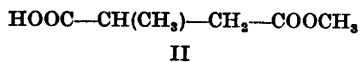
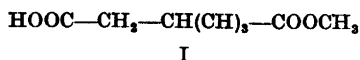


A Method of Preparing Half-esters of Alkylsuccinic Acids with Free Primary Carboxyl Group. Synthesis and Optical Configuration of Optically Active Methyl 2-Methyl-3-carboxypropanoate

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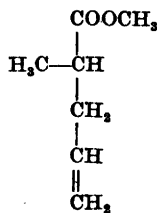
The preparation of the half-ester (I) of methylsuccinic acid has proved difficult because the methods usually employed for the synthesis of monoesters of dibasic acids give mixtures of



the two isomeric half-esters (I) and (II) ^{1,2}. Hancock and Linstead ³ obtained (I) in crystalline form in very poor yield by fractional crystallization of the ester mixture. The half-ester (I) has recently been prepared from citraconic anhydride by Veibel and Pedersen ⁵. None of the methods appears suitable for preparation of (I) in quantity.

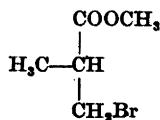
Armstrong and Hilditch ⁴ obtained methyl hydrogen azelate in very good yield by oxidation of methyl oleate in acetone solution with potassium permanganate. It thus appeared possible to prepare half-esters of the type (I) by oxidation of the corresponding esters of alkylallylactic acids. It was found that simple distillation of the oxidation products of methyl methylallylacetate gives crude (I) in yields of 60–68 % of the theoretical. The half-ester may be purified by crystallization from low boiling light petroleum. The melting point of pure (I) was found to be 42.2–42.8° C. (Hancock and Linstead give 42.5–43.5° C and Veibel and Pedersen 42–44° C). The melting point was unchanged after distillation at 0.1 mm pressure.

Methyl ester of optically active methylallylactic acid can be oxidized without racemization to give the enantiomorphs of (I). (+)-Methyl 2L-methyl-4:5-pentenoate (III),



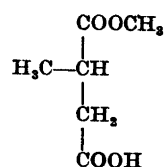
III

$[\alpha]_D^{25} + 17.0^\circ$
(homogeneous)



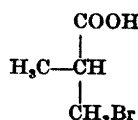
V

$[\alpha]_D^{25} + 13.6$
(homogeneous)



IV

$[\alpha]_D^{25} - 9.3^\circ$
(chloroform $c = 17.5$)



VI

$[\alpha]_D^{25} + 10.1^\circ$
(chloroform $c = 14.4$)

from acid of $[\alpha]_D^{25} + 8.2^\circ$ ^{5,6,7} on oxidation gave (-)-methyl 2L-methyl-3-carboxypropanoate (IV). The active half-ester isolated by means of simple distillation had $[\alpha]_D^{25} - 9.3^\circ$ (chloroform, $c = 17.5$). A part of the specimen was converted into (-)-methyl methylsuccinate of $\alpha_D^{20} - 3.45^\circ$, $l = 0.5$. For the antipode Berner and Leonardsen ⁸ give $\alpha_D^{20} + 6.91^\circ$, $l = 1$. This result shows that the oxidation of (III) by means of potassium permanganate proceeds without partial racemization in contrast to the oxidation of optically active methylallylactic acid with chromic acid ⁹. Levorotatory half-ester (IV) can also readily be obtained by resolution of the inactive ester (I) *via* the quinine salt. A specimen of (IV) obtained in this manner had after distillation $[\alpha]_D^{25} - 9.3^\circ$ (chloroform, $c = 17.4$).

The enantiomorphs of methyl 2-methyl-3-carboxypropanoic acid (I) are key compounds for the synthesis of a number of optically active compounds having a methyl group in α -position to a carboxyl group. Work is in progress on the prepara-

tion of the dextrorotatory antipode of (IV) and on the use of the enantiomorphs as intermediates in the synthesis of optically active compounds. For example, (IV) has *via* Hunsdieckers' procedure¹⁰ been converted into (+)-methyl 2L-methyl-3-bromo-propanoate (V), $[\alpha]_D^{25} + 13.8^\circ$ (homogeneous). (Found: Br 44.3. Calc. Br 44.14). Hydrolysis of the ester (V) with hydrogen bromide in glacial acetic acid gave (+)-2L-methyl-3-bromopropanoic acid ((+)- β -bromoisobutyric acid), $[\alpha]_D^{25} + 10.1^\circ$ (chloroform, $c = 14.4$). (Found Br 48.2. Calc. Br 47.85).

Experimental. For the oxidation of methyl methylallylacetate the following procedure appears to give the best results. Methyl methylallylacetate, b.p. 134.5—135.0°, 760 mm, $n_D^{25} 1.4158$, (52 g) was dissolved in 450 ml of dry acetone (distilled from potassium permanganate) in a 2 l three-necked round-bottomed flask equipped with a reflux condenser and a Hershberg stirrer. Powdered potassium permanganate (400 g) was added in portions as fast as the vigorous reaction allowed. The addition of permanganate lasted 2 h after which time refluxing and stirring was continued for 4 h. The reaction mixture was filtered on a sintered glass funnel. The filtrate contained practically nothing of the desired oxidation product and was discarded. The mass on the filter was washed with about 1 l of a solution of sulfurous acid. The filtrate was acidified with hydrochloric acid and the mixture was extracted several times with ether (it is preferable to use an apparatus for continuous extraction). The ether solution was washed with a small quantity of water and dried with sodium sulphate. The solvent was distilled off and the residue distilled *in vacuo*. The main fraction (37.8 g, 64 % of the theoretical) distilled at 101—103°, 0.1 mm. On cooling to room temperature most of the material solidified to a mass of large crystals, only a very small part remaining liquid. After treatment with charcoal the half-ester was crystallized from light petroleum at -15° . M.p. 42.2—42.8°.

Preparation of the optically active half-ester (IV). a) *by oxidation.* The oxidation was performed as described above starting from optically active methylallylacetate. Once-distilled half-ester (IV) ($n_D^{25} 1.4309$; $[\alpha]_D^{25} -9.3^\circ$

(chloroform, $c = 17.5$)) crystallized on seeding. Crystallization from light petroleum (b. p. 20—40°) after treatment with charcoal gave (IV) with m. p. 31.4—32.3° and $[\alpha]_D^{25} -9.3^\circ$ (chloroform, $c = 17.8$).

b) *by resolution of inactive half-ester (I).* Inactive half-ester (I) (16.7 g) was dissolved in a mixture of acetone and water (1:1 by volume, 450 ml) and quinine (43.4 g) was dissolved in the warm solution. The solution was filtered and crystallization allowed to take place at room temperature. After standing overnight the crystals were collected and recrystallized thrice from progressively smaller amounts of the same solvent. The quinine salt was decomposed by means of hydrochloric acid and the half-ester extracted with ether in an apparatus for continuous extraction. After distillation the optically active half-ester (IV) ($n_D^{25} 1.4309$, super-cooled liquid) showed an optical rotation of $\alpha_D^{25} -0.81^\circ$ (chloroform, $c = 17.4$, $l = 0.5$) $[\alpha]_D^{25} -9.3^\circ$.

The writer is indebted to Professors A. Fredga and E. Stenhagen for advice and interest.

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Received October 8, 1956.