | .00848 | 38.782 | |
| *trans*-2-Octene | − 88 | 123.35 | 750 | .71842 | 1.41281 | 1.41035 | 1.41894 | 1.42349 | .00859 | 38.931 | |
| *cis*-3-Octene | −126 | 122.3 | 741 | .71888 | 1.41246 | 1.41000 | 1.41858 | 1.42328 | .00858 | 38.877 | |
| *trans*-3-Octene | −108 | 122.4 | 741 | .71630 | 1.41241 | 1.41000 | 1.41858 | 1.42330 | .00858 | 39.013 | |
| *cis*-4-Octene | −118 | 121.7 | 739 | .72048 | 1.41361 | 1.41114 | 1.41981 | 1.42449 | .00867 | 38.886 | |
| *trans*-4-Octene | − 94[c] | 121.4 | 739 | .71467 | 1.41157 | 1.40905 | 1.41775 | 1.42244 | .00870 | 39.032 | |
| *cis*-5-Decene | −112 | 169.5–9.6 | 739 | .74451 | 1.42521 | 1.42270 | 1.43139 | 1.43603 | .00869 | 48.192 | 47.913 |
| *trans*-5-Decene | − 73 | 170.2 | 739 | .74012 | 1.42351 | 1.42102 | 1.42964 | 1.43424 | .00862 | 48.309 | |
| 1-Hexyne | −132 | 71.2 | 751 | .71518 | 1.39840 | 1.39617 | 1.40418 | 1.40845 | .00801 | 27.774 | 27.933 |
| 2-Hexyne | − 88 | 83.85 | 742 | .73172 | 1.41346 | 1.41097 | 1.41938 | 1.42404 | .00841 | 28.019 | 28.178 |
| 3-Hexyne | −101 | 81.2–1.3 | 747 | .72307 | 1.41097 | 1.40847 | 1.41714 | 1.42177 | .00867 | 28.204 | 28.178 |
| 1-Heptyne | − 81 | 99.15 | 751 | .73379 | 1.40840 | 1.40596 | 1.41404 | 1.41834 | .00308 | 37.314 | 32.451 |
| 1-Octyne | − 79 | 125.2 | 737 | .74629 | 1.41565 | 1.41328 | 1.42132 | 1.42567 | .00804 | 37.025 | 37.069 |
| 2-Octyne | − 62 | 137.1 | 742 | .75913 | 1.42697 | 1.42464 | 1.43314 | 1.43765 | .00850 | 37.266 | 37.314 |
| 3-Octyne | −105 | 132.8–2.9 | 747 | .75291 | 1.42501 | 1.42252 | 1.43113 | 1.43572 | .00861 | 37.423 | 37.314 |
| 4-Octyne | −102 | 131.8–2.1 | 747 | .75124 | 1.42431 | 1.42184 | 1.43039 | 1.43501 | .00855 | 37.452 | 37.314 |
| 5-Decyne | − 73 | 177.15 | 751 | .76879 | 1.43315 | 1.43067 | 1.43922 | 1.44374 | .00855 | 46.748 | 46.550 |
| *n*-Hexane | − 94 | 68.6 | 747 | .65935 | 1.37458 | 1.37268 | 1.38008 | 1.38330 | .00740 | 29.887 | 29.908 |
| *n*-Heptane | − 90 | 97.6 | 747 | .68390 | 1.38738 | 1.38545 | 1.39216 | 1.39559 | .00671 | 34.523 | 34.526 |
| *n*-Octane | − 57 | 125.1 | 747 | .70305 | 1.39748 | 1.39550 | 1.40238 | 1.40595 | .00688 | 39.166 | 39.144 |
| *n*-Decane | − 30 | 173.4 | 747 | .72998 | 1.41166 | 1.40958 | 1.41678 | 1.42047 | .00720 | 48.463 | 48.380 |
| 2-Me-3-butyn-2-ol | + 2 | 103.2–3.4 | 749 | .8613 | 1.42091 | 1.41847 | 1.42698 | 1.43159 | .00851 | 24.759 | 24.725 |
| 2-Me-3-buten-2-ol (H) | − 39 | 97.2–8.3 | 744 | .8265 | 1.41421 | 1.41183 | 1.42012 | 1.42457 | .00829 | 26.052 | 26.348 |
| 2-Me-3-buten-2-ol (Na) | − 43 | 96.1–7.1 | 744 | .8248 | 1.41676 | 1.41421 | 1.42299 | 1.42771 | .00878 | 26.247 | 26.348 |
| 2-Me-3-octyn-2-ol | − 44 | 181.5–1.6 | 743 | .8506 | 1.44430 | 1.44187 | 1.45068 | 1.45539 | .00881 | 43.815 | 43.857 |
| *cis*-2-Me-3-octen-2-ol | Glass | 176.5–6.8 | 743 | .8378 | 1.44255 | 1.43996 | 1.44900 | 1.45393 | .00904 | 44.964 | 44.820 |
| *trans*-2-Me-3-octen-2-ol | Glass | 177.1–8.4 | 751 | .8301 | 1.43958 | 1.43700 | 1.44598 | 1.45070 | .00898 | 45.122 | 44.820 |

[a] Semi-micro Cottrell method of Willard and Crabtree, *Ind. Eng. Chem., Anal. Ed.*, **8**, 79 (1936), used for all boiling point determinations. [b] (H) indicates 1-alkenes prepared by catalytic hydrogenation, (Na), indicates those prepared by sodium reduction. [c] The f. p. of *trans*-octene-4 is erroneously given as −84° in ref. 3. [d] The triple bond values of Auwers, *Ber.*, **68**, 1635 (1935), were used in calculating the *MR*D values for the acetylenes.

It is now possible to consider the effect of the position of the double bond on the physical constants of straight-chain hexenes and octenes without having to make allowances for mixtures of geometrical isomers. From the data in Table I it is seen that the terminally unsaturated isomer has the lowest boiling point, and the *cis*-2-isomer the highest; the boiling point then decreases as the double bond is moved toward the middle of the chain. In general, also, the 1-isomer has the lowest index of refraction and the lowest density, while the *cis*-2-isomer has the highest. There seems to be no general relationship between the position of the double bond and the freezing point, and this property varies more with the geometrical configuration of the molecule than with the structural form. In all cases, however, the *cis* isomer has a freezing point lower than the *trans* compound.

It was of interest to extend the sodium–liquid ammonia reduction to acetylenes containing a second functional group, and the readily available tertiary acetylenic alcohols were studied. Both dimethylethynylcarbinol and dimethylhexynylcarbinol were smoothly reduced to the corresponding olefinic carbinols in this way, without cleavage into ketones.[7] These acetylenic carbinols were likewise smoothly converted to the olefins by catalytic hydrogenation in the presence of Raney nickel.

Saturated hydrocarbons are easily prepared in a state of purity by catalytic hydrogenation of acetylenes[5]; the constants of some of these are recorded in Table I. Reduction studies are being extended to tertiary aliphatic acetylenes and to aryl derivatives.

## Experimental

**Purification and Physical Constants.**—The compounds involved in this study were purified by repeated distillation through Whitmore–Fenske type columns. The physical constants were measured on freshly-distilled, peroxide-free samples, as it was found that peroxides were formed on

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(7) Babyan, *J. Gen. Chem.* (U. S. S. R.), **9**, 396 (1939).

a few days' standing, and this peroxide formation led to erroneous results, especially in the measurement of densities and indices of refraction. The physical constants were determined with the same precision as reported in our previous paper.[3]

**Acetylenes.**—The monoalkylacetylenes were prepared in the usual manner from alkyl bromides and sodium acetylide in liquid ammonia.[8] The dialkylacetylenes were prepared from alkyl bromides, sodium acetylide and sodamide in liquid ammonia.[9] For the introduction of methyl and ethyl groups the alkyl sulfates were used in preference to the bromides. In the preparation of unsymmetrical dialkylacetylenes the larger group was introduced first.[5] The use of this "one-step" method was satisfactory for all of the dialkylacetylenes reported except 2-octyne. In this case it is preferable to isolate the 1-heptyne and then methylate it, since otherwise purification is difficult owing to the close boiling points of amyl bromide and 2-octyne. The acetylenic carbinols were prepared by the method of Campbell, Campbell and Eby.[10]

**Catalytic Hydrogenations.**—The procedure previously described[3] was used to prepare the *cis*-olefins, and care was taken to keep the reaction temperature below 60°. For the 1-alkenes it was found better to stop the hydrogenation shortly before the calculated amount of hydrogen had been absorbed, since it is easier to free the olefin from acetylene than from saturated hydrocarbon.

The saturated hydrocarbons were prepared in 0.1 mole quantities; the products from several runs were then combined, washed several times with concentrated sulfuric acid to remove any unsaturates, then with water, dried and fractionated.

**Sodium-Liquid Ammonia Reductions.**—These were carried out as described earlier.[3]

## Summary

1. The *cis* forms of 2-hexene and 2-octene have been prepared by catalytic hydrogenation of dialkylacetylenes, and the *trans* forms by sodium-liquid ammonia reduction.

2. The sodium-liquid ammonia method has been applied to the preparation of 1-alkenes and found to yield pure substances.

3. Two acetylenic carbinols have been converted to the olefinic carbinols by both methods of reduction.

4. The physical constants of the isomeric straight-chain hexenes and octenes have been determined, and the relationship between the physical constants and the position of the double bonds has been discussed.

NOTRE DAME, INDIANA RECEIVED JULY 31, 1941

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[8] Hennion, *Proc. Ind. Acad. Sci.*, **47**, 116 (1938).

[9] Bried and Hennion, THIS JOURNAL, **59**, 1310 (1937).

[10] Campbell, Campbell and Eby, *ibid.*, **60**, 2882 (1938).

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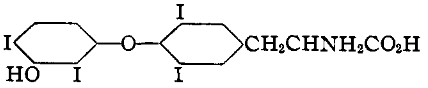
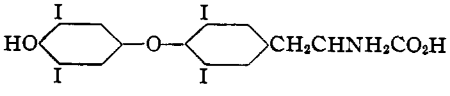
[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 848]

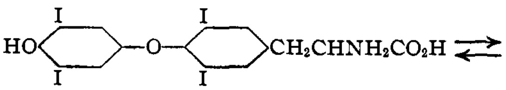
# The Synthesis of *dl*-3,5-Diiodo-4-(3′,5′-diiodo-2′-hydroxyphenoxy)-phenylalanine, a Physiologically Active Isomer of Thyroxine

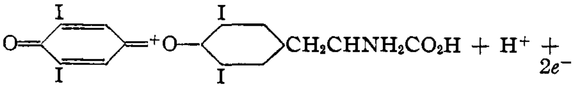
BY CARL NIEMANN AND JAMES F. MEAD

In a previous communication from this Laboratory[1] the synthesis of *dl*-3,5-diiodo-4-(2′,4′-diiodo-3′-hydroxyphenoxy)-phenylalanine (I), a physiologically inactive isomer of thyroxine (II), was described, and it was suggested that thyroxine-like activity is dependent upon the establishment of the equilibrium

I 

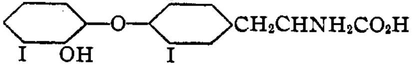
II 





It was therefore predicted that those isomers of thyroxine which could not be converted into a quinoid structure like that above would be inactive and that quantitative differences in the activity of those compounds which could form such structures would be due to the influence of nuclear substituents on the oxidation-reduction potential of the system as a whole.

As a test of this hypothesis we have synthesized *dl*-3,5-diiodo-4-(3′,5′-diiodo-2′-hydroxyphenoxy)-phenylalanine (III)

III 

and have found that this isomer of thyroxine, in

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[1] C. Niemann and C. E. Redemann, THIS JOURNAL, **63**, 1549 (1941).