Synthesis and Chiroptical Properties of Bridged 2,2′-Diaminobiphenyl Derivatives

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The relationship between c.d. spectra and the conformation of chiral 2,2′-diaminobiphenyls was investigated as a function of the torsion angle between the benzene ring planes. The molecular structures of (*S*)-(+)-4,5,6,7,11,12,13,14-octahydro[1]benzazocino[7,6,5-*efg*][1]benzazocine (**22**), (*S*)-(−)-2,2′-diamino-6,6′-dimethylbiphenyl (**25**), and (*S*)-(−)-(6*R*,7*R*)-5,6,7,8-tetrahydro-1,6,7,12-tetramethyldibenzo[*e*,*g*][1,4]diazocine (**27**) were determined by *X*-ray analysis. The shape of the c.d. spectrum of (**22**) (*trans*-conformation) is similar to those of (**25**) and (**27**) (*cis*-conformation). The experimental results and theoretical consideration by the exciton approximation and the π-SCF-MO approximation indicated that the shape of the c.d. spectrum is the same at least for torsion angles of 0—120°. On the other hand, the shape of the c.d. spectrum of the protonated species was inverted with a critical torsion angle of *ca.* 90°.

In connection with the determinations of absolute configurations, the chiroptical properties of biphenyl derivatives have been studied by several investigators.[1-3] The sign of the c.d. bands at longer wavelengths depends strongly on the substitution pattern,[4] whereas the Cotton effect within the conjugation band around 240 nm is determined only by the helicity of the biphenyl system. However, to our knowledge, there is no report on the c.d. spectra of *cis*-skew and *trans*-skew conformations of optically active biphenyls. It would therefore be interesting to see if the sign of the 'conjugation band' Cotton effect is reversed by a change in conformation from *cis*-skew to *trans*-skew in biphenyls of the same absolute configuration. We turned our attention to 2,2′- and 2,6′-bridged 2,2′ -diaminobiphenyl derivatives, since protonation of the amino groups changes the direction of the electric transition dipole moment of each aniline chromophore and would greatly affect the c.d. spectra (Figure 1).

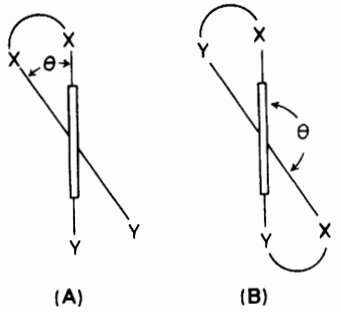
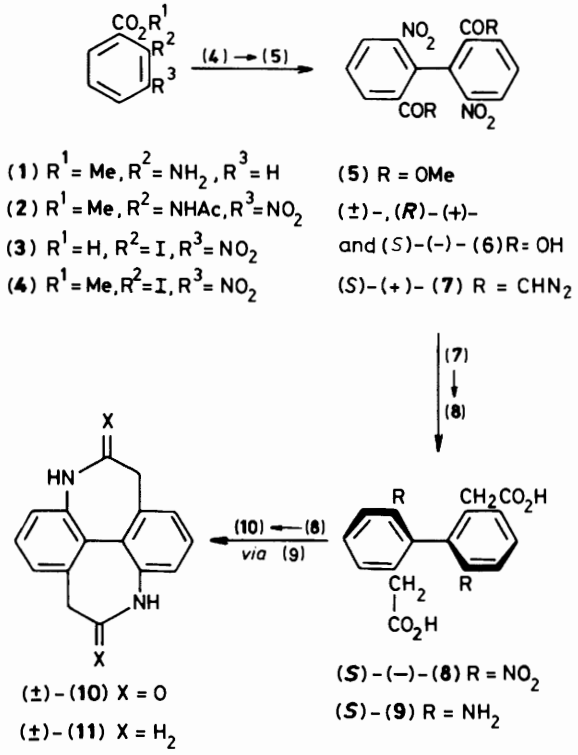


Figure 1. *cis* (A) and *trans* (B) Conformations of bridged biphenyls

Synthesis.—The optically active starting biphenyl, 6,6′-dinitrodiphenic acid (**6**), had been prepared earlier[5] but was synthesized without using mercury(II) acetate according to Scheme 1. Nitration of methyl anthranilate (**1**) gave compound (**2**) and methyl 2-acetamido-5-nitrobenzoate, which could readily be removed by recrystallization. Compound (**2**) was converted into the iodide (**3**) and Ullmann reaction of its methyl ester (**4**) gave the biphenyl derivative (**5**) in higher yield than *via* the bromide, methyl 2-bromo-3-nitrobenzoate.[5] Hydrolysis of the dimethyl ester (**5**) gave the dicarboxylic acid (**6**), which was resolved into optically active acids using (+)- and (−)-α-methylbenzylamine.[5]

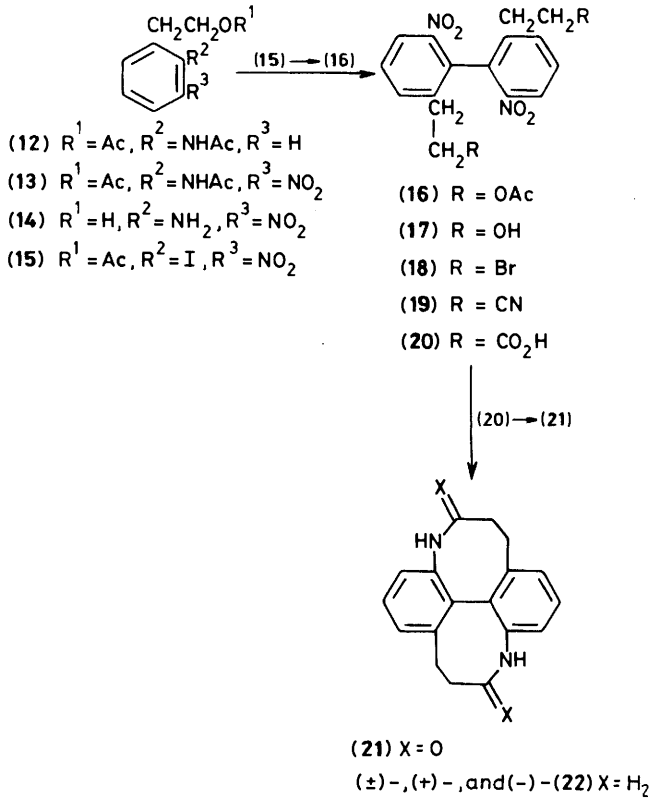


Scheme 1.

A doubly bridged biphenyl derivative (**11**) (θ *ca.* 135°) was synthesized as shown in Scheme 1. The Arndt–Eistert reaction of (*S*)-(−)-(**6**) *via* diazoketone (*S*)-(**7**) gave the homologated dicarboxylic acid (*S*)-(**8**) in good yield. After catalytic hydrogenation of the nitro group, cyclization of the intermediate (**9**) to dilactam (**10**) was carried out at room temperature with dicyclohexylcarbodi-imide (DCC) in dilute solution. However, the product showed no optical activity and the biphenyl racemized during the cyclization step. Furthermore, lactam (**10**) had to be reduced at the refluxing temperature of tetrahydrofuran (THF) with $LiAlH_4$ and thus we gave up trying to synthesize diamine (**11**) in optically active form.

In the transition state of the racemization, the torsional angle is taken to be 0°. The greater the angle θ in the ground state, the

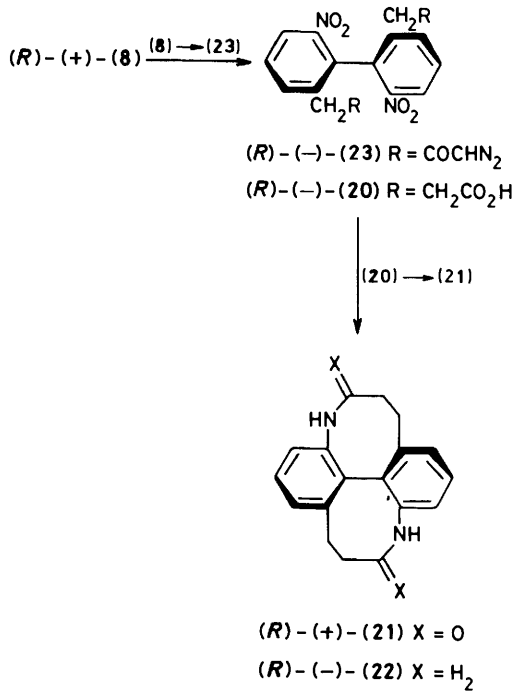
greater the energy barrier will be. We tried to synthesize the double bridged biphenyl with eight-membered rings. First, we chose the optical resolution method to investigate whether the amine was stable for racemization (Scheme 2).



Scheme 2.

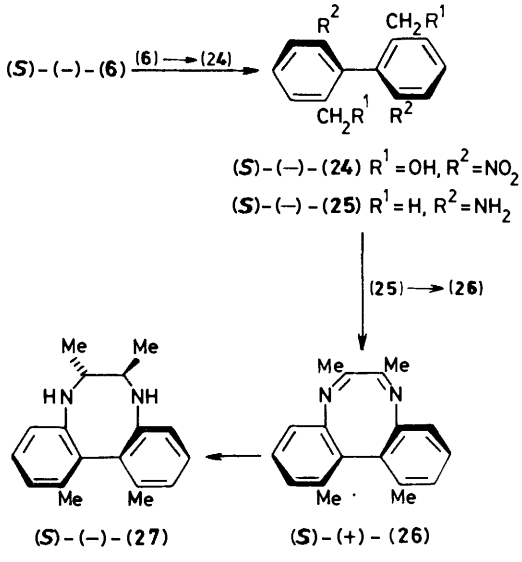
o-Aminophenethyl alcohol was nitrated *via* diacetate (**12**) to give compound (**13**) and 2-(2-acetamido-5-nitrophenyl)ethyl acetate. Nitration at the *ortho*-position dominated that at the *para*-position to the amino group. Separation was carried out by repeated recrystallization [45% yield of (**13**)] or silica gel column chromatography (60% yield). Compound (**13**) was converted into the iodide (**15**) *via* reaction of the amine (**14**) with KI–I_2 in high yield.[6] Ullmann reaction of compound (**15**) gave a biphenyl derivative (**16**), which was hydrolysed to give diol (**17**) in good yield. Diol (**17**) was treated with PBr_3 to give dibromide (**18**), which was converted into dicarboxylic acid (**20**) *via* dinitrile (**19**). Cyclization to dilactam (**21**) was achieved by the method described above (Scheme 1). Reduction of the dilactam was carried out in diglyme at reflux, since it did not proceed in THF. Optical resolution of the products (**22**), was achieved by using (+)-camphorsulphonic acid. Crystallization of the salt from methanol–ethyl acetate afforded needles (first crop) and the mother liquor also gave needles (second crop). Thus we obtained (+)-(**22**) ($[\alpha]_D^{24}$ +77.6°) from the first crop and (−)-(**22**) from the second crop.

Since diamine (**22**) did not racemize at room temperature, we decided to synthesize the optically active form of (**22**) from (*R*)-(+)-(**8**) to determine the absolute configuration of (+)- and (−)-(**22**). The route of the synthesis is summarized in Scheme 3. The Arndt–Eistert reaction was repeated twice from (*R*)-(+)-(**6**) and gave the two-carbon-homologated diacid (*R*)-(−)-(**20**) in good yield. The cyclization of (*R*)-(**20**) to dilactam (*R*)-(+)-(**21**) was achieved without racemization in contrast to the same reaction of (*S*)-(**8**) to dilactam (**10**). The dilactam (*R*)-(**21**) did



Scheme 3.

not racemize in refluxing diglyme. However, optically active diamine (**22**) gradually lost its activity with some decomposition at 109 °C in diglyme. Thus, we could not use the same reduction temperature as that of the racemic dilactam and chose milder reduction condition, that is heating at 105 °C for 5 h in diglyme. The diamine (**22**) obtained was optically active ($[\alpha]_D^{24}$ −77.7° after recrystallization) with some racemization. Clearly, (−)-(**22**) had the (*R*)-configuration and (+)-(**22**) the (*S*)-configuration.



Scheme 4.

Next, we synthesized the optically active singly bridged diamine (**27**), of type (A) in Figure 1, according to Scheme 4. Newman *et al.* have established the preparation of optically active 2,2′-diamino-6,6′-dimethylbiphenyl (**25**) from optically active (**6**) *via* diol (**24**).[7] We chose an improved procedure of

reducing diacid (*S*)-(−)-(**6**) to diol (−)-(**24**) using $NaBH_4$ *via* thiazolidine-2-thione amide[8] and obtained a good yield of the required product. Catalytic hydrogenation and hydrogenolysis gave diamine (*S*)-(−)-(**25**) in good yield. Cyclization of (*S*)-(**25**) to di-imine (*S*)-(+)-(**26**) was achieved according to the method of Hall and Insole.[9] No racemization seemed to occur in this cyclization process, since this type of di-imine is stable up to *ca.* 200 °C. Catalytic hydrogenation of (*S*)-(+)-(**26**) gave diamine (−)-(**27**) as the sole product. The ^{13}C n.m.r. spectrum with nine carbon signals showed that diamine (**27**) had C_2 symmetry. Hydrogen must attack from the less hindered side of the imine group as illustrated in Figure 2. As a result, the absolute configuration of the two asymmetric centres formed was deduced to be *R,R*. This was confirmed by the *X*-ray analysis described below.

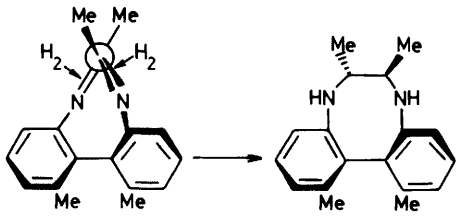


Figure 2. Stereochemistry of reduction mechanism of the di-imino compound (*S*)-(+)-(**26**)

X-*Ray Crystallography*.—Crystallographic analyses were carried out for (**22**), (**25**), and the HNO_3 salt of (**27**) (Figures 3—5; Table 1). As described above, an (*R,R*)-configuration was determined for the diaminoethylene bridge carbon atoms of (**27**).

The angles between the two phenyl mean planes are 118°, 66°, and 93° for (**22**), (**27**), and (**25**), respectively. The angle of (**27**) and the supplementary angle of (**22**) were very close and similar to those found in schizandrin-type lignans having an eight-atom ring.[10]

The cyclo-octadiene ring can be in two conformationally stable forms with C_2 symmetry, twist-boat (TB) and twist-boat-chair (TBC), which exist in almost equal populations in solution.[11] The cyclo-octadiene ring of the HNO_3 salt of (**27**) was in the TBC form in the crystalline state (Figure 4).

Two different kinds of conformers were present as pairs in a unit cell in the crystalline state of (**22**) but the two conformers (**A**) and (**B**) did not differ significantly (Figure 3). Although (**22**) has potential C_2 symmetry as shown in the structural formula, the crystalline state of the two conformers did not have that symmetry. One bridge involved a nearly planar amino group: the sum of the bond angles around nitrogen N(1) was 353(4)°

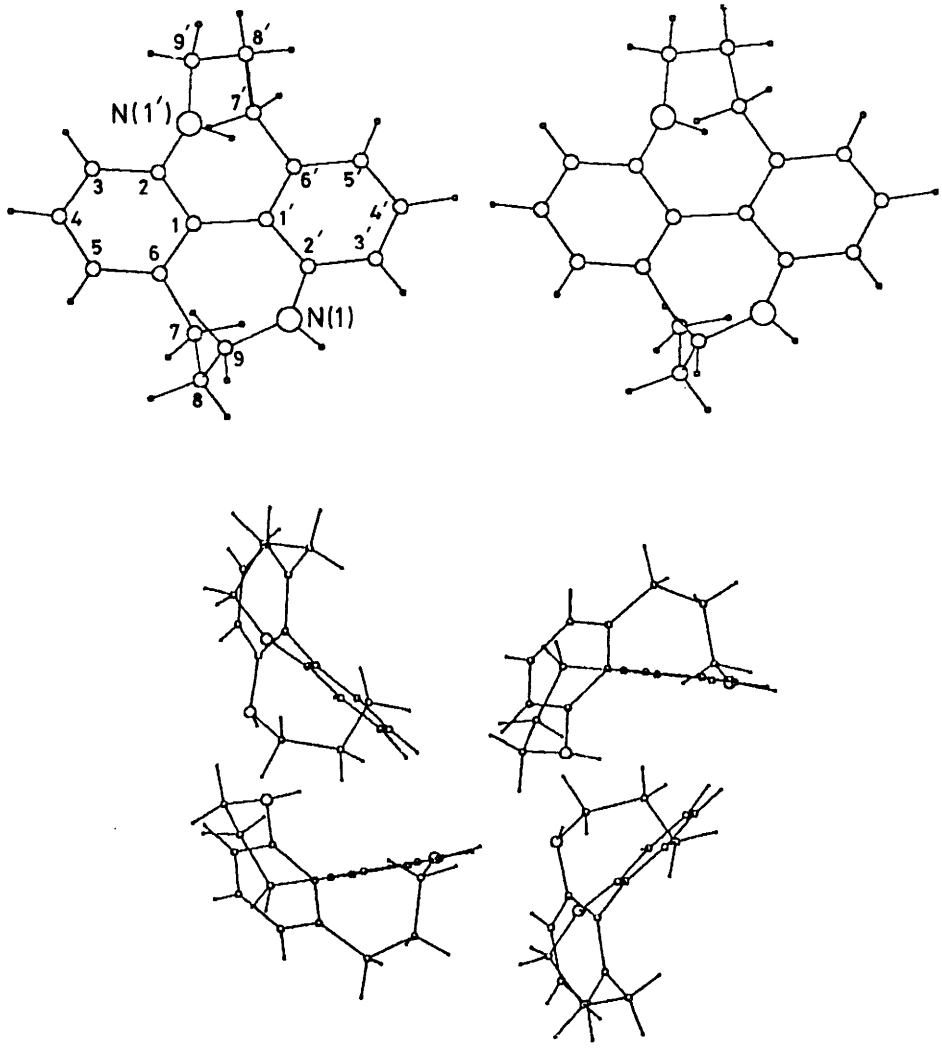


Figure 3. Molecular structure and stereoview of (**22**)

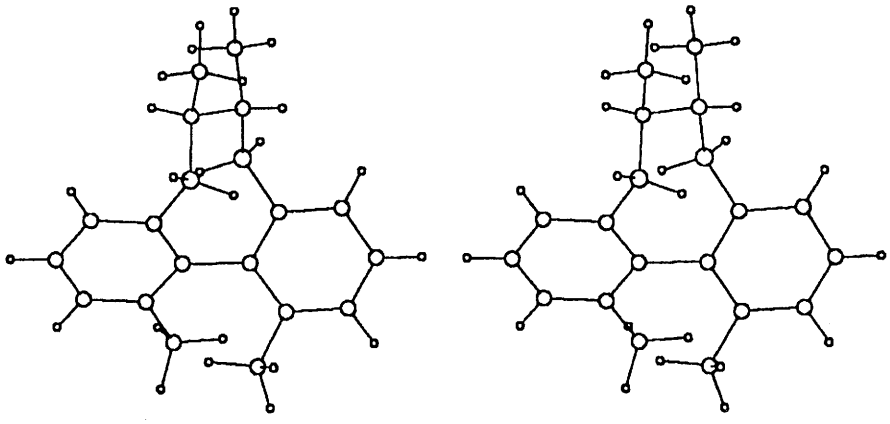


Figure 4. Stereoview of (**27**)

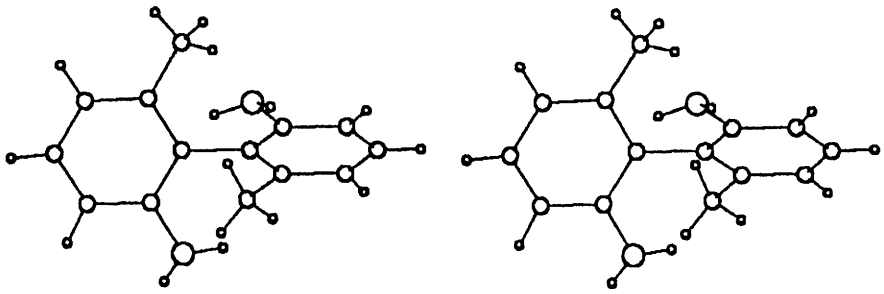


Figure 5. Stereoview of (**25**)

for (**A**) and 355(4)° for (**B**). The π-orbital of the nitrogen was orientated parallel to the π-orbital of the benzene ring and the ring was in the TB form. The other bridge had a pyramidal amino group: the sum of the bond angles around N(1′) was 344(4)° for (**A**) and 335(4)° for (**B**). The lone-pair orbital had a direction which did not allow conjugation with the π-orbital of the benzene ring and the ring was in the TBC form. There was one intramolecular [C(1′)···H–N(1′), 2.43(4) Å for (**A**) and 2.48(4) Å for (**B**)] and two intermolecular [N(1′) (**A**)···H–N(1′) (**B**), 2.16(4) Å; N(1′) (**B**)···H–N(1) (**A**), 2.43(4) Å] short contacts. The former intermolecular contact can be considered to be a hydrogen bond because the distance N(1′)···N(1) was 3.083(4) Å.

The i.r. spectrum of solid (**22**) showed three kinds of NH stretching absorptions at 3 420, 3 320, and 3 220 cm^{-1}, attributable to a free and two hydrogen-bonded NH, according to *X*-ray crystallography results. That of a dilute solution exhibited two kinds of NH stretching vibrations at 3 442 and 3 340 cm^{-1}, attributable to a pyramidal NH and a planar NH absorption. Thus, the amine (**22**) in solution exists in the same conformation as in the crystalline state and/or in an equilibrium between C_2-symmetrical TB and TBC forms.

A dilute solution of (**27**) showed only one NH stretching vibration at 3 345 cm^{-1}, attributable to the pyramidal NH, and therefore (**27**) must be in the same conformation in solution as in the crystalline state.

C.d. Spectra.—The c.d. and u.v. spectra of (*S*)-(+)-(**22**), (*S*)-(−)-(**25**), and (*S*)-(−)-(**27**) are presented in Table 2. Three band systems, in the 220, 240, and 300 nm regions, were observed in the u.v. spectra and were assigned, respectively, to the $^1B_{a,b}$, ^1L_a and ^1L_b bands of the benzene chromophores. Comparison of the c.d. and u.v. spectra of (*S*)-(+)-(**22**) and (*S*)-(−)-(**27**) in methanol indicated that the longest wavelength

Table 1. Fractional atomic co-ordinates and isotropic thermal parameters of (**22**), (**25**), and (**27**)·2HNO_3 with e.s.d.s. in parentheses.

(**22**) Molecule A	*x*	*y*	*z*	B_{eq}/B_{iso}
N(1)A	0.396 0(2)	0.084 8(1)	0.082 2(3)	5.00(7)
C(1)A	0.364 6(2)	0.076 3(1)	0.429 4(3)	2.77(5)
C(2)A	0.410 9(2)	0.102 9(1)	0.551 9(3)	2.82(5)
C(3)A	0.442 6(2)	0.066 5(1)	0.670 6(3)	3.79(7)
C(4)A	0.429 9(2)	0.003 6(1)	0.668 1(4)	3.99(7)
C(5)A	0.388 6(2)	−0.023 3(1)	0.543 2(4)	3.92(7)
C(6)A	0.355 7(2)	0.012 1(1)	0.423 2(3)	3.25(6)
C(7)A	0.318 7(2)	−0.018 0(1)	0.282 7(4)	4.25(7)
C(8)A	0.394 4(3)	−0.025 2(1)	0.162 4(4)	5.13(9)
C(9)A	0.447 9(2)	0.033 1(2)	0.137 7(4)	4.87(8)
N(1′)A	0.428 1(1)	0.167 5(1)	0.558 9(2)	3.08(5)
C(1′)A	0.315 5(2)	0.117 3(1)	0.319 4(3)	2.77(5)
C(2′)A	0.329 6(2)	0.117 5(1)	0.159 7(3)	3.46(6)
C(3′)A	0.276 1(2)	0.155 8(1)	0.067 7(3)	4.32(7)
C(4′)A	0.212 7(2)	0.193 5(1)	0.129 4(4)	4.43(8)
C(5′)A	0.198 3(2)	0.194 2(1)	0.285 4(4)	3.87(7)
C(6′)A	0.249 3(1)	0.156 4(1)	0.380 1(3)	3.06(6)
C(7′)A	0.230 1(2)	0.161 8(1)	0.550 7(4)	3.77(7)
C(8′)A	0.280 4(2)	0.215 1(1)	0.630 3(4)	4.23(7)
C(9′)A	0.377 5(2)	0.200 9(1)	0.675 7(3)	3.89(7)
H[N(1)A]	0.385(3)	−0.085(2)	0.016(5)	5.0
H[C(3)A]	0.473(2)	0.084(2)	0.763(4)	3.8
H[C(4)A]	0.454(3)	−0.021(2)	0.758(4)	4.0
H[C(5)A]	0.382(3)	−0.066(2)	0.541(4)	3.9
H(1)[C(7)A]	0.289(3)	−0.061(2)	0.308(5)	4.2
H(2)[C(7)A]	0.266(3)	0.007(2)	0.232(5)	4.2
H(1)[C(8)A]	0.444(3)	−0.061(2)	0.207(5)	5.1
H(2)[C(8)A]	0.368(3)	−0.041(2)	0.069(5)	5.1
H(1)[C(9)A]	0.476(3)	0.044(2)	0.239(5)	4.9

Table 1. (*continued*)

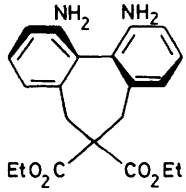
	x	*y*	*z*	B_{eq}/B_{iso}
H(2)[C(9)A]	0.495(3)	0.024(2)	0.060(5)	4.9
H[N(1')A]	0.417(2)	0.184(2)	0.460(4)	3.1
H[C(3')A]	0.287(3)	0.155(2)	−0.044(5)	4.3
H[C(4')A]	0.172(3)	0.228(2)	0.058(5)	4.4
H[C(5')A]	0.153(2)	0.222(2)	0.337(5)	3.9
H(1)[C(7')A]	0.163(2)	0.173(2)	0.560(4)	3.8
H(2)[C(7')A]	0.242(3)	0.122(2)	0.608(4)	3.8
H(1)[C(8')A]	0.281(3)	0.251(2)	0.549(4)	4.2
H(2)[C(8')A]	0.244(3)	0.230(2)	0.723(5)	4.2
H(1)[C(9')A]	0.413(2)	0.244(2)	0.698(4)	3.9
H(2)[C(9')A]	0.378(3)	0.176(2)	0.766(4)	3.9
Molecule B				
N(1)B	0.131 4(2)	0.346 5(1)	0.385 8(3)	3.70(5)
C(1)B	0.331 9(2)	0.367 1(1)	0.363 8(3)	2.61(5)
C(2)B	0.400 1(2)	0.323 7(1)	0.381 9(3)	2.89(5)
C(3)B	0.463 8(2)	0.330 2(1)	0.498 1(3)	3.46(6)
C(4)B	0.459 1(2)	0.379 6(1)	0.596 9(4)	4.21(7)
C(5)B	0.391 5(2)	0.422 6(1)	0.581 8(3)	4.11(7)
C(6)B	0.327 8(2)	0.417 5(1)	0.465 7(3)	3.37(6)
C(7)B	0.249 8(2)	0.461 3(1)	0.457 2(4)	4.39(8)
C(8)B	0.169 8(2)	0.437 5(2)	0.550 2(4)	4.79(8)
C(9)B	0.155 3(2)	0.369 2(1)	0.537 9(3)	3.88(7)
N(1')B	0.407 0(1)	0.270 8(1)	0.286 7(3)	3.47(5)
C(1')B	0.269 5(2)	0.362 0(1)	0.230 4(3)	3.00(5)
C(2')B	0.175 8(2)	0.353 6(1)	0.247 3(3)	3.11(6)
C(3')B	0.122 8(2)	0.346 9(1)	0.115 3(3)	3.72(7)
C(4')B	0.160 1(2)	0.350 0(1)	−0.028 1(3)	4.16(7)
C(5')B	0.250 5(2)	0.358 8(1)	−0.044 9(3)	3.89(7)
C(6')B	0.305 5(2)	0.364 5(1)	0.082 1(3)	3.28(6)
C(7')B	0.405 8(2)	0.371 5(2)	0.054 7(3)	4.45(8)
C(8')B	0.453 7(2)	0.310 2(2)	0.026 6(4)	5.49(10)
C(9')B	0.478 2(2)	0.273 8(2)	0.170 2(4)	4.89(8)
H[N(1)B]	0.068(2)	0.341(2)	0.382(4)	3.7
H[C(3)B]	0.512(2)	0.298(2)	0.510(4)	3.5
H[C(4)B]	0.499(2)	0.385(2)	0.686(4)	4.2
H[C(5)B]	0.388(3)	0.457(2)	0.653(4)	4.1
H(1)[C(7)B]	0.264(3)	0.506(2)	0.495(5)	4.4
H(2)[C(7)B]	0.227(3)	0.469(2)	0.343(5)	4.4
H(1)[C(8)B]	0.183(3)	0.447(2)	0.677(5)	4.8
H(2)[C(8)B]	0.114(3)	0.460(2)	0.518(5)	4.8
H(1)[C(9)B]	0.208(3)	0.347(2)	0.581(4)	3.9
H(2)[C(9)B]	0.096(3)	0.358(2)	0.601(5)	3.9
H[N(1')B]	0.351(2)	0.263(2)	0.242(4)	3.5
H[C(3')B]	0.055(3)	0.335(2)	0.131(4)	3.7
H[C(4')B]	0.122(3)	0.346(2)	−0.123(5)	4.2
H[C(5')B]	0.278(2)	0.362(2)	−0.140(5)	3.9
H(1)[C(7')B]	0.415(3)	0.400(2)	−0.040(5)	4.4
H(2)[C(7')B]	0.438(3)	0.395(2)	0.138(5)	4.4
H(1)[C(8')B]	0.412(3)	0.290(2)	−0.046(5)	5.5
H(2)[C(8')B]	0.515(3)	0.308(2)	−0.042(5)	5.5
H(1)[C(9')B]	0.487(3)	0.228(2)	0.140(5)	4.9
H(2)[C(9')B]	0.531(3)	0.295(2)	0.224(5)	4.9
(25)				
C(1)	0.586 4(3)	0.159 5(1)	0.353 1(3)	3.46(5)
C(2)	0.587 6(3)	0.228 9(1)	0.335 1(3)	3.67(5)
C(3)	0.697 1(3)	0.258 6(1)	0.213 6(3)	4.72(6)
C(4)	0.805 1(3)	0.219 9(2)	0.116 1(3)	5.27(7)
C(5)	0.806 4(3)	0.151 9(1)	0.135 2(3)	5.05(7)
C(6)	0.697 7(3)	0.121 0(1)	0.253 4(3)	4.04(5)
C(7)	0.699 4(4)	0.046 0(1)	0.273 8(4)	6.07(8)
N(2)	0.477 1(3)	0.268 2(1)	0.431 1(3)	4.86(5)
C(1')	0.468 2(3)	0.126 8(1)	0.481 1(3)	3.51(5)
C(2')	0.523 0(3)	0.113 2(1)	0.653 4(3)	4.11(5)
C(3')	0.417 4(4)	0.079 6(1)	0.769 5(3)	5.23(7)
C(4')	0.258 4(4)	0.061 2(1)	0.716 6(4)	5.62(7)
C(5')	0.202 3(3)	0.076 1(1)	0.548 1(4)	5.10(7)
C(6')	0.305 6(3)	0.108 6(1)	0.428 6(3)	4.10(5)
C(7')	0.246 3(3)	0.124 2(2)	0.244 7(4)	5.65(7)
N(2')	0.682 7(3)	0.130 3(1)	0.706 5(3)	5.67(6)

Table 1. (*continued*)

	x	*y*	*z*	B_{eq}/B_{iso}
H[C(3)]	0.691(3)	0.307(1)	0.211(3)	2.2(5)
H[C(4)]	0.877(3)	0.244(1)	0.039(3)	3.4(6)
H[C(5)]	0.882(3)	0.119(1)	0.069(3)	3.3(6)
H(1)[C(7)]	0.787(4)	0.025(2)	0.210(5)	6.3(9)
H(2)[C(7)]	0.723(4)	0.032(2)	0.389(5)	6.6(9)
H(3)[C(7)]	0.593(5)	0.029(2)	0.219(6)	9.9(13)
H(1)[N(2)]	0.513(4)	0.308(1)	0.460(4)	4.6(7)
H(2)[N(2)]	0.436(4)	0.249(1)	0.528(4)	3.5(6)
H[C(3')]	0.463(3)	0.069(1)	0.888(3)	3.4(6)
H[C(4')]	0.192(4)	0.041(2)	0.807(4)	5.0(7)
H[C(5')]	0.087(3)	0.061(1)	0.509(4)	3.5(6)
H(1)[C(7')]	0.139(4)	0.107(2)	0.220(4)	6.2(8)
H(2)[C(7')]	0.236(4)	0.170(2)	0.220(5)	6.8(9)
H(3)[C(7')]	0.321(5)	0.108(2)	0.149(6)	8.9(11)
H(1)[N(2')]	0.704(4)	0.135(1)	0.825(4)	4.8(7)
H(2)[N(2')]	0.737(3)	0.165(1)	0.647(4)	3.7(6)
(27)·2HNO_3				
C(1)	0.007 9(3)	0.063 9(2)	0.164 4(2)	2.74(6)
C(2)	−0.066 2(3)	0.126 6(2)	0.263 1(2)	2.42(5)
C(3)	−0.052 7(4)	0.245 1(2)	0.270 8(3)	3.38(6)
C(4)	0.040 4(5)	0.300 2(3)	0.174 4(3)	4.30(8)
C(5)	0.115 2(5)	0.238 3(3)	0.077 7(3)	4.65(9)
C(6)	0.102 2(4)	0.121 6(2)	0.070 7(3)	3.81(7)
N(7)	−0.155 5(3)	0.067 9(2)	0.368 7(2)	2.59(4)
C(8)	−0.051 9(3)	0.055 1(2)	0.492 0(2)	2.74(5)
C(9)	−0.172 6(5)	0.054 1(4)	0.605 5(3)	5.03(9)
C(10)	0.200 4(8)	0.056 5(4)	−0.031 7(4)	6.41(14)
N	0.450 1(4)	0.149 4(3)	0.350 1(4)	5.21(8)
O(1)	0.564 4(4)	0.197 3(3)	0.393 0(6)	8.40(13)
O(2)	0.309 9(3)	0.149 1(3)	0.372 2(6)	7.88(12)
O(3)a*	0.475 2(12)	0.078 0(6)	0.258 9(7)	6.8(2)
O(3)b*	0.521 4(36)	0.187 0(16)	0.247 4(27)	18.6(10)
H[C(3)]	−0.1063	0.2892	0.2892	3.38
H[C(4)]	0.0520	0.3852	0.1764	4.30
H[C(5)]	0.1800	0.2806	0.0105	4.65
H(1)[N(7)]	−0.1873	−0.0102	0.3376	2.59
H(2)[N(7)]	−0.2567	0.1130	0.3896	2.59
H[C(8)]	0.0265	0.1213	0.5014	2.74
H(1)[C(9)]	−0.2557	−0.0177	0.5943	5.03
H(2)[C(9)]	−0.1046	0.0447	0.6952	5.03
H(3)[C(9)]	−0.2412	0.1326	0.6066	5.03
H(1)[C(10)]	0.3314	0.0711	−0.0164	6.41
H(2)[C(10)]	0.1757	−0.0345	−0.0222	6.41
H(3)[C(10)]	0.1661	0.0848	−0.1268	6.41

* Occupancy = 0.5

band of (+)-(**22**) is shifted to the red relative to that of (−)-(**27**). This may be due to the presence of a nearly planar amino group in a molecule of (+)-(**22**) and a pyramidal amino group in (−)-(**27**), *i.e.* the difference in conjugation of the nitrogen lone-pair orbital with the π-orbital of the benzene ring, as observed in the *X*-ray crystallographic analysis. The pattern of the c.d. spectrum of (+)-(**22**), except for this red shift, is similar to that of (−)-(**27**). Mislow *et al.*[12] have reported the c.d. spectrum of the bridged 2,2'-diaminobiphenyl (*R*)-(**28**), which is fixed in the *cis*-conformation at θ *ca.* 45° by the seven-membered ring.[12] In



(*R*)-(**28**)

Table 2. U.v. and c.d. spectra of biphenyl derivatives

Compound	Medium	λ/nm (ε or Δε)
(*S*)-(−)-(**21**)	MeOH	u.v. 268sh (1 190), 244sh (8 590), 213.5 (47 800)
		c.d. 268 (−3.39), 229.5 (−54.8), 212.5 (−57.0), 200.5 (+11.8)
(*S*)-(+)-(**22**)	MeOH	u.v. 324 (3 580), 274sh (5 540), 250sh (11 300), 222.5 (32 800)
		c.d. 324 (+6.03), 288 (−5.73), 271 (+4.55), 249 (−43.9), 224 (+57.3), 206 (−40.6)
(*S*)-(+)-(**22**)·2HCl	MeOH	u.v. 278.5 (1 050), 270 (913), 262sh (772), 234 (9 150), 210 (36 000)
		c.d 276.5 (+2.37), 272sh (+1.14), 261.5 (−1.97), 231 (+41.5), 214.5 (+48.5), 197sh (−78.2), 190.5 (−107.6)
(*S*)-(+)-(**22**)	KBr	c.d. 330 (+9.2), 290 (−15.3), 257 (−39.1), 240.5 (+34.5), 223 (+23.4)
(*S*)-(−)-(**25**)	MeOH	u.v. 292.5 (4 800), 235 (14 600), 205 (59 000)
		c.d. 299.5 (+2.56), 280 (−3.72), 237 (−10.4), 215.5 (+15.4), 203.5 (−14.9)
(S)-(−)-(**25**)	heptane	u.v. 293 (5 490), 236.5 (15 100), 206 (56 800)
		c.d. 298 (+4.52), 281 (−6.39), 238 (−15.0), 215 (+17.9), 201 (−25.1)
(S)-(−)-(**25**)·2HCl	MeOH	u.v. 271 (945), 266sh (969), 263 (1 050), 212sh (22 500)
		c.d. 270.5 (+0.17), 267sh (+0.10), 255 (−0.14), 250 (−0.12), 245 (−0.11), 222sh (+1.73), 217 (+2.18)
(*S*)-(−)-(**25**)[a]	KBr	c.d. 302 (+2.75), 282 (−2.34), 240 (−16.2)
(*S*)-(+)-(**26**)	MeOH	u.v. 276 (3 170), 213 (35 500)
		c.d. 285.5 (+43.9), 223 (+23.0), 208 (+2.55)
(*S*)-(−)-(**27**)	MeOH	u.v. 290 (1 890), 251sh (9 810), 226sh (28 900), 215 (30 800)
		c.d. 292 (+10.1), 273sh (+5.73), 247 (−50.9), 222 (+7.45), 209 (−40.6)
(*S*)-(−)-(**27**)·2HCl	MeOH	u.v. 275sh (1 600), 267sh (1 990), 233sh (12 700), 212sh (32 300), 199 (39 200)
		c.d. 271sh (+2.42), 264 (+3.82), 227sh (−12.0), 215 (−34.5), 197 (+63.0)

[a] The enantiomer was measured.

Table 3. Calculated c.d. spectra of (*S*)-2,2′-diaminobiphenyls

θ (°)	λ/nm (Δε)
66	291 (+12.7), 267 (+9.12), 247 (−18.2), 208 (−16.0)
93	285 (+5.33), 265 (+2.02), 248 (−16.9), 205 (−0.38)
118	299 (+6.75), 279 (−0.60), 271 (+0.51), 250 (−39.7), 210 (−57.2)

spite of the difference in conformation, *cis*-skew and *trans*-skew, the similarity of the c.d. spectrum of (*S*)-(**28**) to those of (*S*)-(+)-(**22**) and (*S*)-(−)-(**27**) is particularly interesting. This suggests that the pattern of the c.d. spectra in the short-wavelength region, 200—250 nm, remains unchanged with an alteration of the torsion angle at least from 0° to 120°. Mislow *et al.*[13] have shown that, in the case of biphenyls, the sign and magnitude of the Cotton effect around 250 nm reflect the sign and size of the torsion angle between the aromatic rings, *i.e.* positive for the M-helicity. The empirical results have been supported by the investigation of c.d. spectra of aporphines of widely differing substitution patterns,[4,14] in which the ^1L_a band (conjugation band) is at longer wavelength (270—280 nm) and the intensity of the associated c.d. band is sensitive to alterations in the position of substituents in the biphenyl nucleus. The above observation in the presence of strong conjugation between the aromatic nuclei suggests that the influence of substituents on the c.d. intensity increases with decreasing conjugation between the aromatic rings.

For the case of (*S*)-(−)-(**25**), with the torsion angle of nearly 90° between the planes of the benzene rings, the transition moments are largely equivalent to those of two aniline moieties. For example, if the angle between the electric transition dipole vector and the long axis of the biphenyl skeleton is 60° instead of 90°, the pattern of the c.d. spectrum will be the same for the torsion angles of 0—130° (0° for the coplanar *cis*-conformation) according to the theory of dipole coupling.

Unbridged diamine (**25**) was reported to be in the *cis*-conformation from a comparison with the c.d. spectra of (**28**)[12] and measurement of the dipole moment in benzene.[15] But since the sign will be the same at least for the torsion angles of 0—120°, the assignment of the conformation is difficult by comparison of only the c.d. spectra of (**25**) and (**28**). As described above, the torsion angle was 93° for crystalline (**25**). We measured the c.d. spectrum for crystalline (+)-(**25**) with a KBr disc. The spectrum obtained was similar to that of (+)-(**25**) in solution. Thus we can assume that the torsion angle must be similar in the solution and in the crystalline state, and must be larger than 90°, as found for dinitro compounds.[12]

The c.d. spectra of the HCl salts of (*S*)-(**22**) and (*S*)-(**27**) suggested that these compounds were almost enantiomeric (Table 2): the signs were opposite and the magnitudes were almost the same. The Cotton effect seems to invert at a torsion angle θ of *ca.* 90°. This inversion may be caused by the similarity in the magnitude of the perturbation of the ammonium group and the methylene group.

The c.d. spectrum of the 2HCl salt of (*S*)-(**25**) showed a similar pattern to that of (*S*)-(**22**)·HCl and was antipodal to that of (*S*)-(**27**)·2HCl (Table 2). However, the magnitude of the c.d. spectrum of (*S*)-(**25**)·2HCl was far smaller than those of (*S*)-(**22**)·2HCl and (*S*)-(**27**)·2HCl. This suggests that the torsion angle θ of (*S*)-(**25**)·2HCl would be slightly larger than 90° in solution. Mislow *et al.* have reported that the torsion angle was larger than 90° owing to the repulsion between the two positive charges.[12] As described before, the torsion angle θ of (*S*)-(**25**) was more than 90° and the repulsion between the positive charges did not always make the torsion angle larger than 90°.

We calculated the theoretical rotational strength of the diaminobiphenyl compounds by the dipole velocity method using π-SCF-MO-CI. The following torsion angles were used: θ = 118°, 66°, and 93°; these were obtained by *X*-ray analysis. A resonance integral $\beta_{1-1'}$ of the 1-1′ bond was estimated from the relation of $\beta_0 \cdot \cos\theta$, where $\beta_0 = -2.371$ eV. The calculated energies and rotational strengths were converted into a theoretical c.d. spectrum on the assumption that the spectrum represented a sum of Gaussian bands.[16]

The theoretical curves agreed well with the experimental ones (Table 3). In particular, the negative Cotton effects at around 250 nm, characteristic of the (*S*)-configuration of the diamino

compounds, could be reproduced for three compounds by this method. The major shortcoming of the calculation was the failure to produce the positive Cotton effect at *ca.* 220 nm.

Experimental

M.p.s are uncorrected. Optical rotations were determined with a Perkin-Elmer Model 141 polarimeter, using a 1.0 dm microcell. C.d. curves were obtained using a JASCO Model J-40 spectropolarimeter. I.r. spectra were recorded on a JASCO-A702 spectrophotometer. N.m.r. spectra were measured with Varian XL200 and EM390 spectrometers using tetramethylsilane as the internal standard. U.v. spectra were obtained on a Hitachi Model 323 spectrophotometer. Mass spectra were taken with a HITACHI M-68 mass spectrometer. *X*-Ray diffraction data were collected on a Rigaku diffractometer with graphite-monochromatized Cu-K_α radiation (λ 1.5418 Å) for (**22**) and the nitrate of (**27**), and Mo-K_α radiation (λ 0.7107 Å) for (**25**).

Methyl 2-Acetamido-3-nitrobenzoate (**2**).—A solution of methyl anthranilate (**1**) (21 ml) in Ac_2O (170 ml) was stirred for 1 h at room temperature. A mixture of Ac_2O (35 ml), AcOH (30 ml), and 60% HNO_3 (50 ml) was added dropwise to the stirred solution during 2 h at 10 ± 5 °C. The mixture was stirred at that temperature for 2.5 h and was then poured into ice–water (100 ml) and the precipitates (A) were collected by filtration and washed with water. The filtrate was extracted with chloroform and the extract was dried (Na_2SO_4). The solvent was removed under reduced pressure to give an oily residue which was crystallized from ether (6.59 g).

The precipitates (A) were recrystallized from chloroform–methanol to give methyl 2-acetamido-5-nitrobenzoate (10.4 g). The mother liquor was concentrated under reduced pressure and the residue was crystallized from ether to give the *3-nitro ester* (**2**) (16.1 g; total yield 59%), m.p. 115—117 °C; $\nu_{max.}$(KBr) 3 320, 1 723, 1 682, and 1 535 cm^{-1}; δ($CDCl_3$) 2.23 (3 H, s), 3.96 (3 H, s), 7.31 (1 H, t, *J* 3 Hz), and 8.04—8.37 (2 H, m); *m/z* 238 (Found: C, 50.55; H, 4.05; N, 11.85. $C_{10}H_{10}N_2O_5$ requires C, 50.4; H, 4.25; N, 11.75%).

2-Iodo-3-nitrobenzoic Acid (**3**).—The ester (**2**) (106.8 g) was hydrolysed with aqueous KOH (220 g in 500 ml). The orange needles (75.5 g) were collected by filtration and suspended in a mixture of conc. HCl (400 ml) and water (800 ml). A solution of $NaNO_2$ (40 g) in water (120 ml) was added at 2 ± 2 °C during 1.5 h. The diazonium solution was then added to a solution of KI (95 g) and I_2 (75 g) in dimethyl sulphoxide (DMSO) (1.5 l) at 5 °C during 20 min and the mixture was stirred at 50 °C for 20 min. After being cooled, the mixture was extracted with ethyl acetate. The extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to obtain the acid (**3**) as a crystalline powder which was washed with n-hexane (114.5 g, 87%), m.p. 210—212 °C [lit.,[17] 210—212 °C]; $\nu_{max.}$(KBr) 1 712, 1 542, and 1 378 cm^{-1}; δ([$^2H_6$]acetone) 7.65—8.01 (3 H, m); *m/z* 293 (Found: C, 28.8; H, 1.65; N, 4.9. Calc. For $C_7H_4INO_4$: C, 28.7; H, 1.4; N, 5.0%).

Methyl 2-Iodo-3-nitrobenzoate(**4**).—A solution of the acid (**3**) (18.4 g) in methanol (400 ml) and conc. H_2SO_4 (15 ml) was heated under reflux overnight and extracted with chloroform. The extract was washed successively with 5% aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was crystallized from chloroform–n-hexane and gave yellow needles (18 g, 93%), m.p. 65—66 °C [lit.,[17] 64—66 °C]; $\nu_{max.}$(KBr) 1 705, 1 532, and 1 350 cm^{-1}; δ($CDCl_3$) 3.97 (3 H, s) and 7.53—7.83 (3 H, m); *m/z* 307 (Found: C, 31.1; H, 2.15; I, 41.4; N, 4.6. Calc. for $C_8H_6INO_4$: C, 31.3; H, 1.95; I, 41.35; N, 4.55%).

Dimethyl 6,6′-Dinitrobiphenyl-2,2′-dicarboxylate (**5**).—A mixture of (**4**) (6.4 g) and activated Cu powder (5 g) was heated at 100—180 °C during 3 h under nitrogen. The mixture was extracted with chloroform and the extract was chromatographed on silica gel with chloroform as eluant. The residue (3.42 g, 91%) was recrystallized from methylene dichloride–n-hexane and gave the diester (**5**) as yellow prisms which were identical with an authentic sample.[5]

6,6′-Dinitrodiphenic Acid (*6,6′-Dinitrobiphenyl-2,2′-dicarboxylic Acid*) (**6**).—The dimethyl ester (**5**) (60 g) was hydrolysed at 70 °C for 3 h in a solution of KOH (50 g) in methanol (1 l). The solution was concentrated under reduced pressure and acidified with conc. HCl to give the acid (**6**) as a powder (48.1 g, 87%) which was identical with an authentic sample.

(S)-(+)-*2,2′-Bisdiazoacetyl-6,6′-dinitrobiphenyl* (**7**).—A suspension of (*S*)-(−)-(**6**) (3.5 g) and thionyl chloride (10 ml) in benzene (40 ml) was heated under reflux for 2 h. The volatile materials were removed by distillation under reduced pressure. The residue was dissolved in benzene (30 ml) and the solution was added to a stirred excess of diazomethane in ether at 5 °C. The solution was stirred for 1 h and concentrated under reduced pressure. The residue was crystallized from benzene, to give the *diazo compound* as yellow prisms (3.55 g, 89%), m.p. 145—146 °C (decomp.); $[\alpha]_D^{23}$ +28.9° (*c* 0.391 in $CHCl_3$); $\nu_{max.}$(KBr) 2 120, 1 625, 1 617, and 1 610 cm^{-1}; δ($CDCl_3$) 5.60 (1 H, s), 7.60 (1 H, t, *J* 7 Hz), 7.73 (1 H, dd, *J* 7 and 3 Hz), and 8.28 (1 H, dd, *J* 7 and 3 Hz); *m/z* 342 (Found: C, 50.7; H, 2.45; N, 21.95. $C_{16}H_8N_6O_4$ requires C, 50.55; H, 2.1; N, 22.1%).

(S)-(−)-*6,6′-Dinitrobiphenyl-2,2′-diacetic Acid* (**8**).—A warm solution of (*S*)-(+)-(**7**) (390 mg) in dioxane (5 ml) was added dropwise during 45 min to a stirred suspension of Ag_2O, freshly prepared from 10% $AgNO_3$ (5 ml), at 65 °C. Next, a small portion of Ag_2O was added every 15 min. The mixture was kept at 65 °C for 30 min, then the temperature was raised to 90 °C during 50 min. After being cooled the mixture was made alkaline with dil. NaOH and the insoluble materials were removed by filtration. The filtrate was acidified with 10% aqueous HCl and extracted with ether. The solution was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was crystallized from acetone–benzene and gave yellow prisms of the *acid* (**8**) (280 mg, 76%), m.p. 197—200 °C; $[\alpha]_D^{23}$ −18.0° (*c* 0.266 in MeOH); $\nu_{max.}$(KBr) 1 705 and 1 531 cm^{-1}; δ([$^2H_6$]acetone) 3.33 (2 H, s), 7.33 (1 H, t, *J* 8 Hz), 7.93 (1 H, dd, *J* 8 and 2 Hz), and 8.21 (1 H, dd *J* 7 and 2 Hz) (Found: C, 53.6; H, 3.45; N, 7.6. $C_{16}H_{12}N_2O_8$ requires C, 53.35; H, 3.35; N, 7.8%).

4,5,6,10,11,12-*Hexahydro*[1]*benzazepino*[6,5,4-def][1]*benzazepine-5,11-dione* (**10**).—(*S*)-(−)-(**8**) (360 mg) was hydrogenated in methanol (20 ml) with PtO_2 (200 mg). The catalyst was then filtered off and washed with methanol. The solvent was removed from the combined filtrate and washings under reduced pressure. The residue [(**9**)] was suspended in methylene dichloride (450 ml). A solution of DCC (618 mg) in methylene dichloride (20 ml) was added to the stirred suspension at 0 °C. The mixture was stirred at room temperature for 24 h and the solvent was removed under reduced pressure. The residue was chromatographed on Sephadex LH-20 with methanol–chloroform (7:3) as eluant and gave the *product* (**10**) as prisms (137 mg, 52%). The product was too insoluble to allow measurement of its $[\alpha]_D$ value; however, the c.d. spectrum did not show a Cotton effect in methanol. The product had m.p. >300 °C; $\nu_{max.}$(KBr) 1 671 cm^{-1}; $\lambda_{max.}$(MeOH) 305.5 (ε 2 500), 296.5 (1 860), and 239.0 nm (16 400); *m/z* 264 (Found: C, 72.55; H, 4.45; N, 10.6. $C_{16}H_{12}N_2O_2$ requires C, 72.7; H, 4.6; N, 10.6%).

4,5,6,10,11,12-*Hexahydro*[1]*benzazepino*[6,5,4-def][1]*benzazepine* (**11**).—A suspension of the dilactam (**10**) (80 mg) in dry THF (20 ml) was added to a stirred slurry of $LiAlH_4$ (150 mg) in THF (30 ml) at 0 °C. The mixture was stirred at room temperature for 30 min and then heated under reflux for 5 h. A solution of methanol in ether was added to decompose excess of $LiAlH_4$ and the entire mixture was poured into 10% aqueous KOH and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was crystallized from chloroform–methylene dichloride–ether to give the *diamine* (**11**), m.p. 225—227 °C; $\nu_{max.}$(KBr) 3 355 cm^{-1}; δ($CDCl_3$) 2.50—2.87 (4 H, m), 3.17 (2 H, br s), 3.50—3.77 (4 H, m), and 6.67—7.77 (6 H, m); *m/z* 236 (Found: C, 81.15; H, 6.65; N, 11.9. $C_{16}H_{16}N_2$ requires C, 81.3; H, 6.8; N, 11.85%).

2-(2-*Acetamido*-3-*nitrophenyl*)*ethyl Acetate* (**13**).—A solution of 60% aqueous HNO_3 (3 ml), Ac_2O (2 ml), and AcOH (1.8 ml) was added dropwise to a stirred suspension of 2-(2-acetamidophenyl)ethyl acetate (**12**) (2.8 g) in Ac_2O (15 ml) at 0—10 °C during 30 min. The solution was stirred at 5 °C for 2 h and then poured into ice–water. The precipitates were collected by filtration. The filtrate was extracted with chloroform and the extract was washed with water, dried (Na_2SO_4) and concentrated under reduced pressure. The precipitates and the residue were chromatographed on silica gel with chloroform–acetonitrile as eluant and the eluate was crystallized from chloroform–ether to give (**13**) (1.82 g, 60%).

In another run, the precipitates were recrystallized from chloroform–ether several times and gave the *ester* (**13**) in 45% yield, m.p. 150 °C; $\nu_{max.}$(KBr) 3 270, 1 730, and 1 659 cm^{-1}; δ($CDCl_3$) 2.04 (3 H, s), 2.22 (3 H, s), 3.00 (2 H, t, *J* 7 Hz), 4.28 (2 H, t, *J* 7 Hz), 7.30 (1 H, t, *J* 8 Hz), 7.53 (1 H, dd, *J* 8, 2 Hz), 7.85 (1 H, dd, *J* 8 and 2 Hz), and 8.32 (1 H, br s) (Found: C, 54.15; H, 5.35; N, 10.45. $C_{12}H_{14}N_2O_5$ requires C, 54.15; H, 5.3; N, 10.5%).

2-(2-*Amino*-3-*nitrophenyl*)*ethanol* (**14**).—A mixture of (**13**) (2.46 g) in 20% aqueous KOH (50 ml) was warmed at 80 °C for 30 min and then cooled to room temperature. Orange needles (99%) were collected by filtration, washed with water and hexane, and used in the next preparation without further purification, $\nu_{max.}$(KBr) 3 505, 3 465, and 3 345 cm^{-1}; δ($CDCl_3$) 1.80 (1 H, t, *J* 4 Hz), 2.87 (2 H, t, *J* 6 Hz), 3.97 (2 H, m), 6.60 (1 H, dd, *J* 7 and 8 Hz), 6.60 (2 H, br s), 7.23 (1 H, dd, *J* 7 and 1.5 Hz), and 8.02 (1 H, dd, *J* 8 and 1.5 Hz).

2-(2-*Iodo*-3-*nitrophenyl*)*ethyl Acetate* (**15**).—A solution of $NaNO_2$ (850 mg) in water (2.5 ml) was added dropwise to a stirred suspension of compound (**14**) (2.24 g) in a mixture of conc. HCl (7.5 ml) and water (17 ml) at 0 °C. A small amount of urea was added and then the solution was rapidly filtered by suction. Next, 42% aqueous HBF_4 (3.7 ml) was added to the filtrate and a solution of KI (2.25 g) and I_2 (1.75 g) in DMSO (30 ml) was added to the stirred diazonium solution at room temperature. The mixture was stirred at room temperature for 1 h and warmed at 40 °C for 30 min. Then $FeSO_4 \cdot 7H_2O$ (4 g) was added and the mixture was extracted with ethyl acetate. The extract was washed successively with aqueous $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated under reduced pressure. The oily residue was acetylated with Ac_2O (20 ml) and pyridine (15 ml) at room temperature overnight. The mixture was treated in the usual manner and the residue was recrystallized from chloroform–n-hexane to give yellow prisms of the *iodo compound* (**15**) (4.04 g, 98%), m.p. 75.5—77 °C; $\nu_{max.}$(Nujol) 1 725 cm^{-1}; δ($CDCl_3$) 2.03 (3 H, s), 3.23 (2 H, t, *J* 6.5 Hz), 4.30 (2 H, t, *J* 6.5 Hz), and 7.35 (3 H, s) (Found: C, 35.6; H, 3.1; N, 4.45; I, 37.95. $C_{10}H_{10}INO_4$ requires C, 35.84; H, 3.01; N, 4.18; I, 37.85%).

2,2′-*Bis*-(2-*acetoxyethyl*)-6,6′-*dinitrobiphenyl* (**16**).—A mixture of (**15**) (4.04 g) and activated Cu powder (3.03 g) was heated at 100 °C for 1 h under N_2. The temperature was then slowly raised to 160 °C during 2 h. After being cooled the mixture was extracted with chloroform–acetone and the extract was evaporated under reduced pressure. The oily residue was chromatographed on silica gel with chloroform as eluant. The residue (2.2 g, 88%) from the eluate was used in the next preparation without further purification, δ($CDCl_3$) 1.96 (6 H, s), 2.56 (4 H, t, *J* 7 Hz), 7.47 (2 H, t, *J* 7 Hz), 7.63 (2 H, dd, *J* 7, 2.5 Hz), and 7.98 (2 H, dd, *J* 7 and 2.5 Hz).

2,2′-*Bis*-(2-*hydroxyethyl*)-6,6′-*dinitrobiphenyl* (**17**).—The diacetate (**16**) (22.7 g) was stirred with a solution of KOH (25 g) in methanol (250 ml) at room temperature for 2 h. Next, water (700 ml) was added and the mixture was extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was crystallized from chloroform–benzene to give the *diol* (**17**) as pale yellow prisms (14.76 g, 81%), m.p. 93—94 °C; $\nu_{max.}$(KBr) 3 340, 1 522, and 1 350 cm^{-1}; δ($CDCl_3$) 2.48 (2 H, t, *J* 6 Hz), 2.52 (2 H, t, 6 Hz), 3.70 (4 H, t, *J* 6 Hz), 7.54 (2 H, t, *J* 8 Hz), 7.72 (2 H, dd, *J* 8 and 2 Hz), and 8.03 (2 H, dd, *J* 8 and 2 Hz); *m/z* 314 (Found: C, 57.85; H, 4.95; N. 8.5. $C_{16}H_{16}N_2O_6$ requires C, 57.85; H, 4.85; N, 8.45%).

2,2′-*Bis*-(2-*bromoethyl*)-6,6′-*dinitrobiphenyl* (**18**).—A mixture of the diol (**17**) (8.7 g) and PBr_3 (6.5 ml) was stirred and heated at 100 °C under N_2 for 70 min, poured into ice–water, and extracted with chloroform. The extract was washed successively with aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on silica gel with chloroform as eluant and recrystallized from chloroform–ether, to give pale yellow prisms of the *dibromide* (**18**), m.p. 118.5—119.5 °C; $\nu_{max.}$(KBr) 1 529 and 1 352 cm^{-1}; δ($CDCl_3$) 2.78 (2 H, t, *J* 8 Hz), 2.81 (2 H, t, *J* 7 Hz), 3.38 (2 H, t, *J* 7 Hz), 3.40 (2 H, t, *J* 8 Hz), 7.60 (2 H, t, *J* 7.5 Hz), 7.72 (2 H, dd, *J* 7.5 and 2.5 Hz), and 8.08 (2 H, d, *J* 7.5 and 2.5 Hz); *m/z* 457 and 459 (Found: C, 41.65; H, 3.15; Br, 34.75; N, 6.05. $C_{16}H_{14}Br_2N_2O_4$ requires C, 41.95; H, 3.1; Br, 34.9; N, 6.1%).

2,2′-*Bis*-(2-*cyanoethyl*)-6,6′-*dinitrobiphenyl* (**19**).—A mixture of the dibromide (**18**) (820 mg), NaCN (351 mg), and DMSO (4 ml) was stirred and heated at 80 °C for 10 min. Chloroform was added and the insoluble materials were filtered off and washed with chloroform. The combined filtrate and washings were washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on silica gel with chloroform as eluant and, after work-up, showed $\nu_{max.}$($CHCl_3$) 2 245, 1 531, and 1 352 cm^{-1}; δ($CDCl_3$) 2.51 (8 H, m), 7.57—7.80 (4 H, m), and 8.80 (2 H, dd, *J* 6.5 and 3 Hz); *m/z* 350.

(R)-(−)-2,2′-*Bis*-(3-*diazo*-2-*oxopropyl*)-6,6′-*dinitrobiphenyl*, (R)-(−)-(**23**).—Oxalyl dichloride (3 ml) was added to a suspension of (*R*)-(+)-(**8**) (536 mg) in benzene (20 ml). The mixture was heated under reflux for 1.5 h. The volatile materials were removed under reduced pressure and the residue was stirred with an excess of diazomethane in ether at 0 °C for 4 h. The volatile materials were removed by distillation. The residue was chromatographed on silica gel with chloroform as eluant. Work-up gave the *diazo compound* (**23**) as yellow prisms (328 mg, 54%) which were recrystallized from benzene, m.p. 139 °C (decomp.); $[\alpha]_D^{22}$ −42.9 ± 2.6° (*c* 0.319 in MeOH); $\nu_{max.}$(KBr)

2 100 cm^{-1}; δ($CDCl_3$) 3.27 (4 H, s), 5.03 (2 H, s), 7.5—7.7 (4 H, m), and 8.03 (2 H. dd. *J* 6.5 and 2.5 Hz); *m/z* 380 (*M* − N_2) (Found: C, 53.0; H, 3.1; N, 20.45. $C_{18}H_{12}N_6O_6$ requires C, 52.95; H, 2.95; N, 20.6%).

(R)-(−)- *and* (±)-2,2′-*Bis*-(2-*carboxyethyl*)-6,6′-*dinitrobiphenyl*, (R)-(−)- *and* (±)-(**20**).—(i) A solution of (*R*)-(−)-(**23**) (664 mg) in dioxane (10 ml) was added dropwise to a stirred suspension of Ag_2O, prepared from 10% aqueous $AgNO_3$ (10 ml), in 1% aqueous $Na_2S_2O_3$ (40 ml) at 65 °C during 1.5 h. During the addition, a small amount of a mixture of Ag_2O and 1% aqueous $Na_2S_2O_3$ was added several times. The temperature was then raised to 90 °C during 2 h. The insoluble materials were removed by filtration and 10% aqueous HCl (50 ml) was added. The mixture was extracted with ether and the extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The crystalline residue was recrystallized from acetone–benzene to give the *diacid* (**20**) as pale yellow prisms, m.p. 219—222 °C; $[\alpha]_D^{22}$ −18.4 ± 1.9° (*c* 0.311 in MeOH); $\nu_{max.}$(KBr) 1 709 cm^{-1}; δ($CDCl_3$) 2.37—2.72 (8 H, m), 7.70 (2 H, t, *J* 8 Hz), 7.90 (2 H, dd, *J* 8 and 2 Hz), and 8.10 (2 H, dd, *J* 8 and 2 Hz); $\lambda_{max.}$(MeOH) 309sh (ε 3 660), 261.5 (70 300), and 209sh nm (33 500); *m/z* 389 (Found: C, 55.35; H, 3.95; N, 7.35. $C_{15}H_{16}N_2O_8$ requires C, 55.65; H, 4.15; N, 7.2%).

(ii) A mixture of the nitrile (**19**) (81 mg) and 50% aqueous H_2SO_4 (20 ml) was heated at 160 °C (bath temp.) for 4 h and poured into water. The precipitates (60 mg) were collected by filtration and the filtrate was extracted with ether. The extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure to give the diacid as a crystalline powder (14 mg, total 82%). The n.m.r. spectrum was identical with that of the (*R*)-(−)-isomer.

(R)-(+)-4,5,6,7,11,12,13,14-*Octahydro*[1]*benzazocino*[7,6,5-efg][1]*benzazocine*-5,12-*dione*, (R)-(+)-(**21**).—A mixture of (*R*)-(−)-(**20**) (615 mg) and PtO_2 (0.1 g) in methanol (10 ml) was stirred for 2 h under hydrogen. The catalyst was then filtered off and washed with methanol. The filtrate and washings were concentrated under reduced pressure. The residue was suspended in a mixture of methylene dichloride (350 ml) and acetonitrile (100 ml) and DCC (1.306 g) was added. The mixture was stirred at room temperature for 24 h and concentrated under reduced pressure. The residue was chromatographed on silica gel with chloroform–methanol as eluant. The residue from work-up was recrystallized from acetone to give the *tetracyclic dione* (**21**) as pale yellow needles (238 mg), m.p. > 300 °C; $[\alpha]_D^{22}$ +225.7 ± 12.9° (*c* 0.206 in MeOH); $\nu_{max.}$(KBr) 1 658 cm^{-1}; $\lambda_{max.}$(MeOH) 268sh (ε 1 190) and 213.5 nm (47 800) (Found: C, 73.65; H, 5.65; N, 9.45. $C_{18}H_{16}N_2O_2$ requires C, 73.95; H, 5.5; N, 9.6%).

(R)-(−)-4,5,6,7,11,12,13,14-*Octahydro*[1]*benzazocino*[7,6,5-efg][1]*benzazocine*, (*R*)-(−)-(**22**).—A mixture of a large excess of $LiAlH_4$ and (*R*)-(+)-(**21**) (87 mg) in diglyme (75 ml) was heated at 105 °C for 5 h. Excess of $LiAlH_4$ was decomposed with methanol and then 50% aqueous KOH. The mixture was extracted with ether and the extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was crystallized twice from chloroform–methanol to give the *tetracycle* (**22**), $[\alpha]_D^{24}$ −77.7 ± 6.4° (*c* 0.184 in MeOH); m.p. 204.5—206.5 °C; $\nu_{max.}$(KBr) 3 420 and 3 320 cm^{-1}; δ($CDCl_3$)1.4—3.6 (10 H, m) and 6.7—7.3 (6 H, m); δ_C (CD_2Cl_2) 32.0, 47.9, 119.4, 121.5, 126.8, 129.2, 143.0 and 150.5 p.p.m.; *m/z* 264 (Found: C, 81.65; H, 7.7; N, 10.45. $C_{18}H_{20}N_2$ requires C, 81.8; H, 7.65; N, 10.6%).

Optical Resolution of (**22**).—A solution of (+)-camphor-10-sulphonic acid (645 mg) in methanol (5 ml) was added to a solution of the diamine (**22**) (367 mg) in methanol (30 ml). The solution was concentrated to *ca.* 4 ml and ethyl acetate (30 ml) was added. The solution was kept at room temperature for 28 h. The salt was collected by filtration and recrystallized from methanol–ethyl acetate, $[\alpha]_D^{24}$ +30.8 ± 1.0° (*c* 0.701 in MeOH).

The salt (65 mg) was treated with aqueous KOH. The amine (25 mg) was recrystallized from methanol, and had $[\alpha]_D^{24}$ +77.6 ± 6.8° (*c* 0.174 in MeOH); m.p. 204.5—206.5 °C. The salt thus possessed two molecules of acid per molecule of base.

The mother liquor of the salt was concentrated under reduced pressure. The residue was crystallized twice from methanol–ethyl acetate to give a second salt, $[\alpha]_D^{24}$ +21.9 ± 0.8° (*c* 0.754 in MeOH).

The second salt (7 mg) was treated as above to give the antipodal amine (3.3 mg), $[\alpha]_D^{24}$ −64.9 ± 4.4° (*c* 0.1665 in MeOH); thus this second salt possessed one molecule of acid per molecule of base.

(S)-(−)-2,2′-*Bis*(*hydroxymethyl*)-6,6′-*dinitrobiphenyl*, (S)-(−)-(**24**).—A mixture of (*S*)-(−)-(**6**) (5.60 g, 16.8 mmol) and $SOCl_2$ (40 ml) was heated under reflux for 2 h. The volatile materials were removed by distillation. The residue was dissolved in THF (100 ml) and thiazolidine-2-thione (4.05 g, 34 mmol) and triethylamine (5.7 ml) were added to the stirred solution. The mixture was stirred at 50 °C for 30 min and then cooled. A solution of $NaBH_4$ (5 g) in water (30 ml) was added and the mixture was stirred overnight. Next, 10% aqueous HCl (70 ml) was added and the mixture was extracted with ether. The extract was washed successively with 10% aqueous KOH and water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on a short column of silica gel containing 10% $AgNO_3$, with chloroform as eluant. The residue from work-up was crystallized from benzene, to give the diol (**24**) as pale yellow plates (3.09 g, 60%), m.p. 120—121 °C (lit.,[7] 120—121 °C); $[\alpha]_D^{23}$ −64.6 ± 2.1° (*c* 0.492 in EtOAc) (lit.,[7] −65°).

(S)-(−)-2,2′-*Diamino*-6,6′-*dimethylbiphenyl*, (S)-(−)-(**25**).—A mixture of (*S*)-(−)-(**24**) (1.65 g, 5.43 mmol), trifluoroacetic anhydride (12 ml), and pyridine (10 ml) was stirred at room temperature for 4 h, poured into ice–water, and extracted with methylene dichloride. The extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was extracted with 10% aqueous HCl and this extract was washed with methylene dichloride made alkaline with 10% aqueous KOH, and extracted with methylene dichloride. The extract was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was crystallized from ethanol to give the diamine (**25**) as prisms (840 mg, 73%), m.p. 157—159 °C (lit.,[7] 156—158 °C); $[\alpha]_D^{23}$ −51.7 ± 2.4° (*c* 0.385 in EtOH) (lit.,[7] −49°).

(S)-(+)-1,6,7,12-*Tetramethyldibenzo*[e,g][1,4]*diazocine*, (S)-(+)-(**26**).—This *compound* was prepared from (*S*)-(−)-(**25**) (370 mg) according to a literature procedure[9] for the preparation of the racemic compound, and was crystallized from n-hexane as pale yellow prisms, m.p. 111.5—112.5 °C; $[\alpha]_D^{23}$ +1 438 ± 16° (*c* 0.1163 in MeOH); $\nu_{max.}$(KBr) 1 649 and 1 640 cm^{-1}; δ($CDCl_3$) 1.93 (6 H, s), 1.99 (6 H, s), 6.85 (2 H, dd, *J* 7.5 and 1.5 Hz), 7.00 (2 H, dd, *J* 7.5 and 1.5 Hz), and 7.20 (2 H, t, *J* 7.5 Hz); *m/z* 262 (Found: C, 82.35; H, 6.95; N, 10.75. $C_{18}H_{18}N_2$ requires C, 82.4; H, 6.9; N, 10.7%).

(S)-(−)-(6R,7R)-5,6,7,8-*Tetrahydro*-1,6,7,12-*tetramethyldibenzo*[e,g][1,4]*diazocine*, (S)-(−)-(**27**).—A mixture of (*S*)-(+)-(**26**) (217 mg, 0.828 mmol) and PtO_2 (80 mg) in methanol (15 ml) was stirred under hydrogen for 2 h. The catalyst was filtered

off and the filtrate was concentrated under reduced pressure to give an oily residue, δ($CDCl_3$) 1.19 (6 H, m), 2.13 (6 H, s), 2.74 (2 H, br s), 2.83 (2 H, m), 7.00 (2 H, d, *J* 8 Hz), 7.02 (2 H, d, *J* 8 Hz), and 7.24 (2 H, t, *J* 8 Hz); δ_C($CDCl_3$) 20.1, 22.4, 66.3, 122.0, 125.4, 128.8, 131.3, 137.4, and 149.7 p.p.m.

The HCl salt was crystallized from ethanol–ethyl acetate, m.p. 221—225 °C; $[\alpha]_D^{24}$ −118.4 ± 71° [*c* 0.223 in MeOH + 1M NaOH (2 drops ml^{-1})]; $[\alpha]_{365}^{24}$ −29.1 ± 1.5° (*c* 0.447 in 1M HCl); *m/z* 266 (Found: C, 62.9; H, 6.95; N, 8.15; Cl, 20.35. $C_{18}H_{24}N_2Cl_2 \cdot \frac{1}{4}H_2O$ requires C, 62.9; H, 7.2; N, 8.15; Cl, 20.6%).

The HNO_3 salt was crystallized from methanol–ethyl acetate, m.p. 211 °C (decomp.); $\nu_{max.}$(KBr) 1 551 and 1 384 cm^{-1} (Found: C, 55.05; H, 6.2; N, 14.25. $C_{18}H_{24}N_4O_6$ requires C, 55.1; H, 6.15; N, 14.3%).

X-*Ray Structure Determination of* (**22**), (**25**), *and* (**27**).—Crystals with dimensions of 0.2 × 0.2 × 0.2 mm (**22**), 0.3 × 0.4 × 0.4 mm (**25**), and 0.2 × 0.3 × 0.4 mm (**27**)·2-HNO_3 were used. Integrated intensities were measured in the range θ ≤ 65° with an ω–2θ scan. Independent reflections, 2 760, 1 261, and 990, were recorded for (**22**), (**25**), and (**27**)·2HNO_3, respectively. Lorentz and polarization corrections were applied, but not the absorption correction.

Crystal Data.—(**22**): $C_{18}H_{20}N_2$, orthorhombic, space group $P2_12_12_1$, a = 14.901(1), b = 21.817(2), c = 8.744(1) Å V = 2842.8(4) $Å^3$, Z = 8, D_x = 1.235 g cm^{-1}. (**25**): $C_{14}H_{16}N_2$, orthorhombic, space group $P2_12_12_1$, a = 7.976(2), b = 20.126(3), c = 7.559(1) Å, V = 1213.3(4) $Å^3$, Z = 4, D_x = 1.162 g cm^{-1}. (**27**)·2 HNO_3: $C_{18}H_{24}N_4O_6$, orthorhombic, space group $P2_12_12$, a = 8.094(1), b = 11.673(1), c = 10.304(1) Å, V = 973.5(1) $Å^3$, Z = 4, D_x = 1.339 g cm^{-1}.

The structures were solved using the program MULTAN 78.[18] A difference-electron-density map was calculated after block-diagonal least-squares refinement, which revealed the positions of all the hydrogen atoms. Successive refinement of the positional parameters of all the atoms and the anisotropic thermal parameters of the non-hydrogen atoms gave an R value ($\Sigma|\Delta F|/\Sigma|F_o|$) of 0.037 (2 392 observed reflections) for (**22**), 0.033 (1 034) for (**25**), and 0.070 (859) for the (**27**)·2HNO_3. The weighting scheme employed was $w = 1/\sigma^2(F_o)$ for $|F_c| \geq 3\sigma(F_o)$ and $w = 0$ for $|F_c| < 3\sigma(F_o)$ or $|\Delta F| > 3\sigma(F_o)$. $\sigma(F_o)$ Was estimated by the relation $\sigma(F_o) = [\sigma_1^2(F_o) + c|F_o|^2]^{\frac{1}{2}}$, where $\sigma_1(F_o)$ is the e.s.d. depending on the counting errors,[19] c being 0.001 36 for (**22**), 0.000 59 for (**25**), and 0.007 34 for (**27**)·2HNO_3. Atomic co-ordinates are given in Table 1. Bond lengths and angles, anisotropic temperature factors, and structure factors are given in Supplementary Publication No. SUP 23989 (45 pp.)*

* For details of the Supplementary Publications Scheme see Instructions for Authors (1984), *J. Chem. Soc., Perkin Trans. 1*, 1984, Issue 1.

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