Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Hydrogen-bonded chains in racemic 2-benzyl-3-(2-bromophenyl)propiononitrile and hydrogen-bonded sheets in methyl 2-benzyl-2-cyano-3-phenylpropionate

Guillermo Calderón,[a] Luz Marina Jaramillo-Gómez,[a] José M. de la Torre,[b] Justo Cobo,[b] John N. Low[c] and Christopher Glidewell[d]*

[a]Departamento de Química, Universidad de Valle, AA 25360 Cali, Colombia, [b]Departamento de Química Inorgánica y Orgánica, Universidad de Jaén, 23071 Jaén, Spain, [c]Department of Chemistry, University of Aberdeen, Meston Walk, Old Aberdeen AB24 3UE, Scotland, and [d]School of Chemistry, University of St Andrews, Fife KY16 9ST, Scotland
Correspondence e-mail: cg@st-andrews.ac.uk

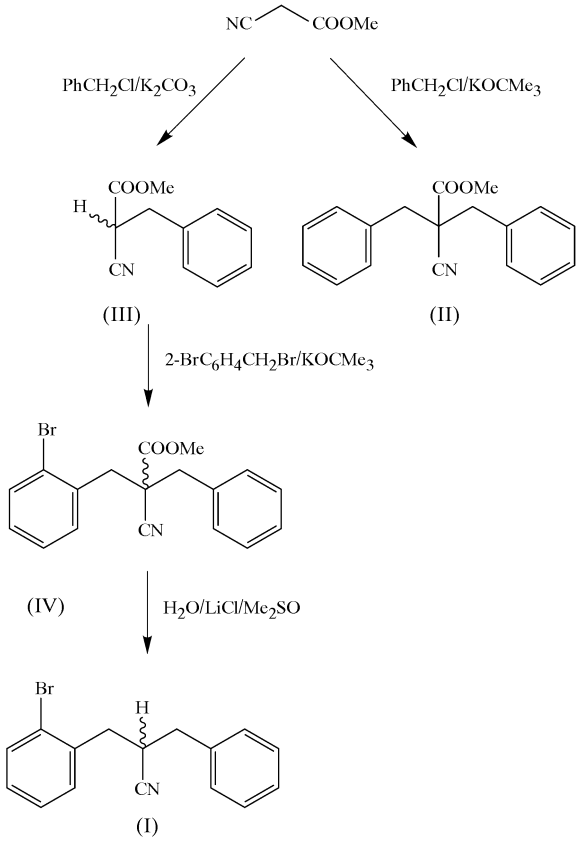
Received 8 August 2006
Accepted 16 August 2006
Online 31 August 2006

The molecules of 2-benzyl-3-(2-bromophenyl)propiononitrile, $C_{16}H_{14}BrN$, are linked into chains by a single C—H···N hydrogen bond. The molecules of methyl 2-benzyl-2-cyano-3-phenylpropionate, $C_{18}H_{17}NO_2$, are linked into sheets by a combination of C—H···O and C—H···π(arene) hydrogen bonds.

Comment

The synthesis of heterocyclic systems containing pyrrolidine fragments is an important goal because of the widespread occurrence of such systems both in biologically active natural products and in therapeutic agents. We present here the molecular and supramolecular structures of two compounds prepared for use as intermediates in the synthesis of pyrrolidines using radical cyclization methodology. 2-Benzyl-3-(2-bromophenyl)propiononitrile, (I), was obtained in three steps (see scheme) through successive alkylation of methyl 2-cyanoacetate with benzyl chloride and potassium carbonate to give the intermediate ester (III), and then with 2-bromobenzyl bromide and potassium *tert*-butoxide to give (IV), followed by controlled hydrolysis and decarboxylation of the resulting cyano ester. By contrast, when potassium *tert*-butoxide was employed as the base in the first alkylation step, this gave a double alkylation leading directly to methyl 2-benzyl-2-cyano-3-phenylpropionate, (II). These two closely related nitriles (Figs. 1 and 2), each containing two benzyl substituents, have supramolecular structures that exhibit different types of hydrogen bonding leading to completely different patterns of supramolecular aggregation.

In (I) (Fig. 1), atom C2 is a stereogenic centre and the molecules are chiral. The compound is racemic, and the centrosymmetric space group $P2_1/n$ accommodates equal numbers of the *R* and *S* enantiomers; the selected reference molecule has *R* configuration. In addition, the skeletal conformation does not exhibit even approximate symmetry, as shown by the leading torsion angles, particularly those around the C1—C17 and C2—C27 bonds (Table 1). By contrast, the conformation adopted by the molecule of (II) (Fig. 2), where there are no stereogenic centres, has approximate mirror symmetry (Table 3), but the modest deviations from exact symmetry are sufficient to render the molecules chiral. The chirality is a consequence only of the conformation in the solid state but, in the absence of inversion twinning, each crystal of (II) contains only a single enantiomer. In both compounds, the C1—C2 bonds are very long, as is characteristic of nitriles (Allen *et al.*, 1987), with short C1—N1 bonds; the remaining bond lengths and angles present no unusual features.



The molecules of (I) are linked into simple chains by means of a single C—H···N hydrogen bond (Table 2). Aryl atom C13 in the molecule at (*x*, *y*, *z*) acts as a hydrogen-bond donor to atom N1 in the molecule at ($\frac{3}{2} - x$, $\frac{1}{2} + y$, $\frac{3}{2} - z$), so forming a *C*(8) (Bernstein *et al.*, 1995) chain running parallel to the [010] direction and generated by the 2_1 screw axis along ($\frac{3}{4}$, *y*, $\frac{3}{4}$) (Fig. 3). Two chains of this type, related to each other by inversion and hence antiparallel, pass through each unit cell, but there are no direction-specific interactions between adjacent chains.

The molecules of (II) are linked by a combination of C—H···O and C—H···π(arene) hydrogen bonds (Table 4) into

 DOI: 10.1107/S0108270106032689

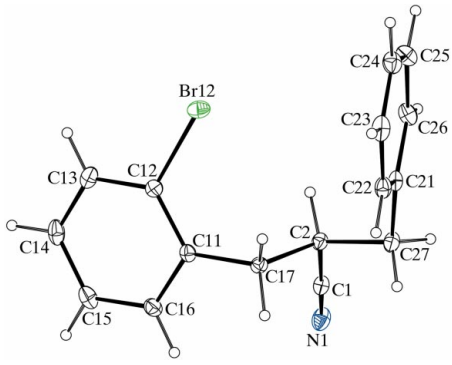


Figure 1
The *R* enantiomer of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

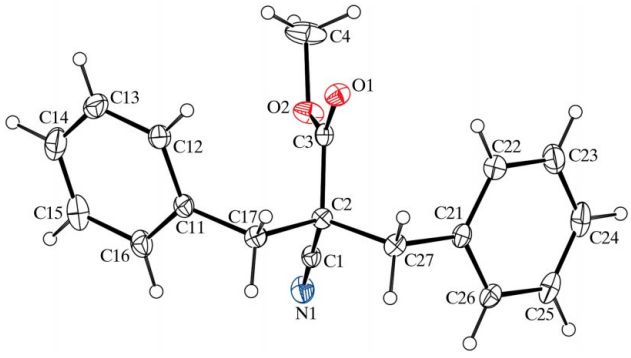


Figure 2
A molecule of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

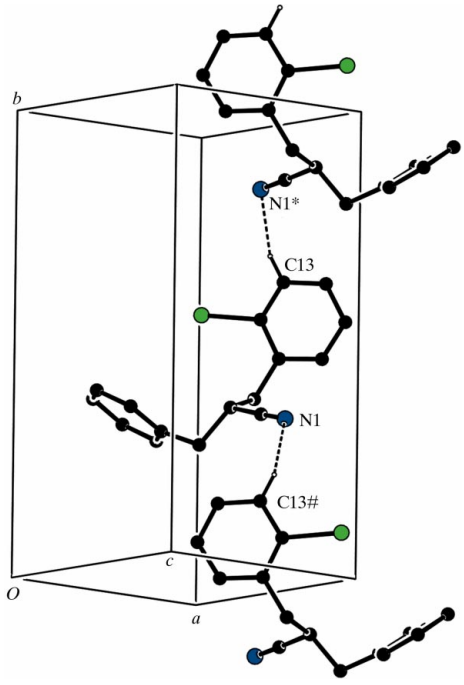


Figure 3
Part of the crystal structure of (I), showing the formation of a $C(8)$ chain along [010] built from C—H···N hydrogen bonds. For the sake of clarity, H atoms not involved in the motif shown have been omitted. Atoms marked with an asterisk (*) or a hash (#) are at the symmetry positions $(\frac{3}{2}-x,\frac{1}{2}+y,\frac{3}{2}-z)$ and $(\frac{3}{2}-x,-\frac{1}{2}+y,\frac{3}{2}-z)$, respectively.

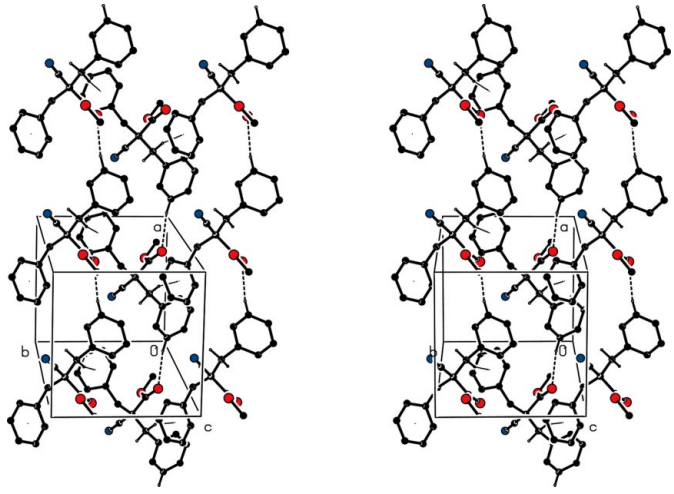


Figure 4
A stereoview of part of the crystal structure of (II), showing the formation of a sheet parallel to (001), formed by the combination of [100] and [010] chains. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

sheets, whose formation is readily analysed in terms of two simple one-dimensional substructures, each involving a single hydrogen bond. In one substructure, aryl atom C25 in the molecule at (x, y, z) acts as a hydrogen-bond donor to carbonyl atom O1 in the molecule at $(-1+x, y, z)$, so generating by translation a $C(8)$ chain running parallel to the [100] direction (Fig. 4). In the second substructure, methylene atom C27 in the molecule at (x, y, z) acts as a hydrogen-bond donor, *via* H27*A*, to the C11–C16 aryl ring of the molecule at $(2-x, -\frac{1}{2}+y, -z+\frac{3}{2})$, so forming a chain running parallel to the [010] direction and generated by the 2_1 screw axis along $(1, y, \frac{3}{4})$ (Fig. 4). The combination of these [100] and [010] chains generates a sheet parallel to (001) (Fig. 4). Two such sheets, generated by the 2_1 screw axes at $z=\frac{1}{4}$ and $z=\frac{3}{4}$, pass through each unit cell, but there are no direction-specific interactions between adjacent sheets. In neither of the structures of (I) and (II) are there any aromatic π–π stacking interactions.

Experimental

For the synthesis of (I), methyl 2-cyanoacetate (0.0128 mol) was added to a hot suspension (bath temperature 313 K) of potassium carbonate (0.048 mol) in tetrahydrofuran (50 ml) and the mixture was stirred for 30 min. Benzyl chloride (0.0245 mol) was then added and the reaction mixture was heated under reflux for 36 h. The mixture was cooled to ambient temperature, quenched by addition of brine and extracted with ethyl acetate (2 × 10 ml). The combined organic extracts were dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (using 6% ethyl acetate in hexane as eluant) to afford methyl 2-cyano-3-phenylpropionate, (III), as a viscous yellow oil (yield 52%). A solution of ester (III) (2.64 mmol) in tetrahydrofuran (3 ml) was added dropwise under argon to a stirred suspension of potassium *tert*-butoxide (2.64 mmol) in anhydrous tetrahydrofuran (36 ml) at 393 K. After stirring for 10 min, 2-bromobenzyl bromide (2.64 mmol) in tetrahydrofuran (3 ml) was

introduced slowly *via* syringe and the mixture was stirred for another 4 h at ambient temperature. The reaction was quenched by addition of brine and the mixture was then extracted with ethyl acetate (2 × 10 ml); the combined organic extracts were dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica (using 5% ethyl acetate in hexane as eluant) to give methyl 2-benzyl-3-(2-bromophenyl)-2-cyanopropionate, (IV), as a white powder (yield 68%, m.p. 365–366 K). A solution of ester (IV) (1.47 mmol) and water (14×10^{-3} ml) in dimethyl sulfoxide (2.0 ml) was added to a heated solution (375 K) of lithium chloride (2.94 mmol) in dry dimethyl sulfoxide (6.0 ml) under argon. This reaction mixture was heated at 405 K for 45 min. After cooling to ambient temperature, the reaction mixture was washed with brine (10 ml) and the organic layer was extracted with *n*-pentane (3 × 10 ml); the combined extracts were dried with magnesium sulfate and the solvent was removed under reduced pressure. The crude solid product was purified by flash chromatography on silica with 10% (*v*/*v*) ethyl acetate/hexane as eluant, affording a white powder, which was recrystallized from a solution of ethyl acetate/hexane to provide colourless crystals of (I) suitable for single-crystal X-ray diffraction (yield 48%, m.p. 351–352 K); MS (*m*/*z*, %): 301/299 (12:11, M^+), 171/169 (18/17, $[CH_2C_6H_4Br]^+$), 91 (100, $[C_7H_7]^+$). For the synthesis of (II), methyl cyanoacetate (1.055 g, 0.01 mol) was added dropwise to a suspension of potassium *tert*-butoxide (1.14 g, 0.01 mol) in anhydrous tetrahydrofuran (130 ml) at room temperature under an argon atmosphere. This mixture was stirred for 15 min, then benzyl chloride (1.287 g, 0.01 mol) was added slowly, followed by stirring for 4 h at ambient temperature. The reaction was then quenched by addition of brine (10 ml) and the mixture was extracted with ethyl acetate (2 × 10 ml); the combined organic extracts were dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The residue was purified by flash chromatography to afford (II) as a white powder; recrystallization from ethyl acetate gave colourless crystals suitable for single-crystal X-ray diffraction (yield 92%, m.p. 354–355 K); MS (*m*/*z*, %): 279 (7, M^+), 188 (20), 156 (6), 91 (100, $[C_7H_7]^+$).

Compound (I)

Crystal data

$C_{16}H_{14}BrN$
M_r = 300.19
Monoclinic, $P2_1/n$
a = 9.7924 (2) Å
b = 14.8921 (2) Å
c = 10.0937 (2) Å
β = 113.392 (2)°
V = 1350.98 (5) Å^3
Z = 4
D_x = 1.476 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 3.02 mm^{-1}
T = 120 (2) K
Plate, colourless
0.20 × 0.15 × 0.08 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.583, T_{max} = 0.794
26393 measured reflections
3077 independent reflections
2554 reflections with $I > 2\sigma(I)$
R_{int} = 0.040
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.062
S = 1.07
3077 reflections
163 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0287P)^2 + 0.3751P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.57 e Å^{-3}

Table 1
Selected geometric parameters (Å, °) for (I).

N1—C1	1.146 (2)	C1—C2	1.472 (2)
C27—C2—C17—C11	170.00 (14)	C17—C2—C27—C21	−74.01 (19)
C2—C17—C11—C12	−81.6 (2)	C2—C27—C21—C22	99.62 (19)

Table 2
Hydrogen-bond geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
C13—H13···N1^{i}	0.95	2.58	3.294 (3)	132

Symmetry code: (i) $-x+\frac{3}{2}, y+\frac{1}{2}, -z+\frac{3}{2}$.

Compound (II)

Crystal data

$C_{18}H_{17}NO_2$
M_r = 279.33
Orthorhombic, $P2_12_12_1$
a = 9.2000 (3) Å
b = 9.3280 (2) Å
c = 18.3031 (5) Å
V = 1570.73 (7) Å^3
Z = 4
D_x = 1.181 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 120 (2) K
Block, colourless
0.70 × 0.45 × 0.32 mm

Data collection

Bruker–Nonius KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
T_{min} = 0.938, T_{max} = 0.976
13755 measured reflections
2053 independent reflections
1845 reflections with $I > 2\sigma(I)$
R_{int} = 0.031
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.076
S = 1.14
2053 reflections
192 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0366P)^2 + 0.1369P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.17 e Å^{-3}
$\Delta\rho_{min}$ = −0.13 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.036 (4)

Table 3
Selected geometric parameters (Å, °) for (II).

N1—C1	1.1428 (18)	C1—C2	1.4773 (19)
C27—C2—C17—C11	174.44 (12)	C17—C2—C27—C21	175.07 (12)
C2—C17—C11—C12	−92.52 (16)	C2—C27—C21—C22	77.05 (17)
C1—C2—C3—O2	6.48 (17)	C2—C3—O2—C4	176.60 (14)

Table 4
Hydrogen-bond geometry (Å, °) for (II).

Cg is the centroid of the C11–C16 ring.

D—H···A	D—H	H···A	D···A	D—H···A
C25—H25···O1^{i}	0.95	2.53	3.467 (2)	169
C27—H27A···Cg^{ii}	0.99	2.77	3.6799 (15)	153

Symmetry codes: (i) $x-1, y, z$; (ii) $-x+2, y-\frac{1}{2}, -z+\frac{3}{2}$.

For compounds (I) and (II), the space groups $P2_1/n$ and $P2_12_12_1$, respectively, were uniquely assigned from the systematic absences. All H atoms were located in difference maps and then treated as riding atoms, with C—H distances of 0.95 (aromatic), 0.98 (CH_3), 0.99 (CH_2) or 1.00 Å (aliphatic CH), and with $U_{iso}(H) = kU_{eq}(C)$, where $k = 1.5$ for the methyl group and 1.2 for all other H atoms. In the absence of significant resonant scattering, the absolute configuration of the molecules of (II) in the crystal selected for data collection could not be established, but this configuration has no chemical significance; accordingly, the Friedel-equivalent reflections were merged prior to the final refinements.

For both compounds, data collection: *COLLECT* (Hooft, 1999); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *OSCAIL* (McArdle, 2003) and *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97* and *PRPKAPPA* (Ferguson, 1999).

X-ray data were collected at the EPSRC National Crystallography Service, University of Southampton, England. The authors thank the staff for all their help and advice. JC and JMT thank the Consejería de Innovación, Ciencia y Empresa (Junta de Andalucía, Spain) and the Universidad de Jaén for financial support; JMT also thanks the Universidad de Jaén for a scholarship grant supporting a short stay at the EPSRC National Crystallography Service. GC and LMJG thank COLCIENCIAS, UNIVALLE (Universidad del Valle, Colombia), for financial support.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG3038). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–19.
Bernstein, J., Davis, R. E., Shimoni, L. & Chang, N.-L. (1995). *Angew. Chem. Int. Ed. Engl.* **34**, 1555–1573.
Burla, M. C., Caliandro, R., Camalli, M., Carrozzini, B., Cascarano, G. L., De Caro, L., Giacovazzo, C., Polidori, G. & Spagna, R. (2005). *J. Appl. Cryst.* **38**, 381–388.
Ferguson, G. (1999). *PRPKAPPA*. University of Guelph, Canada.
Hooft, R. W. W. (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
McArdle, P. (2003). *OSCAIL for Windows*. Version 10. Crystallography Centre, Chemistry Department, NUI Galway, Ireland.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
Sheldrick, G. M. (2003). *SADABS*. Version 2.10. University of Göttingen, Germany.
Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.