Crystal Structure of a Cyclohexanespiropropane Derivative Prepared from 1-(Nitromethyl)-1,2-epoxycyclohexene and Methyl Sodiocyanoacetate

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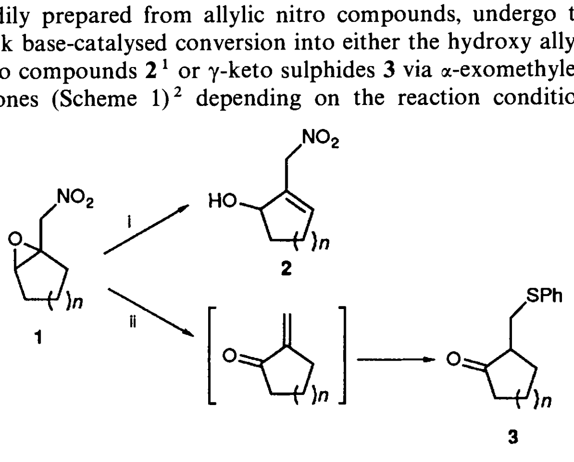
The structure of 2-hydroxycyclohexanespiro(2′-cyano-2′-methoxycarbonyl)cyclopropane, prepared by the reaction of 1,2-epoxy-1-(nitromethyl)cyclohexane with methyl sodiocyanoacetate, has been determined from X-ray diffraction data. There are two independent molecules in an asymmetric unit. The geometry of cyclopropane is discussed.

We have recently reported that β,γ-epoxy nitro compounds **1**, readily prepared from allylic nitro compounds, undergo the weak base-catalysed conversion into either the hydroxy allylic nitro compounds **2**[1] or γ-keto sulphides **3** via α-exomethylene ketones (Scheme 1)[2] depending on the reaction conditions employed. During the course of our studies on the utilization of the β,γ-epoxy nitro compounds as the synthetic equivalent to α-exomethylene ketones, we have obtained an unexpected spiro[2,5]octane derivative **5** as single diastereoisomer in good yield from the reaction of 1-(nitromethyl)-1,2-epoxycyclohexane, **4**, with methyl sodiocyanoacetate. Its structure has been unequivocally determined by X-ray crystallography.



Scheme 1 *Reagents and conditions:* i, Et_3N (0.05 equiv.), CH_3CN; ii, PhSNa (1.0 equiv.), DMF

Experimental

Synthesis.—Sodium hydride (48 mg, 1.20 mmol, 60% dispersion in mineral oil) was placed in a two-necked round-bottom flask equipped with a rubber septum and a stopcock. After washing it with dry pentane (3 × 10 cm^3) and removing pentane under vacuum, the flask was filled with argon through the stopcock and charged with dry *N*,*N*-dimethylformamide (DMF, 9 cm^3) *via* a syringe through the rubber septum. To the slurry was added methyl cyanoacetate, and the mixture was stirred until homogeneous (*ca.* 30 min). 1-(Nitromethyl)-1,2-epoxycyclohexane, **4**, (157 mg, 1.00 mmol) in DMF (1.0 cm^3) was added *via* a syringe and the combined mixture was stirred at 25 °C for 24 h. To the reaction mixture was added saturated aqueous NH_4Cl (50 cm^3). The aqueous mixture was extracted with ether (3 × 30 cm^3). The combined ether extracts were washed with saturated aqueous NaCl (3 × 30 cm^3) and water (30 cm^3), dried ($MgSO_4$) and concentrated *in vacuo*. The remaining methyl cyanoacetate was removed by Kugelrohr distillation. The residual white solid (77%, 161 mg) was almost pure and recrystallized from ether.

5: m.p. 65–66 °C; ν_{max}(Nujol)/cm^{-1} 3400, 2230 and 1730; δ_H(270 MHz; $CDCl_3$) (*J* values in Hz) 3.83 (3 H, s), 3.79 (1 H, br m), 2.00 (1 H, ddd, *J* 13.8, 11.8, 3.0), 1.92–1.65 (5 H, m, *J* 18.5, 14.8, 10.8, 5.5, 4.8), 1.65–1.43 (4 H, m, *J* 16.5, 10.8, 4.8, 3.8) and 1.2 (1 H, m, *J* 13.8, 11.8, 4.0; δ_C(22.5 MHz; $CDCl_3$) 166.2, 118.0, 71.0, 53.5, 42.1, 32.2, 26.3, 24.5, 24.1, 22.9 and 20.2 (Found: C, 63.39; H, 7.20; N, 6.93. Calc. for $C_{11}H_{15}O_3N$: C, 63.14: H, 7.23; N, 6.69%).

X-Ray Structure Analysis.—A colourless rectangular crystal formed by slow evaporation of an ether solution, of dimensions *ca.* 1.0 × 0.5 × 0.5 mm was used. The lattice parameters were obtained from least-squares analysis of 20 reflections with $20.0 < 2\theta < 40.0°$, from graphite monochromated Mo-*K*α radiation on Rigaku-Denki AFC-III diffractometer. Intensity data of 6418 unique reflections were collected at room temperature by ω–2θ scan technique with θ between 1 and 24.5° and $-18 \leqslant h \leqslant 18$, $0 \leqslant k \leqslant 21$, $-8 \leqslant l \leqslant 8$. Intensity and orientation standards were measured again every 100 reflections; no significant decomposition or movement of the crystal was observed. Corrections were made for Lorentz and polarization but not for absorption effects.

The structure was solved by direct methods (MULTAN78).[3] Some atoms came out from one of the E maps with the highest figure of merit and the remaining non-hydrogen atoms were revealed after successive difference Fourier maps. Block-diagonal least-squares refinements on *F* were performed for positional parameters and anisotropic temperature factors.

All of the hydrogen atoms appeared on difference electron density maps after refinements. However all hydrogen atoms were fixed at calculated positions (with C–H = 1.05 Å, O–H = 0.95 Å). The final *R*, R_w values are 0.076, 0.119 for the 4908 unique reflections $[|F_o| > 3\sigma(F_o)]$. A weighting scheme is $w = [\sigma^2(F_o) - 0.750\,|F_o| + 0.005\,|F_o|^2]^{-1}$. The atomic scattering factors were taken from International Tables for X-ray Crystallography.[4] Calculations were performed with UNICS-NAGOYA[5] on HITAC M-680H of the Computer Center of The National Defense Academy.

Full lists of atomic coordinates and tables of thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. (CCDC).†

Results and Discussion

In order to extend our strategy to use β,γ-epoxy nitro compounds as the synthetic equivalent to α-*exo*-methylene ketones, we examined the reaction with other basic nucleophiles such as stabilized carbanions. However, when 1-(nitromethyl)-

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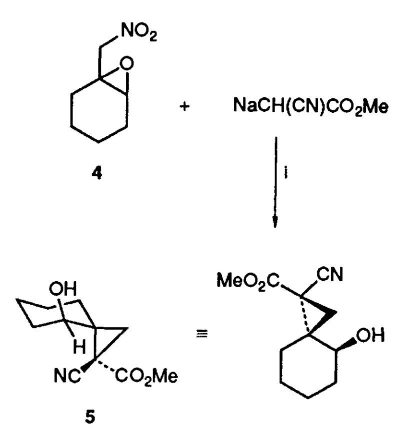
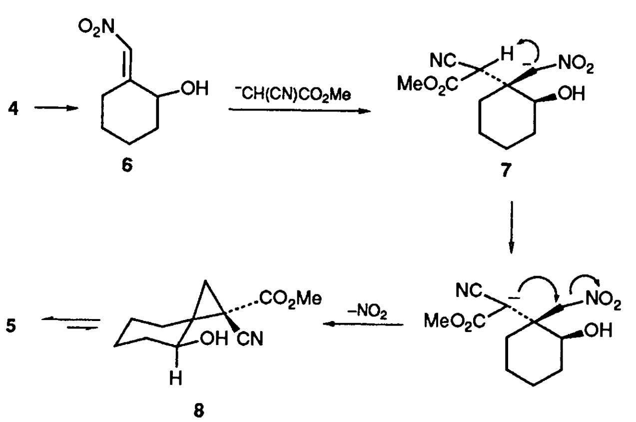
† For details of the deposition scheme, see 'Instruction for Authors (1991),' *J. Chem. Soc., Perkin Trans. 2*, issue 1.



Scheme 2 *Reagents and conditions:* i, DMF, 25 °C, 24 h

Table 1 Final atomic co-ordinates (× 10^4) with esds in parentheses

Atom	*x*	*y*	*z*
O(1A)	2 630(1)	4 037(1)	6 472(3)
O(2A)	975(2)	926(2)	2 817(3)
O(3A)	1 664(1)	848(1)	−670(3)
N(4A)	4 108(2)	1 317((2)	249(4)
C(5A)	2 058(2)	2 640(1)	4 448(4)
C(6A)	891(2)	3 040(2)	4 785(5)
C(7A)	481(2)	3 443(2)	2 804(5)
C(8A)	1 085(2)	4 153(2)	2 654(5)
C(9A)	2 253(2)	3 744(2)	2 301(4)
C(10A)	2 693(2)	3 322(1)	4 239(4)
C(11A)	2 426(2)	1 640(1)	2 789(4)
C(12A)	2 560(2)	1 915(2)	5 502(4)
C(13A)	3 358(2)	1 447(1)	1 333(4)
C(14A)	1 611(2)	1 095(2)	1 703(4)
C(15A)	929(2)	297(2)	−1 942(5)
O(1B)	2 497(2)	5 879(1)	6 921(3)
O(2B)	3 152(2)	9 302(1)	11 338(4)
O(3B)	4 094(2)	8 731(1)	14 015(3)
N(4B)	5 544(2)	6 692(2)	11 360(5)
C(5B)	2 978(2)	7 247(1)	9 157(4)
C(6B)	1 869(2)	7 761(2)	9 948(5)
C(7B)	1 563(2)	7 612(3)	12 263(6)
C(8B)	1 700(3)	6 606(3)	12 002(6)
C(9B)	2 818(2)	6 098(2)	11 166(5)
C(10B)	3 138(2)	6 234(2)	8 878(4)
C(11B)	3 905(2)	7 713(1)	10 264(4)
C(12B)	3 624(2)	7 530(2)	7 633(4)
C(13B)	4 825(2)	7 148(2)	10 873(4)
C(14B)	3 670(2)	8 677(2)	11 886(4)
C(15B)	3 879(3)	9 621(2)	15 815(6)



Scheme 3

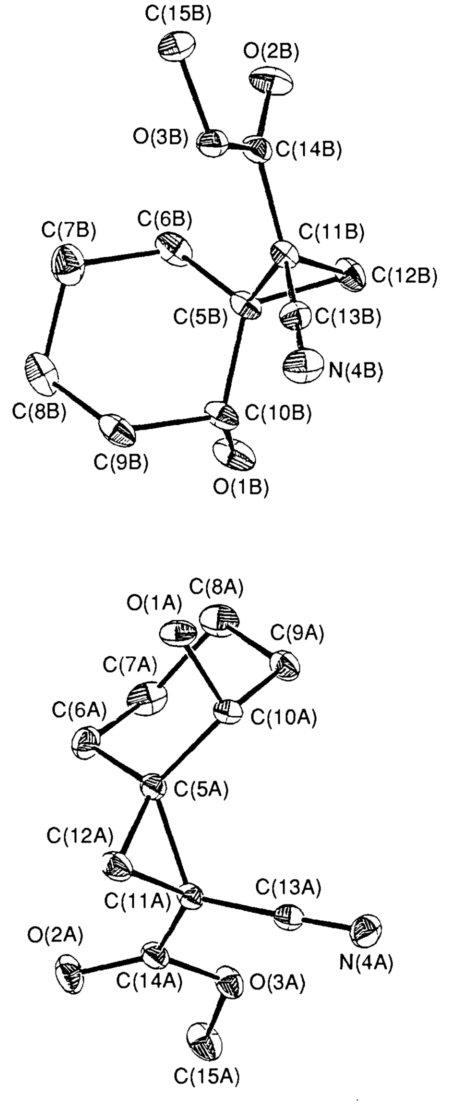


Fig. 1 View of the molecules. Thermal ellipsoids are at the 50% probability level (ORTEP II).[15]

1,2-epoxycyclohexane **4** was allowed to react with methyl sodiocyanoacetate in DMF at 25 °C, contrary to our expectation that the Michael adduct to the α-exomethylene ketone intermediate would be formed, the spiro[2,5]octane derivative **5** was obtained in 77% yield as a single diastereoisomer (Scheme 2). Since the accurate geometry of **5** could not be determined by the NMR studies including the 2D NMR technique, and we needed to know the geometry, for the study on the stereochemistry and the mechanism of this new reaction, the compound was subjected to X-ray crystallographic analysis. As shown below, it was found that three functional groups are arranged so as to diminish the mutual steric repulsion.

From this result we can assume the reaction mechanism is as follows (Scheme 3). The carbanion acts as a base to abstract an acidic α-nitro proton leading to the ring-opening product **6**. Then, prior to the isomerization of the exo-olefin to the endo-isomer, the carbanion adds to the α,β-unsaturated nitro moiety from the face distal to hydroxy group to give adduct **7**. The methoxycarbonyl group of **7** is oriented away from the hydroxy group to avoid steric repulsion. After intramolecular proton exchange between the α-nitro anion and α-cyanoester moiety, intramolecular nucleophilic substitution occurs to give the spiro compound **8**, which must be converted into the more stable conformer **5**. It is noteworthy that a good yield of **5** was obtained, despite such a multistep reaction. Furthermore, it is unusual for a primary nitro group to function as a nucleofuge in a substitution reaction.

We examined the stereoselective synthesis of spiro compounds with analogous five- and seven-membered substrates

Table 2 Bond lengths/Å and angles/° with esds in parentheses

Bond	Length/Å	Bond Angle	Angle/°
O(1A)–C(10A)	1.427(2)	C(14A)–O(3A)–C(15A)	116.0(2)
O(2A)–C(14A)	1.201(3)	C(6A)–C(5A)–C(10A)	112.9(1)
O(3A)–C(14A)	1.328(3)	C(6A)–C(5A)–C(11A)	118.7(1)
O(3A)–C(15A)	1.447(4)	C(6A)–C(5A)–C(12A)	120.7(2)
N(4A)–C(13A)	1.139(3)	C(10A)–C(5A)–C(.11A)	115.7(1)
C(5A)–C(6A)	1.513(3)	C(10A)–C(5A)–C(12A)	118.9(2)
C(5A)–C(10)A	1.523(3)	C(11A)–C(5A)–C(12A)	60.3(1)
C(5A)–C(11A)	1.554(3)	C(5A)–C(6A)–C(7A)	110.8(2)
C(5A)–C(12A)	1.486(3)	C(6A)–C(7A)–C(8)A	111.5(2)
C(6A)–C(7A)	1.521(4)	C(7A)–C(8A)–C(9A)	110.7(2)
C(7A)–C(8A)	1.522(4)	C(8A)–C(9A)–C(10A)	112.3(2)
C(8A)–C(9A)	1.516(4)	O(1A)–C(10A)–C(5A)	108.7(1)
C(9A)–C(10A)	1.525(3)	O(1A)–C(10A)–C(9A)	108.5(1)
C(11A)–C(12A)	1.528(3)	C(5A)–C(10A)–C(9A)	110.9(1)
C(11A)–C(13A)	1.442(3)	C5A)–C(11A)–C(12A)	57.6(1)
C(11A)–C(14A)	1.496(3)	C(5A)–C(11A)–C(13A)	117.1(1)
		C(5A)–C(11A)–C(14A)	118.5(1)
		C(12A)–C(11A)–C(13A)	117.3(2)
		C(12A)–C(11A)–C(14A)	118.6(1)
		C(13A)–C(11A)–C(14A)	115.5(1)
		C(5A)–C(12A)–C(11A)	62.1(1)
		N(4A)–C(13A)–C(11A)	177.5(2)
		O(2A)–C(14A)–O(3A)	124.5(2)
		O(2A)–C(14A)–C(11A)	124.9(2)
		O(3A)–C(14A)–C(11A)	110.6(1)
O(1B)–C(10)B	1.424(3)	C(14B)–O(3B)–C(15B)	116.5(2)
O(2B)–C(14B)	1.195(3)	C(6B)–C(5B)–C(10B)	112.6(2)
O(3B)–C(14B)	1.329(3)	C(6B)–C(5B)–C(11B)	118.5(2)
O(3B)–C(15B)	1.443(4)	C(6B)–C(5B)–C(12B)	121.8(2)
N(4B)–C(13B)	1.137(3)	C(10B)–C(5B)–C(11B)	115.8(1)
C(5B)–C(6B)	1.513(4)	C(10B)–C(5B)–C(12B)	118.2(2)
C(5B)–C(10B)	1.520(3)	C(11B)–C(5B)–C(12B)	60.3(1)
C(5B)–C(11B)	1.551(3)	C(5B)–C(6B)–C(7B)	110.5(2)
C(5B)–C(12B)	1.482(3)	C(6B)–C(7B)–C(8B)	112.0(3)
C(6B)–C(7B)	1.540(5)	C(7B)–C(8B)–C(9B)	110.7(3)
C(7B)–C(8B)	1.514(5)	C(8B)–C(9B)–C(10B)	112.6(2)
C(8B)–C(9B)	1.525(5)	O(1B)–C(10B)–C(5B)	104.9(2)
C(9B)–C(10B)	1.521(4)	O(1B)–C(10B)–C(9B)	111.9(2)
C(11B)–C(12B)	1.524(3)	C(5B)–C(10B)–C(9B)	110.7(2)
C(11B)–C(13B)	1.437(3)	C(5B)–C(11B)–C(12B)	57.6(1)
C(11B)–C(14B)	1.491(3)	C(5B)–C(11B)–C(13B)	117.4(2)
		C(5B)–C(11B)–C(14B)	119.0(2)
		C(12B)–C(11B)–C(13B)	118.6(2)
		C(12B)–C(11B)–C(14B)	118.3(2)
		C(13B)–C(11B)–C(14B)	114.4(2)
		C(5B)–C(12B)–C(11B)	62.1(1)
		N(4B)–C(13B)–C(11B)	178.9(2)
		O(2B)–C(14B)–O(3B)	125.5(2)
		O(2B)–C(14B)–C(11B)	124.0(2)
		O(3B)–C(14B)–C(11B)	110.5(2)

(**1**; $n = 1, 3$). However, although desired spiro compounds were obtained in good yield, stereoselection was not observed in either case; two diastereoisomers, consisting of two epimers at the carbon bearing CN and $COOCH_3$ groups, were formed in an approximately 1:1 ratio.

Crystal Data.—$C_{11}NO_3H_{15}$, $M = 209.2$, triclinic, $a = 13.010(1)$, $b = 15.743(3)$, $c = 5.889(1)$ Å, $\alpha = 108.52(1)$, $\beta = 92.85(1)$, $\gamma = 77.84(1)°$. $V = 1117.9(2)$ Å^3, space group $P\bar{1}$, $Z = 4$, $D_c = 1.243$, $D_x = 1.248(1)$ g cm^{-3}, $\mu = 0.85$ cm^{-1}.

The final atomic co-ordinates with their estimated standard deviations are given in Table 1. The numbering scheme is presented in Fig. 1. The bond distances and angles are shown in Table 2.

There are two independent molecules in an asymmetric unit. Both molecules have similar but not identical conformations. As for the cyclopropane geometry, many studies on cyclopropyl derivatives indicate that π-acceptor substituents produced significant bond-length asymmetry in the ring. The vicinal 1–2, 1–3 bonds are lengthened and the distal 2–3 bond opposite the substituent is shortened.[6–10] This symmetry is explicable in terms of an MO model of cyclopropane bonding.[11–13] From Allen's statistical work,[10] these bond lengths can be estimated as follows: C(5)–C(11) = 1.552, C(11)–C(12) = 1.552, C(5)–C(12) = 1.466 Å. These estimated values do not agree exactly with our observations (Table 2) because we cannot estimate the substituted effect of the spirocyclohexyl group. However, these bond asymmetries are almost explicable in terms of donor–acceptor mixtures of the substituents. The C≡N bond lengths agree well with other workers' values.[8,9] We also observe non-linearity in the C–CN groups (Table 2).[9,14] The cyclohexyl group exists in a chair form. The geometry of the cyclohexyl group agrees well with values reported by Ramasubbu *et al.*[9]

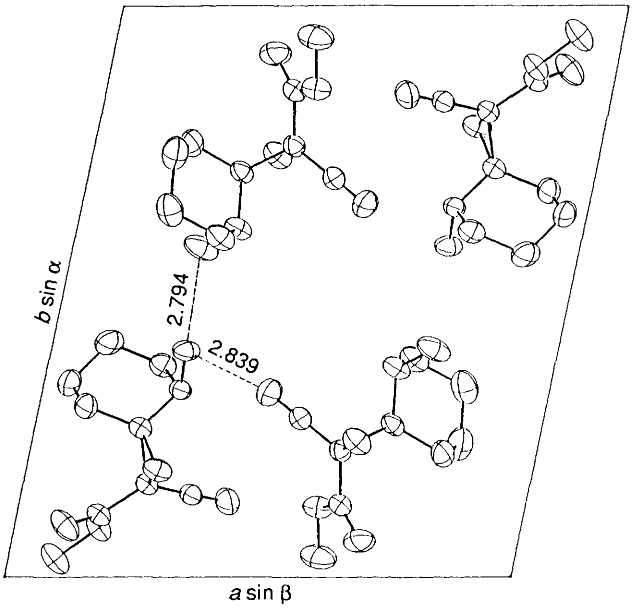


Fig. 2 The packing in the cell

The molecular packing is shown in Fig. 2. There are two kinds of hydrogen bond, one is O(1B)–H···O(1A) (O···O = 2.794 Å, O–H···O = 173.1°), another is O(1A)–H···N(4B) ($1 - x, 1 - y, 2 - z$) (2.839 Å, 132.9°) (Fig. 2).

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