

## Functionalized Hydrocarbons with Condensed Ring Skeletons. VIII. A Dimethyl-Substituted Tricyclo[8.4.0.0<sup>2,7</sup>]tetradec-8-ene

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(Received 16 October 1989; accepted 2 January 1990)

**Abstract.** Tetramethyl 1,2-*trans*-1,10-*trans*-2,7-*cis*-1,7-dimethyltricyclo[8.4.0.0<sup>2,7</sup>]tetradec-8-ene-5,5,12,12-tetracarboxylate, C<sub>24</sub>H<sub>34</sub>O<sub>8</sub>, *M<sub>r</sub>* = 450.53, monoclinic, *P*2<sub>1</sub>, *a* = 7.8649 (23), *b* = 10.9621 (17), *c* = 13.3312 (18) Å, β = 93.279 (15)°, *V* = 1147.5 (4) Å<sup>3</sup>, *Z* = 2, *D<sub>x</sub>* = 1.304 Mg m<sup>-3</sup>, λ(Cu Kα) = 1.54056 Å, μ = 0.76 mm<sup>-1</sup>, *F*(000) = 484, room temperature, final *R* = 0.083 for 1552 observed reflections. The structure consists of three angularly fused six-membered rings *A*, *B* and *C*. Rings *A* and *C* adopt chair conformations with the C1- and C7-methyl groups axial, while ring *B* prefers a half-chair conformation. The relative stereochemistry is *trans* at the *AB* ring junction, *anti* between the C1 methyl and C2 hydrogen, and *cis* at the *BC* ring junction (abbreviated to *TAC*).

**Introduction.** The tricyclic compound (2), a possible natural product precursor, was obtained *via* transannular Diels–Alder reaction of macrocycle (1) (Fig. 1). This is our continued effort (Lamothe, Ndiwami & Deslongchamps, 1988*a,b*) to demonstrate the synthetic utilities of the transannular [4 + 2] cycloaddition in constructing polycyclic molecules with substituted dienes and dienophiles of the macrocycles. The conformational analyses and X-ray studies of other tricyclic molecules synthesized by this new methodology have been reported earlier (Michel, Michel-Dewez & Roughton, 1989). It is expected that the transannular Diels–Alder reaction takes place *via* a boat-like transition state (Lamothe, Ndiwami & Deslongchamps, 1988*a,b*). Consequently, the conformational restraints imposed on the transition state by the triene configuration, substituents and ring size determine the outcome of the relative stereochemistry of the cycloadducts. From a study of the transition state by molecular modelling, it is expected that tricyclic products with both *trans-anti-cis* (*TAC*) and *cis-anti-trans* (*CAT*)

stereochemistry are possible. This is in very good agreement with the result obtained earlier for a similar macrocycle (1) without a methyl substituent on the diene (Lamothe, Ndiwami & Deslongchamps, 1988*b*). Interestingly, the *trans*-annular Diels–Alder reaction of macrocycle (1) produced a single product (2). The relative stereochemistry could not be determined from available spectroscopic data. The crystallographic study presented herein was undertaken to determine the relative stereochemistry of the product (2).

**Experimental.** Crystal 0.20 × 0.20 × 0.20 mm; Enraf–Nonius CAD-4 diffractometer, graphite monochromator, Cu Kα radiation, ω–2θ scan; lattice parameters refined from 24 reflections with 2θ range 60–80°; *hkl* range: –9–9, –13–13 and –15–16; 2θ<sub>max</sub> = 144°; two standard reflections were monitored every 60 min, without significant deviation; 2382 unique measured reflections; 1552 observed with *I*<sub>net</sub> ≥ 2.5σ*I*<sub>net</sub>; structure was solved by direct methods and refined with *NRCVAX* (Gabe, Lee & Le Page, 1985). All non-H atoms were refined anisotropically. All H atoms were calculated and refined. The last least-squares cycle was calculated with 66 atoms; 289 parameters using weights based on counting statistics. The residuals for all the significant reflections are *R<sub>F</sub>* = 0.083, *wR* = 0.039 and *S* = 2.799; the poor quality of the crystal and the high thermal parameters on all the esters prevent better values;

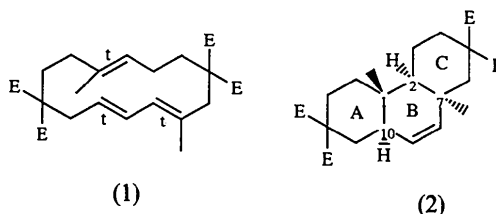


Fig. 1. IUPAC numbering (*E* = COOCH<sub>3</sub>).

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Table 1. Final coordinates and  $B_{eq}$  values for non-H atoms, with e.s.d.'s in parentheses
$$B_{eq} = \frac{1}{3} \pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* a_i \cdot a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	$B_{eq}$ (Å <sup>2</sup> )
C1	0.4331 (8)	0.2222 (6)	0.2460 (4)	3.9 (4)
C2	0.5018 (9)	0.2856 (7)	0.1500 (5)	4.3 (4)
C3	0.5017 (9)	0.1999 (6)	0.0573 (4)	4.3 (4)
C4	0.5513 (9)	0.2743 (7)	-0.0315 (5)	4.7 (4)
C5	0.4643 (9)	0.2757 (7)	-0.1192 (5)	5.1 (4)
C6	0.3012 (9)	0.2020 (8)	-0.1405 (5)	5.1 (4)
C7	0.1898 (9)	0.2546 (7)	-0.2223 (4)	4.8 (4)
C8	0.0433 (9)	0.1736 (6)	-0.2478 (4)	4.1 (4)
C9	-0.0485 (9)	0.1312 (7)	-0.1546 (5)	5.3 (4)
C10	0.0678 (9)	0.0860 (7)	-0.0727 (5)	5.1 (5)
C11	0.2116 (8)	0.1781 (7)	-0.0404 (4)	4.1 (4)
C12	0.3477 (9)	0.1179 (7)	0.0316 (5)	5.0 (4)
C13	0.2746 (9)	0.0644 (7)	0.1334 (5)	5.0 (4)
C14	0.2647 (10)	0.1583 (8)	0.2190 (4)	5.5 (4)
C15	0.6598 (10)	0.1115 (7)	0.0788 (5)	5.6 (5)
C16	0.1328 (9)	0.2938 (7)	-0.0028 (5)	5.0 (4)
C17	0.5684 (9)	0.1477 (7)	0.2985 (5)	5.2 (4)
C18	0.8459 (10)	0.1387 (9)	0.3686 (5)	7.5 (6)
C19	0.3982 (8)	0.3324 (7)	0.3182 (5)	4.9 (4)
C20	0.2791 (9)	0.3759 (8)	0.4731 (5)	6.6 (5)
C21	0.0890 (9)	0.0668 (7)	-0.3132 (5)	4.7 (4)
C22	0.2084 (10)	0.0079 (8)	-0.4628 (5)	6.0 (5)
C23	-0.0889 (9)	0.2445 (6)	-0.3096 (5)	4.6 (4)
C24	-0.3738 (9)	0.2393 (8)	-0.3970 (6)	6.2 (5)
O1	0.5437 (6)	0.0283 (5)	0.3253 (3)	6.0 (3)
O2	0.7087 (6)	0.2079 (5)	0.3205 (3)	5.2 (3)
O3	0.4237 (7)	0.4363 (5)	0.3016 (4)	7.0 (3)
O4	0.3326 (6)	0.28617	0.4015 (3)	5.7 (3)
O5	0.0723 (7)	-0.0394 (5)	-0.2948 (4)	6.9 (3)
O6	0.1576 (6)	0.1066 (5)	-0.3966 (3)	5.6 (3)
O7	-0.0894 (7)	0.3512 (5)	-0.3265 (4)	8.1 (4)
O8	-0.2230 (7)	0.1819 (5)	-0.3458 (4)	7.2 (3)

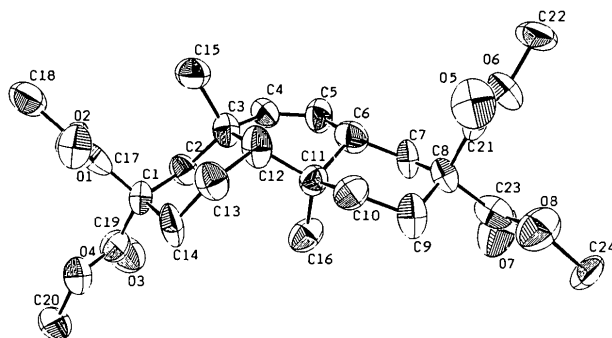


Fig. 2. ORTEP perspective view with crystallographic numbering.

max.  $\Delta/\sigma = 0.462$ . In the final difference map, the deepest hole was  $-0.29 \text{ e } \text{Å}^{-3}$  and the highest peak  $0.27 \text{ e } \text{Å}^{-3}$ . The secondary-extinction coefficient was 0.05 (1). Atomic scattering factors were from *NRCVAX*.

**Discussion.** Table 1 gives the final atomic parameters with their  $B_{eq}$  values.\* Fig. 2 shows the atom numbering and an ORTEP (Johnson, 1976) perspec-

\* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52932 (15 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Molecular geometry

(a) Bond lengths (Å) with e.s.d.'s in parentheses			
C1—C2	1.579 (9)	C10—C11	1.559 (10)
C1—C14	1.523 (10)	C11—C12	1.544 (10)
C1—C17	1.484 (10)	C11—C16	1.509 (11)
C1—C19	1.578 (10)	C12—C13	1.614 (10)
C2—C3	1.554 (9)	C13—C14	1.542 (10)
C3—C4	1.507 (9)	C17—O1	1.271 (9)
C3—C12	1.531 (10)	C17—O2	1.304 (8)
C3—C15	1.589 (10)	C18—O2	1.439 (10)
C4—C5	1.321 (9)	C19—O3	1.180 (9)
C5—C6	1.529 (10)	C19—O4	1.350 (8)
C6—C7	1.476 (9)	C20—O4	1.449 (8)
C6—C11	1.566 (9)	C21—O5	1.198 (9)
C7—C8	1.478 (10)	C21—O6	1.337 (8)
C8—C9	1.544 (9)	C22—O6	1.466 (9)
C8—C21	1.516 (10)	C23—O7	1.191 (9)
C8—C23	1.505 (10)	C23—O8	1.325 (9)
C9—C10	1.470 (10)	C24—O8	1.475 (9)

(b) Valence angles (°) with e.s.d.'s in parentheses			
C2—C1—C14	110.1 (5)	C6—C11—C10	103.1 (5)
C2—C1—C17	110.8 (5)	C6—C11—C12	105.8 (5)
C2—C1—C19	103.7 (6)	C6—C11—C16	110.8 (6)
C14—C1—C17	116.7 (6)	C10—C11—C12	111.1 (6)
C14—C1—C19	108.5 (6)	C10—C11—C16	109.3 (6)
C17—C1—C19	106.2 (5)	C12—C11—C16	115.9 (5)
C1—C2—C3	113.2 (6)	C3—C12—C11	113.5 (6)
C2—C3—C4	108.0 (6)	C3—C12—C13	109.9 (5)
C2—C3—C12	119.8 (6)	C11—C12—C13	114.2 (6)
C2—C3—C15	105.1 (5)	C12—C13—C14	114.5 (6)
C4—C3—C12	112.3 (5)	C1—C14—C13	113.7 (6)
C4—C3—C15	103.7 (5)	C1—C17—O1	122.4 (6)
C12—C3—C15	106.5 (6)	C1—C17—O2	113.7 (6)
C3—C4—C5	123.9 (7)	O1—C17—O2	123.7 (7)
C4—C5—C6	123.0 (6)	C1—C19—O3	125.9 (6)
C5—C6—C7	112.8 (6)	C1—C19—O4	107.6 (6)
C5—C6—C11	110.1 (5)	O3—C19—O4	126.4 (6)
C7—C6—C11	114.7 (6)	C8—C21—O5	126.9 (6)
C6—C7—C8	111.0 (6)	C8—C21—O6	110.3 (6)
C7—C8—C9	113.0 (5)	O5—C21—O6	122.8 (7)
C7—C8—C21	112.9 (6)	C8—C23—O7	127.2 (7)
C7—C8—C23	108.8 (6)	C8—C23—O8	116.3 (6)
C9—C8—C21	111.5 (6)	O7—C23—O8	116.5 (6)
C9—C8—C23	104.8 (6)	C17—O2—C18	115.9 (6)
C21—C8—C23	105.2 (5)	C19—O4—C20	115.2 (5)
C8—C9—C10	113.5 (6)	C21—O6—C22	113.4 (6)
C9—C10—C11	113.4 (6)	C23—O8—C24	123.3 (6)

tive view of the tricyclic compound. Bond lengths and angles are given in Tables 2(a) and 2(b). The relative stereochemistry of (2) was found to be *trans-anti-cis* (TAC) instead of *CAT*. From recent results obtained in this laboratory (Deslongchamps, 1989), the transition state of the transannular Diels–Alder reaction on a 14-membered ring prefers a chair-boat-chair conformation. Although cycloadducts with both *TAC* and *CAT* stereochemistry could be approached *via* a chair-boat-chair transition state from macrocycle (1), the substituents on rings A and C of the *TAC* product experience much weaker steric interactions. Therefore, the formation of tricyclic (2) with *TAC* stereochemistry is energetically favored. The proposed transition state with chair-boat-chair conformation does not remain in the final product; presumably the boat-like ring B scrambles into a half-chair conformation which is energetically preferred. This leads to the C15- and C16-methyl groups being in the axial positions while rings A and C still adopt chair conformations, as demonstrated by the crystal structure. No abnormally short contact distances were observed.

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## Functionalized Hydrocarbons with Condensed Ring Skeletons. IX. A Trioxotricyclo[8.4.0.0<sup>2,7</sup>]tetradecane

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(Received 8 September 1989; accepted 2 January 1990)

**Abstract.** Methyl 1,2-*trans*-1,10-*cis*-2,7-*cis*-7-methyl-6,8,14-trioxotricyclo[8.4.0.0<sup>2,7</sup>]tetradecane-1-carboxylate, C<sub>17</sub>H<sub>22</sub>O<sub>5</sub>, *M<sub>r</sub>* = 306.36, monoclinic, *P*2<sub>1</sub>/*c*, *a* = 10.3072 (2), *b* = 14.9042 (3), *c* = 10.5568 (3) Å, β = 109.552 (2)°, *V* = 1528.22 (6) Å<sup>3</sup>, *Z* = 4, *D<sub>x</sub>* = 1.332 Mg m<sup>-3</sup>, λ(Cu Kα) = 1.54056 Å, μ = 0.76 mm<sup>-1</sup>, *F*(000) = 665.93, room temperature, final *R* = 0.037 for 2500 observed reflections. The structure consists of three angular fused six-membered rings *A*, *B* and *C*. The *AB* ring junction is *cis*, the C1 ester and the C2 proton (IUPAC numbering) are in an *anti* relationship, and the *BC* ring junction is *cis* (abbreviated to *CAC*). Rings *A*, *B* and *C* adopt chair conformations.

**Introduction.** Quassinoids are a class of degraded triterpenes found mostly in the bitter principles of 'Simaroubaceous' plants growing in central Asia (Polonsky, 1973, 1985). Some members of that family display interesting and potent biological activities and some have antineoplastic properties. In the course of studies directed toward the synthesis of compounds belonging to this family of natural products we prepared β-diketone (3) (Fig. 1) in a stereoselective fashion from the base-catalyzed [4 + 2] cycloaddition of β-ketoester (1) and dienophile (2) followed directly by an acidic decarboxylation-hydrolysis step (Spino & Deslongchamps, 1989). The stereochemistry shown for compound (3) was assigned on the basis of previous studies on similar systems (Deslongchamps & Lavallée, 1988)

and was consistent with a high-resolution <sup>1</sup>H NMR spectroscopic analysis. We decided to look at the alkylation reaction of β-diketones like (3) and its stereochemistry as a means of introducing the C8 methyl group present in many quassinoids. Only a few examples of the alkylation of systems like compound (3) have so far appeared in the literature (Duthaler & Maienfisch, 1982; Chan & Prasad, 1987). On the basis of stereoelectronic control, we would expect the alkylation of the enolate of (3) to yield, as the major product, the tricyclic compound having the *trans* fused junction between rings *B* and *C*. However, the methyl ester at C1 could direct the attack of the alkylating agent, by way of steric hindrance, to the opposite face of the molecule giving the product with the *cis-BC* ring junction. The alkylation with methyl iodide actually proceeded to 65% yield to give predominantly the *cis-BC* ring junction product (4) along with its *trans* isomer in a 2:1 ratio.† The two isomeric products could easily be separated by column chromatography on silica gel, but their respective structures could not be determined by spectroscopic means. That no epimerization had occurred at C9 (Fig. 2) under the reaction conditions was verified simply by recovering (3), unchanged, after protonation of the potassium enolate generated in an identical manner. We report herein the X-ray diffraction analysis of the major isomer, compound (4), undertaken to determine its relative stereochemistry and, therefore, also that of the minor isomer.

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† In addition, 8% of *O*-alkylated products were isolated.