Synthesis and Absolute Configuration of (−)-Bisnoradamantan-2-one [(−)-Tricyclo[3.3.0.0^{3,7}]octan-2-one]

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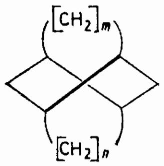
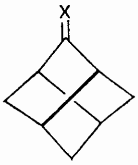
Summary (−)-Tricyclo[3.3.0.0^{3,7}]octane-2-carboxylic acid (**6**) was converted into (−)-bisnoradamantan-2-one (**5**) whose c.d. spectrum indicated the (1*R*,3*R*,5*R*,7*R*) absolute configuration.

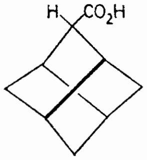
Bridging the 1,4- and 2,5-positions of cyclohexane with polymethylene chains affords rotatory chiral (gyrochiral)[1] tricyclic compounds (**1**; $m \neq n \neq 1$); we reported syntheses and absolute configurations of two representative compounds, (+)-twistane (**2**) having D_2 symmetry,[2] and (+)-twist-brendane (**3**) having C_2 symmetry.[3] These compounds have an intrinsically chiral framework which is in contrast to tricyclo[3.3.0.0^{3,7}]-octane ('bisnoradamantane')[4] (**4**) which has D_{2d} symmetry and is achiral. Molecular models show that (**4**) consists of two enantiomeric D_2-twisted cyclohexane species fused together resulting in two pairs each of enantiotopic and homotopic methylene groups.



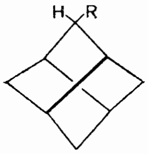
(1)
(2), $m = n = 2$
(3), $m = 1, n = 2$



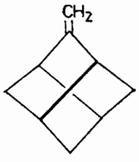
(4), X = H_2
(5), X = O



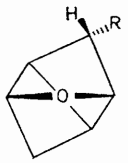
(6)



(7), R = $CONMe_2$
(8), R = CH_2NMe_2
(9), R = $CH_2\overset{\downarrow}{N}Me_2$ O



(10)



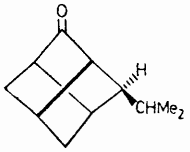
(11), R = H
(13), R = $CHMe_2$

Table. C.d. spectra of (−)-bisnoradamantan-2-one (**5**) and (1*R*,3*R*,4*S*,5*R*,7*R*)-4-isopropylbicyclo[3.3.0.0^{3,7}]octan-2-one (**12**) in iso-octane.

Compound	λ/nm	[θ]
(**5**)	281·6sh	$-9{\cdot}71 \times 10^3$
	286·3	$-1{\cdot}05 \times 10^4$
	290·4sh	$-9{\cdot}91 \times 10^3$
	296·2sh	$-7{\cdot}77 \times 10^3$
(**12**)	299·5	$-2{\cdot}48 \times 10^3$
	304sh	$-2{\cdot}43 \times 10^3$

Conversion of one of the methylene groups into an oxo-group breaks the D_{2d} symmetry furnishing bisnoradamantan-2-one (**5**) with C_2 symmetry. As part of a program to synthesise high symmetry chiral cage compounds, we report here the synthesis and absolute configuration of (**5**).

Optical resolution of racemic tricyclo[3.3.0.0^{3,7}]octane-2-carboxylic acid[5] (**6**) *via* the (+)-2-(1-aminoethyl)naphthalene salt furnished (−)-(**6**) {$[\alpha]_D^{14}$ − 22·5° ($CHCl_3$), m.p. 85—86 °C}. Treatment of (**6**) with thionyl chloride in benzene, followed by anhydrous dimethylamine, produced the (−)-dimethylamide (**7**) {$[\alpha]_D^{12}$ − 3·2° ($CHCl_3$), m.p. 82—84 °C}.† Compound (**7**) was reduced with $LiAlH_4$ to give the (+)-dimethylaminomethyl derivative (**8**) {$[\alpha]_D^{13}$ +5·7° ($CHCl_3$), b.p. 102—103 °C at 20 mmHg} which, on treatment with hydrogen peroxide, afforded the amine oxide (**9**). Pyrolysis of (**9**) gave the olefin (**10**) {$[\alpha]_D^{12}$ − 29·7° ($CHCl_3$), [θ] − 6·96 × 10^4 at 192 nm (iso-octane), b.p. 92—93 °C at 120 mmHg, yield 59%} whose structure was confirmed by i.r. [ν(film) 3060, 1683, and 860 cm^{-1}] and ^1H n.m.r. [δ(CCl_4) 1·42 (6H, s), 2·38 (4H, m), and 4·09 (2H, s)] spectroscopy. Ozonization of the olefin (**10**) in methylene chloride followed by treatment with zinc powder and acetic acid, gave (−)-bisnoradamantan-2-one (**5**) {33%, $[\alpha]_D^{13}$ − 55·9° (EtOH), m.p. 103—105 °C}, the i.r. and n.m.r. spectra of which were identical with those of the racemic form prepared by Sauers' procedure.[6]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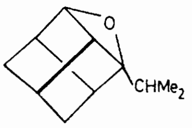
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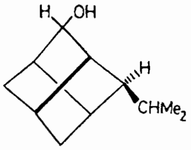
(15)

C.d. spectra[2,3,7] of various tricyclic ketones, prepared from intermediates of known absolute configurations, indicate that the sign of c.d. curve due to the *n*–π* transition around 300 nm can be predicted by applying the octant rule to the 'outer ring'[8] in the projection formula which holds the carbonyl group at the 'point of twist'.[9] Applying this generalization to (−)-bisnoradamantan-2-one (**5**) with a negative Cotton effect (see Table), we assigned the absolute configuration (**11**) which led to the absolute configuration (−)-(1*R*,3*R*,5*R*,7*R*)-tricyclo[3.3.0.0^{3,7}]octan-2-one. This conclusion was further supported by the negative Cotton effect (see Table) exhibited by (1*R*,3*R*,4*S*,5*R*,7*R*)-4-isopropyltricyclo[3.3.0.0^{3,7}]octan-2-one (b.p. 125 °C at 20 mmHg) (**12**) whose projection formula can be illustrated as (**13**). Compound (**12**) was prepared from the (−)-oxetane (**14**) with known absolute configuration[7] *via* the secondary alcohol[10] (**15**) {$[\alpha_D^{17}]$ +2·8° (EtOH), b.p. 119—122 °C at 25 mmHg}.

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† Satisfactory elemental analyses were obtained for new compounds and their i.r. and n.m.r. spectra are in accord with the assigned structures.

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