

Songwen Xie,<sup>a</sup> Cal Y. Meyers<sup>a</sup>  
and Paul D. Robinson<sup>b\*</sup><sup>a</sup>Meyers Institute for Interdisciplinary Research in Organic and Medicinal Chemistry and the Department of Chemistry and Biochemistry, Southern Illinois University-4409, Carbondale, IL 62901, USA, and <sup>b</sup>Department of Geology, Southern Illinois University-4324, Carbondale, IL 62901, USA

Correspondence e-mail: robinson@geo.siu.edu

## Key indicators

Single-crystal X-ray study  
T = 155 K  
Mean  $\sigma(\text{C}-\text{C}) = 0.004 \text{ \AA}$   
Disorder in main residue  
R factor = 0.073  
wR factor = 0.232  
Data-to-parameter ratio = 15.1For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.***N,N'*-Dicyclohexyl-*N*-[(1*RS*,2*RS*,6*SR*)-4-(4-methoxyphenyl)-2,6-dimethyl-3-cyclohexene-1-carbonyl]urea: an unusual crystalline enantiomeric pairing**

The synthesis of (1*SR*,2*SR*,5*RS*,6*RS*)-5-ethyl-4-(4-methoxyphenyl)-2,6-dimethyl-3-cyclohexenecarboxylic acid was accompanied by the formation of a by-product shown to differ only by the absence of the 5-ethyl group. That mixture was subjected to an enantiomer resolution process utilizing (–)-menthol and dicyclohexylcarbodiimide (DCC), and the expected diastereomers of both compounds were formed along with their anhydrides and an unexpected, but related, compound in both cases. The unexpected compound formed from the substrate lacking the 5-ethyl group was unequivocally identified by X-ray analysis as the title compound, C<sub>29</sub>H<sub>42</sub>N<sub>2</sub>O<sub>3</sub>, (I), a result that, together with the NMR spectra, similarly identified the corresponding product from the compound possessing the 5-ethyl substituent. The two enantiomers of (I) appear to be disordered and superimposed in the asymmetric unit, differing only in the position of the double bond, a rare phenomenon made possible by the unusual stereochemistry of (I).

## Comment

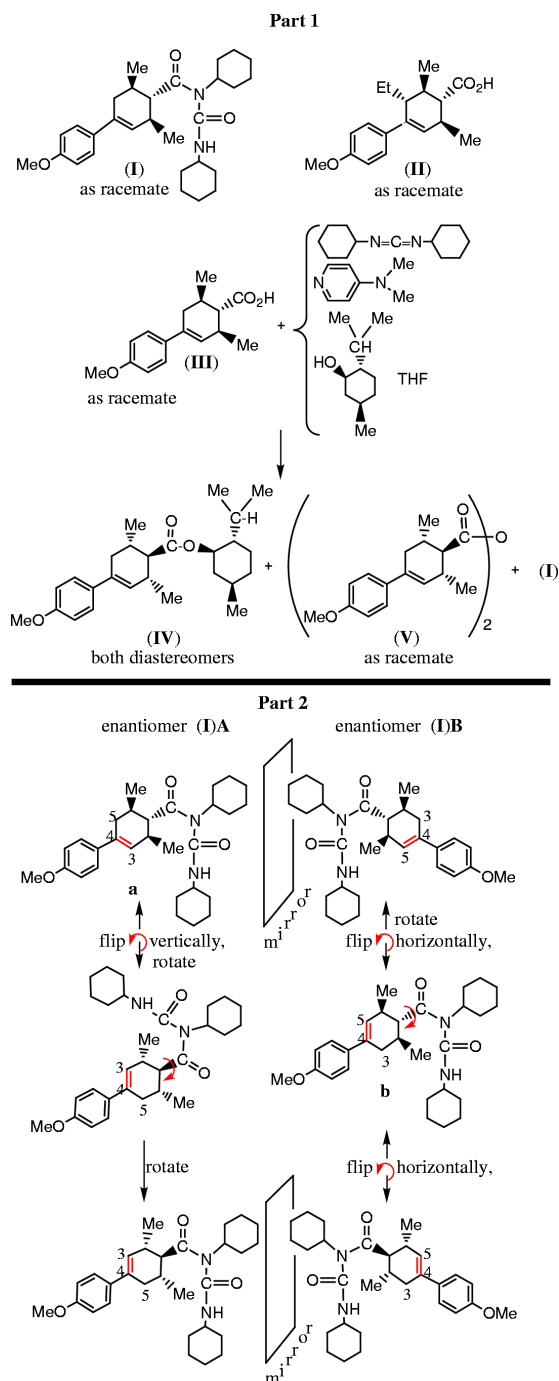
Crenshaw *et al.* (1974) reported the preparation of racemic 5-ethyl-4-(4-methoxyphenyl)-2,6-dimethyl-3-cyclohexenecarboxylic acid, but they did not determine its diastereomeric structure although, with four distinct asymmetric centers, eight different diastereomers were possible. Carrying out this synthesis exactly as it was reported, we isolated and unequivocally determined the diastereomeric structure of this product by X-ray analysis as (1*SR*,2*SR*,5*RS*,6*RS*)-5-ethyl-4-(4-methoxyphenyl)-2,6-dimethyl-3-cyclohexenecarboxylic acid, (II) (Xie *et al.*, 2002). In one of our enantiomer resolution attempts of this racemate with (–)-menthol and dicyclohexylcarbodiimide (DCC), we used impure (II) and found that it contained a small amount of a related product, (III), lacking only the 5-ethyl group of (II), that was co-formed during the synthesis. This resolution reaction provided the (–)-menthyl ester diastereomers (IV) of (III) and the corresponding diastereomers of (II), along with the unexpected anhydride (V) of (III) and the corresponding anhydride of (II) identified by NMR, and another unexpected product unequivocally characterized by X-ray analysis as racemic *N,N'*-dicyclohexyl-*N*-[(1*RS*,2*RS*,6*SR*)-4-(4-methoxyphenyl)-2,6-dimethyl-3-cyclohexene-1-carbonyl]urea, (I). The reaction sequence is illustrated in Part 1 of the scheme and the crystal structure with the atom numbering of (I) is shown in Fig. 1. From this X-ray characterization and NMR spectra of (I) and the similar NMR spectra of the corresponding unexpected product formed during the enantiomer resolution of (II), we determined that the unexpected compound formed in the resolution reaction of (II) was its racemic carbonylurea

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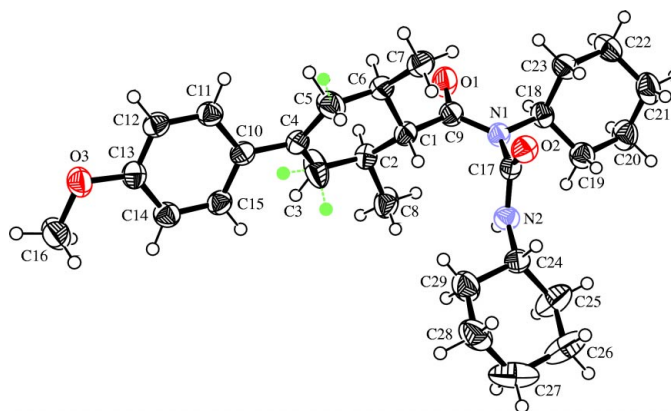
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derivative similar to (I). In a related reaction of a carboxylic acid with a non-optically active alcohol in the presence of DCC, Boden & Keck (1985) likewise reported the formation of a carbonylurea similar to (I).



The structure of (I) was initially solved and refined using a room-temperature data set, which resulted in quite large thermal displacement parameters for several atoms. The structure was then refined using a low-temperature (173 K) data set (results reported in this study) which significantly attenuated the unruly displacements, although they are still in evidence. The cyclohexene ring exhibits a shorter than normal



**Figure 1**

The molecular structure and atom-numbering scheme for (I), with displacement ellipsoids at the 50% probability level. The drawing shows two disordered enantiomers which completely overlap, with the exception of the three H atoms shown in green. These atoms were not included in the model.

C4—C5 distance (Table 1) and atoms C3 and C5 have somewhat higher than expected displacement parameters, indicating possible minor disorder in that portion of the ring. These combined observations and Fig. 1 suggest a superimposition of the two disordered enantiomers, one having the double bond at C3—C4 and the other at C4—C5. That such is quite likely the case is illustrated in Part 2 of the scheme, showing that enantiomers (I)A and (I)B differ only in the position of the double bond, *viz.* C3=C4 in A (see *a*) and C4=C5 in B (see *b*) (the atom numbering in A is retained). This result was presented at the 15th Midwest Organic Solid State Symposium (Xie *et al.*, 2004). Two enantiomers differing only in the position of their double bond is extremely rare. Although either enantiomer can be present in the asymmetric unit, the labeled enantiomer shown in Fig. 1 is the major one present. This view is supported by the fact that the allylic H atoms on C5 and the vinyl H atom on C3 can be clearly seen in a difference Fourier map while no evidence for the reverse situation could be found. Also the C3—C4 bond distance is significantly shorter than that of C4—C5 (Table 1). Thus, in the refinement, the H atoms in question were assigned full occupancy for enantiomer A and were ignored for enantiomer B [although their theoretical positions are shown in Fig. 1 (in green)]. *PLATON* (Spek, 2003) reports a possible hydrogen bond involving N2—H2a...O2( $\frac{1}{2} - x, y - \frac{1}{2}, \frac{1}{2} - z$ ); that possibility is remote, the donor–acceptor distance being excessive [3.401 (2) Å].

## Experimental

A solution of racemic (1*SR*,2*SR*,6*RS*)-4-(4-methoxyphenyl)-2,6-dimethyl-3-cyclohexenecarboxylic acid, (III) [0.500 g, approximately 1.73 mmol, containing (II) (Xie *et al.*, 2002)], (–)-menthol (0.697 g, 4.46 mmol), DCC (0.753 g, 3.65 mmol), and 4-dimethylaminopyridine (0.218 g, 1.78 mmol) in 20 ml of freshly distilled tetrahydrofuran was flushed with argon and stirred at room temperature. The solution became turbid in 2 h. After 26 h, the stirring was stopped, and the resulting white precipitate was removed by filtration. The filtrate was

evaporated, leaving a light-yellow oil, to which  $\text{CH}_2\text{Cl}_2$  was added. The white solid which formed was removed by filtration. The filtrate was again diluted with  $\text{CH}_2\text{Cl}_2$  and the resulting white solid was removed. This process was repeated until no more white solid was formed. The residual  $\text{CH}_2\text{Cl}_2$  solution was washed with 0.5 N HCl, followed by saturated aqueous  $\text{NaHCO}_3$  and water, dried and evaporated. The resultant mixture was fractionally eluted by column chromatography with 60:1 to 10:1 hexane–ethyl acetate, providing four fractions. The first contained the (–)-menthyl esters of carboxylic acids (II) and (III), the second contained both anhydrides, and the third was the carbonylurea derivative (prepared from DCC) of (II), identified by NMR. The last fraction was evaporated to a solid which was recrystallized from 2,2,4-trimethylpentane–ethanol; white crystals (m.p. 534–535 K). The melt crystallized immediately when cooled below the melting point, and the crystalline mass exhibited the identical m.p. as the original crystals.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.06 (*d*, *J* = 6.6 Hz, 3H), 1.20 (*m*, 5H), 1.32–1.51 (*m*, 6H), 1.62 (*s*, 3H), 1.63–1.83 (*m*, 6H), 1.91–2.19 (*m*, 6H), 2.50 (*d*, *J* = 10.8 Hz, 1 H), 2.78 (*m*, 1H), 3.70 (*m*, 1H), 3.81 (*s*, 3H), 4.32 (*t*, *J* = 10.8 Hz, 1H), 5.20 (*d*, *J* = 8.1 Hz, 1H), 5.81 (*s*, 1H), 6.85 (*d*, *J* = 8.7 Hz, 2H), 7.33 (*d*, *J* = 8.7 Hz, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  19.8, 20.5, 22.1, 24.7 (2C), 25.3, 25.4, 25.9 (2C), 31.3 (2C), 32.79, 32.9 (2C), 35.9, 36.2, 50.4, 53.4, 55.3, 113.6 (2C), 126.0 (2C), 127.9, 134.2, 153.6, 154.7, 220.9, 221.0. These crystals were used in this X-ray study which unequivocally identified them as the racemic carbonylurea derivative (I) of carboxylic acid (II).

Crystal data

$\text{C}_{29}\text{H}_{42}\text{N}_2\text{O}_3$	$D_x = 1.168 \text{ Mg m}^{-3}$
$M_r = 466.65$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 9091 reflections
$a = 15.0059 (3) \text{ \AA}$	$\theta = 2.3\text{--}29.2^\circ$
$b = 10.4719 (2) \text{ \AA}$	$\mu = 0.08 \text{ mm}^{-1}$
$c = 16.9266 (3) \text{ \AA}$	$T = 155 (2) \text{ K}$
$\beta = 93.547 (1)^\circ$	Prism, colorless
$V = 2654.76 (9) \text{ \AA}^3$	$0.50 \times 0.35 \times 0.19 \text{ mm}$
$Z = 4$	

Data collection

Bruker SMART CCD area-detector diffractometer	3507 reflections with $I > 2\sigma(I)$
$\phi$ and $\omega$ scans	$R_{\text{int}} = 0.031$
Absorption correction: none	$\theta_{\text{max}} = 25.0^\circ$
17643 measured reflections	$h = -17 \rightarrow 17$
4675 independent reflections	$k = -12 \rightarrow 12$
	$l = -20 \rightarrow 20$

Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.1585P)^2 + 0.2847P]$
$R[F^2 > 2\sigma(F^2)] = 0.073$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.232$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.10$	$\Delta\rho_{\text{max}} = 0.47 \text{ e \AA}^{-3}$
4675 reflections	$\Delta\rho_{\text{min}} = -0.32 \text{ e \AA}^{-3}$
310 parameters	
H-atom parameters constrained	

Table 1

Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ ).

C1–C2	1.535 (3)	C5–C6	1.504 (3)
C2–C3	1.495 (3)	C1–C6	1.542 (3)
C3–C4	1.386 (3)	C2–C8	1.521 (3)
C4–C5	1.415 (3)	C6–C7	1.520 (3)
C1–C2–C3	111.22 (19)	C6–C1–C2	110.71 (17)
C2–C3–C4	123.3 (2)	C5–C6–C7	111.0 (2)
C3–C4–C5	119.2 (2)	C1–C6–C7	112.18 (18)
C4–C5–C6	121.2 (2)	C3–C2–C8	110.7 (2)
C5–C6–C1	110.46 (18)	C1–C2–C8	112.11 (18)

The rotational orientations of the methyl groups were refined by the circular Fourier method available in *SHELXL97* (Sheldrick, 1997). All H atoms were treated as riding, with C–H and N–H distances ranging from 0.88 to 1.00  $\text{\AA}$  and  $U_{\text{iso}}(\text{H})$  values equal to 1.5 (methyl H atoms) or 1.2 (all other H atoms) times  $U_{\text{eq}}$  of the parent atom.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINTE* (Bruker, 2001); data reduction: *SAINTE*; program(s) used to solve structure: *SIR92* (Burla *et al.*, 1989); program(s) used to refine structure: *LS* in *TEXSAN* (Molecular Structure Corporation, 1997) and *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *TEXSAN*, *SHELXL97* and *PLATON* (Spek, 2003).

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