CrystEngComm

Cite this: *CrystEngComm*, 2012, **14**, 3972–3981

www.rsc.org/crystengcomm

PAPER

Investigation on the weak interactions assembling the crystal structures of Betti bases†‡

Cosimo Cardellicchio,*[a] Maria Annunziata M. Capozzi,[b] Angel Alvarez-Larena,[c] Joan F. Piniella[c] and Francesco Capitelli[d]

Received 29th September 2011, Accepted 9th March 2012
DOI: 10.1039/c2ce06295j

The crystal structures of (*S*, *S*)-aminobenzylnaphthols, easily produced by a chromatography-free highly stereoselective Betti reaction, were investigated by means of single crystal X-ray diffraction analysis, and the main intra- and intermolecular interactions were described. The presence of a strong intramolecular hydrogen bond was confirmed, whereas the whole crystal building was found to be due mainly to other bondings, such as CH···O and CH···π interactions. As far as the last interactions were concerned, we observed many short distances from one hydrogen atom to an aryl plane, together with the appropriate geometric requirements for the assemblies. The observations suggest that these interactions can play a relevant role in the crystal building. The absence of similar short distance CH···π interactions in the crystal of a diastereomeric (*R*, *S*)-aminobenzylnaphthol could be a suggestion of the preferential crystallisation of the (*S*, *S*)-stereoisomer and, consequently, its prevalence as a product of the Betti reaction.

Introduction

Crystal engineering is concerned both with the understanding of the intermolecular interactions in the context of crystal packing, and with the application of the relevant ideas to the design of new solids having desired physical and chemical properties.[1] Hydrogen bond, that is both strong and directional, is the most reliable among such intermolecular interactions.[1–3] In recent times, the concept of hydrogen bond was extended also to C–H···O, C–H···N, O–H···π, and finally to C–H···π interactions,[4–8] that could be considered the weakest form of the hydrogen bond,[1–3] even if no general consensus[6] has been expressed towards this position. The main criticism is due to the multi-atom nature of the π-acceptor and to the somehow missing directionality requirements.[2,3] Since each crystal structure is a result of many compromises, weaker hydrogen bonds are more likely to be bent. However, higher bonding energies were calculated when the angle between the CH bond and the projection of the H-atom on the aryl plane gets closer to 180°, and the offset of this projection from the centroid of the aryl moiety is minimal.[2–5]

In the C–H···π interactions, the distances from the hydrogen atom to the aryl plane were reported to occur in the range between 2.6 and 3.0 Å,[7,8] whereas cases of shorter distances were also reported.[9] The strength of these weak interactions could be increased if both the donor and the acceptor component were activated, for example by increasing the proton donating ability, or the electron density of the π-system. In fact, shorter distances from the hydrogen atom to the aryl plane were observed in these circumstances, a fact that suggests that a real bonding interaction is occurring.[2,3]

Even if weaker with respect to the other hydrogen bonds, the possibility of multiple co-operative interactions of the same kind can lead to a considerable total energy.[2–4,10] In fact, CH···π interactions have been reported to play a crucial role in many different areas, such as supramolecular assemblies, protein folding and drug–receptor interactions.[4,5] Theoretical investigations corroborated its relevance also in asymmetric synthesis,[11] as reported, among others, by Noyori *et al.*[12] in the enantioselective hydrogen transfer to carbonyl compounds from a chiral arene-ruthenium(II) complex, by Nishibayashi *et al.*[13] in the enantioselective propargylic substitution reaction with a chiral ruthenium complex, by Dudding, Houk *et al.* in a hetero-Diels–Alder reaction,[14] and by some of us[15,16] in the enantioselective oxidation of aryl benzyl sulfides in the presence of a chiral titanium complex.

Another fruitful research theme was the investigation on the relative stability of the diastereomeric couples employed in the enantiomer resolutions.[17] Usually, the less soluble salt melts at

[a]*CNR Istituto di Chimica dei Composti OrganoMetallici, Dipartimento di Chimica, via Orabona 4, 70125 Bari, Italy.*
E-mail: cardellicchio@ba.iccom.cnr.it; Fax: +39-0805539596;
Tel: +39-0805442077
[b]*Dipartimento di Chimica, via Orabona 4, 70125 Bari, Italy*
[c]*Department of Geology, Universitat Autònoma de Barcelona, Campus Universitari UAB, 08193, Bellaterra, Spain*
[d]*CNR Istituto di Cristallografia, via Salaria km 29,300, 00015 Monterotondo (Roma), Italy*

† Electronic Supplementary Information (ESI) available: Table of the dihedral angles between mean aryl planes; NMR spectra of already reported compounds. See DOI: 10.1039/c2ce06295j/

‡ Dedicated to Prof. Alfredo Ricci on the occasion of his retirement.

higher temperature and with a larger enthalpy of fusion.[17] This stability was sometimes explained by invoking C–H···π interactions. Cases of particular interest were reported by Saigo *et al.*[18–20] For example, more effective C–H···π interactions were found in the crystal structures of the less soluble salts of 2-naphthylglycolic acid with 1-arylethylamines.[18] Another work investigates the salts of 2-naphthylglycolic acid with 1-phenylethylamine derivatives, or the salts of *cis*-1-aminoindan-2-ol with arylalkanoic acids. Numerous CH···π interactions were present in the most stable isomer of the diastereomeric couples,[19,20] thus contributing to the stability of the crystal. This result was also confirmed by theoretical calculations.[20]

The research by some of us in the enantioselective synthesis of sulfoxides[15,16] was also accompanied by an investigation of their crystal structures.[21] Another research theme in asymmetric synthesis deals with chiral nonracemic aminobenzylnaphthols, easily produced by using the so-called Betti reaction.[22] In this straightforward procedure, three small components (2-naphthol, ammonia or amines, and aryl aldehydes) condense to yield the corresponding aminobenzylnaphthol, or Betti base. The aminobenzylnaphthtols that were produced by using this procedure can be easily resolved into their enantiomers.[22]

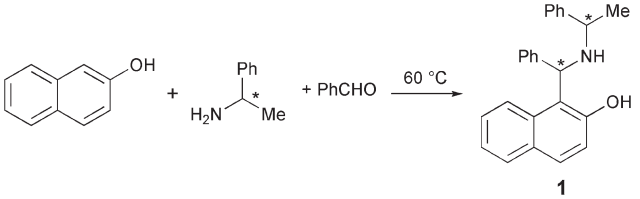
After our first papers on the Betti reaction,[23,24] several research groups[22] applied this valuable procedure to prepare new chiral nonracemic aminobenzylnaphthols. Among these investigations, a new fruitful research line started with the contemporary works of the groups of Palmieri,[25,26] Forlani[27] and Chan.[28] In their research, 2-naphthol was reacted with an aryl aldehyde and with (*R*)- or (*S*)-1-arylethylamine. (*R*, *R*)- or (*S*, *S*)-aminobenzylnaphthols were obtained, when the (*R*)- or the (*S*)-1-arylethylamine was employed, respectively. For instance, the reaction of 2-naphthol with benzaldehyde and (*R*)-1-phenylethylamine at 60 °C without any solvent (Scheme 1)[25] yielded the corresponding (*R*, *R*)-aminobenzylnaphthol **1** in high yield (93%) and with a very high diastereomeric ratio (> 99 : 1).

The Palmieri group explained this high stereoselectivity by invoking an asymmetric transformation of the second kind, in which the (*R*, *R*)-stereoisomer crystallises preferentially, and can thus be obtained as diastereomerically pure.[25] At this stage, we decided to investigate the main interactions building the crystal structures of a series of similar aminobenzylnaphthols **1–9**, looking for a plausible explanation of the high asymmetric induction observed in the Betti reaction.

Results and discussion

1. Synthesis of aminobenzylnaphthols.

(*S*, *S*)-Aminobenzylnaphthols **1**,[25,27] **2**, **3**,[25,29] **4**,[29] **5**,[30] and **6–9** were obtained by a Betti reaction of commercially available 2-naphthol, benzaldehyde or *p*-halobenzaldehyde with (*S*)-1-arylethylamine (Scheme 2).



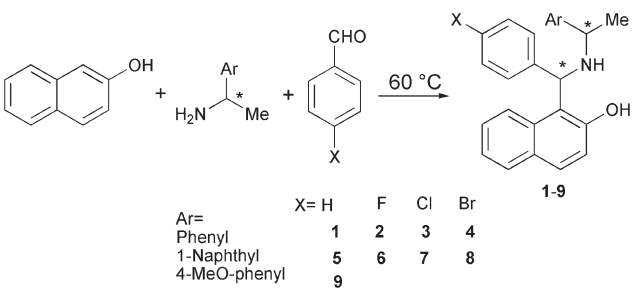
Scheme 1 The Betti reaction with nonracemic 1-phenylethylamine.

The aminobenzylnaphthols **1–9** are constituted by three different aryl groups, *i.e.* the naphthyl and the phenyl moieties (Fig. 1), and a further aryl group deriving from the employed 1-arylethylamine, *i.e.* phenyl (molecules **1–4**), 1-naphthyl (molecules **5–8**), or 4-methoxyphenyl group (molecule **9**). The last aryl groups are indicated with a B label (see Fig. 1) to distinguish them from the main naphthyl or phenyl groups.

From a synthetic point of view, the aryl aldehyde and the (*S*)-1-arylethylamine were first mixed without any solvent to yield the corresponding imine. Then, 2-naphthol was added and the reaction mixture was kept at 60 °C for two days. An analysis of the crude reaction mixture shows many products, among which the (*S*, *S*)-stereoisomers **1–9** and the corresponding unreacted imines were predominant.

After two days, the addition of small amounts of ethanol caused the precipitation of a solid, that was collected and recrystallised to yield (*S*, *S*)-aminobenzylnaphthol **1–9** free from significant amount of the (*R*, *S*)-stereoisomer (de > 98%). With this easy, solventless and chromatography-free procedure, isolated yields in the range 51-68% were obtained for the (*S*, *S*)-aminobenzylnaphthol **1–9** (see Experimental section). Additional material could be recovered from the mother liquor, provided that a chromatographic separation was employed.

Since the high stereoselectivity of the reaction was reported to be related with the crystallisation of a particular molecular form,[25] we reasoned that a comparison between the interactions present in the crystal structures of the (*S*, *S*)- and of the (*R*, *S*)-stereoisomers could shed light on the selectivity of the process. However, the preparation of the crystals of the last species appeared to be an uphill task with the previous experimental procedure. First, we were not able to obtain satisfactory amounts of the (*R*, *S*)-stereoisomers from the crude reaction mixture and then, as already reported,[25] spontaneous transformation into the (*S*, *S*)-counterparts occurred when the crystal



Scheme 2 Stereoselective Betti reaction between 2-naphthol, aryl aldehydes and (*R*)- or (*S*)-1-arylethylamine.

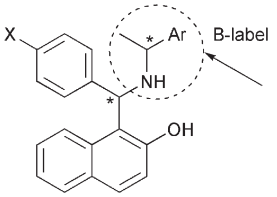


Fig. 1 Naming of the aryl groups in the aminobenzylnaphthols **1–9**.

was grown. Finally, we succeeded in producing small amounts of only (*R*, *S*)-**1** by using a variation of the method reported by Forlani *et al.*,[27] in which a mixture of almost equal amounts of the two diastereoisomers was produced. The (*R*, *S*)-**1** was isolated after crystallisations (see Experimental section), and soon analysed. We observed that the aminobenzylnaphthol (*R*, *S*)-**1** has a low melting point (135–137 °C against 155–156 °C for (*S*, *S*)-**1**). A DSC analysis confirmed these values.

2. Crystal structures of the aminobenzylnaphthols

2.1 General considerations. A systematic synthetic work was performed to prepare (*S*, *S*)-**2–4** and **6–8** aminobenzylnaphthols, in which the sequence fluorine–chlorine–bromine atoms was added to the prototypal (*S*, *S*)-**1** or (*S*, *S*)-**5** compounds. Molecule **9** completes the screening. The crystal structures of (*S*, *S*)-aminobenzylnaphthols **2–4** and **6–9** were determined in this work, whereas the crystal structures of (*S*, *S*)-**1** and (*R*, *R*)-**5**, reported by Forlani *et al.*[27] and Szatmari *et al.*,[30] respectively, are considered herein for comparison.

The crystal structures of (*S*, *S*)-**2–4** and **6–9** are orthorhombic and their space group is $P2_12_12_1$. The molecular representation and the atomic numbering are reported in Fig. 2–8, whereas crystallographic data are reported in Table 1. Intramolecular hydrogen bonds and intermolecular CH···O interactions are summarised in Table 2.

The common characteristic of the aminobenzylnaphthols **1–9** is a strong O–H···N intramolecular hydrogen bond formed by a hydroxyl group and a nitrogen atom, observed for the Betti base since 1954 with IR spectroscopy.[31] In structures (*S*, *S*)-**1–9**, the H···N distances are in the range 1.70–1.93 Å (Table 2).

The O–H···N angles are in the range 139–151°. In principle, the presence of the nitrogen atom in the aminobenzylnaphthols investigated herein could provide a further acceptor for donor-H···N hydrogen bonds. However, we observed that this atom is not involved into any interaction in the aminobenzylnaphthols **2–9**, a situation that occurred also in an investigation on similar structures reported by Alfonsov *et al.*[32]

The most interesting aspect of the aminobenzylnaphthols **1–9** is the presence of a series of short distance CH···π interactions.

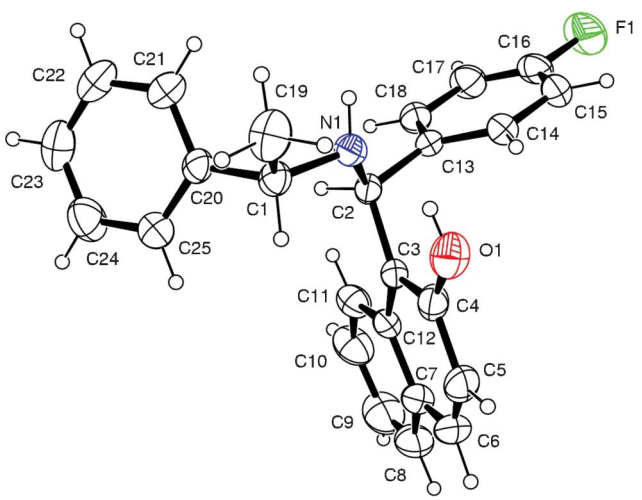


Fig. 2 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**2**.

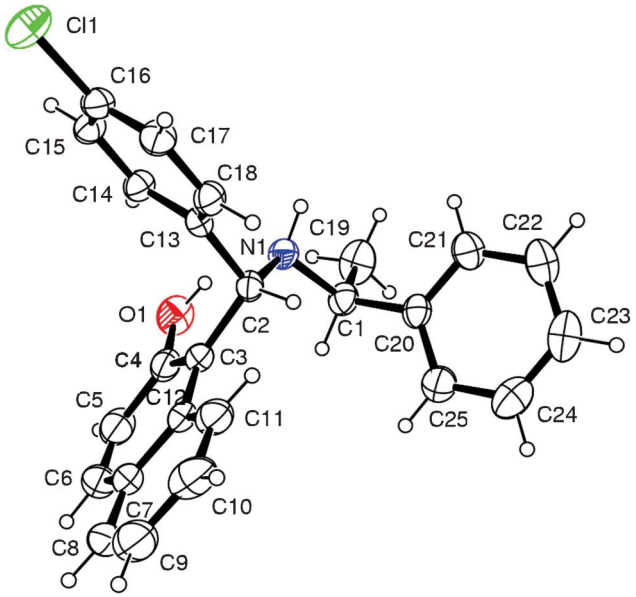


Fig. 3 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**3**.

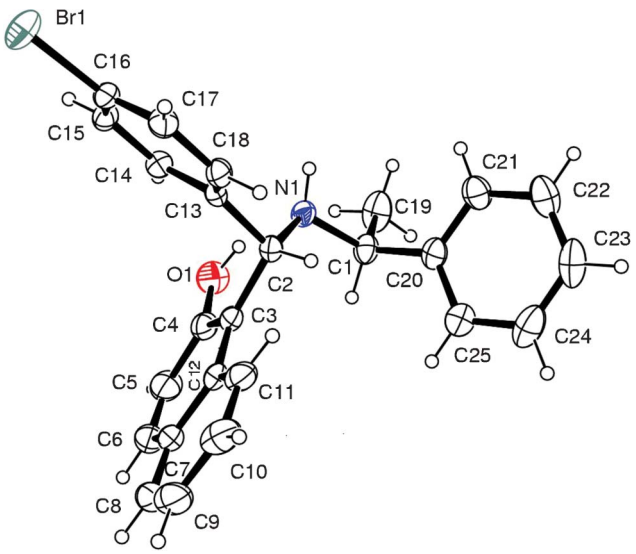


Fig. 4 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**4**.

When these interactions involve aryl hydrogen atoms as donors, a characteristic T-shape arrangement of the aryl groups is observed. In Table 3, we have collected a selection of the most relevant distances and angles describing these interactions.[4–7]

2.2 (*S*, *S*)-1 stereoisomer. The investigation on the crystal structure of the prototypal aminobenzylnaphthol (*S*, *S*)-**1**[27] showed that two molecules are present in the asymmetric unit and are bound together by a series of mutual C–H···π interactions (Fig. 9). In fact, the H_{ortho} and the H_{meta} of the phenyl^B group of one molecule interact with the naphthyl moiety of the other molecule, the distances from these atoms to the naphthyl plane being 2.49 Å (Table 3, C21–H21···Np2) and 2.82 Å (Table 3, C22–H22···Np1) respectively. The value of 2.49 Å is one of the shortest distances ever reported for this type of interaction.[4-5,9] The distance from the projection of this atom

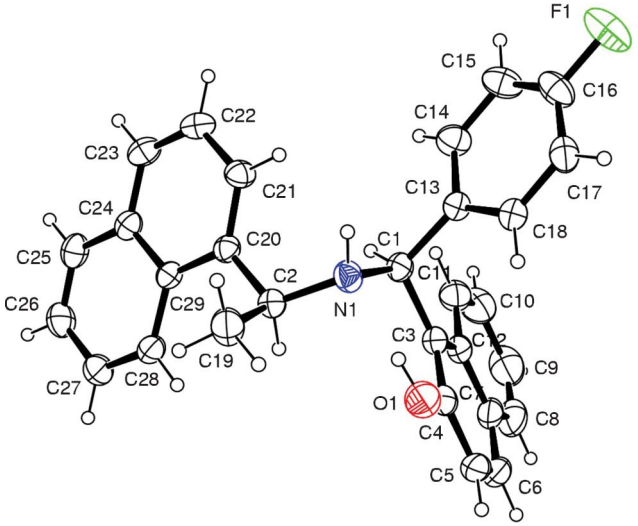


Fig. 5 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**6**.

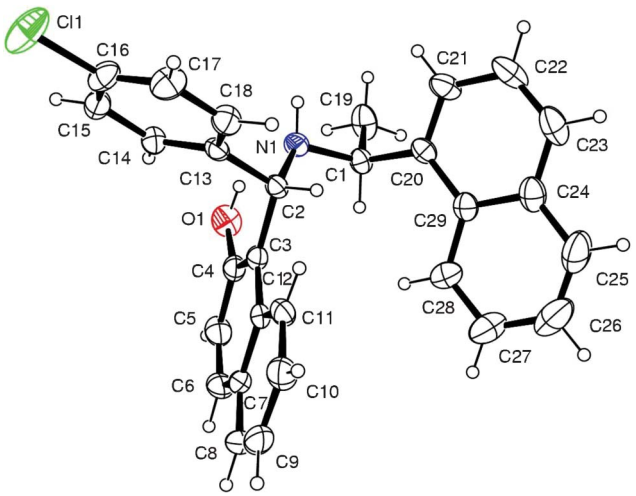


Fig. 6 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**7**.

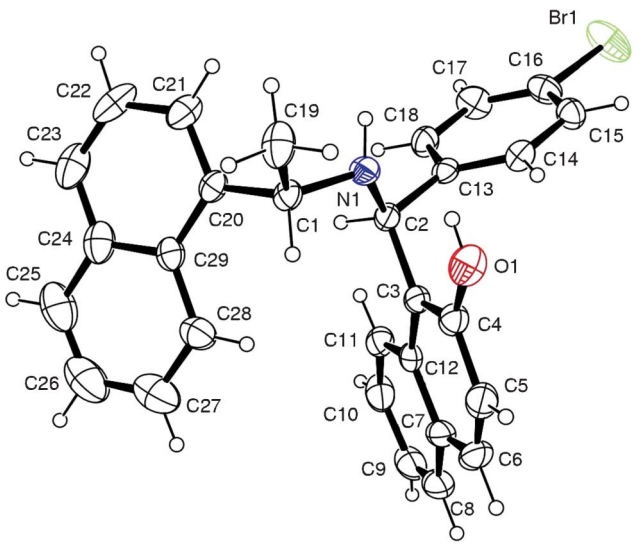


Fig. 7 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**8**.

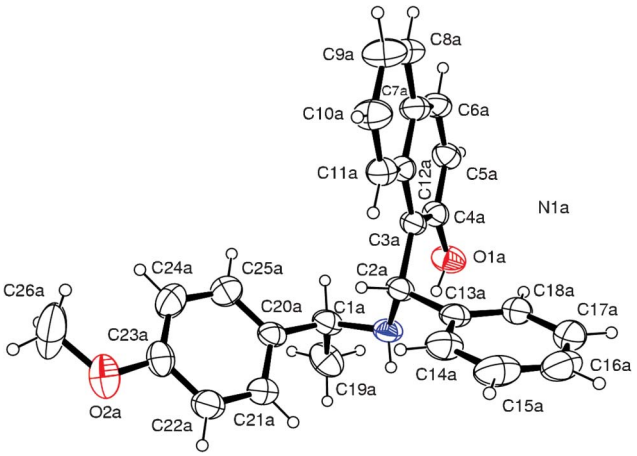


Fig. 8 ORTEP plot of aminobenzylnaphthol (*S*, *S*)-**9**.

to the centroid of the aryl group is 0.39 Å and the angle between the C–H bond and the projection of the hydrogen atom in the mean aryl plane is 153°. These geometric characteristics corroborate the fact that this interaction should be relatively strong.

The phenyl^{B} group is also the H-acceptor of a different interaction with one hydrogen atom of the phenyl^{B} group of the other molecule (Table 3, C25–H25···Ph^{B}), the distance from the hydrogen atom to the aryl plane being 2.74 Å (C–H···Hp angle of 172°). Finally, one hydrogen atom of the naphthyl group interacts with the naphthyl moiety of the other molecule (Table 3, C8–H8···Np2). The distance from the hydrogen atom to the naphthyl plane is 2.69 Å and a 0.10 Å distance from the projection of this atom to the centroid of the aryl group was measured.

The contemporary measure of various short distances from the hydrogen atoms to the aryl planes, together with suitable orientation requirements, suggest that these CH···π interactions should give a large contribution to the stabilisation of the structure.[4–7]

2.3 (*R*, *S*)-1 stereoisomer. The crystal structure of (*R*, *S*)-**1** stereoisomer is monoclinic and its space group is $P2_1$ (Fig. 10). Only one molecule is hosted in the asymmetric unit. Only one main CH···π interaction was observed, involving the H_{meta} of the phenyl^{B} group, which is 2.81 Å distant from the plane of the naphthyl group (Table 3, C17–H17···Np1). This distance is much longer than the many distances hydrogen atom/aryl plane observed in the (*S*, *S*)-stereoisomer, thus suggesting a weaker interaction and a consequent less stable crystal, as indicated also by a lower melting point.

The safest way to detect the presence of CH···π interactions is by far the measurement, in the analysis of the crystal structures, of distances in the range 2.6–3.0 Å, or below, from the hydrogen atom to the aryl planes, together with appropriate directionality requirements.[4–8]

However, other confirmations could be obtained also by using spectroscopic techniques.[4,5] For example, we examined the IR spectra of the couple (*S*, *S*)-**1** and (*R*, *S*)-**1**. A low-frequency shift (5–22 cm^{-1}) is expected when this type of interaction is present.[5] In this respect, since the crystal structure analysis revealed the

Table 1 Crystallographic data

	(*S*, *S*)-2	(*S*, *S*)-3	(*S*, *S*)-4	(*S*, *S*)-6
Code name	G15	F9	F13	G11
Empirical formula	$C_{25}H_{22}FNO$	$C_{25}H_{22}ClNO$	$C_{25}H_{22}BrNO$	$C_{29}H_{24}FNO$
Diffractometer	Nonius Kappa CCD	Bruker SMART APEX	Bruker SMART APEX	Nonius Kappa CCD
Data collection software	COLLECT[a]	SMART[b]	SMART[b]	COLLECT[a]
Formula weight	371.44	387.89	432.35	421.49
T/K	293(2)	293(2)	293(2)	293(2)
Radiation, λ/Å	Mo-Kα, 0.71073	Mo-Kα, 0.71073	Mo-Kα, 0.71073	Mo-Kα,0.71073
Cell reflections, θ range	128, 3.21°–20.03°	2160, 2.53°–20.71°	4533, 2.29°–22.52°	108, 3.11°–20.57°
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Orthorhombic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a/Å	10.687(2)	10.6982(8)	10.6828(6)	8.2095(5)
b/Å	12.122(2)	12.1633(9)	12.1716(7)	14.0391(8)
c/Å	15.549(3)	15.7632(12)	15.9649(9)	19.7711(12)
β (°)	90	90	90	90
V/Å^3	2014.3(7)	2051.2(3)	2075.8(2)	2278.7(2)
Z, ρ_c/Mg m^{-3}	4, 1.225	4, 1.256	4, 1.383	4, 1.229
μ/mm^{-1}	0.080	0.201	1.995	0.079
F(000)	784	816	888	888
Crystal size/mm	0.56 × 0.34 × 0.20	0.28 × 0.24 × 0.23	0.58 × 0.52 × 0.50	0.40 × 0.40 × 0.20
Shape, Colour	prism, colourless	prism, colourless	block, colourless	prism, colourless
Data collection θ range	2.13–29.18°	2.11–29.03°	2.10–29.02°	1.78–29.06°
Refl. collected/unique	14 042/4931	14 206/4998	14 211/5019	15 886/5561
R(int)	0.030	0.036	0.027	0.024
Max. and min. trans.	0.9841 and 0.9564	0.9552 and 0.9458	0.4353 and 0.3908	0.9843 and 0.9689
Refinement method	FMLS on F^2	FMLS on F^2	FMLS on F^2	FMLS on F^2
Data/restraints/param.	4931/0/257	4998/0/257	5019/0/257	5561/0/293
GOF	1.006	1.1015	0.898	1.032
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0471; wR_2 = 0.0836	R_1 = 0.0490; wR_2 = 0.0887	R_1 = 0.0356; wR_2 = 0.0666	R_1 = 0.0460; wR_2 = 0.0994
Final *R* indices (all data)	R_1 = 0.0919; wR_2 = 0.0976	R_1 = 0.0922, wR_2 = 0.1060	R_1 = 0.0552, wR_2 = 0.0707	R_1 = 0.0662, wR_2 = 0.1080
Flack parameter	0.3(11)	0.02(7)	0.008(7)	0.0(10)
Larg. diff. peak/hole/e Å^{-3}	0.122 and −0.129	0.120 and −0.193	0.637 and −0.238	0.129 and −0.149

	(*S*, *S*)-7	(*S*, *S*)-8	(*S*, *S*)-9	(*R*, *S*)-1
Code name	FF4	FF3	F1	CB63
Empirical formula	$C_{29}H_{24}ClNO$	$C_{29}H_{24}BrNO$	$C_{26}H_{25}NO_2$	$C_{25}H_{23}NO$
Diffractometer	Nonius Kappa CCD	Nonius Kappa CCD	Bruker SMART APEX	Nonius Kappa CCD
Data colletion software	COLLECT[a]	COLLECT[a]	SMART[b]	COLLECT[a]
Formula weight	437.94	482.40	383.47	353.44
T/K	293(2)	293(2)	293(2)	293(2)
Radiation, λ/Å	Mo-Kα, 0.71073	Mo-Kα, 0.71073	Mo-Kα, 0.71073	Mo-Kα, 0.71073
Cell reflections, θ range	147, 3.95°–20.03°	144, 4.32°–18.49°	3366, 2.17°–18.65°	95, 3.60°–20.28°
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_1$
a/Å	10.7520(7)	10.7830(5)	15.510(3)	7.1201(6)
b/Å	13.3730(17)	13.4940(19)	15.661(3)	8.2128(7)
c/Å	16.005(3)	15.938(2)	17.891(4)	17.3792(6)
β (°)	90	90	90	101.64(1)
V/Å^3	2301.3(5)	2319.1(5)	4345.5(15)	995.4(1)
Z, ρ_c/Mg m^{-3}	4, 1.264	4, 1.382	8, 1.172	2, 1.179
μ/mm^{-1}	0.187	1.794	0.073	0.071
F(000)	920	992	1632	376
Crystal size/mm	0.45 × 0.50 × 0.55	0.50 × 0.50 × 0.55	0.52 × 0.34 × 0.23	0.75 × 0.25 × 0.20
Shape, colour	prism, colourless	prism, colourless	block, colourless	prism, colourless
Data collection θ range	5.03°–27.50°	5.01°–27.50°	1.73°–29.02°	5.07°–27.53°
Refl. collected/unique	16 091/5123	21 983/5188	30 166/10 679	11 734/4444
R(int)	0.074	0.071	0.044	0.126
Max. and min. trans.	0.9121 and 0.9121	0.4674 and 0.4387	0.9833 and 0.9628	0.9859 and 0.9486
Refinement method	FMLS on F^2	FMLS on F^2	FMLS on F^2	FMLS on F^2
Data/restraints/param.	5123/0/293	5188/0/293	10 679/0/531	4444/1/248
GOF	1.062	1.088	0.931	1.008
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0579; wR_2 = 0.0968	R_1 = 0.0517; wR_2 = 0.1021	R_1 = 0.0499; wR_2 = 0.0849	R_1 = 0.0719; wR_2 = 0.1051
Final *R* indices (all data)	R_1 = 0.1217; wR_2 = 0.1191	R_1 = 0.1258; wR_2 = 0.1264	R_1 = 0.1532; wR_2 = 0.1114	R_1 = 0.1836; wR_2 = 0.1386
Flack parameter	−0.01(9)	0.046(12)	0.4(12)	0(3)
Larg. diff. peak/hole/e Å^{-3}	0.167 and −0.272	0.292 and −0.519	0.106 and −0.093	0.168 and −0.166

[a] Nonius, COLLECT and EVAL. 2002 Nonius BV, Delft, The Netherlands. [b] Bruker, SMART. 2002 Bruker AXS Inc., Madison, Wisconsin, USA.

presence of some T-shape interactions between the aryl moieties, we focused on the signals relative to these groups. In particular, we detected the aryl CH-stretching. Among the others, we observed in the IR spectra (KBr pellets) a sequence of signals of 3065, 3057, 3049 and 3031 cm^{-1} for the (*R*, *S*)-**1** compound, whereas the same sequence moves to 3056, 3048, 3034 and 3023 cm^{-1} for the (*S*, *S*)-**1**, as expected from the presence of these interactions in the (*S*, *S*)-**1** stereoisomer.

Usually, another confirmation of the presence of CH···π interactions is the upfield variation of the chemical shifts of the involved proton in the ^{1}H-NMR spectra.[4,5,33] In the case of the couple of stereoisomers (*S*, *S*)-**1** and (*R*, *S*)-**1**, we observed a clearly different pattern between the aryl hydrogen atoms of the (*S*, *S*)-**1** and those of (*R*, *S*)-**1**. Most of the aryl signals of (*S*, *S*)-**1** moved upfield (see ESI),† but the complexity of the spectra did not allow to attribute each signal. However, it seems safer to draw our conclusions on the unambiguous results deriving from the structural data of the crystals and of the IR spectra, since NMR spectra refer to samples in solution.

2.4 (*S*, *S*)-Stereoisomers 2–9. Only one molecule is hosted in the asymmetric unit of the (*S*, *S*)-**2–8** molecules. The crystal structures of compounds (*S*, *S*)-**2**, (*S*, *S*)-**3**, and (*S*, *S*)-**4**, differing only in the type of halogen atom, are isostructural (Fig. 11). The RMS of the distances between equivalent carbon, nitrogen, and oxygen atoms after performing a best molecular fit (BMF) is 0.041 for **2** and **3**, 0.050 for **3** and **4**, and 0.079 for **2** and **4**.

Beyond the cited strong O–H···N hydrogen bond (Table 2), in the **2–4** molecules an intermolecular C–H···O interaction involving the H_{meta} of the phenyl group and the hydroxyl oxygen atom is present (C15–H15···O1, Table 2). Fig. 12 shows a representative example of these bondings in aminobenzylnaphthol **2**.

On the other hand, a relevant intramolecular T-shape arrangement is found between the phenyl and the naphthyl group (Table 3, C18–H18···Np2). In particular, the distances from the hydrogen atom of the phenyl group to the naphthyl plane are short in the case of compounds **3** and **4** (2.65 Å and 2.60 Å, Table 3) and slightly longer in molecule **2** (2.73 Å Table 3). The distances from the projections of the hydrogen atoms to the centroid of the aryl groups are in the range 0.33–0.46 Å, another hint that these interactions are strong and should contribute largely to the stabilisation of the crystals. Representative compound **4** and its interactions are depicted in Fig. 13.

Another CH···π interaction drawn in Fig. 13 for the representative compound **4** involves one hydrogen atom of the naphthyl with the plane of the phenyl^B group (Table 3, C8–H8···Ph^B). The distances from this hydrogen atom to the phenyl^B plane are in the range 2.72–2.78 Å for compounds **2–4**, slightly longer than the other ones, but having the C–H···Hp angles in the range 172–176°.

A further CH···π interaction, characterised by a longer hydrogen atom/aryl plane distance, was found from one hydrogen atom of the phenyl^B group (Table 3, C21–H21···Np1) to the plane of the naphthyl moiety, the distances being in the range 2.78–2.91 Å for compounds **2–4**. A representative example is depicted in Fig. 14 for aminobenzylnaphthol **2**.

The crystal of (*S*, *S*)-**6** results in being isostructural with (*S*, *S*)-**5**, obtained by inverting the structure reported[30] for (*R*, *R*)-**5** (Fig. 15), the RMS of the BMF being 0.102. In this couple, the Ar^B ring adopts a conformation that differs from the molecules **2–4** and **7, 8**. In fact, in these last aminobenzylnaphthols, the angles between the aryl^B plane and the naphthyl plane are in the

Table 2 Distance and angles of hydrogen bond type interactions in aminobenzylnaphthols **1–9**

	D–H···A	D–H (Å)	H··A(Å)	D··A (Å)	D–H··A(°)	Symmetry
(*S*, *S*)-**1**[a]	O1–H1···N1	0.82	1.90	2.585	140	
	O2–H2···N2	0.82	1.88	2.581	142	
(*R*,*S*)-**1**	O1–H4···N1	0.82	1.85	2.574(4)	147	
	C14–H14···O1	0.93	2.79	3.718(5)	172	x−1, +y, +z
	C19–H19A···O1	0.96	2.81	3.552(5)	135	−x+2,+y−1/2,−z+1
(*S*, *S*)-**2**	O1–H4···N1	0.82	1.86	2.575(2)	145	
	C15–H15···O1	0.93	2.52	3.281(3)	139	x+1/2,−y+1/2+1,−z+2
(*S*, *S*)-**3**	O1–H4···N1	0.82	1.86	2.579(3)	146	
	C15–H15···O1	0.93	2.54	3.306(3)	139	x+1/2,−y+1/2+1,−z+2
(*S*, *S*)-**4**	O1–H4···N1	0.82	1.85	2.577(3)	147	
	C15–H15···O1	0.93	2.53	3.296(3)	140	x+1/2,−y+1/2+1,−z+2
(*R*, *R*)-**5**[b]	O1–H1···N12	0.94	1.70	2.562	151	
(*S*, *S*)-**6**	O1–H4···N1	0.82	1.83	2.562(2)	148	
	C15–H15···O1	0.93	2.69	3.274(3)	122	x+1, +y, +z
(*S*, *S*)-**7**	O1–H4···N1	0.82	1.90	2.609(3)	144	
	C15–H15···O1	0.93	2.96	3.553(4)	123	x−1/2, −y+1/2, −z
(*S*, *S*)-**8**	O1–H4···N1	0.82	1.93	2.611(4)	139	
(*S*, *S*)-**9**	O1A–H4A···N1A	0.82	1.84	2.565(2)	147	
	O1B–H4B···N1B	0.82	1.85	2.568(3)	146	
	C5A–H5A···O1B	0.93	2.70	3.522(3)	148	
	C5B–H5B···O1A	0.93	2.51	3.411(3)	163	
	C9A–H9A···O2B	0.93	2.57	3.441(3)	156	x,+y−1,+z
	C22A–H22A···O1B	0.93	2.57	3.454(3)	158	x+1/2,−y−1/2,−z+2
	C9B–H9B···O2A	0.93	2.62	3.520(3)	162	x,+y+1,+z
	C26B–H26F···O2A	0.96	2.57	3.476(5)	158	x−1,+y+1,+z

[a] Reported by Forlani *et al.*[27] [b] Reported by Szatmari *et al.*[30]

Table 3 Selected CH···π interactions in aminobenzylnaphthols **1–9**

D–H···Ar	*h* (Å)[a]	*d* (Å)[b]	CH···Ar(°)[c]	*δ* (Å)[d]
(*S*, *S*)-**1** molecule I[e,f]				
C8–H8···Np2	2.69	2.69	145	0.10
C25–H25···Ph^B	2.74	2.77	172	0.43
(*S*, *S*)-**1** molecule II[e,f]				
C21–H21···Np2	2.49	2.52	153	0.39
C22–H22···Np1	2.82	2.82	139	0.21
(*R*,*S*)-**1**[f]				
C17–H17···Np1	2.81	2.85	146	0.48
(*S*, *S*)-**2**[f]				
C18–H18···Np2	2.73	2.77	146	0.46
C8–H8···Ph^B	2.78	3.26	176	1.71
C21–H21···Np1	2.78	2.93	150	0.91
(*S*, *S*)-**3**[f]				
C18–H18···Np2	2.65	2.68	144	0.42
C8–H8···Ph^B	2.78	3.08	175	1.33
C21–H21···Np1	2.85	2.97	147	0.83
(*S*, *S*)-**4**[f]				
C18–H18···Np2	2.60	2.62	144	0.33
C8–H8···Ph^B	2.72	2.86	172	0.87
C21–H21···Np1	2.91	2.99	147	0.70
(*R*, *R*)-**5**[f,g,h]				
C21–H21···Np1	2.71	2.88	133	0.97
C27–H27···Np^{B}1	2.75	2.76	135	0.20
(*S*, *S*)-**6**[f]				
C21–H21···Np1	2.79	2.97	133	1.02
C27–H27···Np^{B}1	2.82	2.83	137	0.18
(*S*, *S*)-**7**[f]				
C8–H8···Np^{B}1	2.68	2.70	159	0.27
C19–H19C···Np2	2.69	2.73	145	0.43
C19–H19B···Ph	2.86	2.88	176	0.36
(*S*, *S*)-**8**[f]				
C8–H8···Np^{B}1	2.70	2.73	159	0.36
C19–H19C···Np2	2.71	2.75	145	0.46
C19–H19B···Ph	2.79	2.81	177	0.30
(*S*, *S*)-**9** Molecule I[f]				
C21–H21···Np1	2.74	2.87	149	0.86
(*S*, *S*)-**9** Molecule II[f]				
C21–H21···Np1	2.81	2.83	145	0.35

[a] Distance from the H-atom to the mean aryl plane. [b] Distance from the H-atom to the aryl ring centroid. [c] C–H···Hp angle, in which Hp is the projection of the H-atom in the mean aryl plane. [d] Distance from the Hp to the aryl ring centroid. [e] Reported by Forlani *et al.*[27] [f] The two rings of the naphthyl moiety were indicated as Np1 and Np2, Np1 being the rings bonded to the methine carbon atoms. [g] Reported by Szatmari *et al.*[30] [h] The reported structure was relabelled according to our numeration.

range 43.93–47.02°, whereas in compounds **5** and **6** the same angles are 71.20 and 75.35° respectively (see Table A, ESI).†

The most relevant CH···π interaction deals with the C21–H21···Np1 assembly, as depicted in Fig. 14 (Table 3, 2.71–2.79 Å distance from the hydrogen atom to the aryl plane).

The crystal structures of (*S*, *S*)-**7** and (*S*, *S*)-**8**, in which Ar^B = 1-naphtyl, are isostructural, the RMS of the BMF being 0.025 (Fig. 16).

The most interesting CH···π interactions found in these compounds deal with the C8–H8···Np^{B}1 assembly already represented in Fig. 13 (Table 3, 2.68 and 2.70 Å distances from the hydrogen atom to the aryl plane, with a distance from the projection of the hydrogen atom to the centroid of 0.27 and 0.36 Å).

Another CH···π interaction involves the hydrogen atoms of the methyl group that interact with the naphthyl groups (Table 3, C19–H19–Np2). In the case of the couple of molecules **7** and **8**, the distances from the hydrogen atom to the aryl plane are 2.69

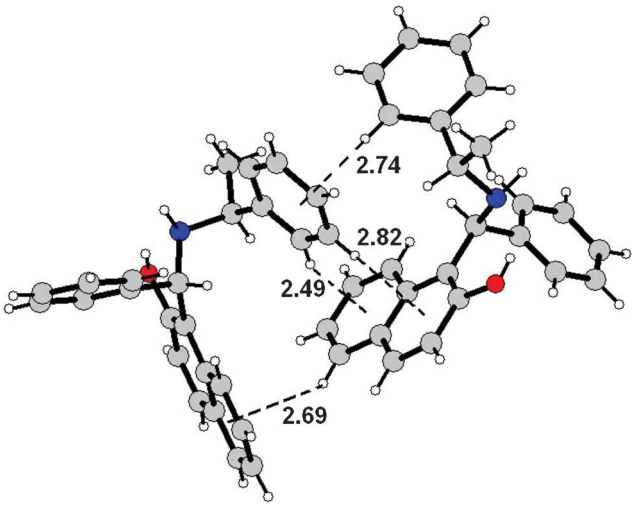


Fig. 9 CH···π interactions in aminobenzylnaphthol (*S*, *S*)-**1**.

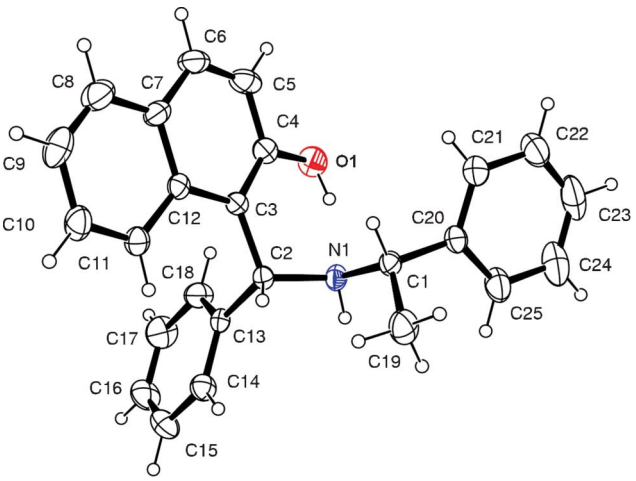


Fig. 10 ORTEP plot of aminobenzylnaphthol (*R*, *S*)-**1**.

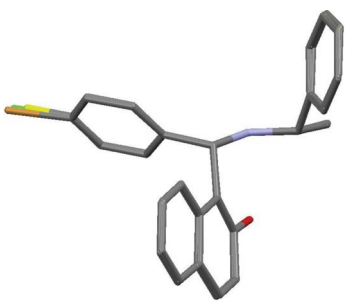


Fig. 11 Best fit of (*S*, *S*)-**2**, (*S*, *S*)-**3** and (*S*, *S*)-**4** structures (including 25 carbon, 1 nitrogen and 1 oxygen atoms).

and 2.71 Å, with a 0.43 and 0.46 Å distance from the projection of the hydrogen atom to the centroid (Fig. 17).

Compound **9** differs from the **2–8** aminobenzylnaphthols because two molecules are hosted in the asymmetric unity. As far as the hydroxyl oxygen is concerned, two CH···O interactions were observed between the oxygen atom and one hydrogen atom of the naphthyl group (Table 2, 2.51 Å distance, C5B–H5B···O1A, and 2.70 Å distance C5A–H5A···O1B). The

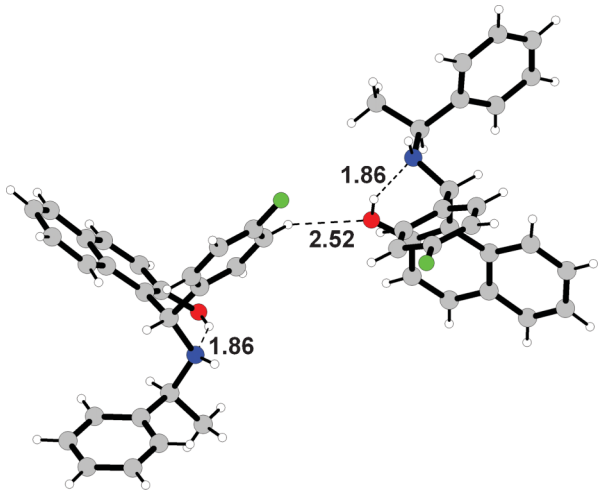


Fig. 12 Intramolecular hydrogen bonds and intermolecular CH···O interaction in aminobenzylnaphthol (*S*, *S*)-**2**.

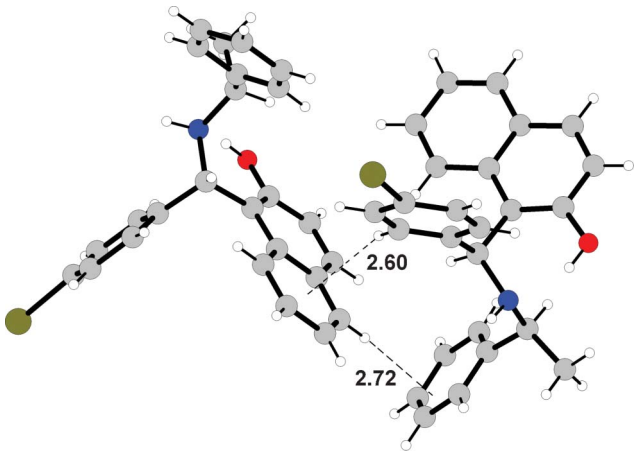


Fig. 13 CH···π interactions in aminobenzylnaphthol (*S*, *S*)-**4**.

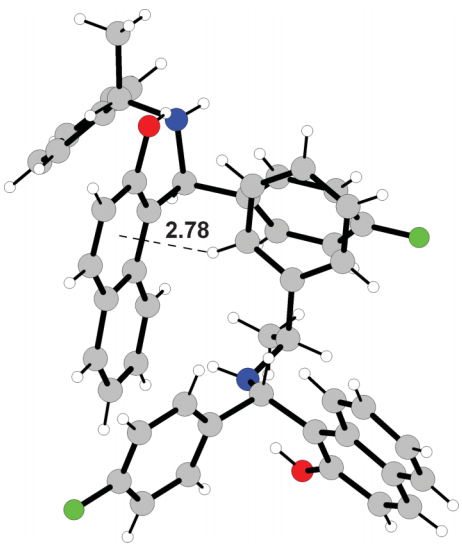


Fig. 14 A CH···π interaction in aminobenzylnaphthol (*S*, *S*)-**2** involving the phenyl^{B} group.

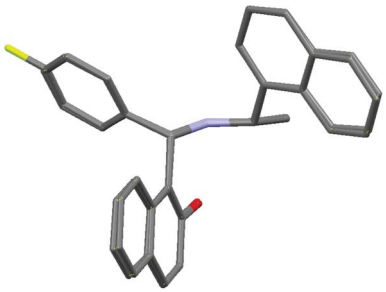


Fig. 15 Best fit of (*S*, *S*)-**5** and (*S*, *S*)-**6** structures (including 31 carbon, 1 nitrogen and 1 oxygen atoms).

presence of a further oxygen atom, belonging to the 4-methoxyphenyl group, originates some further CH···O interactions. The first of these interactions is found between one hydrogen atom of the methyl group and the oxygen atom of the methoxy group (Table 2, 2.57 Å distance, C26B–H26F···O2A), whereas the second one occurs between a hydrogen atom of the naphthyl group and the other methoxy oxygen atom (Table 2, 2.57 Å distance, C9A–H9A···O2B).

In the presence of these interactions involving the oxygen atom, CH···π assemblies are limited to the interaction of the H_{meta} of the phenyl^{B} group with the naphthyl group (Table 3, C21–H21···Np1, 2.81 Å distance from the hydrogen atom to the aryl plane).

Conclusions

The useful, highly stereoselective solvent- and chromatography-free Betti reaction of 2-naphthol with aryl aldehydes and nonracemic amines originated a class of interesting aminobenzylnaphthols, whose crystal structures were investigated by means of X-ray diffraction experiments. The aminobenzylnaphthols obtained by substituting a hydrogen atom with the sequence fluorine–chlorine–bromine atom could be grouped into three classes of isostructural molecules. In the investigated structures, the presence of the known intramolecular hydrogen bonding was confirmed, whereas CH···π interactions appear to play an important role in the intermolecular interactions building the crystals structure. Some cases of very short distances from the hydrogen atoms to the planes of the aryl groups were reported, together with appropriate geometric requirements for these interactions. The missing of the crystal structures of many less accessible (*R*, *S*)-stereoisomers suggests to avoid speculations, but the presence of these interactions only in the crystals of the (*S*, *S*)-aminobenzylnaphthols could be considered a sound hint of a

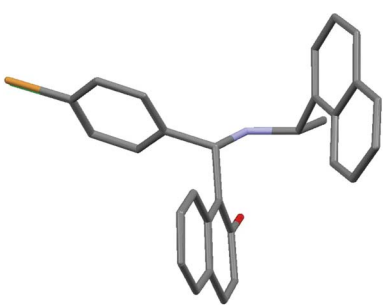


Fig. 16 Best fit of (*S*, *S*)-**7** and (*S*, *S*)-**8** structures (including 29 carbon, 1 nitrogen and 1 oxygen atoms).

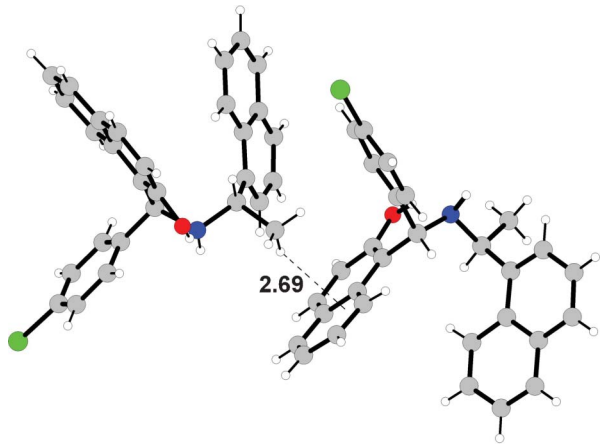


Fig. 17 A CH···π interaction involving the methyl group in aminobenzylnaphthol (*S*, *S*)-**7**.

more stable and, as a consequence, of a preferentially formed crystal.

Experimental

Chemicals were purchased from Sigma-Aldrich and were used as received. NMR spectra were recorded using a Bruker AM500 spectrometer. Elemental analyses were performed on a Carlo Erba CHNS-O EA1108 Elemental Analyzer.

Materials

(*S*, *S*)-Aminobenzylnaphthols **2–4** and **6–9** were synthesised by reacting 2-naphthol, aryl aldehydes and (*S*)-1-arylethylamine for two days at 60 °C without any solvent. After this time, the addition of small amounts of ethanol caused the precipitation of the desired product, that was collected and re-crystallised.

1-[(*S*)-(4-Fluorophenyl)-((1′*S*)-1′-phenylethylamino)-methyl]-naphthalen-2-ol (2). Isolated yield 68%. Mp 108–110 °C (from ethanol). $[\alpha]_D^{25}$ = + 213.3 (*c* = 1.0 in $CHCl_3$). Anal. Calcd for $C_{25}H_{22}FNO$: C 80.84; H 5.97; N 3.77. Found C 80.89; H 5.90; N 4.01. ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 13.40–12.37 (1H, br s, OH), 7.82–7.72 (2H, m, H_{Ar}), 7.45–7.31 (4H, m, H_{Ar}), 7.29–7.16 (7H, m, H_{Ar}), 6.94–6.86 (2H, m, H_{Ar}), 5.49 (1H, s, $CHAr_2$), 3.92 (1H, q, $^3J_{HH}$ 6.9 Hz, CHMe), 3.30–2.80 (1H, br s, NH), 1.53 (3H, d, $^3J_{HH}$ 6.9 Hz, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 162.4 (d, $^1J_{CF}$ 247.4 Hz, C_{Ar}-F), 156.6 (C_{Ar}), 142.1–141.6 (br s, C_{Ar}), 132.3 (C_{Ar}), 130.1 (C_{Ar}), 129.7 (d, $^3J_{CF}$ 8.0 Hz, C_{Ar}), 129.1 (C_{Ar}), 128.9 (C_{Ar}), 128.8 (C_{Ar}), 128.2 (C_{Ar}), 126.9 (C_{Ar}), 126.6 (C_{Ar}), 122.7 (C_{Ar}), 120.8 (C_{Ar}), 119.9 (C_{Ar}), 115.9 (d, $^2J_{CF}$ 21.7 Hz, C_{Ar}), 112.3 (C_{Ar}), 59.4 ($CHAr_2$), 56.9 (CHMe), 22.6 (CH_3).

1-[(*S*)-(4-Chlorophenyl)-((1′*S*)-1′-phenylethylamino)-methyl]-naphthalen-2-ol (3). Isolated yield 52%. Mp 149–150 °C (from *tert*-butanol) (lit.,[27] 132–140 °C for the (*R*, *R*) stereoisomer). $[\alpha]_D^{25}$ = + 205.1 (*c* = 2.0 in $CHCl_3$) (lit.,[27] = −192.0 (*c* = 3.5 in $CHCl_3$) for the (*R*, *R*) stereoisomer).

1-[(*S*)-(4-Bromophenyl)-((1′*S*)-1′-phenylethylamino)-methyl]-naphthalen-2-ol (4). [31] Isolated yield 57%. Mp 138–140 °C (from *tert*-butanol). $[\alpha]_D^{25}$ = + 190.1 (*c* = 1.0 in $CHCl_3$).

1-[(1*S*)-(4-Fluorophenyl)-((1′*S*)-1′-naphthalen-1-yl-ethylamino)-methyl]-naphthalen-2-ol (6). Isolated yield 53%. Mp 157–159 °C (from ethanol). $[\alpha]_D^{25}$ = + 313.1 (*c* = 1.0 in $CHCl_3$). Anal. Calcd for $C_{29}H_{24}FNO$: C 82.63; H 5.74; N 3.32. Found : C 82.67; H 5.81; N 3.43. ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 14.19–13.38 (1H, br s, OH), 7.90–7.84 (2H, m, H_{Ar}), 7.80–7.76 (1H, m, H_{Ar}), 7.74–7.46 (4H, m, H_{Ar}), 7.42–7.29 (2H, m, H_{Ar}), 7.26–6.95 (6H, m, H_{Ar}), 6.92–6.87 (2H, m, H_{Ar}), 5.49 (1H, s, $CHAr_2$), 5.01–4.77 (1H, m, CHMe), 2.66–2.37 (1H, br s, NH), 1.66 (3H, d, $^3J_{HH}$ 6.6 Hz, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 162.2 (d, $^1J_{CF}$ 247.4 Hz, $C_{Ar\text{-}F}$), 157.0 (C_{Ar}), 139.9–139.0 (br s, C_{Ar}), 137.2 (C_{Ar}), 133.8 (C_{Ar}), 132.4 (C_{Ar}), 131.4 (C_{Ar}), 129.9 (C_{Ar}), 129.5 (d, $^3J_{CF}$ 8.0 Hz, C_{Ar}), 128.9 (C_{Ar}), 128.6 (C_{Ar}), 128.2 (C_{Ar}), 126.3 (C_{Ar}), 126.2 (C_{Ar}), 125.8 (C_{Ar}), 125.5 (C_{Ar}), 122.4 (C_{Ar}), 121.0 (C_{Ar}), 120.0 (C_{Ar}), 115.9 (d, $^2J_{CF}$ 20.9 Hz, C_{Ar}), 113.2 (C_{Ar}), 60.3 ($CHAr_2$), 52.1–51.0 (br s, CHMe), 23.0 (CH_3).

1-[(1*S*)-(4-Chlorophenyl)-((1′*S*)-1′-naphthalen-1-yl-ethylamino)-methyl]-naphthalen-2-ol (7). Isolated yield 56%. Mp 142–144 °C (from ethanol). $[\alpha]_D^{25}$ = + 329.8 (*c* = 0.8 in $CHCl_3$). Anal. Calcd for $C_{29}H_{24}ClNO$: C 79.53; H 5.52; N 3.2. Found : C 79.51; H 5.63; N 3.47. ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 14.10–13.30 (1H, br s, OH), 7.94–7.82 (2H, m, H_{Ar}), 7.79–7.35 (5H, m, H_{Ar}), 7.32–6.98 (10H, m, H_{Ar}), 5.45 (1H, s, $CHAr_2$), 4.94–4.74 (1H, m, CHMe), 2.66–2.38 (1H, br s, NH), 1.64 (3H, d, $^3J_{HH}$ 6.7 Hz, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 157.3 (C_{Ar}), 140.2 (C_{Ar}), 140.1–139.4 (br s, C_{Ar}), 134.1 (C_{Ar}), 134.0 (C_{Ar}), 132.6 (C_{Ar}), 131.7 (C_{Ar}), 130.3 (C_{Ar}), 129.4 (C_{Ar}), 129.2 (C_{Ar}), 128.9 (C_{Ar}), 128.5 (C_{Ar}), 126.6 (C_{Ar}), 126.5 (C_{Ar}), 126.1 (C_{Ar}), 125.8 (C_{Ar}), 122.7 (C_{Ar}), 122.6 (C_{Ar}), 121.2 (C_{Ar}), 120.3 (C_{Ar}), 113.2 (C_{Ar}), 60.6 ($CHAr_2$), 52.1–51.1 (br s, CHMe), 23.3 (CH_3).

1-[(1*S*)-(4-Bromophenyl)-((1′*S*)-1′-naphthalen-1-yl-ethylamino)-methyl]-naphthalen-2-ol (8). Isolated yield 51%. Mp 126–128 °C (from ethanol). $[\alpha]_D^{25}$ = + 226.8 (*c* = 1.1 in $CHCl_3$). Anal. Calcd for $C_{29}H_{24}BrNO$: C 72.20; H 5.01; N 2.90. Found : C 72.41; H 5.16; N 3.07. ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 14.02–13.43 (1H, br s, OH), 7.89–7.82 (2H, m, H_{Ar}), 7.73 (1H, d, $^3J_{HH}$ 8.6 Hz, H_{Ar}), 7.68 (1H, d, $^3J_{HH}$ 7.8 Hz, H_{Ar}), 7.65–7.43 (2H, m, H_{Ar}), 7.39 (1H, d, $^3J_{HH}$ 7.4 Hz, H_{Ar}), 7.34–7.29 (2H, m, H_{Ar}), 7.24–7.20 (1H, m, H_{Ar}), 7.17–6.98 (7H, m, H_{Ar}), 5.41 (1H, s, $CHAr_2$), 4.96–4.76 (1H, m, CHMe), 2.69–2.30 (1H, br s, NH), 1.61 (3H, d, $^3J_{HH}$ 6.6 Hz, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 157.1 (C_{Ar}), 140.6 (C_{Ar}), 139.5 (C_{Ar}), 133.9 (C_{Ar}), 132.4 (C_{Ar}), 132.2 (C_{Ar}), 131.5 (C_{Ar}), 130.1 (C_{Ar}), 129.5 (C_{Ar}), 129.0 (C_{Ar}), 128.7 (C_{Ar}), 128.3 (C_{Ar}), 126.3 (C_{Ar}), 125.9 (C_{Ar}), 125.6 (C_{Ar}), 122.5 (C_{Ar}), 122.4 (C_{Ar}), 122.0 (C_{Ar}), 121.0 (C_{Ar}), 120.1 (C_{Ar}), 113.0 (C_{Ar}), 60.5 ($CHAr_2$), 52.0–51.0 (br s, CHMe), 23.1 (CH_3).

1-[(*S*)-(phenyl)-((1′*S*)-1′-4′-methoxyphenylethylamino)-methyl]-naphthalen-2-ol (9). Isolated yield 64%. Mp 127–129 °C (from *tert*-butanol). $[\alpha]_D^{25}$ = + 187.8 (*c* = 2.0 in $CHCl_3$). Anal. Calcd for $C_{26}H_{25}NO_2$: C 81.43; H 6.57; N 3.65. Found C 81.35; H 6.79; N 3.94. ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 13.87–13.69 (1H, br s, OH), 7.76–7.71 (2H, m, H_{Ar}), 7.41–7.38 (1H, m, H_{Ar}), 7.26–7.16 (8H, m, H_{Ar}), 7.12–7.09 (2H, m, H_{Ar}), 6.95–6.91 (2H, m, H_{Ar}), 5.46 (1H, s, $CHAr_2$), 3.88–3.81 (4H, m, CHMe + OCH_3), 2.25–2.13 (1H, br s, NH), 1.48 (3H, d, $^3J_{HH}$ 6.7 Hz, CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ_C 159.3 (C_{Ar}), 157.0 (C_{Ar}), 141.0–140.3 (br s,

C_{Ar}), 134.8–134.0 (br s, C_{Ar}), 132.5 (C_{Ar}), 129.9 (C_{Ar}), 129.0 (C_{Ar}), 128.8 (C_{Ar}), 128.1 (C_{Ar}), 128.0 (C_{Ar}), 127.8 (C_{Ar}), 126.4 (C_{Ar}), 122.5 (C_{Ar}), 121.1 (C_{Ar}), 120.0 (C_{Ar}), 114.3 (C_{Ar}), 112.8–112.4 (br s, C_{Ar}), 60.1 ($CHAr_2$), 55.9 (CHMe), 55.3 (OCH_3), 22.8 (CH_3).

1-[(*R*)-(phenyl)-((1′*S*)-1′-phenylethylamino)-methyl]-naphthalen-2-ol (1). An almost equimolar mixture of (*R*, *S*)-**1** and (*S*, *S*)-**1** was obtained by reacting a solution of 2-naphthol, benzaldehyde and (*S*)-1-phenylethylamine in THF for three days at room temperature. The reaction mixture was crystallised from n-hexane/diethyl ether 99 : 1, and then the recovered solid was re-crystallised from n-hexane/diethyl ether 1 : 1. The mother liquor of this crystallisation yielded some crystals of the (*R*, *S*)-diastereomer upon slow evaporation of the solvent. Mp 135–137 °C (from ethanol). $[\alpha]_D^{25} = -167.7$ (c = 0.25 in $CHCl_3$).

X-Ray experiments

X-Ray data were collected at 293 K by means of single crystal X-ray diffractometers. Unit cell parameters are reported in Table 1. Data were corrected for Lorentz and polarisation effects, and for absorption effects (**3**, **4**, **7**, **8** and **9**).[34] The structures were solved by direct methods (SIR97)[35] and refined by full-matrix-least-square technique on F^2 for all unique measured data (SHELXL-97).[36] Non-hydrogen atoms were refined using anisotropic displacement parameters. Nitrogen-bonded H atoms were located by means of Fourier maps application, and had assigned a fixed isotropic displacement parameter ($U_{iso}(H) = 1.2\ U_{iso}(N)$); the other hydrogen atoms were geometrically imposed with riding-model constraints (C–H_{Ar} 0.93 Å C^{-1}–$H_{Methine}$ = 0.98 Å with $U_{iso}(H) = 1.2U_{iso}(C)$; C–$H_{Methyl}$ 0.96 Å with $U_{iso}(H) = 1.5U_{iso}(C)$; O–H = 0.82 Å with $U_{iso}(H) = 1.5U_{iso}(0)$). Complete crystallographic data are available upon request from the Cambridge Crystallographic Data Centre (12 Union Road, Cambridge, CB2 1EZ, UK; email: deposit@ccdc.cam.ac.uk), by quoting the depository numbers CCDC-822815 ((*S*, *S*)-**2**), 822816 ((*S*, *S*)-**3**), 822817 ((*S*, *S*)-**4**), 822818 ((*S*, *S*)-**6**), 822819 ((*S*, *S*)-**7**), 822820 ((*S*, *S*)-**8**), 822821 ((*S*, *S*)-**9**), 822822 ((*R*, *S*)-**1**).

Acknowledgements

This work was financially supported, in part, by the MIUR Rome (PRIN Project: Stereoselezione in sintesi organica. Metodologie e applicazioni) and by the University of Bari. We thank Dr Gabriella Cannone and Dr Francesco Iannone (Dipartimento di Chimica, Bari, Italy) for preliminary synthetic experiments, Mr Giuseppe Chita (CNR, Istituto di Cristallografia, Bari, Italy) for some X-ray data collection, Dr Francesca Benevelli (Bruker Italia), and Prof. Francesco Naso for helpful discussions.

References

1 (*a*) G. R. Desiraju, *Crystal Engineering. The design of organic solids*, Elsevier, Amsterdam, 1989; (*b*) G. R. Desiraju, J. J. Vittal and A. Ramanan, *Crystal Engineering. A Textbook*. World Scientific Publishing, Singapore, 2011.
2 G. R. Desiraju, *Angew. Chem., Int. Ed.*, 2011, **50**, 52–59.
3 G. R. Desiraju, *Acc. Chem. Res.*, 2002, **35**, 565–573.
4 M. Nishio, *Phys. Chem. Chem. Phys.*, 2011, **13**, 13873–13900.
5 (*a*) M. Nishio, Y. Umezawa, K. Honda, S. Tsuboyama and H. Suezawa, *CrystEngComm*, 2009, **11**, 1757–1788; (*b*) M. Nishio, *CrystEngComm*, 2004, **6**, 130–158.
6 S. Tsuzuki and A. Fujii, *Phys. Chem. Chem. Phys.*, 2008, **10**, 2584–2594.
7 Y. Umezawa, S. Tsuboyama, K. Honda, J. Uzawa and M. Nishio, *Bull. Chem. Soc. Jpn.*, 1998, **71**, 1207–1213.
8 J. Ran and M. W. Wong, *J. Phys. Chem. A*, 2006, **110**, 9702–9709.
9 M. C. Grossel, A. K. Cheetham, D. A. O. Hope and S. C. Weston, *J. Org. Chem.*, 1993, **58**, 6654–6661.
10 K. M. Sureshan, T. Uchimaru, Y. Yao and Y. Watanabe, *CrystEngComm*, 2008, **10**, 493–496.
11 M. Nishio, *Tetrahedron*, 2005, **61**, 6923–6950.
12 M. Yamakawa, I. Yamada and R. Noyori, *Angew. Chem., Int. Ed.*, 2001, **40**, 2818–2821.
13 K. Kanao, Y. Tanabe, Y. Miyake and Y. Nishibayashi, *Organometallics*, 2010, **29**, 2381–2384.
14 C. D. Anderson, T. Dudding, R. Gordillo and K. N. Houk, *Org. Lett.*, 2008, **10**, 2749–2752.
15 F. Naso, M. A. M. Capozzi, A. Bottoni, M. Calvaresi, V. Bertolasi, F. Capitelli and C. Cardellicchio, *Chem.–Eur. J.*, 2009, **15**, 13417–13426.
16 M. A. M. Capozzi, C. Centrone, G. Fracchiolla, F. Naso and C. Cardellicchio, *Eur. J. Org. Chem.*, 2011, 4327–4334.
17 H. Suezawa, S. Ishihara, Y. Umezawa, S. Tsuboyama and M. Nishio, *Eur. J. Org. Chem.*, 2004, 4816–4822.
18 K. Kinbara, Y. Harada and K. Saigo, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1339–1347.
19 T. Shimada, Y. Kobayashi and K. Saigo, *Tetrahedron: Asymmetry*, 2005, **16**, 3807–3813.
20 K. Saigo and Y. Kobayashi, *Chem. Rec.*, 2007, **7**, 47–56.
21 F. Naso, C. Cardellicchio, M. A. M. Capozzi, F. Capitelli and V. Bertolasi, *New J. Chem.*, 2006, **30**, 1782–1789.
22 C. Cardellicchio, M. A. M. Capozzi and F. Naso, *Tetrahedron: Asymmetry*, 2010, **21**, 507–517.
23 C. Cardellicchio, G. Ciccarella, F. Naso, E. Schingaro and F. Scordari, *Tetrahedron: Asymmetry*, 1998, **9**, 3667–3675.
24 C. Cardellicchio, G. Ciccarella, F. Naso, F. Perna and P. Tortorella, *Tetrahedron*, 1999, **55**, 14685–14692.
25 C. Cimarelli, A. Mazzanti, G. Palmieri and E. Volpini, *J. Org. Chem.*, 2001, **66**, 4759–4765.
26 C. Cimarelli, G. Palmieri and E. Volpini, *Tetrahedron: Asymmetry*, 2002, **13**, 2417–2426.
27 C. Boga, E. Di Martino, L. Forlani and F. Torri, *J. Chem. Res.*, 2001, 43–45.
28 D.-X. Liu, L.-C. Zhang, Q. Wang, C.-S. Da, Z.-Q. Xin, R. Wang, M. C. K. Choi and A. S. C. Chan, *Org. Lett.*, 2001, **3**, 2733–2735.
29 M. R. Saidi and N. Azizi, *Tetrahedron: Asymmetry*, 2003, **14**, 389–392.
30 I. Szatmari, R. Sillanpaa and F. Fulop, *Tetrahedron: Asymmetry*, 2008, **19**, 612–617.
31 V. Carassiti and G. B. Fabbri, *Boll. Sci. Fac. Chim. Ind. Bologna*, 1954, **12**, 160–161, (*Chem. Abstr.*, **49**, 10744d).
32 V. A. Alfonsov, K. E. Metlushka, C. E. Mc Kenna, B. A. Kashemirov, O. N. Kataeva, V. F. Zheltukhin, D. N. Sadkova and A. B. Dobrynin, *Synlett*, 2007, 488–490.
33 W. B. Jennings, N. J. P. McCarthy, P. Kelly and J. F. Malone, *Org. Biomol. Chem.*, 2009, **7**, 5156–5162.
34 Bruker. SAINT and SADABS. 2001, Bruker AXS Inc., Madison, Wisconsin, USA.
35 A. Altomare, M. C. Burla, M. Camalli, G. L. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. Moliterni, G. Polidori and R. Spagna, *J. Appl. Crystallogr.*, 1999, **32**, 115–119.
36 G. M. Sheldrick, *SHELXL-97. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany, 1997.