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CIRCULAR DICHROISM OF N-2,4-DINITROPHENYL DERIVATIVES OF CHIRAL 1-ALKYL-2-PROPYNYLAMINES AND 1-ALKYL-2-PROPENYLAMINES

BJÖRN RINGDAHL
Department of Organic Pharmaceutical Chemistry, Biomedical Center,
University of Uppsala, Box 574, S-751 23 Uppsala, Sweden

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Abstract—The sign of the Cotton effects near 320 and 400 nm in the CD spectra of the N-2,4-dinitrophenyl derivatives of chiral 1-alkyl-2-propynylamines and 1-alkyl-2-propenylamines correlates with their absolute configurations. The Cotton effects are generated by the coupled oscillator methanism and their sign is the same as the chirality (right-handed screw for positive chirality) of the interaction of the dominant oscillators of the 2,4-dinitrophenylamino chromophore with that of the amine moiety, the chirality of the interaction being deduced by conformational analysis.

2,4-Dinitrofluorobenzene is known to react readily with amino acids to give coloured crystalline derivatives with high specific rotation.[1] In methanol solution the DNP (= 2,4-dinitrophenyl) derivatives of amino acids exhibit an absorption band centered around 350 nm and a shoulder in the 400 nm region.[2] The CD spectra of the DNP derivatives of aromatic amino acids show in methanol a characteristic pattern of two bands above 300 nm. The sign of the longer wavelength Cotton effect correlates with the absolute configuration of the aromatic amino acid (the DNP aromatic rule).[3] Although DNP derivatives of aliphatic α-amino acids display very weak Cotton effects their acylanilides exhibit CD spectra with a strong Cotton effect near 400 nm, the sign of which is determined by the absolute configuration at the α-C atom.[4] Recently, the DNP aromatic rule has been extended to include a wide variety of chiral amines all containing aromatic groups.[5] However, the application of the rule to aliphatic compounds has not been successful.[5]

In a recent publication, the synthesis of some chiral 1-alkyl-2-propenylamines and the determination of their absolute configuration is described.[6] Our continuing interest in the chiroptical properties of alkyl-substituted 2-propynylamines[6,7] and the availability of the above 1-alkyl-2-propenylamines prompted us to synthesize the DNP-derivatives of some of these amines (Table 1, **1a–d** and **2a–c**) and to examine their electronic absorption (EA) and CD spectra in both methanol and cyclohexane solution. Previous CD studies on DNP-derivatives have been restricted to methanol solution, presumably because strongly polar solvents are normally required to dissolve DNP amino acids. In the present study the DNP derivatives of two saturated amines (Table 1, **3a–b**) have also been included.

RESULTS AND DISCUSSION

Electronic absorption spectra. The electronic absorption spectra (Table 1) of the DNP derivatives of the 1-alkyl-2-propynylamines (**1a–d**), of the 1-alkyl-2-propenylamines (**2a–c**) and of the saturated amines (**3a–b**) in methanol exhibit a shoulder in the 400 nm region and an absorption maximum at 342–353 nm, designated as bands I and II, respectively.

In cyclohexane, band I appears as a broad but distinct maximum at 387–404 nm due mainly to a substantial hypsochromic shift relative to methanol solution of band II, whose maximum appears at 325–335 nm.

Bands I and II are most probably intramolecular charge-transfer (CT) bands due to electronic transitions accompanied by a partial electron transfer from the amino group to the 2- and 4-nitro group, respectively.[8] The observed solvent effect is in agreement with such an assignment.

Circular dichroism spectra. The DNP derivatives show CD spectra with multiple Cotton effects (Table 1).

Since the Cotton effects arise from strong absorption bands, and since there are other strongly absorbing groups present in the molecules, it can be assumed that the rotatory strength is developed primarily from the dipole–dipole coupling mechanism.[9] Thus in the 1-alkyl-2-propynylamine (**1a–d**) and 1-alkyl-2-propenylamine derivatives (**2a–c**) the dominant contribution to the dichroic absorption of bands I and II arise from the interaction of the 2,4-dinitrophenylamino chromophore with the lowest energy $\pi \rightarrow \pi^*$ transition of the ethynyl ($^1A_{1u} \leftarrow {}^1A_{1g}$ of acetylene at *ca* 152 nm[10]) and the ethenyl group [$^1B_{1u} \leftarrow {}^1A_{1g}$ (N–V) of ethylene at *ca* 175 nm[10]], both red shifted by alkyl substitution. The electric transition moments of these transitions are directed along the multiple bond.[10] In the intramolecularly H-bonded 2,4-dinitrophenylamino chromophore the transition moments of band I (μ_1) and band II (μ_2) are directed as shown in **4**.[2] The chirality of μ_1 and μ_2 with the triple and double bond in the 1-alkyl-2-propynylamine and 1-alkyl-2-propenylamine derivatives, respectively, which determines the sign of the Cotton effects associated with bands I and II, depends on both the absolute configuration and the preferred conformation of the respective derivatives.

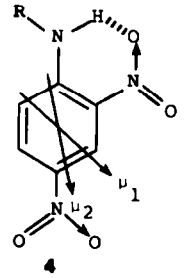

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Table 1. Electronic absorption and circular dichroism data for the N-2,4-dinitrophenyl derivatives of some chiral amines

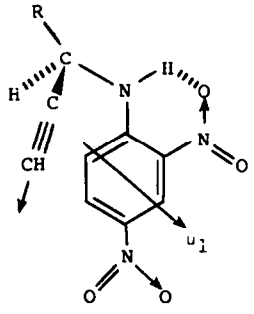
N-2,4-Dinitrophenyl derivative	Amine R_1	Amine R_2	Amine R_3	Methanol: Electronic absorption λnm (log ε)	Methanol: Circular dichroism λnm ([θ][a])	Cyclohexane: Electronic absorption λnm (log ε)	Cyclohexane: Circular dichroism λnm ([θ][a])
(R)-1a	CH_3	C=CH	H	~395 (3.79)[b]	394 (-7.200)	388 (3.71)	382 (-8.000)
				342 (4.22)	326 (+7.400)	325 (4.22)	316 (+12.300)
				263 (3.99)	265 (-2.300)	261 (3.98)	264 (-4.000)
					225 (+16.100)		224 (+21.400)
(R)-1b	CH_2CH_3	C=CH	H	~395 (3.80)[b]	395 (-6.500)	388 (3.71)	384 (-7.200)
				343 (4.22)	326 (+7.400)	327 (4.23)	317 (+12.900)
				264 (3.99)	265 (-1.900)	262 (3.99)	264 (-3.400)
					225 (+16.900)		224 (+22.600)
(S)-1c	C=CH	$CH_2CH_2CH_3$	H	~395 (3.79)[b]	397 (+5.600)	387 (3.72)	386 (+6.800)
				343 (4.23)	330 (-8.600)	327 (4.25)	319 (-13.800)
				263 (3.99)	266 (+1.100)	262 (4.01)	264 (+3.100)
					224 (-17.100)[b]		223 (-23.600)
(R)-1d	C=CH	CH_2CH_3	CH_3	~395 (3.80)[b]	403 (-2.400)	396 (3.71)	396 (-2.400)
				343 (4.23)	330 (+4.100)	329 (4.24)	324 (+5.200)
				265 (4.00)	265 (-1.300)	264 (4.00)	264 (-1.000)
					214 (+9.200)		212 (+11.300)
(R)-2a	CH_3	$CH=CH_2$	H	~400 (3.79)[b]	400 (-5.200)	397 (3.74)	387 (-5.800)
				347 (4.22)	320 (+800)	329 (4.26)	315 (+2.100)
				264 (3.95)	266 (-4.300)	257 (3.99)	263 (-6.900)
					226 (+14.600)		227 (+23.400)
(S)-2b	$CH=CH_2$	CH_2CH_3	H	~400 (3.81)[b]	405 (+4.700)	397 (3.73)	293 (+4.800)
				348 (4.23)	320 (-870)	330 (4.27)	320 (-3.150)
				266 (3.96)	266 (+3.900)	257 (3.98)	265 (+6.300)
					225 (-17.400)		227 (-24.700)
(R)-2c	CH_2CH_3	$CH=CH_2$	CH_3	~405 (3.80)[b]	417 (-870)	400 (3.73)	
				350 (4.24)		332 (4.26)	
				266 (3.97)	267 (-3.000)	262 (3.98)	262 (-3.800)
					227 (+4.700)		229 (+6.500)
(R)-3a	CH_3	CH_2CH_3	H	~410 (3.79)[b]	412 (-1.300)	403 (3.74)	400 (-1.100)
				352 (4.24)	350 (-1.400)	333 (4.26)	330 (-1.900)
				264 (3.97)		256 (3.99)	
(R)-3b	CH_2CH_3	$CH_2CH_2CH_3$	H	~410 (3.81)[b]	415 (-1.450)	404 (3.74)	400 (-1.200)
				353 (4.25)		335 (4.26)	
				264 (3.98)		255 (4.00)	

[a] Molecular ellipticity

[b] Shoulder

^{1}H NMR data for the DNP derivatives are summarized in Table 2 which also contains data for the DNP derivative of 1-ethyl-1-methylpropylamine (3c) included for comparison purposes. In the 1-alkyl-2-propynylamine derivatives (1a–d), especially in (R)-1d, the H-6 proton doublet (and to some extent the H-5 split doublet) is shifted downfield compared to its position in the corresponding saturated amine derivatives [(R)-1a vs (R)-3a, (S)-1c vs (R)-3b and (R)-1d vs 3c]. On the other hand, in the 1-alkyl-2-propenylamine derivatives and their saturated counterparts the chemical shifts of the H-5 and H-6 protons correspond closely [(R)-2a vs (R)-3a and (R)-2c vs 3c]. Furthermore, the relatively constant position of the H-3 proton doublet within the whole series of compounds contrasted with the substantial effect on the chemical shift of the H-6 proton on introducing two alkyl groups at the chiral centre [(R)-1d vs (R)-1b, (R)-2c vs (S)-2b and 3c vs (R)-3b] suggests that the resonance position of the H-6 proton is affected primarily through steric and/or magnetic anisotropy effects from the substituents at the chiral centre and that differences in electronic effects of delocalisation of the nitrogen lone-pair electrons are of minor importance. Thus it is reasonable to assume that in the preferred conformations of the 1-alkyl-2-propynylamine and 1-alkyl-2-propenylamine derivatives, the ethynyl group is close enough to the aromatic ring to exert a magnetic anisotropy effect on the H-6 proton whereas the ethenyl group is not.

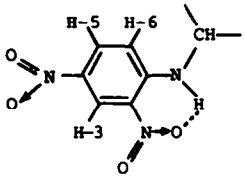
In view of the extremely low steric requirements of the H atom at the chiral centre and the deshielding effect of the ethynyl group on the aromatic H-6 proton, the preferred conformation for the intramolecularly H-bonded (R)-N-2,4-dinitrophenyl-1-alkyl-2-propynylamines may be depicted as (R)-5.



(R)-5

The chirality (right-handed screw for positive chirality) of the transition moment of band I of the chromophore

Table 2. Proton magnetic resonance data for the N-2,4-dinitrophenyl derivatives of some chiral amines



N-2,4-Dinitrophenyl derivative	δ, [a] ppm			
	H-3[b]	H-5[c]	H-6[d]	N-CH[e]
(R)-1a	9.10	8.33	7.15	4.48
(R)-1b	9.10	8.33	7.16	4.33
(S)-1c	9.08	8.30	7.14	4.36
(R)-1d	9.14	8.30	7.70	
(R)-2a	9.11	8.25	6.97	4.35
(S)-2b	9.09	8.23	6.97	4.11
(R)-2c	9.13	8.18	7.20	
(R)-3a	9.11	8.25	6.98	3.80
(R)-3b	9.12	8.25	6.99	3.70
3c	9.13	8.20	7.18	

[a] Chemical shift downfield from Me_4Si = 0, solvent $CDCl_3$

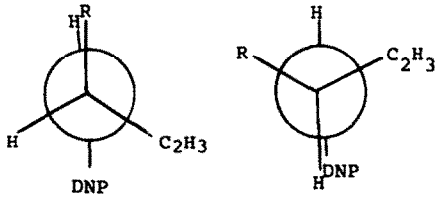
[b] Doublet J = 2.5 Hz [c] Split doublet J_1 = 9.5 Hz, J_2 = 2.5 Hz

[d] Doublet J = 9.5 Hz [e] Multiplet

(μ_1) and that of the ethynyl group as shown in (R)-5 is negative and the DNP derivatives (R)-1a (Fig. 1) and (R)-1b show negative Cotton effects for band I in both methanol and cyclohexane solution. The derivative (S)-1c, with the enantiomeric configuration, displays a positive Cotton effect. Since an Et group is larger in effective bulk size than a Me group the derivative (R)-1d should have a preferred conformation similar to (R)-5, the Me and Et groups replacing the H atom and the R group, respectively. However, the relatively large downfield shift of the aromatic H-6 proton of this derivative (Table 2) suggests a small rotation about the chiral C–N bond as compared to (R)-5, forcing the ethynyl group towards and the Me group away from the aromatic ring. The chirality of the two transition moments in this conformation is negative and the dichroic absorption of band I is negative. The reduced molecular ellipticity for this maximum can be explained on the basis of a reduced preference for the conformer of lowest energy since the difference in size between a Me and an Et group is smaller than that between a H atom and an alkyl group and/or a reduced dihedral angle between the two transition moments compared to (R)-5.

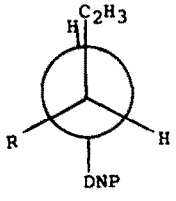
The interpretation of the Cotton effects associated with the 1-alkyl-2-propenylamine derivatives (2a–c) is complicated by the greater conformational mobility of these compounds as compared to the 1-alkyl-2-propynylamine derivatives, since the size of a Me and an Et group is closer to that of an ethenyl group than to an ethynyl one. Moreover, since a symmetry axis for the ethenyl group is absent, the direction of the transition moment for its lowest energy π–π^* transition will depend on the preferred conformation about the attachment bond of the group.

The three conformers of lowest energy for a (R)-N-2,4-dinitrophenyl-1-alkyl-2-propenylamine are depicted as (R)-6a–c.



(R)-6a

(R)-6b



(R)-6c

Although the absence of any shielding or deshielding influence of the ethenyl group on the aromatic H-6 proton would indicate that (R)-6a is less favoured, its occurrence cannot be fully excluded. (R)-6b is similar to the conformation deduced for DNP derivatives of aromatic amines and amino acids.[5] The conformational preference about the ethenyl group attachment bond in 6a–c is illustrated in (R)-7. Preferred conformations

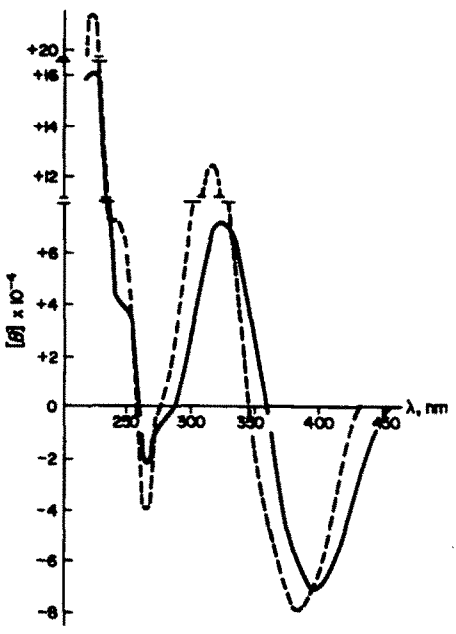
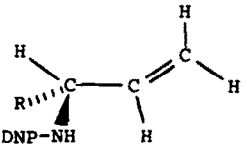


Fig. 1. CD spectra of (R)-N-2,4-dinitrophenyl-1-methyl-2-propynylamine [(R)-1a] in methanol (——) and cyclohexane (– – –).

analogous to (R)-7 was proposed for N-salicylidene-1-alkyl-2-propenylamines[7] and have been demonstrated for 3,3-dialkylpropenes.[11]



(R)-7

In the intramolecularly H-bonded N-2,4-dinitrophenyl-1-alkyl-2-propenylamines, the sign of the Cotton effect associated with band I is determined by the chirality of the double bond with the attachment bond of the 2,4-dinitrophenylamino chromophore, since the transition moment of band I of the chromophore is approximately parallel to the chromophore attachment bond. The orientation of the chromophore about its attachment bond will have little effect on the strength of CD maximum associated with band I. The chirality of the relevant bonds as shown in (R)-7 is negative and the DNP derivative (R)-2a (Fig. 2) exhibits a negative Cotton effect for band I. A positive Cotton effect is observed for (S)-2b. The derivative (R)-2c should have a preferred conformation similar to (R)-7, the Me and Et groups replacing the H atom and the R group, respectively. The reduced molecular ellipticity in methanol and the absence of any observable Cotton effect in cyclohexane for band I of this derivative can be explained much the same way as for the reduced ellipticity of band I of (R)-1d.

The Cotton effects associated with band I of the saturated amine derivatives, (R)-3a and (R)-3b, are also most likely generated by the coupled oscillator mechanism.[9,12] Since the polarizability of a C–H bond is negligible compared with that of a C–C bond,[12] only the C–C bond vicinal to the chromophore attachment bond need to be considered as inducing dichroic absorption in the chromophoric group of (R)-3a. Of the two con-

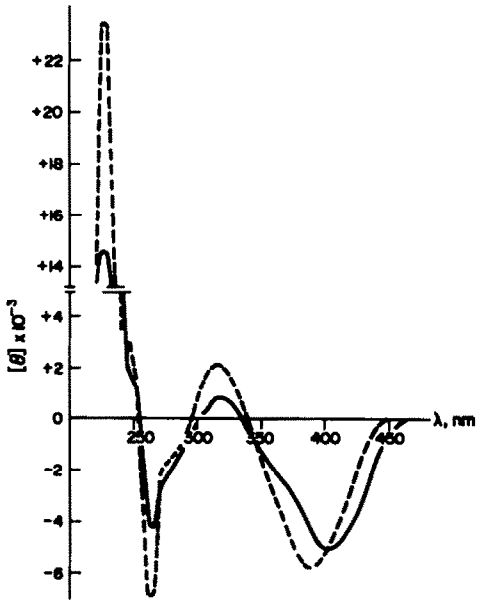
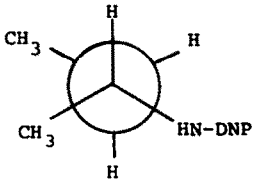
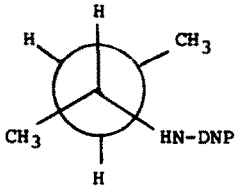


Fig. 2. CD spectra of (R)-N-2,4-dinitrophenyl-1-methyl-2-propenylamine [(R)-2a] in methanol (———) and cyclohexane (– – –).

formers of lowest energy, (R)-8a and (R)-8b, owing to rotation about the Et group attachment bond, only (R)-8b with negative chirality of the relevant bonds is important for dichroic absorption, and the observed Cotton effect is negative. The derivative (R)-3b, having two C–C bonds vicinal to the chromophore attachment bond, also displays a negative Cotton effect for band I, but because of its many conformational possibilities no statement concerning the chirality of the relevant bonds can be made.



(R)-8a

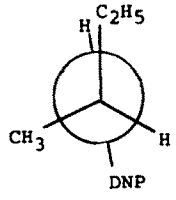


(R)-8b

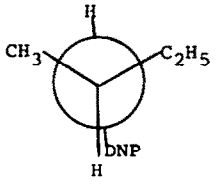
The direction of the transition moment μ_2 of band II of the chromophore as shown in 4 does not deviate greatly from the phenyl group-amine nitrogen bond. For an intramolecularly H-bonded (R)-N-2,4-dinitrophenyl-1-alkyl-2-propynylamine of the conformation shown in (R)-5, the sign of the Cotton effect associated with band II is determined by the chirality of the phenyl group-amine nitrogen bond and the ethynyl group attachment bond. The DNP derivatives (R)-1a (Fig. 1), (R)-1b and (R)-1d, having positive chirality of the relevant bonds, display positive Cotton effects for band II. On the other hand, the derivative (S)-1c exhibits a negative Cotton effect. The difference in the position of band II in the EA and CD spectra, most pronounced in methanol solution (Table 1), can be explained by band overlap with the oppositely signed Cotton effect of band I. Accordingly, in cyclohexane, where the dichroic absorption of band II is greatly enhanced, the band is closer to its position in the EA spectrum.

In the 1-alkyl-2-propenylamine derivatives, the chirality of the phenyl group-amine nitrogen bond and the double bond determines the sign of the Cotton effect displayed by band II. For a given absolute configuration, the chirality of the bonds depends on the preferred conformation about the attachment bond of both the chromophore and the ethenyl group. Taking the preferred conformation as shown in (R)-6b or (R)-6c and and (R)-7, the chirality of the relevant bonds of the derivative (R)-2a is positive and the observed Cotton effect is positive (Fig. 2). (S)-2b exhibits a negative Cotton effect. The remarkable decrease in ellipticity for band II of the 1-alkyl-2-propenylamine derivatives as compared to the 1-alkyl-2-propynylamine derivatives is due primarily to the much greater conformational mobility of the former and to the reduced dihedral angle between the effective transition moments.

For the derivatives (R)-3a and (R)-3b the sign of the Cotton effect associated with band II depends on the chirality of the phenyl group-amine nitrogen bond and the C–C bonds attached to the chiral centre. Of the two conformers of lowest energy, (R)-9a and (R)-9b, owing to rotation about the chromophore attachment bond of (R)-3a, the latter, having two C–C bonds symmetrically disposed about the chromophore, is rotationally less important. The chirality of the relevant bonds in (R)-9a is negative and (R)-3a displays a negative Cotton effect also for band II. The derivative (R)-3b should have a preferred conformation analogous to (R)-9b and thus no Cotton effect for band II is observed.



(R)-9a



(R)-9b

The spectral region below 300 nm is rather complex with several maxima and shoulders. In the CD spectra of the 1-alkyl-2-propynylamine (1a–d) and 1-alkyl-2-propenylamine (2a–c) derivatives distinct maxima are observed at 265 and 225 nm both more intense in cyclohexane than in methanol.

The results reported for the 400 nm band are in agreement with what has been found for the 400 nm Cotton effect of aromatic amino acids.[3] Thus the DNP aromatic rule[3] can be extended to include derivatives of chiral amines containing no aromatic group.

EXPERIMENTAL

Optical rotations at the sodium D line were measured in a 1-dm tube with a Perkin–Elmer 141 spectropolarimeter. Electronic absorption (EA) spectra were obtained with a Zeiss Spektralfotometer Pm QII. CD spectra were recorded on a Jasco J-41 spectropolarimeter at 20° with cell lengths of 1 and 2 mm. ^{1}H NMR spectra were recorded with a Perkin–Elmer R 12B spectrometer at 37°. Elemental analyses were done at the Microanalytical Laboratory, Royal Agricultural College, Uppsala, Sweden.

N-2,4-Dinitrophenyl derivatives were prepared from the respective amines[6,13–15] (1.0 mmol) by stirring with 2,4-dinitrofluorobenzene (1.2 mmol) in the presence of a slight excess of $NaHCO_3$ for 2–4 hr in 50% EtOH. The soln was filtered and the solid was washed with EtOH-water and recrystallized. In

Table 3. Physical and analytical data for the N-2,4-dinitrophenyl derivatives of some chiral amines

N-2,4-Dinitrophenyl derivative	M.p. °C	Recryst. solvent[a]	$[\alpha]_D^{22}$ deg. (c ethanol)	Elemental analyses					
				Calc.			Found		
				C	H	N	C	H	N
(R)-1a	122-123	EtOH	+ 64.1 (0.8)	51.1	3.9	17.9	51.0	3.9	17.7
(R)-1b	78-79	EtOH-H_2O	+ 85.8 (1.2)	53.0	4.5	16.9	52.9	4.5	16.7
(S)-1c	59-60	Et_2O-P	- 86.5 (0.7)	54.8	5.0	16.0	54.6	4.9	15.7
(R)-1d	99-100	EtOH-H_2O	+ 3.9 (1.1)	54.8	5.0	16.0	54.8	4.9	15.7
(R)-2a	52-53	Et_2O-P	-146 (1.0)	50.6	4.7	17.7	50.3	4.6	17.4
(S)-2b	42-43	P	+118 (1.1)	52.6	5.2	16.7	52.9	5.3	16.7
(R)-2c	108.5-109.5	EtOH-H_2O	- 22.5 (0.5)	54.3	5.7	15.8	54.2	5.8	15.8
(R)-3a	54-55	Et_2O-P	- 69.4 (0.9)	50.2	5.5	17.6	50.1	5.3	17.3
(R)-3b	28.5-29.5	P	- 22.5 (0.5)	53.9	6.4	15.7	53.7	6.2	15.5
3c	86-87	EtOH-H_2O		53.9	6.4	15.7	53.7	6.6	15.7

[a] P = petroleum ether

cases where the derivative formed an oil the EtOH was evaporated *in vacuo* and the mixture extracted with ether which was evaporated. The residue was treated with 2N NaOH for 5 hr to remove excess of 2,4-dinitrofluorobenzene. Extraction with ether and evaporation yielded a solid which was recrystallized. Physical and analytical data for the derivatives are given in Table 3.

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