overnight under an atmosphere of argon. Removal of the urea and concentration of the filtrate gave a residue which was purified by flash chromatography (60:35:5 MeOH/$CHCl_3$/HOAc) and then crystallization from MeOH/acetone to afford **20a** (201.0 mg, 50% yield): mp 170–174 °C; TLC (20% MeOH/$CHCl_3$ and some HOAc) R_f 0.26; $[\alpha]^{22}_D$ +4.7 (*c* 0.0143, MeOH); IR (Nujol) 3255, 1686, 1646, 1462 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.09 (s, NH), 9.04 (s br, 2 H, amidine), 8.75 (s, br, 2 H, amidine), 8.31 (t, 5.9, NH), 7.90 (s, NH), 7.16 (d, 1.4, 1 H), 6.81 (d, 1.4, 1 H), 4.14 (dd, 3.9, 7.3, 1 H), 3.79 (s, NCH_3), 3.48 (q, 5.9, 2 H), 2.59 (t, 5.9, 2 H), 2.41–1.85 (m, 4 H); FAB-MS, *m/z* (relative intensity) 320 (M – Cl, 6.2). Anal. Calcd for $C_{14}H_{21}N_6O_3Cl\cdot H_2O$ (374.45): C, 44.9; H, 6.1. Found: C, 45.5; H, 6.1.

(5*S*)-3-[1-Methyl-4-(2-pyrrolidone-5-carboxamido)-pyrrole-2-carboxamido]propionitrile (22a). A suspension of nitrile **17** (943.7 mg, 4.25 mmol) in MeOH (30.0 mL) was hydrogenated over 5% Palladium on charcoal (404 mg) at room temperature and atmospheric pressure. Removal of the catalyst and concentration of the filtrate gave an oily residue, which was coevaporated with dry CH_2Cl_2 (twice, 40 mL) to give amine **21** as a foamy off-white material. Owing to the instability of the amine, it was used directly in the following reaction. A mixture of acid **8a** (884.0 mg, 6.85 mmol), DMAP (78.0 mg, 0.64 mmol), and amine **21** was dissolved in dry DMF (15.0 mL) and chilled (0 °C). To this solution was added DCC (1.36 g, 6.50 mmol) in dry DMF (8.0 mL). After 15 min at 0 °C, the reaction mixture was stirred at room temperature overnight. Removal of the urea and the solvent gave a solid residue, which was recrystallized from MeOH to afford **22a** as a white powder (915.1 mg, 71% yield): mp 245–246 °C; TLC (10% MeOH/$CHCl_3$) R_f 0.35; IR (Nujol) 3263, 2318, 1692, 1673, 1655, 1533, 1464, 1377 cm^{-1}; ^1H NMR (DMSO-d_6) δ 10.00 (s, 1 H), 8.36 (t, 6.2, 1 H), 7.87 (s, 1 H), 7.16 (d, 1.5, 1 H), 6.79 (d, 1.5, 1 H), 4.11 (dd, 4.2, 8.0, 1 H), 3.79 (s, 3 H), 3.90 (q, 6.2, 2 H), 2.72 (t, 6.2, 2 H), 2.29 (m, 1 H), 2.15 (m, 2 H), 1.92 (m, 1 H); exact MS, *m/z* (relative intensity) for $C_{14}H_{17}N_5O_3$ 303.1334 (M, 25.3), for $C_9H_{12}N_{14}O_2$ 192.1014 (M – pyroglutamoyl group, 55.9).

***R* Stereoisomers.** Compounds (4*R*)-(+)-**11b**, (4*R*)-(+)-**14b**, (4*R*)-(–)-**7b**, and (5*R*)-(–)-**20b** all gave IR, MS, and ^1H NMR data similar to those of the corresponding *S* isomers. The specific rotations, $[\alpha]^{22}_D$, are +2.0° (*c* 0.0051, MeOH), +7.7° (*c* 0.0044, H_2O), –6.3° (*c* 0.0050, MeOH), and –4.6° (*c* 0.0142, MeOH), respectively.

Determination of DNA Binding Constants. The relative binding constants were estimated by displacement of intercalative binding of ethidium to calf thymus DNA and employment of a value of $K_{assoc} = 1 \times 10^6$ M^{-1} at pH 7.0, 37 °C, and 40 mM NaCl for ethidium bound to calf thymus DNA.[20] It was determined that none of the oligopeptides interferes with the fluorescence measurements, which were performed on a Turner 430 spectrofluorometer. The procedure, which involves following the displacement of the ethidium upon titrating in the drugs and determining the concentration of drug required to displace 50% of the ethidium, follows that of Morgan and co-workers[20a] and gives relative rather than absolute values for binding constants. Higher concentrations of lexitropsins displace all the ethidium from the DNA.

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Registry No. **7a**, 111136-83-5; (4*R*)-(–)-**7b**, 111136-84-6; **8a**, 98-79-3; **9a**, 4931-66-2; **11a**, 110971-80-7; (4*R*)-(+)-**11b**, 110971-85-2; **13a**, 65571-69-9; **14a**, 110971-81-8; (4*R*)-(+)-**14b**, 110971-86-3; **15**, 110971-82-9; **17**, 3185-95-3; **18**, 24064-13-9; **19**, 78395-16-1; **20a**, 110971-83-0; (5*R*)-(–)-**20b**, 110971-87-4; **21**, 97950-77-1; **22a**, 110971-84-1.

Synthesis of 1,2,5,6-Tetrahydrophosphorin 1-Oxides and 1,2-Dihydrophosphorin 1-Oxides from 2,5-Dihydro-1*H*-phosphole 1-Oxide–Dichlorocarbene Adducts

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Reaction of 6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 1-oxides **1** with silver nitrate in alcohols or in water leads to the regioisomers of alkoxy- or hydroxy-1,2,3,6-tetrahydrophosphorin 1-oxides **2A** and **2B** or **3A** and **3B**. Each isomer consists of diastereoisomers. Water elimination from the hydroxy derivatives **3** results in the formation of the regioisomers of 1,2-dihydrophosphorin 1-oxides **4A** and **4B**. Constitution and stereostructure of the compounds has been elucidated by ^1H, ^{13}C, and ^{31}P NMR spectroscopy.

Although the enlargement of five- and six-membered unsaturated rings by the addition of dihalocarbene and subsequent transformations is a well-established method,[1-3] there have been no reports on this kind of ring expansion for phosphorus-containing heterocycles. Recently we reported on the dichlorocarbene addition to 2,5-dihydro-1*H*-phosphole 1-oxides and on the spontaneous transformation of certain adducts to 1,2-dihydrophosphorin 1-oxides.[4] In this paper the synthesis of dihydrophosphorins through tetrahydrophosphorins starting from stable 1*H*-phosphole–dichlorocarbene adducts is discussed.

Results and Discussion

Dihalocarbene adducts can be enlarged in several ways; one of them involves the use of silver salts.[1,3] Reaction of

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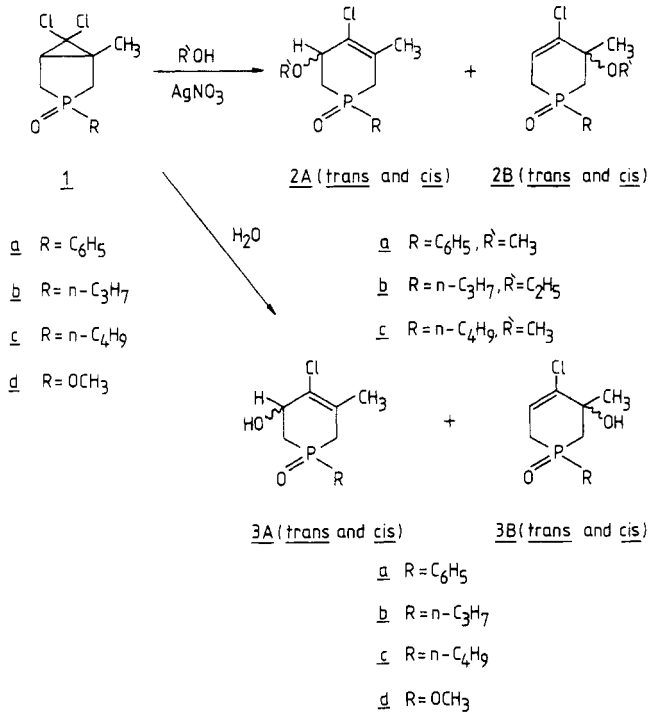
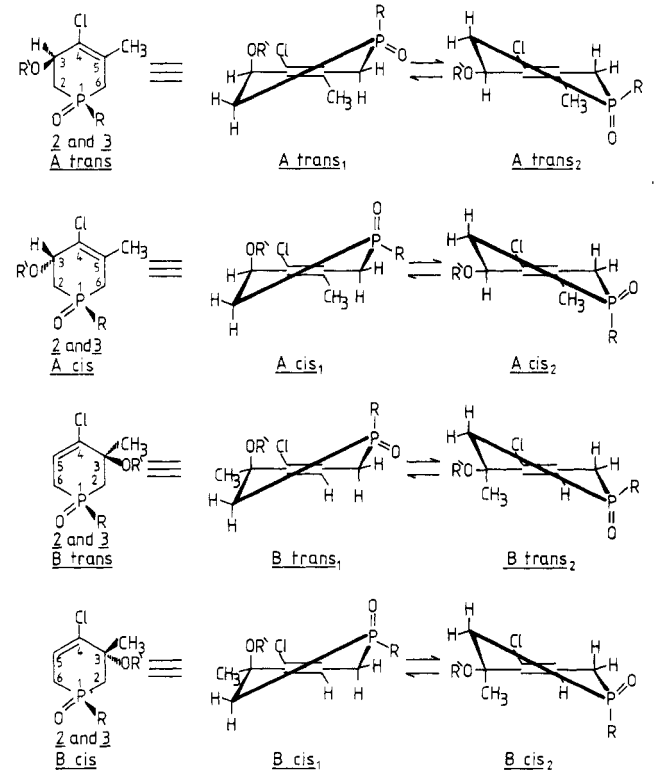
0022-3263/87/1952-5721$01.50/0

Scheme I



Scheme II



the dihalocarbene adducts of cyclopentene in aqueous methanol in the presence of silver nitrate gives hydroxy- and methoxyhalocyclohexenes.[1] No efforts have been made to prepare the methoxy compounds separately.

Now the analogous reaction of the dichlorocarbene adducts of 2,5-dihydro-3-methyl-1*H*-phosphole 1-oxides (**1a–d**)[4] was examined. It was found that on boiling the alcoholic or aqueous solution of dichlorocarbene adducts **1a–d** with silver nitrate, the cyclopropane ring opened to give two regioisomers of the alkoxy- or the hydroxytetrahydrophosphorins **2A** and **2Ba–c** or **3A** and **3Ba–d**, respectively both as a mixture of trans and cis epimers (Scheme I, Table I). No hydrolysis occurred when the aqueous solution of phosphinic acid ester derivative **1d** was reacted.

Table I. Product Compositions for the Diastereomers of 3-Substituted 5- and 3-Methyl-4-chloro-1,2,3,6-tetrahydrophosphorin 1-Oxides 2a–c and 3a–d

	product composition,[a] %				
compd	A-trans	A-cis	B-trans	B-cis	ratio base
2a	43	15	27	15	a
2b	52	14	26	8	c
2c	45	15	29	11	a
3a	40	12	32	16	d
3b	53	33	14	0	b
3c	47	35	18	0	d
3d	33	25	21	21	d

[a] The ratio of the regioisomers was calculated from the relative intensity of the HC–O and HC= ^{1}H NMR signals, that of the diastereomers from the relative ^{1}H NMR intensities of the methoxy (a) or the HC–O signals (b) or from the ^{13}C NMR intensities of the H_2CO (c) or H_2CP signals (d).

Identification of the Products. Since the isomeric tetrahydrophosphorins **2** or **3** could not be separated, the mixtures were subjected to spectroscopic investigations.

The distinction of the regioisomers **A** and **B** and the determination of their ratio was possible on the basis of the ^{1}H NMR signals of the HC–O proton in series **A** (δ ~4.3) and on the basis of the olefinic proton in series **B** (δ ~6.0). Regiomers **A** were predominant in every case. The presence of both possible diastereomers in each regioisomer was indicated by the duplication of signals in the ^{1}H, ^{13}C, and ^{31}P NMR spectra. Practically the same isomeric ratios were determined from the ^{1}H, and ^{13}C NMR spectra. Product compositions are shown in Table I; it was assumed that the trans form was the major diastereomer. Inspection of Dreiding models suggests that compounds **2** and **3** can exist both in a half-chair and in a twist-boat conformation. Because of the eclipsed positions in the latter it seems to be reasonable to consider only the half-chair conformers. Interconversion of these forms at room temperature should be fast on the NMR time scale (Scheme II).

In series **A** the H–CO signal is a triplet (^3J ~ 6 Hz), but this provides no direct information about the conformational situation since both the conformers A-trans$_1$ and A-cis$_1$ alone and a fast ring inversion involving also the A-trans$_2$ and A-cis$_2$ forms are expected to give rise to a triplet pattern. More useful information can be obtained by applying the Karlplus equation for $^3J_{PH}$. For the A-trans$_1$ and A-cis$_1$ conformers, in which the atoms P and the H-3 are in trans position, $^3J_{PH}$ ~ 35 Hz, while for the A-trans$_2$ and A-cis$_2$ conformers, where the atoms concerned are in gauche disposition $^3J_{PH}$ ~ 5 Hz can be expected.[5] The experimental values of $^3J_{PH}$ = 14–23 Hz (cf. Tables II and III) support the involvement of fast equilibria with nearly identical population of the conformers for both the trans and cis diastereomers.

Because ^{1}H and ^{13}C chemical shifts for the trans and cis isomers are rather close (Tables II–V) their unambiguous assignment is not possible. inspection of the molecular

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Table II. ^{1}H NMR Data for the Diastereomers of 5- and 3-Methyl-3-alkoxy-4-chloro-1,2,3,6-tetrahydrophosphorin 1-Oxides 2a-c

compd (R, R′)		^{1}H NMR[a,b,d] δ, (mult, integral, J)				
		A-trans	A-cis	B-trans	B-cis	unresolved
2a (C_6H_5, CH_3)	CCH_3	1.98 (s, 1.29 H)	2.07 (s, 0.45 H)	1.20 (s, 0.81 H)	1.70 (s, 0.45 H)	2.15-3.20 (m, 4 H, $P(CH_2)_2$), 7.30-7.97 (m, 5 H, Ar)
	OCH_3	3.42 (s, 1.29 H)	3.40 (s, 0.45 H)	3.28 (s, 0.81 H)	3.24 (s, 0.45 H)	
	HC-O or HC=	4.25 (dt, $^3J_{PH}$ = 21.4, $^3J_{HH}$ = 5.7)[c,e]	4.19 (dt, $^3J_{PH}$ ~ 21, $^3J_{HH}$ ~ 6)[c,e]	6.25 (dt, $^3J_{PH}$ = 25.7, $^3J_{HH}$ = 5.7)[c,f]	6.20 (dt, $^3J_{PH}$ ~ 26, $^3J_{HH}$ ~ 6)[c,f]	
2b (n-C_3H_7, C_2H_5)	CCH_3	1.95 (s, 1.98 H)		1.47 (s, 1.02 H)		0.96-1.32 (m, 6 H, OCH_2CH_3, $(CH_2)_2CH_3$), 1.55-1.86 (m, 4 H, $(CH_2)_2$), 1.99-3.07 (m, 4 H, $P(CH_2)_2$)
	OCH_2	3.57 (q, $^3J_{HH}$ = 7.1)[c,g]		3.34 (q, $^3J_{HH}$ = 7.1)[c,g]		
	HC-O or HC=	4.19 (dt, 0.66 H, $^3J_{PH}$ = 17.1, $^3J_{HH}$ = 5.7)		6.02 (dt, 0.34 H, $^3J_{PH}$ = 24.3, $^3J_{HH}$ = 5.7)		
2c (n-C_4H_9, CH_3)	CCH_3	1.97 (s, 1.80 H)		1.49 (s)[c,h]		0.84-1.04 (m, 3 H $(CH_2)_3CH_3$), 1.24-1.86 $((CH_2)_3)$,[c,h] 2.02-3.10 (m, 4 H, $P(CH_2)_2$)
	OCH_3	3.40 (s, 1.35 H)	3.42 (s, 0.45 H)	3.22 (s, 0.87 H)	3.19 (s, 0.33 H)	
	HC-O or HC=	4.15 (dt, 0.60 H, $^3J_{PH}$ = 18.6, $^3J_{HH}$ = 5.7)		6.10 (dt, 0.40 H, $^3J_{PH}$ = 24.3, $^3J_{HH}$ = 5.7)		

[a] $CDCl_3$ solution. [b] J given in Hz. [c] The two signals are partly overlapped. [d] Total intensity denoted by e-h. [e] 0.58 H. [f] 0.42 H. [g] 2 H. [h] 7.2 H.

Table III. ^{1}H NMR Data for the Diastereomers of 5- and 3-Methyl-4-chloro-3-hydroxy-1,2,3,6-tetrahydrophosphorin 1-Oxides 3a-c

compd (R)		^{1}H NMR[a,b,d] δ (mult, integral, J)				
		A-trans	A-cis	B-trans	B-cis	unresolved
3a (C_6H_5)	CCH_3	1.90 (s, 1.56 H)		1.42 (d, 0.96 H, $^4J_{PH}$ = 1.4)	1.62 (s, 0.48 H)	1.99-2.88 (m, 4 H, $P(CH_2)_2$), 4.83 (br s, 1 H, OH), 7.19-7.92 (m, 5 H, Ar)
	HC-O or HC=	4.44 (dm, 0.52 H, $^3J_{PH}$ = 20.0)		5.92 (dt, $^3J_{PH}$ = 22.9, $^3J_{HH}$ = 5.7)[c,e]	5.84 (dt, $^3J_{PH}$ ~ 24, $^3J_{HH}$ ~ 6)[c,e]	
3b (n-C_3H_7)	CCH_3	1.97 (s, 2.58 H)		1.59 (s)[c,f]		0.90-1.20 (m, 3 H, $(CH_2)_2CH_3$), 1.40-1.87 (m, $(CH_2)_2$),[c,f] 2.10-2.94 (m, 4 H, $P(CH_2)_2$), 4.95 (br s, 1 H, OH)
	HC-O or HC=	4.42 (dt, 0.53 H, $^3J_{PH}$ ~ 14, $^3J_{HH}$ = 6.4)	4.58 (dt, 0.33 H, $^3J_{PH}$ ~ 23, $^3J_{HH}$ = 5.0)	5.81 (dt, 0.14 H, $^3J_{PH}$ = 24.8, $^3J_{HH}$ = 5.1)		
3c (n-C_4H_9)	CCH_3	1.97 (s, 2.46 H)		~1.6[c,g]		0.76-1.06 (m, 3 H, $(CH_2)_3CH_3$), 1.06-1.88 (m, $(CH_2)_3$),[c,g] 2.06-2.97 (m, 4 H, $P(CH_2)_2$), 4.77 (br s, OH)[c,h]
	HC-O or HC=	4.43 (dt, $^3J_{PH}$ ~ 16, $^3J_{HH}$ = 6.1)[c,h]	c,h	5.82 (dt, 0.18 H, $^3J_{PH}$ = 24.9, $^3J_{HH}$ = 5.1)		
3d (OCH_3)	CCH_3	1.94 (br s, 1.74 H)		1.53 (d, 0.63 H, $^4J_{PH}$ = 1.4)[i]	1.58 (0.63 H, $^4J_{PH}$ = 2.9)[i]	2.04-2.72 (m, 4 H, $P(CH_2)_2$), 4.42 (br s, OH)[c,l]
	OCH_3	3.79 (d, $^3J_{PH}$ = 11.4)[j]		3.73 (d, $^3J_{PH}$ = 11.4)[j,k]	3.77 (d, $^3J_{PH}$ = 11.4)[j,k]	
	HC-O or HC=	~4.6 (dt, $^3J_{HH}$ = 5.7)[c,l]		5.85 (dt, $^3J_{PH}$ = 30.0, $^3J_{HH}$ = 5.7)[c,n,o]	5.84 (dt, $^3J_{PH}$ = 31.4, $^3J_{HH}$ = 5.7)[c,n,o]	

[a] $CDCl_3$ solution. [b] J given in Hz. [c] The signals are partly overlapped. [d] Total intensity denoted by e-h, j, l, n. [e] 0.48 H. [f] 4.42 H. [g] 6.54 H. [h] 1.82 H. [i,k,o] May be reversed. [j] 3 H. [l] 1.58 H. [n] 0.42 H.

Table IV. ^{13}C NMR Data for the Diastereomers of 5- and 3-Methyl-3-alkoxy-4-chloro-1,2,3,6-tetrahydrophosphorin 1-Oxides 2a–c

compd (R, R′)	C	^{13}C NMR,[a,b] δ (J_{P-C}) A-trans	A-cis	B-trans	B-cis	other
2a (C'_6H_5, $C(1'')H_3$)	C_2	34.6 (63.7)	35.2 (63.7)	38.6 (64.5)	36.5 (63.0)	for the major isomer: $\delta_{C_{2'}}$ 128.9 (J = 11.7),[d] $\delta_{C_{3'}}$ 129.7 (J = 8.8), $\delta_{C_{4'}}$ 132.1 (J = 2.9)[e]
	C_3	79.7 (5.9)	78.9 (6.6)	77.8 (3.7)	c	
	C_4	138.9 (11.0)	138.5 (8.0)	C_5 122.7 (6.6)	122.31 (8.1)	
	C_6	33.0 (68.1)	33.6 (6.96)	28.1 (66.7)	29.2 (65.9)	
	CCH_3	23.0 (8.1)	c	26.6 (5.9)	26.0 (2.9)	
	$C_{1''}$	56.6		50.9	50.4	
2b[f] ($C(3')H_3C$-$(2')H_2C(1')H_2$, $C(2'')H_3C$-$(1'')H_2$)	C_2	31.7 (60.8)	31.3 (63.4)	35.2 (57.9)	31.4 (63.0)	unresolved signals: $\delta_{C_{2'}}$ 14.0 (J = 4.4), $\delta_{C_{3'}}$ 14.7 (J = 9.5), $\delta_{C_{2''}}$ 14.2
	C_3	76.5 (4.4)	76.7 (6.6)	76.1 (3.7)	c	
	C_4	137.2 (11.0)	137.6 (8.1)	127.7 (11.0)	c	
	C_5	127.7 (5.1)	c	121.6 (6.6)	120.9 (7.3)	
	C_6	30.3 (63.0)	26.7 (63.0)	26.3 (61.6)	26.7 (63.0)	
	CCH_3	22.1 (8.1)	22.4 (7.3)	22.9 (4.4)	c	
	$C_{1''}$	63.3	64.6	57.6	57.2	
	$C_{1'}$	29.8 (68.1)	c	29.8 (68.1)	c	
2c[f] ($C(4')H_3C$-$(3')H_2C(2')H_2C$-$(1')H_2$, $C(1'')H_3$)	C_2	31.8 (60.8)	32.3 (60.1)	34.8 (58.6)	33.8 (59.0)	unresolved signals: $\delta_{C_{2'}}$ 22.4, $\delta_{C_{3'}}$ 23.1 (J = 14.7) $\delta_{C_{4'}}$ 12.8
	C_3	78.3 (5.1)	78.6 (5.9)	76.7 (3.7)	76.3 (3.7)	
	C_4	136.8 (11.0)	137.2 (8.0)	127.4 (11.0)	126.6 (12.9)	
	C_5	128.3 (5.1)	128.1 (7.3)	122.3 (5.9)	121.5 (7.3)	
	C_6	29.9 (63.0)	29.0 (59.4)	26.5 (62.3)	26.8 (62.3)	
	CCH_3	22.3 (8.1)	c	26.6 (3.7)	c	
	$C_{1''}$	55.4	56.7	49.8	49.6	
	$C_{1'}$	27.9 (68.1)	c	27.6 (68.9)	c	

[a] $CDCl_3$ solution. [b] J given in Hz. [c] Not resolved. [d] Common for all isomers. [e] Other signals in the 128.0–135.4 ppm region could not be resolved. [f] Assignation C_2, C_6, and $C_{1'}$ is tentative.

Table V. ^{13}C NMR Data for the Diastereomers of 5- and 3-Methyl-4-choro-3-hydroxy-1,2,3,6-tetrahydrophosphorin 1-Oxides 3a–d

compd (R)	C	^{13}C NMR,[a,b] δ (J_{P-C}) A-trans	A-cis	B-trans	B-cis	other
3a (C'_6H_5)	C_2	34.2 (66.7)	35.0 (65.9)	39.2 (65.2)	40.5 (62.3)	for the major isomer: $\delta_{C_{2'}}$ 129.0 (J = 11.7), $\delta_{C_{3'}}$ 129.8 (J = 9.5), $\delta_{C_{4'}}$ 132.6 (J = 2.9)[f]
	C_3	70.3 (5.9)	68.5 (2.2)	72.1 (5.9)	71.9 (3.7)	
	C_4	c	c	141.1 (13.2)	e	
	C_5	126.2 (5.9)	126.5 (5.0)	118.5 (7.3)	118.3 (5.1)	
	C_6	33.7 (65.2)	34.7 (65.2)	28.7 (66.7)	29.1 (65.9)	
	CCH_3	23.3 (9.5)	19.5 (12.5)	29.6 (9.5)	28.3	
3b ($C(3')H_3C(2')H_2C(1')H_2$	C_2	32.0 (63.7)	32.2 (65.2)	30.3 (63.7)		unresolved signals: $\delta_{C_{2'}}$ 14.4 (J = 3.7), $\delta_{C_{3'}}$15.1 (J = 14.7)
	C_3	68.9 (2.9)	68.6 (5.1)	71.2 (3.7)		
	C_4	130.9 (9.5)	130.3 (11.0)	140.3 (11.0)		
	C_5	125.3 (4.4)	125.9 (5.1)	117.9 (6.6)		
	C_6	29.4 (68.9)	31.0 (67.4)	26.8 (62.3)		
	CCH_3	23.0 (9.5)		28.9 (3.7)		
	$C_{1'}$	32.4 (60.1)		38.4 (59.3)		
3c ($C(4')H_3C(3')H_2C(2')H_2C(1')H_2$)	C_2	31.6 (63.0)[g]	31.8 (63.0)[g]	29.0 (68.9)		unresolved signals: $\delta_{C_{2'}}$ 22.4, $\delta_{C_{3'}}$ 23.1 (J = 13.9), $\delta_{C_{4'}}$ 12.8
	C_3	68.4	68.2	70.8 (3.7)		
	C_4	130.6 (9.5)	130.0 (11.0)	141.1 (10.3)		
	C_5	125.0 (5.1)	125.5 (5.1)	117.6 (6.6)		
	C_6	26.6 (68.1)	28.4 (68.1)	27.7 (68.1)		
	CCH_3	22.6 (9.5)		28.5 (5.1)		
	$C_{1'}$	32.0 (60.8)		38.1 (58.6)		
3d ($C(2')H_3O(1')$)	C_2	31.7 (85.7)[h]	32.3 (85.7)[h]	38.1 (83.5)		
	C_3	70.0 (2.9)[i]	70.4 (4.4)[j]	73.0 (2.2)[j]	73.1 (2.2)[j]	
	C_4	130.5 (12.5)[k]	131.3 (10.3)[k]	140.4 (11.7)[l]	140.7 (11.7)[l]	
	C_5	126.5 (4.4)[n]	127.3 (5.1)[n]	118.5 (5.9)[p]	119.0 (5.9)[p]	
	C_6	31.8 (88.7)[q]	31.8 (90.9)[q]	26.7 (89.4)[r]	26.6 (90.9)[r]	
	CCH_3	23.4 (12.5)[u]	23.5 (11.7)[u]	28.6 (5.9)[v]	29.2 (7.3)[v]	
	$C_{2'}$	51.2 (5.9)[z]		51.5 (6.6)[z]		

[a] $CDCl_3$ solution. [b] J given in Hz. [c] Overlapped by the signals of the aromatic carbons. [d] Footnote deleted on revision. [e] Not resolved. [f] Other signals in the 128.5–139.0 ppm region could not be resolved. [g–z] May be reversed.

Table VI. ^{31}P NMR Shifts for the Diastereomers of 3-Substituted 5- and 3-Methyl-4-chloro-1,2,3,6-tetrahydrophosphorin 1-Oxides 2a–c and 3a–d

	δ_{31P} (in $CDCl_3$)			
compd	A-trans	A-cis	B-trans	B-cis
2a	29.9	29.9	29.6	32.5
2b	38.5	36.6	37.0	37.5
2c[a]	39.2	38.4	37.7	37.7
3a	30.3	30.3	30.3	28.9
3b	39.6	38.2	39.6	
3c	38.6	40.0	40.0	
3d	45.0	46.4	46.4	44.6

[a] After adding a drop of methanol to the sample, four signals at 44.0, 43.2, 42.5 and 43.0 ppm could be observed.

Table VII. MS Data for 5- and 3-Methyl-3-alkoxy-4-chloro-1,2,3,6-tetrahydrophosphorin 1-Oxides 2a–c

	relative intensity		
fragment (m/e)	**2a**	**2b**	**2c**
M^+[a]	40	23	22
$[M - R']^+$	43	40	48
$[M - R]^+$		46	20
$[M - R'O]^+$	100	100	100
$[M - R'OH]^+$	68	35	44
$[M - Cl]^+$	23	9	17
$[M - CH_2CHOR']^+$		9	20
$[M - CH_2C(CH_3)OR']^+$	8	48	42
$[M - (R'O + P(O)R)]^+ + H$ (116)		15	13
$[M - (R'O + P(O)R)]^+$ (115)	21	13	33
$[P(O)RH]^+$	68	7	4
$[P(O)R]^+$	13		

[a] m/e values for the molecular ions of **2a** and **2b**,**c** are 270 and 250, respectively.

Table VIII. MS Data for 5- and 3-Methyl-4-chloro-3-hydroxy-1,2,3,6-tetrahydrophosphorin 1-Oxides 3a–d

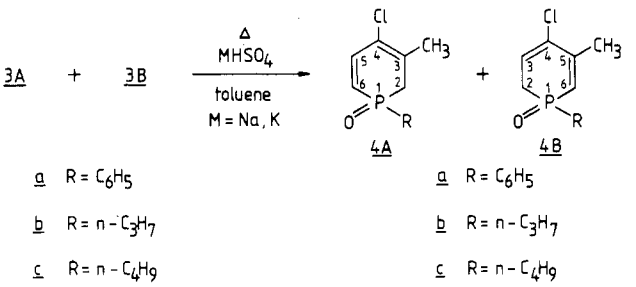
	relative intensity			
fragment (m/e)	**3a**	**3b**	**3c**	**3d**
M^+[a]	50	47	58	14
$[M - CH_3]^+$	56	38	27	65
$[M - OH]^+$	13	34	35	9
$[M - H_2O]^+$	46	69	66	24
$[M - Cl]^+$	100	100	100	89
$[M - CH_2CHOH]^+$		8	3	9
$[M - CH_2C(CH_3)OH]^+$		12	9	4
$[M - (H_2O + Cl)]^+$		11	10	6
$[M - (H_2O + R)]^+ + H$ (162)		25	24	6
$[M - (H_2O + R)]^+$ (161)		7	6	7
$[P(O)RH]^+$	66	6	4	100
$[P(O)R]^+$	30	3	3	99
$[PO]^+$ (47)		17	29	49

[a] m/e values for the molecular ions of **3a**, **3b**, **3c**, and **3d** are 256, 222, 236, and 210, respectively.

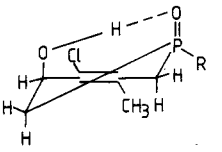
Table IX. Ratio of the Isomers and ^{31}P NMR Chemical Shifts for 3- and 5-Methyl-4-chloro-1,2-dihydrophosphorin 1-Oxides 4a–c

	product compostn, %		δ_{31P} (in $CDCl_3$)	
compd	A	B	A	B
4a	74	26	15.3	14.2
4b	73	27	25.0	24.2
4c	75	25	26.0	25.2

Scheme III



model shows, however, that in the A-cis$_1$ form there is an unfavourable electric interaction between the oxygen atoms of the OR′ and P=O groups, and therefore we assumed that it was the trans form which was predominant. For tetrahydrophosphorins **3Ab–d** having an electron-releasing substituent at phosphorus a shift in favor of the cis stereoisomer (Table I) can be explained by the possibility of the formation of an intramolecular hydrogen bridge in the A-cis$_1$ form.



3Ab–d
cis$_1$

For the regioisomers **2B** and **3B** the existence of B-trans$_1$ ⇌ B-trans$_2$ and a B-cis$_1$ ⇌ B-cis$_2$ type equilibria was again substantiated on the basis of the measured $^3J_{PC}$ values (3.7–9.5 Hz) (cf. Tables IV and V). For the trans disposition of the P and C atoms $^3J_{PC} \sim 19$ Hz, while for the gauche relationship $^3J_{PC} \sim 2$ Hz is expected.[6]

^1H NMR data characteristic for the isomers of **2** and **3** are listed in Tables II and III, respectively. It can be seen from Table II that the difference of the ^1H NMR shifts for the methoxy groups in the two regioisomers of **2a** and **2c** is ~0.18 ppm, while this difference for their diastereomers is ~0.03 ppm. In the ^{13}C spectra only part of the signals were resolved for the individual isomers. For the assignment of signals the attached proton test (APT) technique was used (cf. Tables IV and V). The isomers of **2** and **3** were characterized by ^{31}P NMR chemical shifts (Table VI). Signal overlap was often observed.

Mass spectral (MS) data for **2** and **3** are presented in Tables VII and VIII, respectively. Fragmentation of alkoxy and hydroxy derivatives is similar, the base peak is $[M - R'O]^+$ for **2a–c** and $[M - Cl]^+$ for **3a–c**.

When reactions were carried out in methanol–water mixture, the isomers of both the methoxy and hydroxy derivatives (**2** and **3**) were formed according to ^{31}P NMR.

Dehydration of Hydroxytetrahydrophosphorines 3. Isomeric mixtures of **3** were refluxed in toluene in the presence of potassium or sodium hydrogen sulfate[7] to give dihydrophosphorins **4A** and **4Ba–c** (Scheme III, Table IX). Their ratio could be calculated from the relative intensity of the methyl signals in the ^1H NMR spectra. This appears in the minor isomer (B) as a doublet (J = 1.5 Hz) due to the allylic coupling. A shift in the ratios

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Table X. ^{1}H NMR Data for 3- and 5-Methyl-4-chloro-1,2-dihydrophosphorin 1-Oxides 4a–c

compd		^{1}H NMR,[a,b,d] δ (mult, integral, J) A	B	other
4a	CH_3	2.07 (s, 2.22 H)	2.17 (d, 0.78 H, $^4J_{PH}$ = 1.5)	2.60–3.10 (m, 2 H, PCH_2), 7.25–7.90 (m, Ar, 5 H)
	PCH=	6.15 (t, $^2J_{PH}$ = $^3J_{HH}$ = 14.0)[c,e]	*c,e*	
	PCH=C*H* or PCH_2CH=	6.86 (dd, 0.74 H, $^3J_{PH}$ = 35.7, $^3J_{HH}$ = 14.0)	6.23 (dt, $^3J_{PH}$ ~ 20, $^3J_{HH}$ = 7.1)[c,e]	
4b	CH_3	2.06 (s, 2.19 H)	2.15 (d, 0.81 H, $^4J_{PH}$ = 1.5)	0.85–1.22 (m, 3 H, CH_2CH_3), 1.38–2.02 (m, 4 H, $(CH_2)_2$), 2.27–3.14 (m, 2 H, PCH_2)
	PCH=	6.13 (t, $^2J_{PH}$ = $^3J_{HH}$ = 13.2)[c,f]	*c,f*	
	PCH=C*H* or PCH_2CH=	6.72 (dd, 0.73 H, $^3J_{PH}$ = 32.9, $^3J_{HH}$ = 13.2)	6.25 (dt, $^3J_{PH}$ ~ 20, $^3J_{HH}$ 7.1)[c,f]	
4c	CH_3	2.05 (s, 2.25 H)	2.11 (s, 0.75 H)	0.72–1.09 (m, 3 H, CH_2CH_3), 1.09–1.95 (m, 6 H, $(CH_2)_3$), 2.20–3.09 (m, PCH_2)
	PCH=	6.11 (t, $^2J_{PH}$ = $^3J_{HH}$ = 13.2)[c,g]	*c,g*	
	PCHC*H* or PCH_2CH=	6.68 (dd, 0.75 H, $^3J_{PH}$ = 32.9, $^3J_{HH}$ = 13.2)	*c,g*	

[a] $CDCl_3$ solution. [b] J given in Hz. [c] The signals are partly overlapped. [d] Total intensity denoted by *e–g*. [e] 1.26 H. [f] 1.27 H. [g] 1.25 H.

Table XI. ^{13}C NMR Data for 3- and 5-Methyl-4-chloro-1,2-dihydrophosphorin 1-Oxides 4a–c

compd (R)		^{13}C NMR[a,b] δ (J_{P-C}) A	B	other
4a (C'_6H_5)	C_2	35.5 (71.1)	29.6 (71.8)	common for the two isomers: $\delta_{C_{2'}}$ 127.8 (J = 12.5), $\delta_{C_{3'}}$ 129.8 (J = 10.3), $\delta_{C_{4'}}$ 131.4 (J = 2.9)
	C_3	122.8 (19.8)	122.2 (11.0)	
	C_4	129.7[c] (13.9)	*d*	
	C_5	143.4	149.0	
	C_6	118.5 (93.8)	118.0 (97.5)	
	CCH_3	22.5 (8.8)	24.1 (13.2)	
	$C_{1'}$	132.1 (81.3)		
4b ($C(3')H_3C(2')H_2C(1')H_2$)	C_2	32.0 (74.0)	31.5 (74.0)	common for the two isomers: $\delta_{C_{2'}}$ 14.8 (J = 3.7), $\delta_{C_{3'}}$ 15.1 (J = 11.0)
	C_3	123.4 (19.1)	122.5 (10.3)	
	C_4	130.5 (9.5)	131.4 (19.3)	
	C_5	142.5	148.0	
	C_6	119.0 (88.7)	118.5 (92.3)	
	CCH_3	22.9 (8.1)	24.1 (11.7)	
	$C_{1'}$	33.4 (67.4)	27.5 (68.1)	
4c ($C(4')H_3C(3')H_2C(2')H_2C(1')H_2$)	C_2	28.9 (74.7)	28.5 (74.7)	common for the two isomers: $\delta_{C_{2'}}$ 22.7, $\delta_{C_{3'}}$ 23.0 (J = 14.7), $\delta_{C_{5'}}$ 12.6
	C_3	122.7 (18.3)	122.2 (10.3)	
	C_4	130.1 (9.5)	130.7 (19.0)	
	C_5	142.1	147.6	
	C_6	118.2 (88.7)	117.7 (92.3)	
	CCH_3	22.5 (10.3)	23.7 (11.7)	
	C_1	32.6 (67.4)	26.7 (68.1)	

[a] $CDCl_3$ solution. [b] J given in Hz. [c] Partly overlapped. [d] Overlapped by the aromatic carbon signals.

3A/3B and **4A/4B** may be the consequence of the workup. The ^{31}P, ^{1}H, and ^{13}C NMR analysis as well as the MS data for **4a–c** are listed in Tables IX–XII. ^{13}C NMR assignments were confirmed by APT spectra. MS fragmentation is similar to that of analogous compounds.[4]

The alkoxy derivatives **2a–c** failed to react under similar circumstances, in contrast to, e.g., 3-ethoxycyclohexene, which readily gave cyclohexadiene on distillation from potassium hydrogen sulfate.[7]

Experimental Section

^{31}P, ^{1}H, and ^{13}C NMR spectra were taken on a JEOL FX 100-MHz instrument operating at 40.26, 100.0, and 25.0 MHz, respectively. Chemical shifts are downfield relative to 85% phosphoric acid, (for ^{31}P NMR) and to tetramethylsilane (for ^{1}H and ^{13}C NMR) and have a positive sign. All coupling constants are given in hertz. Infrared spectra were recorded on a SPECORD 75 spectrometer. Mass spectra were obtained on a JEOL-01SG-2 instrument at 75 eV.

Starting materials **1a–d** were prepared as described earlier.[4]

5- and 3-Methyl-1-*n*-butyl-4-chloro-3-methoxy-1,2,3,6-tetrahydrophosphorin 1-Oxide 2c. A mixture of **1c** (1.5 g, 5.88 mmol) and silver nitrate (18.0 g, 0.106 mol) in methanol (50 mL) was boiled for 24 h. The residue obtained after evaporating the solvent was taken up in chloroform and the solvent evaporated after filtration. The crude product was purified by column chromatography using silica gel and chloroform–methanol (96:4) to give **2c** (0.75 g, 51%) as an oily mixture of isomers (Table I): M^+_{found} = 250.0879, $C_{11}H_{20}ClO_2P$ requires 250.0890; IR (neat) 2930, 1650, 1460, 1170, 1075, 750 cm^{-1}.

5- and 3-Methyl-4-chloro-3-methoxy-1-phenyl-1,2,3,6-tetrahydrophosphorin 1-Oxide 2a was prepared in the same way as **2c**: yield, 64%; M^+_{found} = 270.0605, $C_{13}H_{16}ClO_2P$ requires 270.0577; IR (neat) 2910, 1640, 1440, 1180, 1070, 750 cm^{-1}.

Table XII. MS Data for 3- and 5-Methyl-4-chloro-1,2-dihydrophosphorin 1-Oxides 4a-c

fragment (m/e)	relative intensity 4a	4b	4c
M^{+a}	100	84	100
$[M - Cl]^+$	19	20	22
$[M - C_2H_4]^+$		12	3
$[M - C_2H_5]^+$		3	8
$[M - C_3H_6]^+$		65	56
$[M - C_3H_7]^+$		31	6
$[M - C_4H_8]^+$			54
$[M - C_4H_9]^+$			24
$[M - P(O)R]^+ + H$ (115)	12	14	12
$[M - P(O)R]^+$ (114)	12	15	16
$[M - P(O)R]^+ - H$ (113)	6	12	12
$[C_7H_9]^+$ (91)	14	14	8
$[M - (Cl + P(O)R)]^+$ (79)	46	100	82
$[C_6H_5]^+$ (77)	70	82	68
$[PO]^+$ (47)	77	34	22

[a] m/e values for the molecular ions of 4a, 4b, and 4c are 238, 204, and 218, respectively.

5- and 3-Methyl-4-chloro-3-ethoxy-1-*n*-propyl-1,2,3,6-tetrahydrophosphorin 1-Oxide 2b was prepared similarly from **1b** in ethanol: yield, 49%; M^+_{found} = 250.0874, $C_{11}H_{20}ClO_2P$ requires 250.0890; IR (neat) 2970, 1650, 1460, 1180, 1080, 750 cm^{-1}.

Product compositions, ^1H, ^{13}C, and ^{31}P NMR, and MS data for the mixtures containing the isomers of **2a-c** are listed in Tables I, II, IV, VI, and VII, respectively.

5- and 3-Methyl-1-*n*-butyl-4-chloro-3-hydroxy-1,2,3,6-tetrahydrophosphorin 1-Oxide 3c. A solution of **1c** (4.3 g, 16,9 mmol) and silver nitrate (28.7 g, 0.169 mol) in water (110 mL) was refluxed for 2 h. The mixture was filtered and extracted with two portions of chloroform (220 mL). The crude product obtained after drying over sodium sulfate and evaporating the solvent was purified by column chromatography using silica gel and chloroform-methanol (97:3) to give **3c** (1.8 g, 45%) as a mixture of isomers (Table I): M^+_{found} = 236.0709, $C_{10}H_{18}ClO_2P$ requires 236.0734; IR (neat) 3220, 2940, 1640, 1460, 1390, 1140, 750 cm^{-1}.

5- and 3-Methyl-4-chloro-3-hydroxy-1-phenyl-1,2,3,6-tetrahydrophosphorin 1-Oxide 3a was prepared in the same way as **3c** except that five times more water was used: yield, 40%; M^+_{found} = 256.0471, $C_{12}H_{14}ClO_2P$ requires 256.0420.

5- and 3-Methyl-4-chloro-3-hydroxy-1-*n*-propyl-1,2,3,6-tetrahydrophosphorin 1-Oxide 3b was prepared similarly: yield, 42%; mp 103-111 °C; M^+_{found} = 222.0554, $C_9H_{16}ClO_2P$ requires 222.0577; IR (KBr disk) 3220, 2950, 1630, 1450, 1390, 1150, 800 cm^{-1}.

5- and 3-Methyl-4-chloro-3-hydroxy-1-methoxy-1,2,3,6-tetrahydrophosphorin 1-Oxide 3d was prepared similarly: yield, 35%; M^+_{found} = 210.0241, $C_7H_{12}ClO_3P$ requires 210.0213.

Product compositions, ^1H, ^{13}C, and ^{31}P NMR, and MS data for the isomers of **3a-d** are listed in Tables I, III, V, VI, and VIII.

3- and 5-Methyl-1-*n*-butyl-4-chloro-1,2-dihydrophosphorin 1-Oxide 4c. **3c** (1.2 g, 5.07 mmol) and sodium hydrogen sulfate (0.53 g, 5.07 mmol) in toluene (90 mL) was boiled for 14 h. The residue obtained after filtering and evaporating the solvent was purified by column chromatography using silica gel and chloroform-methanol (98:2) to give **4c** (0.78 g, 70%) as an oily mixture of isomers: M^+_{found} = 218.0654, $C_{10}H_{16}ClOP$ requires 218.0629; IR (neat) 2950, 1620, 1565, 1470, 1370, 1170, 750 cm^{-1}.

3- and 5-Methyl-4-chloro-1,2-dihydro-1-phenylphosphorin 1-Oxide 4a was prepared similarly: yield, 61%; M^+_{found} = 238.0387, $C_{12}H_{12}ClOP$ requires 238.0315; IR (neat) 2940, 1610, 1550, 1430, 1365, 1180, 740 cm^{-1}.

3- and 5-Methyl-4-chloro-1,2-dihydro-1-*n*-propylphosphorin 1-Oxide 4b was prepared similarly: yield, 66%; M^+_{found} = 204.0451, $C_9H_{14}ClOP$ requires 204.0472; IR (neat) 2955, 1620, 1560, 1460, 1370, 1180, 730 cm^{-1}.

Product compositions and ^{31}P NMR chemical shifts can be found in Table IX and ^1H and ^{13}C NMR and MS data in Tables X-XII.

Acknowledgment. The support of the Hungarian Academy of Sciences is thanked for the NMR measurements.

Registry No. **1a**, 109011-51-0; **1b**, 109011-52-1; **1c**, 109011-53-2; **1d**, 109011-54-3; A-*trans*-**2a**, 109890-86-0; A-*cis*-**2a**, 109890-93-9; B-*trans*-**2a**, 109891-00-1; B-*cis*-**2a**, 109891-07-8; A-*trans*-**2b**, 109890-87-1; A-*cis*-**2b**, 109890-94-0; B-*trans*-**2b**, 109891-01-2; B-*cis*-**2b**, 109891-08-9; A-*trans*-**2c**, 109890-88-2; A-*cis*-**2c**, 109890-95-1; B-*trans*-**2c**, 109891-02-3; B-*cis*-**2c**, 109891-09-0; A-*trans*-**3a**, 109890-89-3; A-*cis*-**3a**, 109890-96-2; B-*trans*-**3a**, 109891-03-4; B-*cis*-**3a**, 109891-10-3; A-*cis*-**3b**, 109890-97-3; A-*trans*-**3b**, 109890-90-6; B-*trans*-**3b**, 109891-04-5; A-*trans*-**3c**, 109890-91-7; A-*cis*-**3c**, 109890-98-4; B-*trans*-**3c**, 109891-05-6; A-*trans*-**3d**, 109890-92-8; A-*cis*-**3d**, 109890-99-5; B-*trans*-**3d**, 109891-06-7; B-*cis*-**3d**, 109891-11-4; A-**4a**, 109891-12-5; B-**4a**, 109891-15-8; A-**4b**, 109891-13-6; B-**4b**, 109891-16-9; A-**4c**, 109891-14-7; B-**4c**, 109891-17-0.

Notes

Crystal Structures of 4,5-Dimethyl- and 4-Methylphenanthrenes. Planarity of Congested Phenanthrene Molecules

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In view of the steric interaction in the bay region of phenanthrene, which consists of the C4, C4a, C4b, and C5 carbon atoms, there is interest in the planarity of this region in methylphenanthrenes because some of them are carcinogenic.[2] However, the molecular structures of 4,5-dimethylphenanthrene (1) and 4-methylphenanthrene (2) have not been determined. The phenanthrene ring in 1 is considered to be nonplanar on the basis of observations of the racemization process for some of its derivatives[3] and the crystal structures of related compounds.[4,5] During an

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