CD Spectra of 2,4-Dinitrophenyl Derivatives of α-Amino Acids Having Polynuclear Aromatic Group in the Side Chain. Absolute Configuration of 3-(9-Anthryl)alanine

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Synopsis. CD spectra of 2,4-dinitrophenyl (Dnp) derivatives of α-amino acids having polynuclear aromatic group in the side chain with L- and D-configuration showed negative and positive Cotton effect, respectively, around 400 nm in consistent with previously proposed Dnp-aromatic rule. Application of the rule revealed D-configuration of levorotatory 3-(9-anthryl)alanine, which was further confirmed by chiroptical comparison of the 2,4-dinitrophenyl derivative and its *p*-methoxyanilide.

CD spectra of 2,4-dinitrophenyl (Dnp) derivatives of L-α-amino acids having aromatic side chain exhibit characteristic negative Cotton effect around 400 nm.[1,2] A general rule named Dnp-aromatic rule was proposed as described in Fig. 1: *i.e.*, Dnp derivatives of general formula **1** and **1′**, having stereochemistry corresponding to aromatic α-amino acids with L- and D-configuration, show negative and positive Cotton effect, respectively, at the longest wavelength band of DnpNH chromophore.[2]

As examples of aromatic α-amino acids having polynuclear condensed aromatic group in the side chain, L-3-(1-naphthyl)alanine,[3] L-3-(2-naphthyl)alanine,[3] D-1-naphthylglycine,[4] D-2-naphthylglycine,[4] and D-3-(1-pyrenyl)alanine[5] were converted into the corresponding Dnp derivatives **2a—e**. As summarized in Table 1 all of these compounds exhibited intense Cotton effect around 400 nm, and in agreement with Dnp-aromatic rule the sign of the Cotton effect was negative and positive for the derivatives with L- and D-configuration, respectively. Thus Dnp-aromatic rule was shown to be valid for these polynuclear aromatic α-amino acid derivatives.

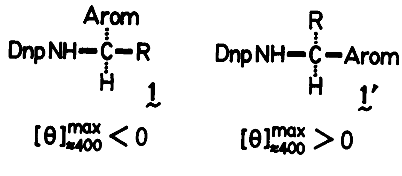
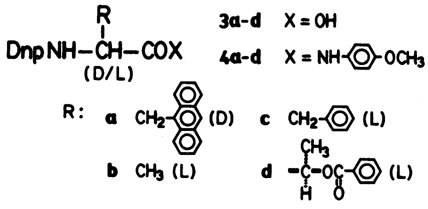


Fig. 1. Dnp-aromatic rule.
Arom implies an achiral group which contains an aromatic chromophore. R implies a nonaromatic group.

Optically active 3-(9-anthryl)alanine hydrochloride ($[\alpha]^{21}_{D}$ −43°, c 0.058, ethanol) was synthesized,[6] but its absolute configuration was not known yet. CD spectrum of Dnp derivative **3a** of the anthrylalanine exhibited an outstanding positive Cotton effect ([θ] +50800) at 414 nm, which indicated D-configuration of the amino acid.



p-Methoxyanilides, such as **4b**, of Dnp-L-α-amino acids with nonaromatic side chain, which correspond to general formula **1′**, exhibit prominent Cotton effect around 400 nm.[2,7] Positive contribution of the anilide chromophore to $[\theta]^{max}_{\approx 400}$ value of Dnp-L-α-amino acids was also observed for the *p*-methoxyanilides, **4c** and **4d**, of Dnp-L-phenylalanine **3c**[1,2] and *N*-Dnp-*O*-benzoyl-L-threonine **3d**,[8] respectively (Table 2). The threonine derivative **3d** was known to exhibit positive Cotton effect at 403 nm,[9] in spite of L-configuration of the α-carbon, which is due to the presence of additional chiral center in the chromophore-bearing side chain.[8] Thus introduction of *p*-methoxyanilide group to Dnp-α-amino acids with L- and D-configuration was assumed to give positive and negative contribution, respectively, to the Cotton effect.

Magnitude of the positive Cotton effect of Dnp-(9-anthryl)alanine *p*-methoxyanilide **4a** is smaller than that of **3a** as shown in Table 2 indicating negative contribution of the anilide chromophore, which is consistent with above-assigned D-configuration of this amino acid residue.

TABLE 1. COTTON EFFECT AROUND 400 nm OF Dnp DERIVATIVES OF α-AMINO ACIDS HAVING POLYNUCLEAR AROMATIC GROUP IN THE SIDE CHAIN

	Formula	Configuration of α-carbon	Arom	R	$[\theta]^{max}$(λ/nm)
2a	**1**	L	(1-Naphthyl)methyl	CO_2H	−19300 (403)
2b	**1**	L	(2-Naphthyl)methyl	CO_2H	−17500 (403)
2c	**1′**	D	1-Naphthyl	CO_2H	+17100 (400)
2d	**1′**	D	2-Naphthyl	CO_2H	+25600 (396)
2e	**1′**	D	(1-Pyrenyl)methyl	CO_2H	+30800 (410)

Table 4. CD spectral data of Dnp–amino acids and *p*-methoxyanilides recorded in methanol

Compd	Molecular ellipticity ($[\theta]\times10^{-3}$) and wavelength (λ/nm) in parentheses.[a]
2a	−19.3(403), 0(336), +5.4(316 sh), +9.5(297), +8.5(292), +9.3(285), 0(272), −12(250 sh), −116(223), −32(215)
2b	−17.5(403), 0(343), +6.3(318), 0(288), −6.9(263), 0(248), +69(229), 0(225), −160(220 sh)
2c	+17.1(400), 0(342), −6.0(310), −3.2(293), −5.8(260), 0(249), +13(235), 0(232), −232(220 sh)
2d	+25.6(396), 0(355), −18.4(330), −5.0(290), −286(230), 0(218), +32(215), 0(212)
2e	+30.8(410), 0(368), −68.8(341), −10.9(331), −13.5(328), 0(322), +8.8(319), +4.5(310 sh), 0(302), +5.4(288 sh), −33.9(276), −11.6(268), −13.0(265), −5(254 sh), −2(249), −214(240), −100(234 sh), −29(220)
3a	+50.8(414), 0(389), −13.7(382), −12.7(378), −22.8(368), 0(349), +17.3(329), 0(295), −2.4(289), 0(284), +141(260), 0(253), −97(228), 0(215)
4a	+34.3(418), 0(392), −22.3(381 sh), −27.5(368), 0(349), +24.2(327), +3.4(288), +65.8(265), 0(255), −77(242 sh), −95(226)
4c	+4.4(395), 0(371), −18.6(335), −4.6(290), −62(252), −26(223)
4d	+14.2(390), 0(354), −13.4(320), −5.4(290), −41(250 sh), −50(240), −16(224)

a) sh: Shoulder.

Table 2. Comparison of $[\theta]^{\max}$ values around 400 nm of Dnp-α-amino acids (**3a**—**d**) and their *p*-methoxyanilides (**4a**—**d**)

	$[\theta]^{\max}_{\approx400}$ of **3**	$[\theta]^{\max}_{\approx400}$ of **4**	Contribution of the anilide	Configuration of α-carbon
a	+50800	+34300	−	D
b	+1600	+12900	+	L
c	−9100	+4400	+	L
d	+5000	+14200	+	L

Table 3. Melting points, solvent of crystallization, and molecular formula of Dnp–amino acids and *p*-methoxyanilides

Compd	Mp θ_m/°C	Solvent of Crystallization	Formula[a]
2a	90—93	H_2O[b]	$C_{19}H_{15}N_3O_6\cdot1/4H_2O$
2b	196—198	$CHCl_3$	$C_{19}H_{15}N_3O_6\cdot3/4H_2O$
2c	133—138	Methanol-H_2O	$C_{18}H_{13}N_3O_6\cdot1/2H_2O$
2d	105—110	Methanol-H_2O	$C_{18}H_{13}N_3O_6\cdot1/2H_2O$
2e	211—215	Ethyl acetate	$C_{25}H_{17}N_3O_6\cdot CH_3CO_2C_2H_5$
3a	206—210	Ethyl acetate-Hexane	$C_{23}H_{17}N_3O_6$
4a	265—268	Acetone-Methanol	$C_{30}H_{24}N_4O_6$
4c	203—204	Benzene	$C_{22}H_{20}N_4O_6$
4d	139—141	Benzene	$C_{24}H_{22}N_4O_8$

a) Satisfactory analytical data (C, H, N ±0.35%) were obtained for the given formula. b) Precipitate from aquaous acidic solution.

Experimental

Dnp-amino acids were prepared from parent amino acids using 1-fluoro-2,4-dinitrobenzene and $NaHCO_3$ in ethanol-H_2O (2:1). *p*-Methoxyanilides, **4a** and **4c**, were synthesized from Dnp-amino acids, **3a** and **3c**, respectively, and *p*-anisidine using dicyclohexylcarbodiimide. *N*-Dnp-*O*-benzoyl-L-threonine *p*-methoxyanilide **4d** was prepared by benzoylation of Dnp-L-threonine *p*-methoxyanilide[2] with benzoyl chloride-pyridine.

Melting points were uncorrected and were listed in Table 3 along with solvents of recrystallization. CD spectra were recorded in methanol solutions at room temperature on a JASCO J-40C spectropolarimeter and were summarized in Table 4.

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9) The $[\theta]$ values of **3d** were erroneously given in Table 1 of Ref. 8, which must be corrected as follows: $[\theta]_{403}$ +5000, $[\theta]_{350}$ 0, $[\theta]_{318}$ −1500, $[\theta]_{298}$ 0, $[\theta]_{266}$ +4600, $[\theta]_{244}$ 0, and $[\theta]_{222}$ −14800.