# Electrochemical Reactions. Part XVI.[1] Stereochemistry of Two Known Diketonic Hydrodimers from Reduction of Carvone

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Electrochemical reduction of (+)-carvone (p-mentha-6,8-dien-2-one) is known to give two crystalline diketonic hydrodimers, along with oily dimeric products. Each crystalline dimer on treatment with sulphuric acid gives a different enantiomer of 2,2'-bi-p-meth-4-ene-6,6'-dione. On the basis of this and the n.m.r. spectra (solutions in CDCl₃ and C₆D₆) the hydrodimers are identified as (−)-(1S,2S,4S)-2,2'-bi-p-menth-8-ene-6,6'-dione (α-dicarvelone), m.p. 150—151°, $[\alpha]_D^{20}$ −85·8° (CHCl₃) and (+)-(1R,2R,4S)-2,2'-bi-p-menth-8-ene-6,6'-dione, m.p. 149—150°, $[\alpha]_D^{20}$ +41·0° (CHCl₃). Both cyclohexane rings in a given dimer have the same absolute stereochemistry. The stereochemistry of the related 2,2'-bi-p-menth-4-ene-6,6'-dione (γ-dicarvelone) and 4,4'-bicarane-2,2'-dione (β-dicarvelone) is also discussed.

REDUCTION of a conjugated enone by chemical or electrochemical means gives the saturated ketone and dimeric products of three types, which are illustrated by the reduction products of 4,4-dimethylcyclohex-2-enone (1).[2] For convenience in the subsequent discussion, the dimers may be considered to arise by

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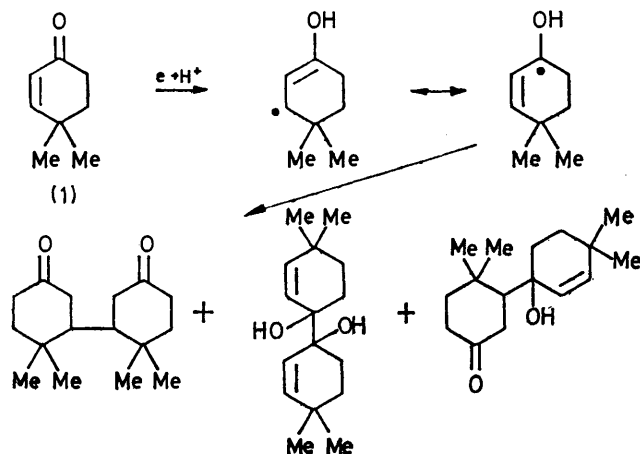
coupling of a radical intermediate, but the exact mechanism of this reaction is still under discussion. When *meso-* and (±)-modifications of the ε-diketonic product can be formed the stereoselectivity depends on the solvent and supporting electrolyte used in the reaction.[3] The relative yields of the three types of dimer depend in part on the degree of steric hindrance to coupling of the radical intermediates. Thus cyclohexenone[4] gives mainly ε-diketones with some ketol dimer, while cholestenone[3,5] gives pinacols. Progress towards an understanding of the factors responsible for stereoselectivity in the formation of ε-diketones is hampered by the difficulty of quantitative isolation of all the reaction products and frustrated by a lack of knowledge, in many instances, of the stereochemistry of these products.

Two crystalline diketonic hydrodimers comprising together 40—50% of the reaction mixture were isolated in 1912 by fractional crystallisation of the products of electrochemical reduction of (+)-carvone and characterised as their dioximes.[6] We will refer to these as dimer A, m.p. 150—151°, and dimer B, m.p. 149—150°. They show a large depression in m.p. on admixture. α-Dicarvelone, previously obtained by Wallach[7] and others[8] from the dissolving metal reduction of carvone, is identical with dimer-A. Wallach[9] proposed structure (4) for α-carvelone and this has been confirmed[10] by modern spectroscopic techniques, but no stereochemical assignments were made. We now present evidence for the stereochemistry of the two crystalline diketones. All the structural formulae given in this paper are for the products which can be prepared from (+)-carvone with the absolute stereochemistry as shown in (2).[11] The enantiomers of many of these products were also prepared from (−)-carvone.

The diketones from (+)-carvone may formally be regarded as derived by union of two radicals (3). They can be grouped under three formulae (4)—(6) in such a way that within each group the members will form an equilibrium mixture under the alkaline reaction conditions, by epimerisation of the asymmetric centres adjacent to the ketone functions. Reduction of (±)-carvone would give a potentially more complex mixture containing the racemic forms of (4)—(6) along with other isomers formed by the union of one radical from (+)-carvone with one from (−)-carvone.

Wallach converted dimer A (α-dicarvelone) by the action of concentrated sulphuric acid into an isomer, γ-dicarvelone, which was given the structure (7) although its stereochemistry was not elucidated.[7,9] γ-Dicarvelone shows λ_max. 236 nm (ε 27,600) which is expected for structure (7) with two αβ-unsaturated ketone chromophores in the molecule. Piperitone, for example, has λ_max. 236 nm (ε 17,800).[12] The n.m.r.

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[2] J. Wiemann, S. Risse, and P. F. Casals, *Bull. Soc. chim. France,* 1966, 381.

[3] For a review see A. J. Fry, *Fortschr. chem. Forsch.,* 1972, **34,** 38.

[4] E. Touboul, F. Weisbuch, and J. Wiemann, *Compt. rend.,* 1969, **268C,** 1170.

[5] H. Lund, *Acta Chem. Scand.,* 1957, **11,** 283; P. Bladon, J. W. Cornforth, and R. H. Jaeger, *J. Chem. Soc.,* 1958, 863.

[6] H. D. Law, *J. Chem. Soc.,* 1912, **101,** 1016.

[7] O. Wallach and H. Lohr, *Annalen,* 1899, **305,** 223.

[8] C. Harries and F. Kaiser, *Ber.,* 1898, **31,** 1806; 1899, **32,** 1320.
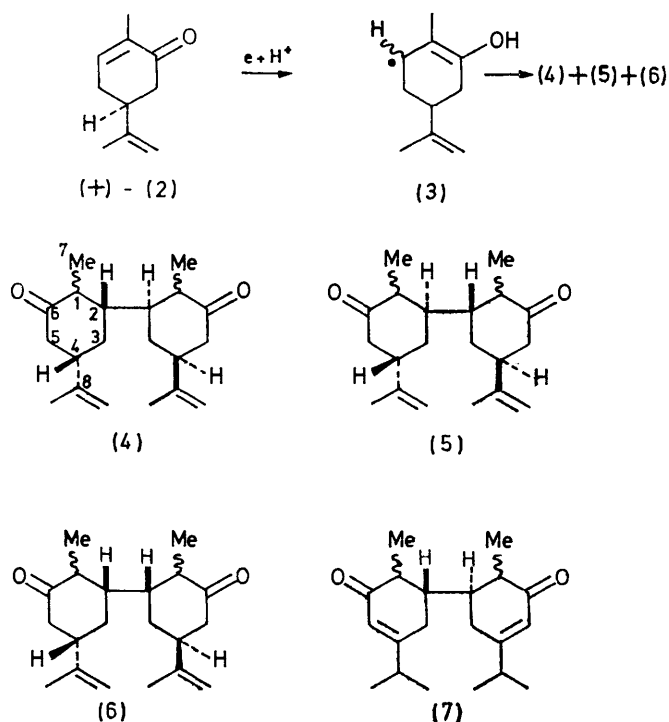
[9] O. Wallach and A. Erben, *Annalen,* 1914, **403,** 101.

[10] T. C. Jain, R. J. Striha, and E. Stewart, *Experientia,* 1968, **24,** 105.

[11] A. J. Birch, *Ann. Reports,* 1950, **47,** 192; K. Freudenberg and W. Lwowski, *Annalen,* 1954, **587,** 213.

[12] A. E. Gillam and T. F. West, *J. Chem. Soc.,* 1945, 95.

spectrum of γ-dicarvelone in $CDCl_3$ shows one signal at τ 4·09 due to the two olefinic protons. There is

(+) - (2)

(3)

(4)

(5)

(6)

(7)

an eighteen-proton doublet at τ 8·86 with J 7·0 Hz which must be due to all six methyl groups. Of the remaining signals, a symmetrical quintet with τ 7·56 (J 7·0 Hz) and intensity ratios of 6 : 15 : 20 : 15 : 6 is

Specimens of γ-dicarvelone with identical m.p. and i.r. spectra were obtained from dimer A and dimer B, themselves prepared from (+)-carvone. These specimens show equal but opposite specific rotations and on admixture in equal parts form (±)-γ-dicarvelone, m.p. 112—113°, showing no depression on admixture with the racemate prepared from (±)-dimer A. Thus dimer A and dimer B prepared from (+)-carvone are each converted into a different enantiomer of γ-dicarvelone. Dimer A and dimer B must therefore be represented by one of the formulae in group (4) and one in group (5), though we do not yet know in which group to place each dimer. A dimer having formula (6) will give a *meso*-isomer of γ-dicarvelone because under the conditions for this conversion enolisation of the ketone functions will result in racemisation of the adjacent asymmetric centres.

In the n.m.r. spectrum of dimer A (see Table) there is only one doublet for the two methyl groups adjacent to the ketone functions, one line for the methyl protons of the two isopropenyl groups, and one line (at 220 MHz this is separated into a doublet) with some fine structure for all four olefinic protons. These results and the conversion into γ-dicarvelone indicate that dimer A has a two-fold axis of symmetry orthogonal to the bond joining the two rings. The lines due to protons of the methylene groups adjacent to the carbonyl functions are not readily seen in the spectrum of dimer A in $CDCl_3$ but are well separated from other lines when C_6D_6 is used as solvent. In the n.m.r. spectrum of cyclohexanone the corresponding protons appear at τ 7·78 ($CDCl_3$) and are magnetically equivalent

N.m.r. data for the two crystalline hydrodimers obtained from reduction of (+)-carvone and their transformation products; in each compound the cyclohexane rings are equivalent

Dimer	τ ($CDCl_3$)	τ (C_6D_6)	Assignment
Dimer A (8), m.p. 151°	9·03 (d, J 6·5 Hz)	9·12 (d, J 6·5 Hz)	CH·CH_3
	8·24 (s)	8·51 (s)	CH_2=C·CH_3
	7·5—7·7 (m) {	7·90 (q, J 14·0 and 6·0 Hz)	HCH·CO
		7·45 [d, J 14·0 (lines broad) Hz]	HCH·CO
	5·19 (s)	5·22 (s)	C=HCH
	5·22 (s)	5·22 (s)	C=HCH
Dimer B (9), m.p. 149°	9·03 (d, J 6·5 Hz)	9·15 (d, J 6·5 Hz)	CH·CH_3
	8·27 (s)	8·50 (s)	CH_2=C·CH_3
	7·52 (q, J 14·0 and 6·5 Hz)	Not assigned	HCH·CO
	7·39 (q, J 14·0 and 4·0), also peaks split by *ca.* 1·5 Hz	Not assigned	HCH·CO
	5·12 (s)	5·28 (s)	C=HCH
	5·33 (s)	5·37br	C=HCH
γ-Dicarvelone (10)	8·86 (d, J 7·0 Hz {	9·15 (d, J 6·5 Hz) and 9·14 (d, J 6·5 Hz)	CH_3·CH·CH_3
		8·97 (d, J 6·0 Hz)	CO·CH·CH_3
	7·56 (quintet, J 7·0 Hz)	Not assigned	CHMe_2
γ-Dicarvelone (11)	8·95 (d, J 6·0 Hz)	Not examined	CO·CH·CH_3
	8·83 (s), 8·81 (s)		CMe_2

well separated at the low-field end of the methylene envelope. This is part of the septet from the two equivalent isopropyl methine protons, and the two outermost lines of unit intensity are not visible above the background. The evidence agrees with Wallach's structure (7) for γ-dicarvelone.

at room temperature.[13] The influence of solvent on the spectra of ketone is well established.[14,15] The $-CH_3$·CO– protons of dimer A form two pairs of equivalent nuclei. The signal due to one pair of equivalent protons is shifted

[13] K. B. Wiberg and B. J. Nist, *J. Amer. Chem. Soc.*, 1961, **83**, 1226.

[14] D. H. Williams and N. S. Bhacca, *Tetrahedron*, 1965, **21**, 1641, 2021.

[15] S. Bory, M. Fetizon, and P. Laszlo, and D. H. Williams, *Bull. Soc. chim. France*, 1965, 2541.

upfield in C_6D_6 to τ 7·90, so these protons must be axial. They give rise to a quartet with J 14·0 and 6·0 Hz. The signal due to the second pair of protons is shifted slightly downfield in C_6D_6 to τ 7·45, so these protons must be equatorial. These latter give rise to a doublet of broadened lines with J 14·0 and $ca.$ 1·0 Hz. The smaller coupling in each pair is due to the proton attached to the same carbon atom as the isopropenyl group, and the large difference between these vicinal coupling constants is consistent with the chair cyclo-hexanone carrying an equatorial isopropenyl group. The methine proton in the sequence CH·CH₂·CO is then axial with $J_{ax,ax}$ 6·0 and $J_{ax,eq}$ $ca.$ 1 Hz.

The n.m.r. spectrum (at 100 and at 220 MHz) of dimer B (see Table) indicates that, for this isomer also, both methyl groups adjacent to the carbonyl functions are equivalent, as are both CH₂·CO groups. However two lines each corresponding to two protons are attri-butable to the =CH₂ groups. If this is taken to imply that the two isopropenyl groups are non-equivalent, we know from the relationship of this dimer to (+)-carvone and to γ-dicarvelone that the only possible source of this supposed non-equivalence is that the two CO·CHMe groups have the opposite stereochemistry. Such a supposition is inconsistent with the remainder of the n.m.r. spectrum. Alternatively, if both iso-propenyl groups are equivalent and axial each proton of one =CH₂ group will be in a different magnetic en-vironment owing to the anisotropy of the carbonyl function, and so both =CH₂ groups will give rise to two lines, each of which corresponds to two protons. This latter alternative is in agreement with an analysis of the part of the n.m.r. spectrum due to the protons of the equivalent CH·CH₂·CO groups. Lines due to these methylene protons are well separated in the spectrum taken in CDCl₃ (220 MHz) whereas in C_6D_6 solution they overlap with others. One pair of protons has τ 7·52, with J 14·0 and 6·5 Hz; the second pair has τ 7·39, with J 14·0 and 4·0 Hz, with a small, possibly long-range coupling of 1·5 Hz. This is consistent with an equatorial methine proton coupled to the methylene protons in a chair cyclohexanone with $J_{eq,ax}$ 6·5 and $J_{eq,eq}$ 4·0 Hz, and necessitates axial isopropenyl groups.

Thus structures with a two-fold axis of symmetry from among groups (4) and (5) are suggested for the two diketones. For both dimers the signals for the methyl protons adjacent to the carbonyl group are moved upfield in the n.m.r. spectrum by 0·10 p.p.m. on changing the solvent from CDCl₃ to C_6D_6, which indicates these methyl groups to be equatorial. For comparison, under the same conditions the signal for the equatorial methyl groups in 2,2,6-trimethylcyclo-hexanone is shifted slightly downfield by 0·04 p.p.m. and that of the axial methyl group strongly upfield by 0·30 p.p.m.[15]

[16] D. L. Robinson and D. W. Theobald, $Quart.$ $Rev.$, 1967, **21**, 314.
[17] R. D. Stolow, T. Groom, and D. I. Lewis, $Tetrahedron$ $Letters$, 1969, 913; R. D. Stolow, A. A. Gallo, and J. L. Marini, $ibid.$, p. 4655.

Conformation (8) can be drawn for the structure among group (4) which satisfies the deductions from the spectral properties of dimer A. However it has been shown [16,17] that interactions between bulky vicinal

(8)   (9)

(10)   (11)
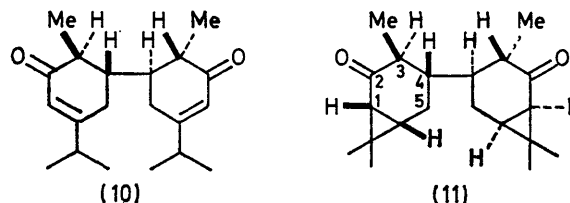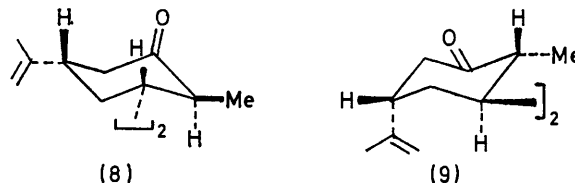
$trans$-substituents in a cyclohexanone can sometimes be large enough to ensure that conformers other than the chair form contribute significantly.

Dimer B is given structure (9) from among group (5). The conformation drawn shows an axial isopropenyl group and an equatorial methyl group as suggested by the n.m.r. data. First we can look at the free energy differences between axial and equatorial sub-stituents attached to a cyclohexane ring. We could find no value in the literature for the isopropenyl group, but values ranging from 2·11 to 2·62 kcal mol⁻¹ at 25 °C are given for isopropyl.[18] Only one determination of the conformational energy for a cyclohexyl substituent (2·15 kcal mol⁻¹)[19] has been made, and this can be compared with the value for an isopropyl substituent (2·22 kcal mol⁻¹)[20] determined by an identical method at 30 °C. In the carvone dimers, the methyl group adjacent to the carbonyl function increases the steric interactions of the axial cyclohexanone ring while the axial isopropenyl group will be subject to less steric interactions than the axial isopropyl group. Thus it is possible that in structure (9) a preferred chair con-former will have the axial isopropenyl group. Secondly, the energy difference between the flexible and chair forms of cyclohexanone is about 2·4—2·8 kcal mol⁻¹.[16] Flexible forms can therefore be expected to contribute significantly to the conformational equilibrium of dimer B along with the chair conformation (9).

γ-Dicarvelone is formed under conditions which epimerise position 1 and it must have an axis of sym-metry orthogonal to the bond joining the two cyclo-hexanone rings. In C_6D_6 the signals due to isopropyl methyl groups which are prochiral are moved upfield relative to the n.m.r. spectrum in CDCl₃, a shift ex-

[18] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, ' Conformational Analysis,' Interscience, New York, 1965.
[19] J. Reisse, J. C. Celotti, D. Zimmermann, and G. Chiurdoglu, $Tetrahedron$ $Letters$, 1964, 2145.
[20] A. H. Lewin and S. Winstein, $J.$ $Amer.$ $Chem.$ $Soc.$, 1962, **84**, 2464.

pected for a γ-substituent on the αβ-unsaturated ketone function,[21] and show a slight non-equivalence. The proton resonances of the methyl groups at positions 1 and 1′ are almost unchanged, which suggests that these groups are equatorial. The stereochemistry shown in (10) can be assigned to (−)-γ-dicarvelone if we assume that the substituents at positions 1 and 2 will prefer the equatorial conformation. The isopropenyl group of carvone is known to prefer the equatorial conformation even though in the axial position there is no axial hydrogen atom on the same side of the ring.[22]

Wallach converted dimer A into an isomer, β-dicarvelone, which he considered to be the cyclopropane derivative (11), by treating the bishydrobromide with base.[7,9] The u.v. spectrum of β-dicarvelone is in agreement with this structure and the u.v. spectra of β- and γ-dicarvelone bear the same relationship to each other as the spectra of trans-caran-2-one (carone) and cholesten-3-one [23] or trans-caran-2-one and piperitone.[12] trans-Caran-2-one has $\lambda_{max.}$ 220 nm (ε 2000), whereas β-dicarvelone, with two such chromophores, has $\lambda_{max.}$ 226 nm (ε 3700). The n.m.r. spectrum also indicates the presence of a gem-dimethyl group attached to a carbon atom with no hydrogen substituent. Under the alkaline reaction conditions the asymmetric centre adjacent to the ketone function in β-dicarvelone may isomerise, and the most stable arrangement will have substituents at positions 3 and 4 both in pseudoequatorial and staggered conformations. (+)-β-Dicarvelone is therefore assigned the stereochemistry shown in (11). This structure is a derivative of trans-caran-2-one with an equatorial substituent in position 4, and the trans-isomer is known to predominate in the cis–trans equilibium of caran-2-one.[24]

EXPERIMENTAL

I.r. spectra were measured for solutions in CS_2, u.v. spectra for solutions in EtOH and n.m.r. spectra for solutions in either $CDCl_3$ or C_6D_6 with Me_4Si as internal reference at 100 and (if necessary) at 220 MHz. N.m.r. data for the assigned peaks are given in the Table. Commercial samples of carvone showed α_D^{20} +59·2 and α_D^{20} −59·0 (neat liquid).

Carvone shows similar polarographic behaviour to other cyclohexenones.[25] Cyclohexenone in water shows $E_{\frac{1}{2}}$ −1·31 V at pH 5·4, and −1·62 V at pH 13 (versus s.c.e.).[26] Cyclohexanone has $E_{\frac{1}{2}}$ −2·28 at pH 13.[26]

Reduction of (+)-Carvone (2).—(a) Law's procedure (alcoholic potassium hydroxide as electrolyte but with a mercury cathode) was followed.

(b) Carvone (3·0 g) was added to a 0·1M-solution (100 ml) of tetraethylammonium bromide in 90% ethanol containing acetic acid (1·0 ml), which was then placed in the cathode compartment of a two-compartment cell with Hg cathode and Ag anode. The mixture was reduced at a cathode potential of −1·7 to −1·8 V (versus s.c.e.)

and the reaction was followed by means of a hydrazine coulometer.[27] The current fell to a low value after passage of 1 faraday per mol (15 h). The mixture was then evaporated and the residue extracted with ether after addition of water. The extract was washed with aqueous sodium hydrogen carbonate and water, dried (MgSO₄), and evaporated, and the residue (2·73 g) was chromatographed on neutral alumina (grade I). Elution with pentane afforded first a little carvone and dihydrocarvone and later a mixture of solid diketones (1·0 g), m.p. 120—148°, which could be more readily eluted with pentane–ether (9 : 1). Elution with pentane–ether (1 : 1) afforded an oil (1·0 g) from which no pure compound could be obtained. The product, m.p. 120—148°, was recrystallised from ether by slow evaporation to give dimer A, m.p. 150—151°. Evaporation of the mother liquors gave a solid from which dimer B, m.p. 149—150°, was obtained by crystallisation from light petroleum (b.p. 60—80°). The separation is very tedious.

(−)-(1S,2S,4S)-2,2′-Bi-p-menth-8-ene-6,6′-dione [(−)-dimer-A] (8) crystallised from ether as square plates, m.p. 150—151°, $[\alpha]_D^{20}$ −85·8 (c 2 in $CHCl_3$) (lit.,[6,7] m.p. 149 and 150°, $[\alpha]_D^{18}$ −73·9°), ν_{CO} 1713 cm⁻¹. The enantiomer, prepared from (−)-carvone, had $[\alpha]_D^{20}$ +86·7 (c 1 in $CHCl_3$), and the racemate, m.p. 118—119° (lit.,[7] 120—121°).

(+)-(1R,2R,4S)-2,2′-Bi-p-menth-8-ene-6,6′-dione [(+)-dimer-B] (9) crystallised from light petroleum (b.p. 60—80°) as rhombic prisms, m.p. 149—150°, $[\alpha]_D^{20}$ +41·0° (c 1 in $CHCl_3$) (lit.,[6] m.p. 149—150°, dextrorotatory). The enantiomer prepared from (−)-carvone, had $[\alpha]_D^{20}$ −43·8° (c 1 in $CHCl_3$), and the racemate, m.p. 135—136°.

Action of Sulphuric Acid.—(−)-Dimer A from (+)-carvone (0·20 g) was stirred with concentrated sulphuric acid (5 ml) at room temperature. It dissolved to give a yellow solution which was poured on ice after 1 h. The precipitate was collected and crystallised from methanol–water (3 : 1) to yield (−)-(1S,2S)-2,2′-bi-p-menth-4-ene-6,6′-dione (10) (γ-dicarvelone), m.p. 126—127°, $[\alpha]_D^{20}$ −240° (c 0·5 in $CHCl_3$) (lit.,[7] m.p. 126°, $[\alpha]_D^{18}$ −213°), ν_{CO} 1670 cm⁻¹, $\lambda_{max.}$ 236 nm (ε 27,600). (+)-Dimer A gave (+)-γ-dicarvelone, $[\alpha]_D$ +245°, and from these (+)-γ-dicarvelone, m.p. 112—113° (lit.,[7] 112°), was prepared.

(+)-Dimer B, from (+)-carvone, gave (+)-γ-dicarvelone, m.p. 126—127°, showing no depression on admixture with the product from (+)-dimer A, $[\alpha]_D^{20}$ +242°. This (+)-γ-dicarvelone on admixture with (−)-γ-dicarvelone from (−)-dimer A gave (±)-γ-dicarvelone, m.p. and mixed m.p. 112—113°. (−)-Dimer B gave (−)-γ-dicarvelone $[\alpha]_D^{20}$ −238°. All specimens of γ-dicarvelone had identical i.r. spectra (KBr disc and CS_2 solution).

(+)-4,4′-Bicarane-2,2′-dione (11).—(−)-Dimer A from (+)-carvone was converted into the hydrobromide and the crude product was treated with alkali to yield (+)-β-dicarvelone, m.p. 215—216° (from aqueous methanol), $[\alpha]_D^{20}$ +81·5 (c 1 in $CHCl_3$) (lit.,[7] m.p. 206—207°, $[\alpha]_D^{18}$ +79°), ν_{CO} 1680 cm⁻¹, $\lambda_{max.}$ 226 nm (ε 3760).

[21] C. J. Timmons, Chem. Comm., 1965, 576; J. Ronayne, M. V. Sargent, and D. H. Williams, J. Amer. Chem. Soc., 1966, 88, 5288.
[22] R. E. Ballard, S. F. Mason, and G. W. Vane, Discuss. Faraday Soc., 1963, 35, 43.
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[24] W. Cocker, P. V. R. Shannon, and P. A. Staniland, J. Chem. Soc. (C), 1967, 485.
[25] K. Schwabe and H. Berg, Z. Elektrochem., 1952, 56, 952.
[26] E. J. Denney and B. Mooney, J. Chem. Soc. (B), 1968, 1410.
[27] J. A. Page and J. J. Lingane, Analyt. Chim. Acta, 1957, 16, 175.