Optically Active Nine-membered Rings incorporating the 8- and 8'-Positions of 1,1'-Binaphthyl. Part 2.[1] Oxygen, Sulphur, and Selenium Heterocycles. Synthesis, 1H Nuclear Magnetic Resonance Spectra, and Absolute Configuration

By **Margaret M. Harris** * and **Piyushbhai K. Patel,** Department of Chemistry, Bedford College, Regent's Park, London NW1 4NS

The preparation of 8-oxa-, 8-thia-, 8-selena-, and 8-dioxothia-8,9-dihydro-7*H*-cyclonona[1,2,3-*de* : 4,5,6-*d'e*']di-naphthalene, racemic and optically active, is described. Enantiomeric forms were synthesised from optically active precursors of known absolute configuration, thus the absolute configurations of the new compounds are established. 1H N.m.r. spectra are discussed.

8,8'-BISBROMOMETHYL-1,1'-BINAPHTHYL reacts with sodiodiethyl malonate to form a nine-membered ring [1] in the same manner as 2,2'-bisbromomethylbiphenyl reacts to give a seven-membered ring. This indication that the geometry of the nucleophilic displacement which closes the ring is favourable for both the substrates has led us to explore further nine-membered ring closures using 8,8'-disubstituted 1,1'-binaphthyls, experimenting with methods previously found successful in the biphenyl seven-membered ring series [2-8] (nine-membered rings incorporating 2,2'-biphenyl are in quite a different category).[7]

2,2'-Bishydroxymethylbiphenyls react with dilute sulphuric acid [2] or with dilute hydrobromic acid [3] to give oxepins, and 2,2'-bisbromomethylbiphenyl forms an oxepin when a solution in aqueous acetone is treated with silver oxide; [5] these conditions failed to give cyclic products from 8,8'-disubstituted 1,1'-binaphthyls: however, 8,8'-bishydroxymethyl-1,1'-binaphthyl did follow the reaction mode of the biphenyl (and 2,2'-disubstituted 1,1'-binaphthyl) series [5,6] when boiled with toluene-*p*-sulphonic acid in benzene and gave the oxonin (1). Little adaptation of the methods used for seven-membered rings [4-6] was needed in order to prepare the nine-membered rings with sulphur (2) or selenium (3) as heteroatom. The dioxothia compound (4) was prepared from (2) by oxidation using hydrogen peroxide.

By starting with the optically active bisbromomethyl-1,1'-binaphthyls or bishydroxymethyl-1,1'-binaphthyls [9] it was possible to prepare both enantiomers of each of the new ring compounds. The substrates are optically labile, but are sufficiently resistant to racemisation to yield optically active cyclic products; the rings when formed are optically stable. The absolute configuration of the optically active precursors is already estab-

lished [10] by notionally stringing together various pieces of synthetic work with optically active compounds into pathways which lead to compounds whose absolute
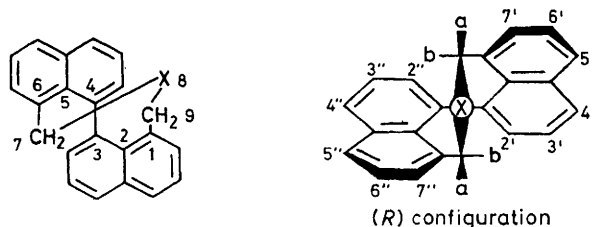
(R) configuration

(1) X = O
(2) X = S
(3) X = Se
(4) X = SO$_2$

configuration is known from asymmetric Meerwein–Ponndorf–Verley reduction [11] or from anomalous *X*-ray diffraction structure determination,[12,13] or by close correspondence of chiroptical properties within a set of related compounds.[6,10,14,15] In this way (+)-(1), (+)-(2), (+)-(3), and (+)-(4) are shown all to have the (*S*)-configuration.

1H N.m.r. Spectra.—Conformational mobility of these nine-membered rings is improbable.[1] The spectra at 100 MHz in deuteriochloroform show clearly defined groups of signals (Table 1). Two well separated doublets [Δ(in Hz)/J 9—11] affirm the chemical shift non-equivalence of the two pairs of diastereotopic [16] geminal protons H$_a$ and H$_b$ (in contrast with the spectra of singly-bridged, otherwise unsubstituted biphenyls which show a sharp singlet in the methylene region, except for the thiepin where there is a small separation, $\Delta\delta$ 0.22

[1] M. M. Harris and S. Singh, *J.C.S., Perkin II*, 1976, 793 is taken as Part I.
[2] D. M. Hall and E. E. Turner, *J. Chem. Soc.*, 1951, 3072.
[3] G. Wittig, P. Davis, and G. Koenig, *Chem. Ber.*, 1951, **84**, 627.
[4] W. E. Truce and D. D. Emrick, *J. Amer. Chem. Soc.*, 1956, **78**, 6310.
[5] K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon, and G. H. Wahl, jun., *J. Amer. Chem. Soc.*, 1964, **86**, 1710.
[6] K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, D. H. Weiss, and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1455.
[7] K. Mislow, S. Hyden, and H. Schaefer, *J. Amer. Chem. Soc.*, 1962, **84**, 1449.
[8] R. E. Buntrock and E. C. Taylor, *Chem. Rev.*, 1968, **68**, 209.
[9] Y. Badar, A. S. Cooke, and M. M. Harris, *J. Chem. Soc.*, 1965, 1412.
[10] H. E. Harris, M. M. Harris, R. Z. Mazengo, and S. Singh, *J.C.S. Perkin II*, 1974, 1059.
[11] K. Mislow and F. A. McGinn, *J. Amer. Chem. Soc.*, 1958, **80**, 6036.
[12] H. Akimoto, T. Shioiri, Y. Iitaka, and S. Yamada, *Tetrahedron Letters*, 1968, 97.
[13] S. Yamada and H. Akimoto, *Tetrahedron Letters*, 1968, 3967; H. Akimoto and S. Yamada, *Tetrahedron*, 1971, 5999.
[14] D. M. Hall, *Progr. Stereochem.*, 1969, **4**, 1.
[15] W. Klyne and J. Buckingham, 'Atlas of Stereochemistry, Absolute Configuration of Organic Molecules,' Chapman and Hall, London, 1974.
[16] K. Mislow and M. Raban, *Topics Stereochem.*, 1967, **1**, 1.

p.p.m. at 100 MHz;[5] six-membered ring *peri*-naphth-alenes with similar bridges also show the methylene protons as singlets[17]). The aromatic protons in the the new bridged binaphthyl compounds fall into three distinct groups in the numerical ratio 2 : 3 : 1.

its deshielding zone: they are brought nearer to this 'main plane' by the out-of-plane *peri*-distortion of 1,8-disubstituted naphthalenes.[20-24] The extent of the consequent deshielding is best appreciated by looking at H_a (although H_a is further deshielded by the nearby
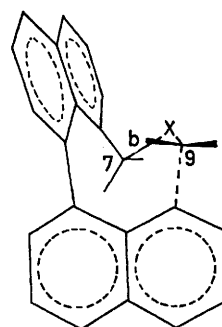
TABLE 1

Chemical shifts (δ; 100 MHz; Me_4Si; $CDCl_3$) of aromatic and methylene protons of compounds (1)—(4)

	Aromatic protons			Methylene protons				
Compound	4',4'',5',5'' (4 H, m)	3',3'',6',6'',7',7'' (6 H, m)	2',2'' (2 H, m)	H_a (2 H, d)	H_b (2 H, d)	$\Delta\delta$	J/Hz	Δ(in Hz)/ J
1	7.96—7.77	7.57—7.35	6.94—6.85	5.47	4.27	1.20	−13	9.2
2	7.91—7.77	7.54—7.24	6.86—6.78	4.76	3.34	1.42	−15	9.5
3	7.86—7.77	7.50—7.19	6.86—6.77	4.88	3.49	1.39	−13	10.7
4	8.06—7.89	7.66—7.34	6.93—6.84	5.06	3.79	1.27	−14	9.1

Methylene protons. The differences $\Delta\delta$ between the chemical shifts of H_a and H_b are all large in the compounds now studied: in the 6,6'-disubstituted 2,2'-bridged biphenyls there is a wide variation in $\Delta\delta$ which in some cases is too small to observe.[14] The separate signals for H_a and H_b are shifted downfield by the electronegativity of the bridging atom, increasing in the order Se $\approx$ S < SO_2 < O:[18] Table 2 gives examples of the effect of oxygen and sulphur in different but related chemical situations. In the carbocyclic analogues bridged by $\rangle C(CO_2Et)_2$, $\rangle C(CO_2Me)_2$, and $\rangle C(CH_2OH)_2$[1] the methylene protons all appear at higher field (δ 3.93 and 3.11; δ 3.98 and 3.09; δ 3.32 and 2.46 respectively). The H_a and H_b signals must be shifted equally by the electronegativity factor from the bridging atom in so far as it operates along bonds: the inequalities must spring from their different spatial relationships with the aromatic nuclei[19] and with groups (if any) attached to

TABLE 2

Chemical Shifts (δ; Me_4Si; $CDCl_3$) of methylene protons in situations comparable to those of (1) and (2)

	(2,6)	($CH_2)_2X$		
O	3.52	4.55	4.34	
S	2.57	3.61	3.44	3.35

(Ref. 25a) (Ref. 5)

the bridge. Models indicate that both H_a and H_b, while not exactly in the 'main plane' of the aromatic system to which the methylene group is joined, are probably in

7' or 7'' aromatic proton, the van der Waals deshielding effect); in H_b, shielding by the opposing naphthalene

Proton shielding in compounds (1)—(4)

system has a compensating influence. For (1), in a rough approximation, working from scale models, H_b lies 1.7 Å above the plane of the opposite naphthalene nucleus and 1.5 Å from the centre of its nearest benzene ring; the procedure of Johnson and Bovey[19] then leads to the conclusion that the long range shielding of H_b could be expected to be at least 1 δ unit greater than that of H_a, shifting the signal upfield.

The coupling constants J_{ab} are quoted in Table 1 with negative values by analogy with those in similar situations.[25b]

The geometry is not as precisely known as it is in the seven-membered ring biphenyl series where angles of torsion have been calculated, 44.1° in the oxepin and 56.6° in the thiepin.[5,14] It seems probable that in nine-membered carboxylic rings incorporating the 8,8'-positions of 1,1'-binaphthyl the dihedral angle is near to 90°.[1,26] Bond lengths and angles quoted for the bridging

[17] A. Biezais-Zirnis and A. Fredga, *Acta Chem. Scand.*, 1971, **25**, 1171.
[18] E. S. Gould, 'Mechanism and Structure in Organic Chemistry,' Holt, Rinehart, and Winston, New York, 1969, p. 39.
[19] C. E. Johnson, jun. and F. A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012.
[20] M. M. Harris and A. S. Mellor, *Chem. and Ind.*, 1961, 557.
[21] A. S. Cooke and M. M. Harris, *J. Chem. Soc.*, 1963, 2365.
[22] V. Balasubramanian, *Chem. Rev.*, 1966, **66**, 567.

[23] J. E. Anderson, R. W. Frank, and W. L. Mandella, *J. Amer. Chem. Soc.*, 1972, **94**, 4608.
[24] R. E. Carter and T. Liljefors, *Tetrahedron*, 1976, 2915.
[25] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 2nd edn., 1969, (*a*) p. 199; (*b*) p. 276; (*c*) p. 205; (*d*) p. 306.
[26] N. L. Allinger, and M. A. Miller, *J. Amer. Chem. Soc.*, 1964, **86**, 2811.

atoms in cyclic situations are: C–O (in 1,4-dioxan) 1.44 $\pm$ 0.03 Å, C–$\widehat{O}$–C 112 $\pm$ 5°; C–S (in 1,4-dithian) 1.80 Å, C–$\widehat{S}$–C 100°; C–Se (in 1,4-diselenan) 1.99 $\pm$ 0.04 Å, C–$\widehat{Se}$–C 97.6 $\pm$ 3.5°; C–SO$_2$ (various, mean taken) 1.75 Å, C–$\widehat{SO}_2$–C 107°.[27] If it is permissible to use these data for the nine-membered rings, the calculated distances between C-7 and -9 are (1) 2.3, (2) 2.84, (3) 3.0, and (4) 2.85 Å: if CH$_2$ is used as X in the bridge the figure is 2.5 Å. The angle of torsion cannot be precisely defined because the naphthalene rings are not planar, but it can be said that the angle subtended by the C-7—C-9 distances at the centre of the pivot bond are near to (1) 52, (2) 63, (3) 68, and (4) 63° and where X = CH$_2$, 55°. The approximate nature of these calculations can hardly be over-stressed, but if the presumption of near orthogonality is correct for the carbocyclic rings then the oxepin (1) has a dihedral angle a little less than 90°, and the others a little greater; the selenium compound approaches, but does not pass, the critical angle of ca. 110° at which Mason[28] predicts that the sign of the shortwave circular dichroism would reverse. It is beyond the scope of this work to do more than to indicate the magnitude of these changes in the geometry of the molecules and to observe that the signals for H$_a$ and H$_b$ will be affected by them.

Aromatic protons. The chemical shifts assigned to 4',4'' and 5',5'' protons (Table 1) are in the region expected for α-positions in naphthalene;[25c] the value for (4) is at somewhat lower field, an observation which can probably be linked with the inductive effect of the *p*-CH$_2$SO$_2$ substituent; the upfield shift of aromatic protons *para*- to a methyl group has been attributed to an inductive effect of opposite direction.[29] Further evidence for this assignment of the lowest field signals comes from a comparison of the n.m.r. spectra of 2,2'-, 8,8'-,[30] and 4,4'-dimethyl-1,1'-binaphthyls.[31] In all three the aromatic protons fall into two groups; for the 2,2'- and 8,8'-disubstituted derivatives the integration ratio lower : higher field is 4 : 8, while for the 4,4'-disubstituted it is 2 : 10, showing that the 4,4'-protons when present are in the lower field group (these protons are labelled 4',4'' in the nine-membered ring series).

Two of the eight β-protons appear upfield from the other six which make up the central multiplet: their signal is a doublet of doublets, *J* 7—7.5 (*ortho*-coupling of two β-positions)[25d] and 2 Hz (*meta*-coupling). These we take to belong to 2',2'' protons rather than 7',7'' because they lie nearer in space to the opposite (shielding) naphthalene nucleus. Also, they are less influenced by the lanthanide shift reagent Pr(fod)$_3$ [tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadionato)praeseodymium].[32] When portions of Pr(fod)$_3$ are added stepwise to (1) in CDCl$_3$ solution there is a progressive

upfield drift in the spectrum; a doublet separates out from the central multiplet and crosses over the doublet assigned to 2',2'' to δ 3.58; meanwhile the presumed 2',2'' signal moves from δ 6.96 to 4.72. The 7',7'' protons are nearer to the oxygen atom both through bonds and through space than are the 2',2'', and so it seems reasonable to consider that they are more sensitive to the shift reagent. While these shifts are taking place the lowest field signals (assigned to 4',4'' and 5',5'') move upfield by *ca.* 1 δ unit. The spectrum of the dioxothiacompound behaves in a similar way in the presence of Pr(fod)$_3$.

U.v. and c.d. of these compounds are currently under investigation.

8-*Oxa*-8,9-*dihydro*-7H-*cyclonona*[1,2,3-de:4,5,6-d'e']-*dinaphthalene* (1).—8,8'-Bishydroxymethyl-1,1'-binaphthyl[9] (10 g) and toluene-*p*-sulphonic acid monohydrate (0.8 g) in benzene (1 080 cm^3) were boiled for 16 h under a Dean–Stark water trap. The solution was washed with 5% sodium carbonate solution and benzene was evaporated off: the residue was purified by chromatography on alumina, using ether–benzene as eluant, and crystallised from benzene to give the *oxonin* (1) (5.5 g, 58%), m.p. 169—170° [Found: C, 89.0; H, 5.4; O, 5.5%; M, 296.119 4 (mass spectrum). C$_{22}$H$_{16}$O requires C, 89.2; H, 5.4; O, 5.4%; M, 296.120 1], ν$_{max.}$ (Nujol) 1 071 and 1 098 cm^{-1} (CH$_2$–O–CH$_2$, cyclic[33]), for ^{1}H n.m.r. spectrum at 100 MHz see Table 1. The signals [δ; tetramethylsilane as standard; 60 MHz; 0.021 1 g (7.1 × 10^{-5} mol) in 0.6 cm^3 CDCl$_3$] moved progressively upfield with the addition of successive quantities of Pr(fod)$_3$. After the addition of 0.449 g (6.16 mole per mole of oxonin) of the shift reagent the signals were at δ 7.34, 7.04, and 6.91 (6 H, 3',3'',4',4'',5',5''), 6.37, 6.24, and 6.11 (2 H, 6'6''), 4.78 and 4.66 (2 H, 2',2''), and 3.58 (2 H, 7',7''). During the addition the Me$_4$Si signal shifted upfield; the δ values reported are measured from the locked Me$_4$Si signal at the start of the measurements.

Optically Active (1).—(a) (−)-Dimethyl 1,1'-binaphthyl-8,8'-dicarboxylate[21] ([α]$_{546}$ −305.7°, chloroform) was reduced to (+)-diol[9] which failed to crystallise but treated as above gave (+)-(1), m.p. 196—197.5°, [α]$_{546}$ +1 119° (c 0.117; l 1.0; chloroform) (Found: C, 89.0; H, 5.5; O, 5.5%): further fractions had [α]$_{546}$ +51, +660, +972, and +1 271°.

(b) A similar preparation from (+)-dimethyl 1,1'-dinaphthyl-8,8'-dicarboxylate gave (−)-(1), m.p. 190—192°, [α]$_{546}$ −1 100° (c 0.106; l 1.0; chloroform); further fraction [α]$_{546}$ −1 215°.

8-*Thia*-8,9-*dihydro*-7H-*cyclonona*[1,2,3-de:4,5,6-d'e']-*dinaphthalene* (2).—8,8'-Bisbromomethyl-1,1'-binaphthyl[9] (7.74 g, 0.017 6 mol) and sodium sulphide nonahydrate (12.72 g, 0.053 mol) in methanol (320 cm^3) and water (16

[27] 'Interatomic Distances,' ed. L. E. Sutton, The Chemical Society, London, 1958; 'Supplement, Special Publication, No. 18,' 1965.

[28] S. F. Mason, R. H. Seal, and D. R. Roberts, *Tetrahedron*, 1974, **30**, 1671.

[29] C. MacLean and E. L. Mackor, *Mol. Phys.*, 1960, **3**, 223.

[30] D. D. Fitts, M. Siegel, and K. Mislow, *J. Amer. Chem. Soc.*, 1958, **80**, 480; W. Dixon, M. M. Harris, and R. Z. Mazengo, *J. Chem. Soc.*, (B), 1971, 775; Y. Badar, A. S. Cooke, and M. M. Harris, *J. Chem. Soc.*, 1965, 142.

[31] E. Clar, V. Sanigök, and M. Zander, *J. Chem. Soc.*, 1957, 4616.

[32] R. E. Rondeau and R. E Sievers, *J. Amer. Chem. Soc.*, 1971, **93**, 1522.

[33] L. J. Bellamy, 'The Infrared Spectra of Complex Molecules,' Methuen, London, 2nd edn., 1958.

cm³) were boiled with stirring for 24 h. The bulk of the methanol was distilled off, ice–water added to the residue, and the crude product boiled in ethanol with charcoal: the ethanol solution deposited 5.0 g (91%) of the *thionin* (2), m.p. 240—241° [Found: C, 84.8; H, 5.2; S, 10.1%; M, 312.097 0 (mass spectrum). $C_{22}H_{16}S$ requires C, 84.6; H, 5.1; S, 10.25%; M, 312.097 2], $\nu_{max.}$ (Nujol) 625, 658, and 705 cm⁻¹ (C–S stretch).[33]

Optically Active (2).—(a) Repetition of the above preparation using (+)-8,8'-bisbromomethyl-1,1'-binaphthyl [9] (2.5 g, $[\alpha]_{546}$ +351°) gave (+)-(2) (1.5 g) m.p. 194—195°, $[\alpha]_{546}$ +832° (c 0.256; l 0.5; NN-dimethylformamide).

(b) (−)-8,8'-Bisbromomethyl-1,1'-binaphthyl (1.5 g; $[\alpha]_{546}$ −396°) gave (−)-(2) (0.80 g), m.p. 190—191°; $[\alpha]_{546}$ −855° (c 0.059; l 1.0; NN-dimethylformamide). In another preparation bisbromomethyl compound of $[\alpha]_{546}$ −353° gave (−)-(2), $[\alpha]_{546}$ −593°.

8-*Selena*-8,9-*dihydro*-7H-*cyclonona*[1,2,3-de:4,5,6-d'e']-*dinaphthalene* (3).—Aqueous potassium selenide was prepared as follows. A cold solution of potassium hydroxide (2.6 g) in water (12 cm³) was saturated with hydrogen selenide gas under nitrogen and further potassium hydroxide added (2.6 g); 18 cm³ of this solution (0.044 mol) was added to a suspension of 8,8'-bisbromomethyl-1,1'-binaphthyl (5.2 g, 0.012 mol) in methanol (320 cm³) under nitrogen and boiled for 24 h with stirring. The solid, remaining after most of the methanol was distilled off, was purified from dark red material on an alumina column with benzene–light petroleum (b.p. 40—60°) as eluant. The residue, after removing the solvent, was boiled with charcoal in light petroleum (b.p. 80—100°). *Compound* (3) crystallised from this solution (2.6 g, 61%), m.p. 240—241° [Found: C, 73.65; H, 4.6; Se, 21.8%; M, 360.042 4 (mass spectrum). $C_{22}H_{16}Se$ requires C, 73.5; H, 4.5; Se, 22.0%; M, 360.041 7].

Optically Active (3).—(a) (+)-8,8'-Bisbromomethyl-1,1'-binaphthyl (2.0 g; $[\alpha]_{546}$ +420.5°) and potassium selenide solution (10 cm³) treated as above gave (+)-(3) (0.83 g), m.p. 232—234°, $[\alpha]_{546}$ +472° (c 0.25; l 0.5; NN-dimethylformamide).

(b) (−)-8,8'-Bisbromomethyl-1,1'-binaphthyl (1.5 g; $[\alpha]_{546}$ −396°) and potassium selenide solution (8 ml) similarly treated gave (−)-(3) (0.65 g), m.p. 232—234°, $[\alpha]_{546}$ −417° (c 0.200; l 1.0; NN-dimethylformamide).

8-*Dioxothia*-8,9-*dihydro*-7H-*cyclonona*[1,2,3-de:4,5,6-d'e']-*dinaphthalene* (4).—The thionin (2) (2.5 g, 0.007 2 mol) in acetic acid (25 cm³) was boiled with 30% hydrogen peroxide (20 cm³) for 90 min. The solution was cooled to −5 °C and kept below 1 °C overnight. Colourless *needles* of (4) separated and were recrystallised from ethanol to give 2.45 g (89%), m.p. 300—302° [Found: C, 76.7; H, 4.7; O, 9.3; S, 9.4%; M, 344.087 4 (mass spectrum). $C_{22}H_{16}O_2S$ requires C, 76.7; H, 4.7; O, 9.3; S, 9.3%; M, 344.087 1], $\nu_{max.}$ (Nujol) 1 150, 1 310, and 1 330 cm⁻¹ ($>SO_2$).[34]

Optically Active (4).—(a) The (+)-thionin (2) (0.5 g; $[\alpha]_{546}$ +832°) treated as above gave (+)-(4) (0.40 g), m.p. 277—280°, $[\alpha]_{546}$ +438° (c 0.244; l 0.5; NN-dimethylformamide).

(b) (−)-(2) (0.5 g; $[\alpha]_{546}$ −593°) similarly treated gave (−)-(4) (0.45 g) m.p. 275—279°, $[\alpha]_{546}$ −365° (c 0.468; l 0.5; NN-dimethylformamide).

[34] L. J. Bellamy and R. L. Williams, *J. Chem. Soc.*, 1957, 863.