Data collection

Enraf–Nonius CAD-4 single-crystal diffractometer	$\theta_{max} = 70°$
ω/θ scans	$h = 0 \rightarrow 16$
Absorption correction: none	$k = 0 \rightarrow 16$
2928 measured reflections	$l = 0 \rightarrow 18$
2928 independent reflections	1 standard reflection frequency: 120 min
2647 reflections with $I > 3\sigma(I)$	intensity decay: 1%

Refinement

Refinement on F	$(\Delta/\sigma)_{max} = 0.03$
$R = 0.046$	$\Delta\rho_{max} = 0.29$ e Å^{-3}
$wR = 0.063$	$\Delta\rho_{min} = 0.22$ e Å^{-3}
$S = 1.870$	Extinction correction: none
2647 reflections	Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)
307 parameters	
H atoms not refined	
$w = 4F_o^2/[\sigma^2(F_o^2) + (0.04F_o^2)^2]$	

Table 1. *Selected geometric parameters (Å, °)*

N1—C1*A*	1.412 (4)	O3′—C3′	1.240 (3)
N2—C1′	1.345 (4)	O4′—C4′	1.197 (5)
N2—C2*A*	1.453 (3)	C1′—C1*A*	1.504 (4)
N3—C2′	1.342 (3)	C2′—C2*A*	1.522 (4)
N3—C3*A*	1.427 (3)	C3′—C3*A*	1.498 (4)
N4—C3′	1.334 (3)	C4′—C4*A*	1.515 (4)
N4—C4*A*	1.450 (4)	C1*A*—C1*B*	1.334 (4)
O1′—C1′	1.234 (3)	C3*A*—C3*B*	1.331 (4)
O2′—C2′	1.227 (3)		
C1′—N2—C2*A*	120.2 (2)	N2—C2*A*—C2′	112.4 (2)
C2′—N3—C3*A*	118.9 (2)	N2—C2*A*—C2*B*	109.7 (2)
C3′—N4—C4*A*	122.1 (2)	N3—C3*A*—C3′	115.5 (2)
N2—C1′—C1*A*	116.1 (2)	N3—C3*A*—C3*B*	124.9 (2)
O1′—C1′—C1*A*	121.6 (3)	N4—C4*A*—C4′	113.1 (3)
O2′—C2′—C2*A*	119.2 (2)	N4—C4*A*—C4*B*	107.9 (2)
N4—C3′—C3*A*	116.5 (2)	C1*A*—C1*B*—C1*C*	128.6 (3)
O3′—C3′—C3*A*	121.8 (2)	C3*A*—C3*B*—C3*C*	132.2 (2)
N1—C1*A*—C1′	117.3 (2)	C1*B*—C1*C*—C1*D*	117.8 (3)
N1—C1*A*—C1*B*	124.0 (3)	C3*B*—C3*C*—C3*D*	125.2 (3)
C2—N1—C1*A*—C1′	−49.2 (4)	C4*A*—N4—C3′—C3*A*	179.4 (2)
C1′—N2—C2*A*—C2′	−60.8 (3)	N2—C1′—C1*A*—N1	−28.0 (3)
C2′—N3—C3*A*—C3′	−56.5 (3)	O1′—C1′—C1*A*—C1*B*	−34.2 (4)
C3′—N4—C4*A*—C4′	48.0 (3)	N3—C2′—C2*A*—N2	−24.1 (4)
C2*A*—N2—C1′—C1*A*	179.5 (2)	N4—C3′—C3*A*—N3	−30.6 (3)
C3*A*—N3—C2′—C2*A*	173.9 (2)	O2—C4′—C4*A*—N4	40.0 (4)

Table 2. *Hydrogen-bonding geometry (Å, °)*

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—HN1···O2′^{i}	0.96	1.950 (2)	2.867 (3)	160.1 (1)
N2—HN2···O3′^{i}	0.92	1.986 (2)	2.856 (3)	156.7 (1)
N3—HN3···O1	0.86	2.087 (2)	2.932 (3)	169.1 (2)
N4—HN4···O1′	0.97	1.976 (2)	2.949 (3)	175.7 (1)

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

H atoms attached to C atoms were placed at idealized positions, while those bonded to N atoms were located from difference Fourier maps. During refinement, all H atoms were allowed to ride with isotropic displacement parameters set at U_{eq} of the carrier atom.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989). Cell refinement: *SDP* (Enraf–Nonius, 1985). Data reduction: *SDP*. Program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1993) (direct methods). Program(s) used to refine structure: *SDP*. Molecular graphics: *ORTEP*II (Johnson, 1976) and *PLUTO* (Motherwell & Clegg, 1978).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SX1026). Services for accessing these data are described at the back of the journal.

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Diastereoselectivity in the Transannular Diels–Alder Reaction of a *trans-trans-trans* 14-Membered Macrocycle Leading to Steroids

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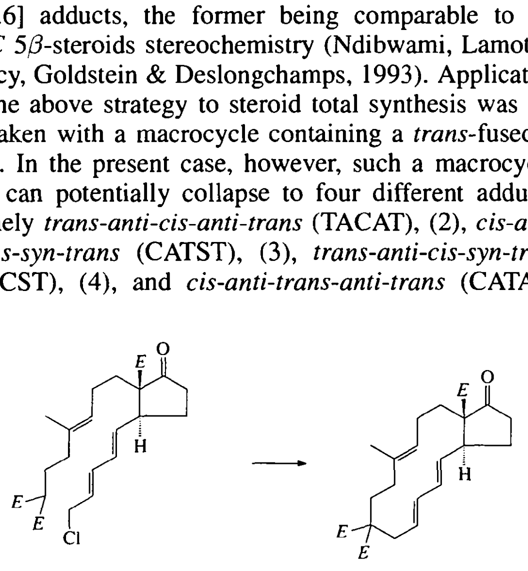
Abstract

A novel 14-membered macrocyclic ring with *trans-trans-trans* triene geometry, trimethyl (4*E*,10*E*,12*E*)-(1*R**,14*S**)-5-methyl-17-oxobicyclo[12.3.0]heptadeca-

4,10,12-triene-1,8,8-tricarboxylate, $C_{24}H_{32}O_7$, which usually undergoes a Diels–Alder cycloaddition upon formation, has been isolated. From four possible contractions, the transannular reaction produces three adducts from which trimethyl *rac*-(5β,9β,10α)-17-oxoandrost-6-ene-3,3,18-tricarboxylate, $C_{24}H_{32}O_7$, was isolated and crystallized.

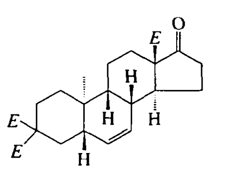
Comment

In the course of our general study on the transannular Diels–Alder (TADA) reaction involving 14-membered macrocyclic trienes (Deslongchamps, 1992), we demonstrated that the *trans-trans-trans* (TTT) geometry leads to the *cis-anti-trans* (CAT) and *trans-anti-cis* (TAC) [6.6.6] adducts, the former being comparable to the *ABC* 5β-steroids stereochemistry (Ndibwami, Lamothe, Soucy, Goldstein & Deslongchamps, 1993). Application of the above strategy to steroid total synthesis was undertaken with a macrocycle containing a *trans*-fused *D* ring. In the present case, however, such a macrocycle, (1), can potentially collapse to four different adducts, namely *trans-anti-cis-anti-trans* (TACAT), (2), *cis-anti-trans-syn-trans* (CATST), (3), *trans-anti-cis-syn-trans* (TACST), (4), and *cis-anti-trans-anti-trans* (CATAT), (5).

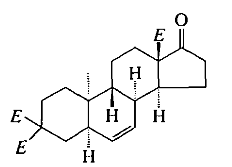


(1′) (1)

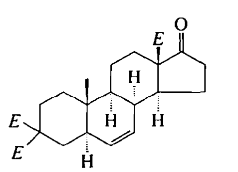
$E = CO_2CH_3$



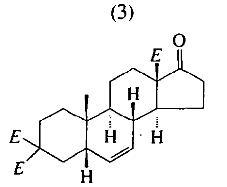
(2)



(3)



(4)



(5)

Since the ratio of final products in the TADA reaction is governed by the energy gap between the corresponding transition-state structures with the incipient *B* ring in a boat conformation (Lamothe, Ndibwami & Deslongchamps, 1988*a*,*b*), we used *AM*1 semi-empirical molecular modelling to predict the stereochemical outcome. Forecasting the CATAT stereoisomer, (5), as the major adduct, the *in situ* generation of macrocycle (1) from allylic chloride (1′) was performed which directly lead to a mixture of three adducts in a 4:1:1 ratio. The major isomer was isolated by crystallization and an X-ray diffraction analysis was undertaken in order to establish unequivocally its relative stereochemistry: it turned out to be the TACAT stereoisomer, (2). This unexpected result prompted us to investigate further with more reliable *ab initio* transition-state modelling and these calculations now corroborate the observed diastereoselectivity (Couturier, Dory, Rouillard, Fortin & Deslongchamps, 1997). During the macrocyclization process in the TTT 14-membered series, the macrocycles are generally not isolated since the ensuing TADA reaction occurs at the reaction temperature of 353 K. However, by deliberately halting the reaction before completion, we were able to isolate, albeit in minute quantities, the intermediate carbocycle (1), which was crystallized, and we were at last able to determine the macrocycle's conformation in this series.

In compound (1), the methyl ester located at the ring junction shows disorder. Successive ΔF maps result in three different orientations. The occupancy refinement converged at values of 0.48 (2) for C23, C24, O5 and O6, 0.23 (2) for C23*A*, C24*A*, O5*A* and O6*A*, and 0.29 (2) for C23*B*, C24*B*, O5*B* and O6*B*. The torsion angle values for C14—C13—C23—O5, C14—C13—C23*A*—O5*A* and C14—C13—C23*B*—O5*B* indicate the differences in their orientations [−62.5 (15), 11 (2) and −31 (2)°, respectively]. The ester is oriented such that O5 or O5*B* could act as an acceptor for C—H···O intramolecular hydrogen bonding. The O···H distances and C—H···O angle values are 2.24 Å and 122.8° for C11—H11*A*···O5, and 2.29 Å and 112.7° for C8—H8···O5*B*, the two most populated conformations. These distances and angles are in good agreement

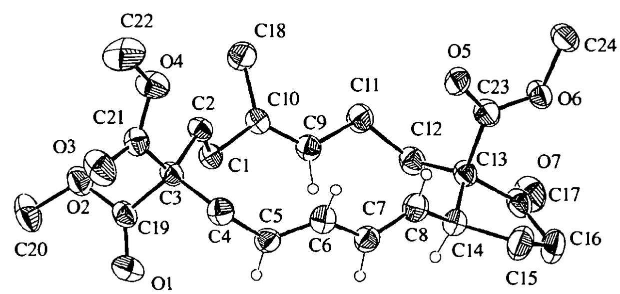


Fig. 1. *ORTEP* (Johnson, 1995) perspective view showing the labelling for compound (1). Displacement ellipsoids are shown at the 30% probability level; H atoms have been omitted for clarity except for those on sp^2-C atoms and those on ring junctions which are drawn as small circles of arbitrary radii. Only one orientation for the disordered methyl ester groups is retained.

with those described by Desiraju, Kashino, Coombs & Glusker (1993). The diene shows a partially broken conjugated system. Indeed, the torsion angle value for C5—C6—C7—C8 is −160.9 (3)°, which is a good indication of the strain in the macrocycle.

Compound (2) crystallizes with two molecules per asymmetric unit. Both skeletons have the same configuration as well as similar global conformations. This chiral crystal structure arises from spontaneous resolution of a racemic mixture. Its absolute configuration has not been determined. One of the two molecules, (2′), shows disorder in rings *A* and *D*. The occupancy refinement converged at 0.553 (7):0.447(7) for C1′–C4′ and C1*B*–C4*B*, and 0.58 (3):0.42(3) for C15′,C16′ and C15*B*,C16*B*. The most important deviations are for the five-membered ring *D*. Indeed, the torsion angles C15—C16—C17—C13 and C12—C13—C17—C16 have values 6.8 (4) and −149.6 (4)°, respectively, in (2), C15′—C16′—C17′—C13′ and C12′—C13′—C17′—C16′ are −16.2 (10) and −135.9 (7)°, respectively, in (2′), and C15*B*—C16*B*—C17′—C13′ and C12′—C13′—C17′—C16*B* are 36.3 (15) and −157.9 (7), respectively, in (2′*B*). The three methyl esters in this molecule are also disordered. In the crystal packing, the molecules form two different layers. The disorder is apparently caused by an intermolecular close contact between C22′ and C20*B* [2.580 (16) Å]. To avoid this contact, molecule (2′) adopts the two conformations observed. All bonds and angles have normal values.

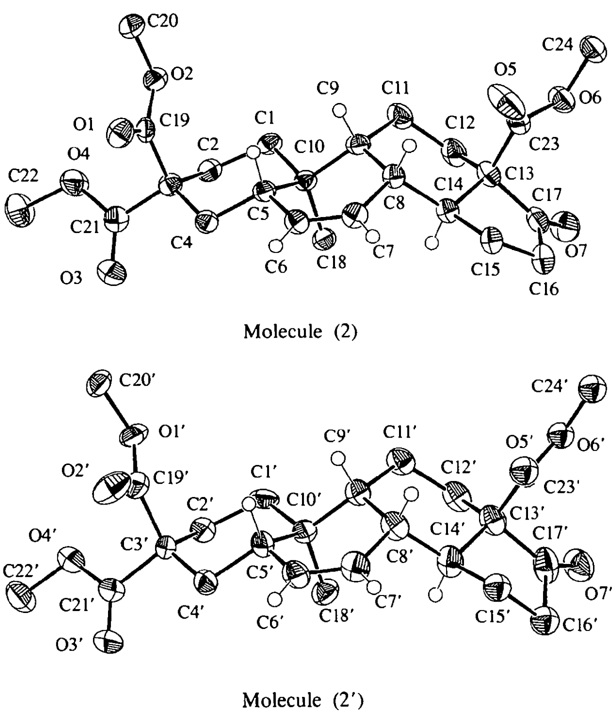


Fig. 2. *ORTEP* (Johnson, 1995) perspective view showing the labelling for molecules (2) and (2′). Displacement ellipsoids are shown at the 30% probability level; H atoms have been omitted for clarity except for those on sp^2-C atoms and those on ring junctions which are drawn as small circles of arbitrary radii. Only one orientation for the disordered methyl ester groups is retained for (2′).

Experimental

Details of the synthesis will be published elsewhere (Couturier, 1997; Couturier, Dory, Rouillard, Fortin & Deslongchamps, 1997).

Compound (1)

Crystal data

$C_{24}H_{32}O_7$
$M_r = 432.51$
Monoclinic
$A2/a$
$a = 23.756$ (2) Å
$b = 6.9151$ (5) Å
$c = 28.381$ (2) Å
$\beta = 95.457$ (6)°
$V = 4641.1$ (6) Å^3
$Z = 8$
$D_x = 1.238$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 24 reflections
$\theta = 20$–25°
$\mu = 0.742$ mm^{-1}
$T = 293$ K
Rectangular
0.20 × 0.15 × 0.05 mm
Colourless

Data collection

Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: none
4819 measured reflections
4279 independent reflections
2600 reflections with $I > 2\sigma(I)$

$R_{int} = 0.023$
$\theta_{max} = 69.85°$
$h = -28 \rightarrow 28$
$k = 0 \rightarrow 7$
$l = 0 \rightarrow 34$
2 standard reflections every 60 reflections intensity decay: none

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.060$
$wR(F^2) = 0.176$
$S = 1.071$
4279 reflections
356 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.0797P)^2 + 0.0298P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = -0.001$
$\Delta\rho_{max} = 0.267$ e Å^{-3}
$\Delta\rho_{min} = -0.243$ e Å^{-3}
Extinction correction: *SHELXL*93
Extinction coefficient: 0.00016 (6)
Scattering factors from *International Tables for Crystallography* (Vol. C)

Compound (2)

Crystal data

$C_{24}H_{32}O_7$
$M_r = 432.50$
Monoclinic
$P2_1$
$a = 7.278$ (4) Å
$b = 12.199$ (2) Å
$c = 24.494$ (7) Å
$\beta = 91.89$ (3)°
$V = 2173.6$ (13) Å^3
$Z = 4$
$D_x = 1.322$ Mg m^{-3}
D_m not measured

Cu $K\alpha$ radiation
$\lambda = 1.54184$ Å
Cell parameters from 24 reflections
$\theta = 20$–25°
$\mu = 0.793$ mm^{-1}
$T = 293$ (2) K
Colourless
0.35 × 0.20 × 0.10 mm
Rectangular

Data collection

Nonius CAD-4 diffractometer	$\theta_{max} = 71.74°$
$\theta/2\theta$ scans	$h = -6 \rightarrow 8$
Absorption correction: none	$k = 0 \rightarrow 14$
4211 measured reflections	$l = 0 \rightarrow 30$
4211 independent reflections	2 standard reflections
4010 reflections with $I > 2\sigma(I)$	frequency: 60 min
	intensity decay: none

Refinement

Refinement on F^2	$\Delta\rho_{max} = 0.323$ e Å^{-3}
$R[F^2 > 2\sigma(F^2)] = 0.060$	$\Delta\rho_{min} = -0.250$ e Å^{-3}
$wR(F^2) = 0.179$	Extinction correction: *SHELXL*93
$S = 1.062$	Extinction coefficient: 0.0014 (4)
4211 reflections	Scattering factors from *International Tables for Crystallography* (Vol. C)
665 parameters	Absolute configuration: Flack (1983)
H atoms riding	Flack parameter = −0.2 (3)
$w = 1/[\sigma^2(F_o^2) + (0.1137P)^2 + 1.7798P]$ where $P = (F_o^2 + 2F_c^2)/3$	
$(\Delta/\sigma)_{max} = -0.013$	

The disordered atoms in (1) were refined using the *SAME*, *SADI* and *SIMU* restraints in *SHELXL*93 (Sheldrick, 1993); the disorded atoms in (2′) were refined using *SAME* and *SADI* restraints. The C15′, C15*B*, C16′, C16*B* and methyl ester disordered atoms at C13 were kept isotropic to avoid unrealistic displacement parameters.

For both compounds, data collection: *NRCCAD DATCOL* (Le Page, White & Gabe, 1986); cell refinement: *NRCCAD TRUANG*; data reduction: *NRCVAX DATRD*2 (Gabe, Le Page, Charland, Lee & White, 1989); program(s) used to solve structures: *NRCVAX SOLVER*; program(s) used to refine structures: *SHELXL*93 (Sheldrick, 1993); molecular graphics: *ORTEP* in *Xtal_GX* (Johnson, 1995); software used to prepare material for publication: *SHELXL*93 *ACTA*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1287). Services for accessing these data are described at the back of the journal.

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Dimethyl *N*,*N*′-Bis(*endo*-himmoyl)-(*R*,*R*)-cystine†

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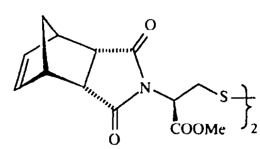
Abstract

The title compound, $C_{26}H_{28}N_2O_8S_2$, contains two norbornene rings, both with *endo* substituents, and an (*M*)-helical disulfide. Both ester groups adopt the *s-cis* conformation, and the bond lengths and angles are within the expected values.

Comment

As part of an ongoing study concerned with the synthesis of biomimetic polymers derived from amino acids (Coles *et al.*, 1994; Biagini *et al.*, 1995), the synthesis of the title compound, (I), was undertaken (Biagini *et al.*, 1995). It was envisaged that polymerization or copolymerization of (I) by a ring-opening metathesis procedure would lead to synthetic polymers in which the cystine units mimic the crosslinking role of cystine residues in proteins. An X-ray structure determination of (I) was undertaken to allow its conformation to be compared with those of other cystine derivatives.



(I)

This study confirmed the structure (Fig. 1) and relative stereochemistry of (I). The imide substituents on both norbornene rings adopt the *endo* configuration, and the two chiral centres (C10 and C10′) have the same

† Alternative systematic name: dimethyl 2,7-bis(1,3-dioxo-1,3,3a,4,7,7a-hexahydro-4,7-methano-2-isoindolyl)-4,5-dithiaoctanedioate.