ABSOLUTE CONFIGURATION AND CHIROPTICAL PROPERTIES OF TRICYCLO[4.4.0.0³,⁸]DECANE (TWISTANE) AND SOME OF ITS DERIVATIVES* **

M. TICHÝ

*Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, 166 10 Prague 6*

Absolute configuration of twistane, twistene and some of their derivatives has been determined by unequivocal chemical way and shown to be opposite to the configuration previously inferred from CD-measurements. The question of the applicability of some of the optical rules to the twistane system is discussed.

The relation between geometry of a chiral compound and its chiroptical properties has been the subject of a vast number of investigations. Although many outstanding results in this area have been achieved (for leading references see[2⁻⁷]) other problems remain about which much less is known. One such still open problem is the question of the so-called "permolecular" effects, *i.e.* the effects of the chirality of the molecular framework as a whole. In most cases these effects are of little importance, but in certain structures they become dominant factor which determines the chiroptical properties[6⁻⁹]. One of the systems, where very pronounced effects in this respect may be expected, is the tricyclo[4,4,0,0³,⁸]decane (twistane) system[10] which exists in two enantiomeric forms *Ia* and *Ib*.

Ia   *Ib*
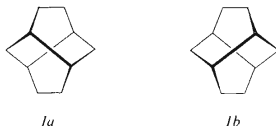
The first synthesis of optically active twistane derivatives was carried out by Adachi and coworkers[11] who repeated in principle the Whitlock's synthesis of twistane[10],

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starting from optically active $(-)$-endo-(2-oxobicyclo[2,2,2]oct-6-yl)acetic acid. The $(-)$-acid (with positive Cotton effect) gave $(+)$-2-twistanone (positive Cotton effect) and further $(+)$-twistane. The Japanese authors assigned absolute configuration to these compounds applying the Octant rule[12] to the first and the Klyne–Djerassi rule[13] to the second ketone: in both cases the application led to the configuration *Ia* for $(+)$-twistane. The same conclusion was reached on the basis of the observed positive Cotton effect of $(+)$-4-twistanone[14]. Moreover, calculation[11] of the optical rotation using the Conformational Dissymmetry Model[6] gave also positive sign of rotation $(M_D + 140°)$ for the enantiomer *Ia*.*

Although these results seemed mutually consistent, they were obtained solely on the basis of optical methods, and therefore a more convincing evidence on the absolute configuration was desirable. We therefore set out to determine the absolute configuration of twistane by chemical way. The unequivocal assignment of absolute configuration to twistane derivatives would thus serve as a test of the applicability of various optical rules to this system.

Synthesis and Correlation of Optically Active Twistane Derivatives

Three routes leading to optically active compounds with twistane system were devised. The first route (Scheme 1) correlates $(+)$-twistane with $(+)$-4-twistanone(($+$)-


$(-)$-*II*; R = H $(+)$-*IV*; R = —OH $(+)$-*VII* $(+)$-*VIII*
$(-)$-*III*; R = CH$_3$ $(+)$-*V*; R, R = —OCSO—
                         $(+)$-*VI*; R = — OCOC$_6$H$_5$

SCHEME 1 $(+)$-*I* ≡ *Ib*

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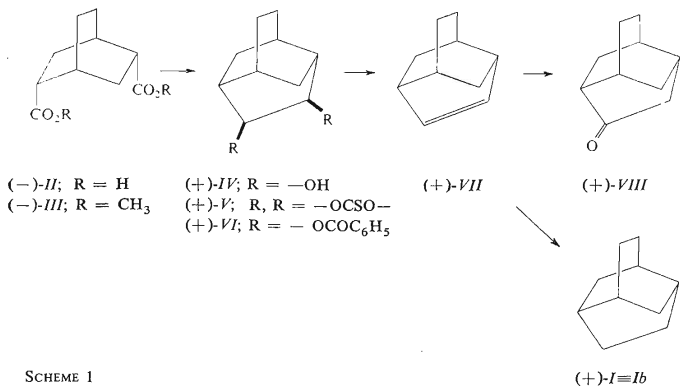
* However, recently Brewster[9] using the Helical Conductor Model[6], concluded that *M*-twistane should have a positive rotation and calculated its $[M]_D$ +484, which is in very good agreement with the found value (570 (ref.[11]), 590 (ref.[14]).

-VIII), (+)-twistene((+)-VII), and with (−)-endo-bicyclo[2,2,2]octane-2,5-di-carboxylic acid ((−)-II). The second route (Scheme 2) starts with the optically active endo-bicyclo[2,2,2]oct-5-ene-2-carboxylic acid((+)-IX) ($[\alpha]_D^{25} +50.9°$), which was obtained by resolution of (±)-IX via its salt with (+)-2-(1-aminoethyl)naphtha-lene. The acid (+)-IX on hydrogenation afforded (−)-(2R)-bicyclo[2,2,2]octane--2-carboxylic acid ((−)-X), $[\alpha]_D^{25} −61.6°$, already correlated with (−)-(2R)-2-hydro-xybicyclo[2,2,2]octane[15,17] ((−)-XI) by Berson and collaborators[17]. Thus, the key compound in the present correlation, (+)-IX, was shown to possess the 2R- configuration.

The acid (+)-IX, (94% optical purity) was transformed via diazo ketone[18] into the tetracyclic ketone (−)-XII, $[\alpha]_D^{25} −49.4°$. Hydrogenation of this compound over palladium gave a mixture of (+)-XIII and (+)-VIII (87.5% and 12.5%, respec-tively), the specific rotation of which corresponded closely to that calculated from the ratio of (+)-XIII : (+)-VIII (calculated 120.1°, found +117.4°). Wolf–Kishner reduction of this mixture afforded a mixture of the two corresponding hydrocarbons XIV and (+)-I (87.3% and 12.7%, respectively) of $[\alpha]_D^{25} +52.1°$. Since the reduction of the ketone (+)-XIII should result in the formation of the inactive hydrocarbon XIV (as was proved by Wolf–Kishner reduction of the pure (+)-XIII), the only con-tribution to the rotation must be due to twistane present in the mixture. Consequently, the specific rotation of the reduction product should be $[\alpha]_D^{25}$ 51.9° (calculated from the optical rotation of twistane given in ref.[14]); this is in excellent agreement with
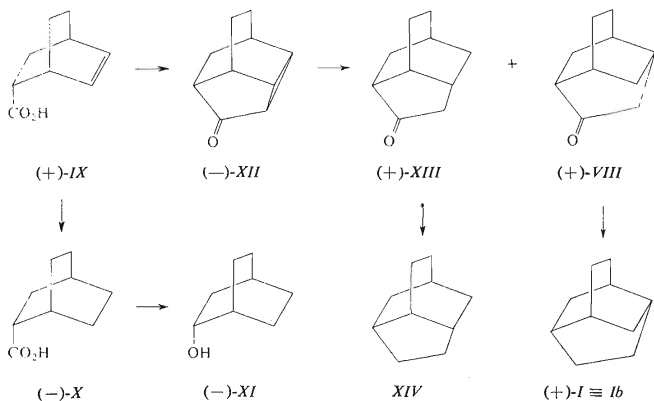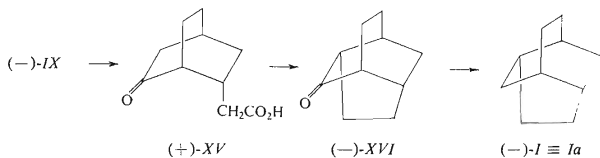

SCHEME 2

the value found. Repeated chromatography separated $(+)$-*VIII*, $[\alpha]_D^{25} +281°$ (corresponding to 95% optical purity — the same as had the starting acid $(+)$-*IX*).

Now, if the acid $(+)$-*IX* has the 2*R* configuration as depicted in Scheme 2, the $(+)$-4-twistanone $((+)$-*VIII*) and $(+)$-twistane $((+)$-*I*) obtained by the shown reaction sequence must have the configuration *M* and not *P* as concluded previously[11,14].*

In order to verify this finding we carried out another sequence of reactions based on the work of Whitlock[10] (Scheme 3) which correlates the acid *IX* with the keto acid *XV* of Adachi[11]. The acid $(-)$-*IX*, (46% optical purity) afforded the dextrorotatory keto acid $(+)$-*XV*, $[\alpha]_D^{25} +16·4°$ (43% optical purity), $\Delta\varepsilon_{295} - 0·25$. In accord with the work of the Japanese authors[11], $(+)$-*XV* was transformed into $(-)$-*XVI* and further into $(-)$-twistane $((-)$-*I*), $[\alpha]_D^{25} -183·0°$ (42% optical purity). The result, thus, is again the same as the result of the preceding correlation (Scheme 2), $(-)$-twistane being related to $(-)$-*IX* and thus being represented by the enantiomer *Ia*. From these data it is evident that the hitherto accepted absolute configuration of twistane is to be reversed.

$(-)$-*IX* → $(+)$-*XV* $(-)$-*XVI* $(-)$-*I* ≡ *Ia*

SCHEME 3

The Applicability of Various Optical Rules to Twistane Derivatives

The present results show that in the case of compounds *VIII*, *XVI* and *XV* the Octant rule[12] and the Klyne–Djerassi rule[13] failed to give the correct answer. The reason for this failure is undoubtedly an ambiguity of application of these rules to twistane structures: *e.g.* according to the Klyne–Djerassi rule, (*M*)-2-twistanone $((+)$-*XVI*) should exhibit a large negative Cotton effect as a result of the sense of the twist of the central ring, whereas the application of the Octant rule leads to a positive Cotton effect (the two substituents nearest to the carbonyl group are in positive octants). Similar situation exists in the case of 4-twistanone where the Octant rule

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* This revision of absolute configuration shows that $(-)$-*endo*-bicyclo[2,2,2]octane-2,5-dicarboxylic acid $((-)$-*II*, Scheme 1), used as the starting material for synthesis of $(+)$-*I*, has in fact 2*R*,5*R*-configuration and not 2*S*, 5*S* as published previously[14].

affords two contradictory results, depending on which of the two six-membered rings is taken as the basis for the octant treatment. It is evident that in these cases the rules are plainly not applicable because of ambiguity of their application.*

In order to obtain information about the extent of the failure of these optical methods we examined chiroptical properties of another type of twistane derivatives, in which the absolute configuration could be deduced from the O—C—C—O segment, applying the dibenzoate method of Nakanishi[20]. Thus, the CD-curve of $(+)$-(M)-cis-twistane-4,5-diol dibenzoate $((+)$-$VI)$ in ethanol exhibits two maxima, the first being positive $(\Delta\varepsilon_{236} +10\cdot0)$ and the second negative $(\Delta\varepsilon_{221} -3\cdot2)$. The same result was obtained with an equimolar mixture of $(+)$-(M)-cis-4,5-twistanediol $((+)$-$IV)$ and tris-dipivaloylmethane europium[21] in tetrachloromethane $(\Delta\varepsilon_{312} +4\cdot2, \Delta\varepsilon_{288} -2\cdot3)$, and with the corresponding thiocarbonyl derivative[22] $(+)$-V of the same absolute configuration $(\Delta\varepsilon_{311} +1\cdot0, \Delta\varepsilon_{255} -0\cdot5)$. The CD-curves of all the three compounds are in accord with a O—C—C—O segment of right-handed chirality[20-22], (Fig. 1B) which corresponds to the absolute configuration found by the chemical correlation. This agreement is probably not fortuitous: in the vicinal derivatives such as dibenzoate the sign of the Cotton effect is determined by the interaction between two (benzoate) chromophores located in a chiral segment "on the periphery" of the molecule, and therefore it is expected to be only little influenced by the chirality of the whole skeleton. Moreover, contrary to the case of the mentioned ketones $VIII$ and XVI, the way how to consider the spatial arrangement of the segment is unequivocal.
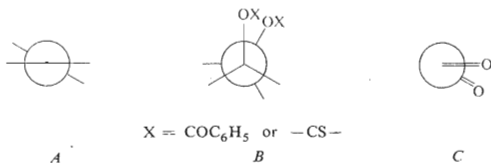

$$X = COC_6H_5 \quad \text{or} \quad -CS-$$

FIG. 1

Projections of a Twisted Double Bond (A), a XO—C—C—OX Segment (B) and a α-Diketone Segment (C) of Right-handed Chirality

On the basis of our[1,14] and Adachi's[11] results, Snatzke[19] concluded that the application of the Octant rule to compounds $(+)$-$VIII$, $(+)$-XVI and $(-)$-XV leads also to results, which agree with the revised absolute configuration, "if applied correctly". We are now, however, of the opinion that to speak in this context about a "correct application" is reasonable only if one already knows the correct answer, and that no serious configurational assignments can be made when there is *a priori* more than one possibility how to apply the rules.

Recently, Hug and Wagnière[23] have calculated that the sign of the $n - \pi^*$ transition Cotton effect (in the 400 nm region) is positive when the helicity (twist) of a cisoid 1,2-dione is right-handed (Fig. 1C). This conclusion was questioned[24], mainly on conformational grounds. A compound, which would be of interest in this connection, would be 4,5-twistanedione (*XVIII*), a rigid, non-enolisable, 1,2-diketone of known absolute configuration. We prepared this derivative by oxidation of the optically active acyloin *XVII* by the dimethyl sulphoxide–acetic anhydride method[25]. The CD-curve of $(-)$-(P)-4,5-twistanedione $((-)$-*XVIII*) exhibits in dioxan three maxima, $\Delta\varepsilon_{445}$ $-1\cdot26$, $\Delta\varepsilon_{282}$ $-1\cdot18$, and $\Delta\varepsilon_{217}$ $+3\cdot17$. The negative sign in the 400 nm region is in accord with the conclusions of Wagnière. Also here, however, one must be careful, as the negative Cotton effect in the 400 nm region might be affected decisively by the chirality of the whole molecular framework (as it presumably is in the case of the ketones).
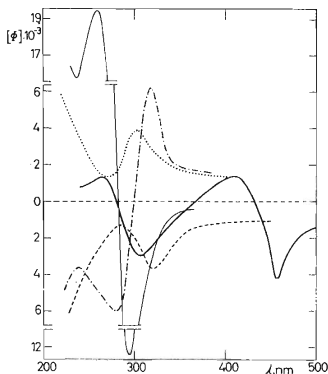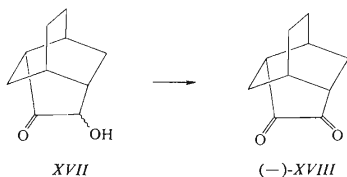

XVII $(-)$-*XVIII*

Fig. 2

ORD- Curves of Compounds $(+)$-*VIII*, $(-)$-*XII*, $(+)$-*XIII* and $(-)$-*XVIII* ——— $(-)$-*XVIII* in dioxan, — — — $(-)$-*XVIII* in methanol, ... $(+)$-*VIII* in ethanol, —·—·— $(+)$-*XIII* in ethanol, ------- $(-)$-*XII* in ethanol.

Another twistane derivative, which promised to be a valuable model, is optically active twistene, with its double bond twisted by about 20° and with a known sense of twist. Scott and Wrixon[26] have proposed a rule, according to which an olefin, twisted in the sense depicted in Fig. 1*A* should exhibit a negative Cotton effect due to $\pi - \pi^*$ transition. Recent calculation of Lewine and Hoffmann[27] suggest that the dominant contribution to the sign of the Cotton effect is that of torsion in the olefin chromophore.

The CD-curve of (*M*)-twistene ((+)-*VII*) at 200 nm is positive $(\Delta\varepsilon +11\cdot6)$; much of its optical activity in the visible region derives from Cotton effects in the vacuum ultraviolet region of a similar type to those of (*M*)-twistane. The positive CD curve contradicts the Scott–Wrixon rule: presumably the "permolecular" chirality here prevails over the torsional contribution.

It is interesting to note that also the heterocyclic analogue, (*P*)-2,7-dioxatwistane[28], has the same sense of optical rotation ($[\alpha]_D^{20}$ $-217°$) as has (*P*)-twistane itself. Similarly, (*P*)-4-azatwistane exhibits a negative sign of optical rotation ($[\alpha]_D^{20}$ $-423°$) (ref.[29]). This indicates that in compounds of this structure the optical rotation is determined predominantly by the molecular framework and only to a small extent by other factors, such as heteroatoms, substituents or unsaturation.

EXPERIMENTAL

(+)-(2S,5S)-endo,endo-Bicyclo[2,2,2]octane-2,5-dicarboxylic Acid ((+)-II)

A solution of (±)-*II* (ref.[18]) (25 g) in warm ethanol (100 ml) was added to a solution of brucine (50 g) in warm ethanol (200 ml). After cooling, the separated salts were filtered off and washed with a small amount of cold ethanol. Crystallisation from boiling water (2·5 l) afforded the almost pure salt of (−)-*II* (29 g). The mother liquors were taken to dryness and crystallised twice from hot water affording the brucine salt of (+)-*II* (10·9 g), m.p. 154–156°C, $[\alpha]_D^{25}$ $-44\cdot6°$ (*c* 0·5, dimethylformamide). The liberated (+)-*II* melted at 198–199°C, $[\alpha]_D^{25}$ $+125\cdot3°$ (*c* 0·5, methanol).

(+)-(M)-cis-4,5-Dihydroxytricyclo[4,4,0,0³,⁸]decane ((+)-IV)

Esterification of (−)-(2R,5R)-endo-2,5-bicyclo[2,2,2]octanedicarboxylic acid[18], (−)-*II*, $[\alpha]_D^{25}$ $-125\cdot0°$ (*c* 0·5, methanol), (12·2 g) with diazomethane gave 13·9 g (98·8%) of the diester (−)-*III*, m.p. 35·5–36·5°C, $[\alpha]_D^{25}$ $-89\cdot5°$ (*c* 0·5, methanol). For $C_{12}H_{18}O_4$ (226·3) calculated: 63·70% C, 8·02% H; found: 63·70% C, 8·07% H. The diester (−)-*III* (13·2 g) was transformed in 33% yield into (+)-*IV*, m.p. 173–173·5°C (ethyl acetate), $[\alpha]_D^{25}$ $+335\cdot8°$ (*c* 0·5, methanol), essentially as described in ref.[18]. For $C_{10}H_{16}O_2$ (168·2) calculated: 71·39% C, 9·59% H; found: 71·31% C, 9·76% H. Dibenzoate, (+)-*VI*, m.p. 85°C (methylcyclohexane) was prepared in 89% yield by benzoylation of (+)-*IV* in pyridine followed by chromatography on a silica gel column with pentane –ether (2 : 1) as eluant; $[\alpha]_D^{25}$ $+164\cdot4°$ (*c* 0·5, ethanol), $\Delta\varepsilon_{236}$ $+10\cdot0$, $\Delta\varepsilon_{221}$ $-3\cdot2$ (ethanol), IR -spectrum: 1 120, 1 280, 1 724 cm⁻¹ (OCOC₆H₅). For $C_{24}H_{24}O_4$ (376·3) calculated: 76·57% C, 6·43% H; found: 76·54% C, 6·37% H. A mixture of (+)-*IV* and Eu(DPM)₃ in tetrachloromethane (0·36 mg (+)-*IV* in 25 ml; molar ratio 1 : 1) had $\Delta\varepsilon_{312}$ $+4\cdot2$, $\Delta\varepsilon_{288}$ $-2\cdot3$.

(+)-(M)-Tricyclo[4,4,0,0^{3,8}]dec-4-ene ((+)-VII)

The diol (+)-IV (2·8 g) was treated with thiocarbonyl-bis-imidazol[18] to give 2·4 g (69%) of its cyclic thiocarbonyl derivative (+)-V, m.p. 225°C (ethyl acetate), $[\alpha]_D^{25} +218·2°$ (c 0·5, ethanol); $\Delta\varepsilon_{311} +1·0$, $\Delta\varepsilon_{255} -0·5$ (dioxane). For $C_{11}H_{14}O_2S$ (210·2) calculated: 62·85% C, 6·71% H; found: 62·98% C, 6·77% H. Transformation of (+)-V into (+)-VII was carried out exactly as described for the racemic compound[18]. The product had the same retention time on gas liquid chromatogram as the racemic compound and melted at 119—120°C, $[\alpha]_D^{25} +416·9°$ (c 0·4, ethanol). ORD (ethanol): plain curve $[\Phi]_{600} +540$, $[\Phi]_{500} +740$, $[\Phi]_{400} +1\,330$, $[\Phi]_{320} +2\,600$. CD (ethanol): $\Delta\varepsilon_{200} +11·7$.

(+)-(M)-Tricyclo[4,4,0,0^{3,8}]decane ((+)-I)

Hydrogenation of (+)-VII gave the title compound in 90% yield, m.p. 161—163·5°C, $[\alpha]_D^{25} +434·4°$ (c 0·48, ethanol). ORD (ethanol): plain curve, $[\Phi]_{500} +790$, $[\Phi]_{400} +1\,380$, $[\Phi]_{320} ++2\,480$.

(+)-(M)-Tricyclo[4,4,0,0^{3,8}]decan-4-one ((+)-VIII)

A stirred mixture of (+)-VII (199·6 mg) and sodium borohydride (37 mg) in diglym (1·5 ml) was treated with boron trifluoride etherate (170 mg) in diglym (1·0 ml) under nitrogen at 0°C, stirred for one hour, treated with sodium hydroxide (30 mg) in water (0·6 ml) followed by 30% hydrogen peroxide (0·4 ml) and stirred for another hour. The reaction mixture was poured into water, extracted four times with pentane, the combined organic layers three times with water and the solvent was evaporated. The residue was dissolved in acetone (10 ml), cooled to 0°C and the stirred solution was oxidized with chromium trioxide (200 mg) and sulphuric acid (0·15 ml) in water (1 ml). After 10 minutes the mixture was taken between pentane and water, the organic layer was taken down and the residue chromatographed on a silica gel column (40 g). Elution with pentane–ether (4 : 1) followed by sublimation afforded 105 mg (47%) of pure (+)-VIII, m.p. 172—174°C, $[\alpha]_D^{25} +295·2°$ (c 0·5, ethanol). ORD (ethanol): $[\Phi]_{400} +1\,300$, $[\Phi]_{302} +3\,800$, $[\Phi]_{271} +1\,300$, $[\Phi]_{240} +2\,120$. CD (ethanol): $\Delta\varepsilon_{285.5} +0·88$. m/e 150.

(+)-(2R)-endo-Bicyclo[2,2,2]oct-5-ene-2-carboxylic Acid ((+)-IX)

A hot solution of the racemic acid (±)-IX (refs[30,31]) (32·4 g) in ethanol (300 ml) was treated with a hot solution of (+)-1-(β-naphthyl)ethylamine[32] (35·2 g) in ethanol (1 200 ml). The separated salt was crystallised six times from ethanol, m.p. 206·5—209°C, $[\alpha]_D^{25} +41·3°$ (c 0·5, dimethylformamide), yield 9·6 g. For $C_{21}H_{25}NO_2$ (323·4) calculated: 77·99% C, 7·79% H, 4·33% N; found: 78·07% C, 8·15% H, 4·29% N. From this salt the acid (+)-IX was liberated by treatment with hydrochloric acid, m.p. 46—47°C, $[\alpha]_D^{25} +50·9°$ (c 0·45, methanol). Further crystallisations of the salt did not alter its constants as well as the constants of the liberated acid. For $C_9H_{12}O_2$ (152·2) calculated: 71·03% C, 7·95% H; found: 71·30% C, 8·12% H.

The combined mother liquors from the crystallisations of the above (+)-salt were taken down and the acid enriched in the (−)-enantiomer was liberated with dilute hydrochloric acid and transformed into its salt with (−)-1-(β-naphthyl)ethylamine. Two crystallisations of this salt afforded (−)-IX, $[\alpha]_D^{25} -23·6°$ (0·5, methanol) : this corresponds to 46% optical purity.

(—)-(2R)-Bicyclo[2,2,2]octane-2-carboxylic Acid ((—)-X)

A solution of (+)-IX, $[\alpha]_D^{25}$ +48·2° (95% optical purity) (102·4 mg), in ethanol (5 ml) was hydrogenated over Adams catalyst (71 mg). The usual work-up procedure afforded 81·3 mg of (—)-X, m.p. 64·5—66°C (without crystallisation), $[\alpha]_D^{25}$ —52·2° (c 0·4, methanol), $[\alpha]_D^{25}$ —61·5° (c 6·8, chloroform). For $C_9H_{14}O_2$ (154·2) calculated: 70·10% C, 9·15% H; found: 70·07% C, 9·32% H.

(—)-(6R)-Tetracyclo[4,4,0,0²,⁴,0³,⁸]decan-5-one ((—)-XII)

A solution of (+)-IX ($[\alpha]_D^{25}$ +45·7°) (4·0 g) in thionyl chloride (7 ml) was stirred for 2 hours, the excess of thionyl chloride removed by stirring for 45 min at 0·5 Torr, and the residue dissolved in ether (40 ml). This solution was added to a stirred ethereal diazomethane (5·2 g in 250 ml of ether) at 0°C and the mixture was stirred for 1 hour. The solvent was removed under reduced pressure, the crystalline diazo ketone dissolved in cyclohexane (170 ml) and boiled for 1 hour with copper bronze (1·5 g). The catalyst was filtered off, the filtrate taken down and the residue chromatographed on a silica gel column (200 g). Elution with pentane-ether (3 : 1) followed by sublimation gave 2·6 g of the ketone (—)-XII, m.p. 108—109°C; $[\alpha]_D^{25}$ —49·4° (c 0·5, methanol); $\Delta\varepsilon_{279}$ —8·2; ORD (in ethanol): $[\Phi]_{350}$ —600, $[\Phi]_{295}$ —12 400, $[\Phi]_{282}$ 0, $[\Phi]_{259}$ +19 400, $[\Phi]_{240}$ +15 200.

(+)-(3S)-Tricyclo[4,3,1,0³,⁷]decan-4-one ((+)-XIII)

The tetracyclic ketone (—)-XII from the preceding experiment was reduced with lithium in liquid ammonia as described for the racemic compound[18]. The chromatographically pure product melted at 114—115°C; $[\alpha]_D^{25}$ +97·8° (c 0·5, methanol). CD (ethanol): $\Delta\varepsilon_{300}$ +2·7; ORD (ethanol): $[\Phi]_{350}$ +1 900, $[\Phi]_{318}$ +6 200, $[\Phi]_{301}$ 0, $[\Phi]_{280}$ —6 000, $[\Phi]_{240}$ —3 500.

Tricyclo[4,3,1,0³,⁷]decane (XIV)

A mixture of (+)-XIII (128 mg), triethylene glycol (5 ml), 100% hydrazine hydrate (1 ml) and acetic acid (0·04 ml) was heated to 100°C for 6 hours. Potassium hydroxide (1·0 g) was added and the mixture was heated to 200—210°C for 8 hours. The mixture was diluted with water, the product extracted with pentane and the pentane solution passed through an activated silica gel column (10 g), taken down (column) and the residue sublimed, m.p. 88—90°C, undepressed on admixture with a specimen prepared from (±)-XIII; $[\alpha]_D^{25}$ —0·1 ± 0·2° (c 1·0, ethanol); yield 94 mg.

Catalytic Reduction of the Ketone (—)-XII

An ethanolic solution (40 ml) of (—)-XII, $[\alpha]_D^{25}$ —49·4°, 90% optical purity, (2·0 g) was hydrogenated over 5% Pd on calcium carbonate (6·0 g). The consumption of hydrogen was 324 ml (107%). After the usual work-up procedure the product (1·9 g) containing 12·5% of (+)-VIII (gas–liquid chromatography) had $[\alpha]_D^{25}$ +117·4° (c 0·5, methanol) and was chromatographed (1·5 g) on a silica gel column (200 g) using a pentane–ether mixture (5 : 1) as eluant. The last fractions, enriched in (+)-VIII, were chromatographed twice on silica gel (40 g) using the same solvent system. The pertinent fractions were combined and the product was sublimed giving 26·6 mg of the completely pure (+)-VIII (gas–liquid chromatography and IR spectra), $[\alpha]_D^{25}$ +281° (c 0·5, ethanol), $\Delta\varepsilon_{285}$ +0·82 (ethanol). Purification of the first fractions from the first chromatography afforded (+)-XIII, m.p. 112—114°C, $[\alpha]_D^{25}$ +96·6° (c 0·5, ethanol).

A part of the reduction product (334 mg) containing 12·5% of (+)-*VIII* was heated with triethylene glycol (8 ml), 100% hydrazine hydrate (2 ml) and acetic acid (0·08 ml) to 90°C for 6 hours, potassium hydroxide (2·5 g) was added and the mixture refluxed for 6 hours. After dilution with water the product was taken up into pentane, passed through an activated silica gel column (10 g), the solvent taken down and the residue sublimed, affording 236 mg of hydrocarbons, containing 12·7% of (+)-*I* (gas-liquid chromatography), $[\alpha]_D^{25} +52·1°$ (0·5, ethanol).

(−)-(*P*)-Tricyclo[4,4,0,0³,⁸]decan-2-one ((−)-*XVI*)

This compound was prepared essentially according to Whitlock and Siefken[10]. In all experiments, except for the iodo-lactonisation, no product was purified by crystallisation. The product of one step was either used directly in the subsequent step in the crude state or it was purified only by column chromatography. (−)-(2*S*)-endo-Bicyclo[2,2,2]oct-5-ene-2-carboxylic acid ((−)-*IX*), $[\alpha]_D^{25} −23·6°$ (*c* 0·5, methanol) −46% optical purity − (8·3 g) was transformed into its methyl ester by treatment with diazomethane. The resulting crude ester was reduced to (−)-(2*S*)-endo-2-hydroxymethylbicyclo[2,2,2]oct-5-ene, b.p. 108°C/10 Torr, $[\alpha]_D^{25} −4·4°$ (*c* 0·69, methanol), yield 6·7 g. This compound was transformed into its methanesulphonate which was subjected without purification to reaction with sodium cyanide followed by hydrolysis with potassium hydroxide in ethylene glycol. The yield of the resulting (−)-(2*R*)-endo-bicyclo[2,2,2]oct-5-en-2-acetic acid, m.p. 38—41°C, was 6·2 g; $[\alpha]_D^{25} −5·6°$ (*c* 1·0, methanol). Iodolactonisation of the crude acid afforded the corresponding iodolactone which on one crystallisation from ethyl acetate (0°C) melted at 121—125°C, $[\alpha]_D^{25} +79·5°$ (*c* 1·0, chloroform), yield 7·0 g. Mother liquor from this crystallisation was taken to dryness (1·2 g), $[\alpha]_D^{25} +122·7°$ (*c* 1·00, chloroform). Hydrogenation of the iodolactone (7·0 g) in the presence of triethylamine gave 3·3 g of the lactone of (2*R*)-endo,endo-6-hydroxybicyclo[2,2,2]octane-2-acetic acid, m.p. 64—67°C. This lactone (2·2 g) was reduced with lithium aluminium hydride to (+)-(2*R*)-endo,endo-6-hydroxy-2-(2′-hydroxyethyl)bicyclo[2,2,2]octane, m.p. 71—74°C, $[\alpha]_D^{25} +22·4°$ (*c* 0·5, chloroform), yield 1·7 g. Oxidation of this diol (111 mg) with Jones reagent afforded (+)-(2*R*)-endo-6-oxobicyclo-[2,2,2]octane-2-acetic acid ((+)-*XV*), m.p. 64—65°C, in 80% yield; $[\alpha]_D^{25} +16·4°$ (*c* 0·6, ethanol), corresponds to 43·5% optical purity; $\Delta\varepsilon_{295} −0·25$, corresponds to 41% optical purity[11].

(+)-(2*R*)-endo,endo-6-Hydroxy-2-(2′-hydroxyethyl)bicyclo[2,2,2]octane (1·35 g) was transformed *via* the oxomethanesulphonate (1·3 g) into (−)-(*P*)-tricyclo[4,4,0,0³,⁸]decan-2-one ((−)-*XVI*) (0·50 g) which after chromatography on silica gel melted at 192—196°C and had $[\alpha]_D^{25} −205·6°$ (*c* 0·6, ethanol) which corresponds to about 50% optical purity[11], $\Delta\varepsilon_{291} −0·59$ (*c* 0·069, ethanol), *i.e.* about 54% optical purity. Wolf–Kishner reduction afforded (−)-(*P*)-tricyclo-[4,4,0,0³,⁸]decane (twistane) ((−)-*I*), $[\alpha]_D^{25} −183·0°$ (*c* 0·5, ethanol), 42% optical purity[14].

(−)-(*P*)-Tricyclo[4,4,0,0³,⁸]decane-4,5-dione ((−)-*XVIII*)

Acyloin condensation of (+)-*III* (3·7 g; prepared from (+)-*II* by treatment with diazomethane), $[\alpha]_D^{25} +88·9°$ (*c* 0·7, methanol) was carried out as described for the racemate[18] and afforded 1·4 g of the acyloin *XVII*, b.p. 96°C/0·1 Torr.

A mixture of *XVII* (408·8 mg), dimethyl sulphoxide (6 ml) and acetic anhydride (4 ml) was allowed to stand for two days. The mixture was diluted with water, extracted with ether (5×), the organic layer washed with water (4×), dried and taken down. The residue was chromatographed on silica gel column (50 g) with benzene–ether (10 : 1) as eluant, yielding 88·8 mg of the yellow product, which was sublimed *in vacuo* and crystallised from methylcyclohexane, m.p.

204—206°C (sealed capillary), $[\alpha]_D^{20}$ —326° (c 0·2, methanol). ORD (dioxan): $[\Phi]_{500}$ —1 440, $[\Phi]_{457}$ —4 180, $[\Phi]_{410}$ +1 370, $[\Phi]_{309}$ —2 880, $[\Phi]_{263}$ +1 300, $[\Phi]_{250}$ +870, ORD (methanol): $[\Phi]_{450}$ —1 070, $[\Phi]_{324}$ —3 530, $[\Phi]_{287}$ —1 230, $[\Phi]_{240}$ —4 680. CD (dioxan): $\Delta\varepsilon_{473}$ 0, $\Delta\varepsilon_{445}$ —1·26, $\Delta\varepsilon_{354}$ 0, $\Delta\varepsilon_{282}$ —1·18, $\Delta\varepsilon_{244}$ 0, $\Delta\varepsilon_{217}$ +3·17. For $C_{10}H_{12}O_2$ (164·2) calculated: 73·15% C 7·37% H; found: 72·79% C, 7·44% H.

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