two steps. Alkylation[11] of the lithium enolate of methyl isobutyrate with propargyl bromide (THF, −78 °C, 80% yield) followed by carbomethoxylation of the resultant terminal acetylene by the method of Tsuji[12] (CO, $PdCl_2$, $CuCl_2$, NaOAc; 72% yield) provided diester **5**.[13] Exposure of **5** (Scheme II) to the Grignard reagent prepared from 2-chloro-6-methyl-5-heptene[14] in the presence of added TMEDA and copper(I) iodide (THF, −78 to 25 °C) resulted in 1,4 addition[15–17] and subsequent cyclization of the intermediate vinylcopper species to yield 48% of cyclopentenone **6**.[10] Selective ozonolysis of the trisubstituted olefin (O_3, CH_2Cl_2, −78 °C; then Me_2S, −78 to 25 °C) generated aldehyde **7**. Treatment of **7** with carbethoxymethylenetriphenylphosphorane (CH_2Cl_2, 40 °C, 6 h) provided the desired diester **4** in 81% yield from **6**.

With ready access to the highly functionalized cyclopentenone **4**, the next stage of the synthesis was to carry out the key photocyclization, and this was accomplished by irradiating a hexane solution of **4** at 366 nm (uranium glass filter). The resulting cyclobutane photoadducts **3** were isolated in 72% yield as a 10:3:1 (**3a**:**3b**:**3c**) mixture of diastereomers. Cleavage of the cyclobutane of **3** with lithium–ammonia[18] at −78 °C led to a 13:1 mixture of spirofused esters **2a**:**2b** in 90% yield. Thus, the two major isomers obtained from the photocycloaddition must contain the same relative stereochemistry at C-9 but are epimeric at the cyclobutyl carbon bearing the carbethoxy group.

The excellent stereoselectivity[19] in the photoannelation might be explained on thermodynamic grounds analogously to the system studied by Oppolzer.[8] However, on the basis of existing data, particularly recent findings by Becker,[20] kinetic control cannot be excluded.

Our next task was to close the remaining five-membered ring to form the basic triquinane skeleton. This was readily accomplished in three high-yield steps (Scheme III). Hydrolysis–decarboxylation of β-keto ester **2a** (HCl, H_2O, HOAc, 6 h, reflux; 90% yield)[21] provided acid **9** (mp 85.5–87 °C). Fischer esterification [CH_3OH, $(CH_3O)_3CH$, p-TSA) gave 97% of ester **10** which was readily cyclized[22] (t-BuO^-K^+, C_6H_6, reflux) to afford a 75% yield of pure dione **11** (mp 71–72 °C) after flash chromatography and recrystallization. The cis stereochemistry of the ring juncture formed in this cyclization is a result of thermodynamic as well as kinetic control.

The remaining portion of the synthesis required differentiation of the two carbonyls of **11**. Selective ketalization was easily achieved to yield ketal **12** due to the vastly different steric environment of the two carbonyls. Thermodynamic reduction (Li, NH_3, CH_3OH) of the ketone gave **13** with the correct stereochemistry of the C-1 hydroxyl. Hydrolysis of the ketal provided keto alcohol **14** in 81% yield from **11**.

Carboxylation of **14** (4 equiv of LDA, CO_2, −78 °C; 10% HCl, −40 °C)[23] followed immediately by diazomethane esterification produced 90% of keto ester **15**. Treatment of **15** with sodium borohydride in methanol generated diol **16** as a mixture of diastereomers in 84% yield. Attempts to selectively mesylate or tosylate **16** to allow introduction of the requisite double bond were unsuccessful. However, bisacetylation (Ac_2O, Et_3N, DMAP)[24] of **16** followed by treatment with DBU gave 90% of the unsaturated ester **18** which was hydrolyzed (KOH, H_2O, MeOH) to pentalenic acid (**1**). Spectra of the methyl ester of synthetic **1** were identical with those of authentic samples.[5a,25]

In summary, an efficient, highly stereoselective synthesis of the important triquinane pentalenic acid (**1**) has been achieved. Similar approaches to other triquinanes utilizing our photocycloaddition–cyclobutane fragmentation sequence are in progress and will be reported in due course.

Acknowledgment. We are deeply indebted to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (AI-20283) for generous financial support. Thanks are due to L. D. Bredon and Dr. D. H. Harris for help in recording 250-MHz ^1H NMR spectra. We also thank Professor David E. Cane, Brown University, for providing us with authentic spectra of methyl pentalenate.

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[25] We thank Professor David E. Cane, Brown University, for providing authentic comparison spectra.

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Cubugene, a Diterpenoid with a Novel Carbon Skeleton from a Termite Soldier (Isoptera Termitidae Termitinae)

Summary: Cubugene (**1**), a unique diterpene hydrocarbon, was isolated from the Kenyan termite soldier *Cubitermes ugandensis* (Fuller), and the structure was elucidated together with its oxidation product (**2**).

Sir: The frontal gland secretion of *Cubitermes* soldiers (Isoptera Termidae Termitinae) is known to consist of diterpene hydrocarbons.[1] We now report the structure of cubugene (**1**), an unstable bicyclic diterpene occuring in the secretion gland of *Cubitermes ugandensis* soldiers, and its oxidation product (**2**).

The termite was collected from Eldama Ravine (elevation 2500 m) in Kenya. The soldiers (1200) were chilled and decapitated, and the heads were crushed in hexane to give 197 mg of crude extract. This was first chroma-

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Table I. NMR Data of Compounds 1 and 2 (in C_6D_6)

	compound 1		compound 2			compound 1					compound 2				
C	δ	mult	δ	mult	H	δ	mult	J, Hz	coupled to[b]	NOE[c]	δ	mult	J, Hz	coupled to[b]	NOE[c]
1	117.9	d	120.7	d	1	6.20	bd	9	2	16, 19	5.50	d	9	2	19 (4%), 16 (3%)
2	126.2	d	60.3	d	2	5.90	bd	9	1, 16	13	2.61	bt	9	1, 6	13 (5.4%), 17 (3%)
3	137.6	s	80.3	s	3										
4	26.1[a]	t	33.1[a]	t	4						1.80			5, 4′, 5′	5
					4′						1.93			5′, 4, 5	
5	28.5[a]	t	31.9[a]	t	5	1.98					1.54	dd	6, 11	4, 4′, 5′, 6	16, 4
					5′	2.23					1.83			4′, 4, 5, 6	
6	125.5	d	48.8	d	6	4.95	vbd		5, 5′, 17		2.01	ddd	1, 8, 11	2, 5, 5′	
7	133.6	s	160.1	s	7										
8	40.0	t	43.0	t	8	2.35	vbt	5	8′, 9′, 9		2.28	md	1, 3, 13	17′, 17, 9, 9′, 8′	8′ (14%)
					8′	1.80	td	1, 5	8, 9, 9′		2.08	dddd	1, 3, 12, 15	17′, 9′, 9, 8	8, 17′ (5%)
9	39.1	t	39.5	t	9	1.41			8, 8′, 9′		1.33	dddd	2, 11, 13, 14	8, 8′, 12, 9′	
					9′	0.90			8, 8′, 9, 12		1.11			8, 8′, 9	
10	46.3	t	46.9	t	10	1.11			11		1.15	(t)	(13)	11, 10′	
					10′						1.24	(dd)	(3, 13)	11, 10	
11	32.2	d	33.4	d	11	1.93			10, 18		1.87	m		18, 10, 10′	
12	44.6	d	44.3	d	12	1.51			9′, 13, 13′		1.58	btd	3, 13	13′, 13, 9	
13	20.7	t	19.0	t	13	2.79	dd	3, 14.5	13′, 12	2	2.92	dd	3, 13	12, 13′	2 (11%), 13′ (11%)
					13′	2.10			13, 12	17, 20	2.05	dd	3, 13	12, 13	20, 13
14	143.9	s	146.0	s	14										
15	37.1	s	37.1	s	15										
16	19.4	q	29.5	q	16	1.63	bs		2	1(10.8)	1.24	s			1 (10%), 5 (3%), 6 (3%)
17	16.1	q	110.0	t	17	1.43	bs		6	13′, 1, 2	5.12	bd	1, 1, 1.5	8, 17′	2 (3%), 17′ (10%)
					17′						5.06	bd	1, 1, 1.5	8′, 8, 17	8′ (7%), 17 (17%)
18	15.6	q	19.5	q	18	0.85	d	7	11	10	0.83	d	7	11	11 (6%)
19	29.4	q	26.7	q	19	1.14[a]				1	1.15	s			1 (15%)
20	27.5	q	24.2	q	20	1.13[a]				13′	1.11	s			1, 13′ (3%), 11 (4%)

[a] Exchangeable. [b] Distinguished coupling are listed. [c] Numerals outside parentheses denote the proton exhibiting the NOE; e.g., in the first line, irradiation of 1-H causes 4% and 3% NOE on 19-H and 16-H, respectively. No indication in parentheses based on 2D-NOE.

tographed on Florisil by elution with hexane to yield 82.5 mg of a hydrocarbon mixture containing 48% cubugene (1) (GLC), which was isolated by flash chromatography using 20:1 hexane/EtOAc over $AgNO_3/SiO_2$ and purified by preparative GLC (15% Carbowax 20M, 250 °C). The hydrocarbon mixture also contained cubitene[2] (3), bifloratriene,[3] cembrene-A,[4] and other unidentified minor congeners as determined by GC/MS.

Cubugene[5] (1), 33 μg/soldier, $C_{20}H_{32}$ (m/z 272.2476, calcd 272.2504) exhibited the following fragments in its electron-impact mass spectrum (EI-MS): m/z 272 (relative intensity) (M^+, 50), 257 ($M^+ - CH_3$, 20), 229 ($M^+ - C_3H_7$, 10), 187 ($M^+ - C_6H_{13}$, 60), and 105 (C_8H_9, 100). Catalytic hydrogenation (Pd/C) followed by EI-MS measurement, $C_{20}H_{38}$, showed 1 to be a bicyclic hydrocarbon with three double bonds. From the ^1H NMR (300 MHz, C_6D_6) data, five methyl groups at δ 0.85 (d, J = 7, 11-Me), 1.13 (s, 15-*gem*-Me), 1.14 (s, 15-*gem*-Me), 1.43 (s, 7-Me), and 1.63 (s, 3-Me, weakly coupled to 5.90, 2-H) were observed, along with a trisubstituted double bond at 4.95 (br d, 6-H), an allylic proton at 2.79 (dd, J = 3, 14.5, 13-H) coupled to 2.10 (13′-H), and a downfield AB quartet (J_{AB} = 9.0) at 6.20 (J = 9, 1-H) and 5.90 (J = 9, 2-H), weakly coupled to 3-Me) of a transoid diene system (UV: λ_{max} 247 nm, ε 18200; CD $[\theta]_{240}$ −1.51 × $10^{3\circ}$ in cyclohexane). 2D-FT homonuclear J-correlation (COSY)[6] indicated the coupling

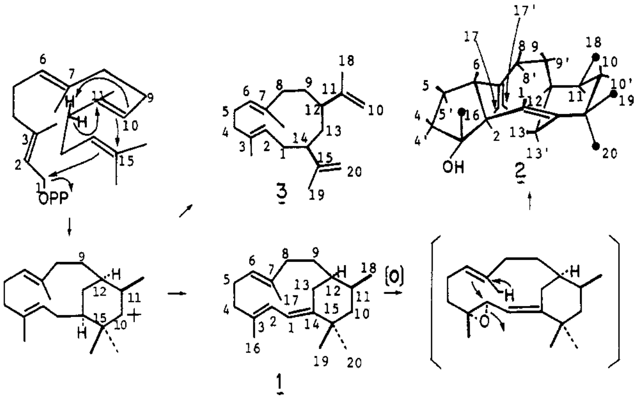

Figure 1. Proposed biogenetic relationship between 1, 2, and 3.

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(4) Wiemer, D. F.; Meinwald, J.; Prestwich, G. D.; Miura, I. *J. Org. Chem.* **1979**, *44*, 3950.

(5) Cubugene was first isolated in 1977 by G.D.P. from the following species: *Cubitermes ugandensis* (Fuller), *C. muneris* (Sjostedt), *C. tenuiceps* (Sjostedt), *C. glebae*, *C.* sp. N.D., and *Crenetermes mixtus* (Williams). The limited amount, its ready oxidation (to 2), and unavailability of crystals suited for X-ray studies eluded its structure determination. NMR data in this text are those of the sample that was isolated from fresh secretions collected in 1983.

(6) Bax, A.; Freeman, R.; Morris, G. *J. Magn. Reson.* **1981**, *42*, 164.

protons[7] (Table I) on the linked carbons (C-8, 9, 12 and 13 in Figure 1). No couplings was observed between H-11 and H-12 as the dihedral angle is close to 90°. The NOE between the proton at 1-H and 3-Me(16-H) and one of the *gem*-dimethyls (19-H) indicated the locations of three methyls on the transoid diene system. 2D-NOE[8] of 1 (3-Me/1-H, 19-H(Me)/1H, 2-H/13-H, 13′-H/20-H(Me), 13′-H/7-Me) revealed the gross conformation which is similar to that of its oxidation product 2.[9] The location of the *sec*-methyl was suggested from the NOE between the 20-Me and 11-H of 2. ^{13}C NMR (25 MHz) data (C_6D_6) also indicated a bicyclic structure with three trisubstituted double bonds (Table I); the assignments are based on the (INEPT)[10] method, selective decoupling, and the comparison with the data of 2.

Compound 2, $C_{20}H_{32}O$ (m/z 288.2452, calcd 288.2498) was isolated from the stored (6 years at −20 °C) hexane extract of *C. ugandensis* soldier heads by column chromatography using 10:1 hexane/EtOAc over SiO_2. The tricyclic nature of compound 2 was disclosed from the ^{13}C NMR data, which showed the presence of one trisubstituted double bond, an exocyclic disubstituted double bond, and a strongly shielded triplet carbon (19.0 ppm, C-13; shielded by the 7,17-ene) (Table I). The ^{13}C NMR assignments are based on heteronuclear chemical shift correlation spectroscopy (CSCM).[11] ^{1}H NMR (360 or 300 MHz) with COSY,[6] 2D-NOE,[8] sequential additions of lanthanide shift reagent [Eu(fod)$_3$-d_{27}], extensive homonuclear difference decoupling, and NOE measurements allowed for complete proton assignments (Table I) and also established the relative configurations 2. A possible biogenesis[12] of cubugene 1 together with the co-occurring irregular cubitene 3[2] is shown in Figure 1.

Acknowledgment. We are grateful to Dr. Darlington for the second collection of *Cubitermes ugandensis*. We also thank the grants from the NSF, the A. P. Sloan Foundation, and the Camille and Henry Dreyfus Foundation.

Registry No. 1, 89890-83-5; 2, 89890-84-6; 3, 66723-19-1; bifloratriene, 69636-81-3; cembrene A, 31570-39-5.

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(7) The present numbering is based on biogenetic considerations, even though the cubugene skeleton does not follow a regular head-to-tail biogenesis. The numbering differs from that employed earlier for the cooccurring cubitene 3.[2]

(8) Kumar, A.; Wagner, G.; Ernst, R. R.; Wuthrich, K. *Biochem. Biophys. Res. Commun.* **1980**, *96*, 1156. We thank Dr. LeRoy F. Johnson of Nicolet Instrument, Freemont, CA, for the improved 2D-NOE pulse sequence.

(9) The compound 2 was obtained as the major oxidation product by treatment of 1 with *m*-chloroperbenzoic acid in CH_2Cl_2. The initial epoxidation is stereoselective, since the exo face of the 2,3-ene (the *re,re* face) is more readily accessible.

(10) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760. Morris, G. A. *Ibid.* **1980**, *102*, 428. Burum, D. P.; Ernst, R. E. *J. Magn. Reson.* **1980**, *39*, 163.

(11) Mandsley, A. A.; Kumar, A.; Ernst, R. R. *J. Magn. Reson.* **1977**, *28*, 463. Bax, A. "Two-dimentional Nuclear Magnetic Resonance in Liquids"; Kluwer Boston Inc.: Hingham, MA, 1981; p 61.

(12) We are grateful to a referee who suggested revision of a previous biogenetic scheme to the one shown.

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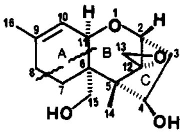
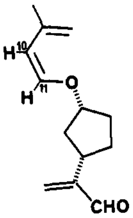
A Novel Type of Intramolecular Diels–Alder Reaction Involving Dienol Ethers: An Unusual Preference for a Boat Transition State in the Incipient Ring Formation

Summary: Cis and trans dienol ethers 2 and 3 have been stereospecifically synthesized and their intramolecular Diels–Alder reactions studied. While 3 did not cyclize upon prolonged heating, the cis dienol ether 2 underwent smooth cyclization through an unusual boat transition state to provide a novel trichothecane-like skeleton 13.

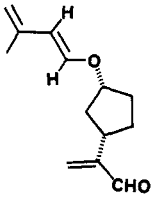
Sir: Notwithstanding the extensive efforts directed at understanding the stereochemical outcome in the intramolecular Diels–Alder reaction, there have been few comparative studies reported on the reactivity and stereoselection imposed by the configuration at the diene moiety.[1,2] Furthermore, while 1-oxygenated dienes have been widely employed in the intermolecular Diels–Alder reaction,[3] there are virtually no examples known for the intramolecular version of this reaction.[2] As part of a synthetic approach toward a trichothecane skeleton such as verrucarol (1),[4] we had occasion to examine these aspects in the thermal cyclization using the two stereospecifically synthesized dienol ethers 2 and 3. In the following, we report that while the latter did not change upon prolonged heating, the former underwent cyclization, involving a unique boat-like transition state during the formation of the incipient B ring, to provide a novel trichothecane-like skeleton.



1



2



3

The synthesis of the two stereoisomeric dienol ethers 2 and 3 commenced from the *exo*-methylene lactone 4,[5,6] as summarized in Scheme I. Deprotonation of the α-alkoxy ester 5 with LDA followed by treatment with methacrolein afforded a 29:71 mixture of threo and erythro β-hydroxy esters 6a and 6b, respectively, in 87% yield.[7] These threo

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(1) Reviews: (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Oppolzer, W. *Synthesis* **1978**, 793. (c) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63.

(2) After the completion of this manuscript, we learned that in a recent paper Burke et al. (*Tetrahedron Lett.* **1984**, *25*, 19) studied the configurational effect on the stereochemical outcome of the intramolecular Diels–Alder reaction using the 1-(silyloxy)-1,3-butadiene system (isomeric at the 3-ene).

(3) Reviews: (a) Danishefsky, S. *Acc. Chem. Res.* **1981**, *14*, 400. (b) Petrzilca, M.; Grayson, J. I. *Synthesis* **1981**, 753.

(4) For the synthesis of the trichothecanes, see the following and references cited therein: (a) Trost, B. M.; McDougal, P. G.; Haller, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 383. (b) Roush, W. R.; D'Ambra, T. E. *Ibid.* **1983**, *105*, 1058.

(5) All new compounds reported herein have spectral (360-MHz ^{1}H and 90.56-MHz ^{13}C NMR, IR, UV, and MS) and microanalytical data consistent with the assigned structure.

(6) Obtained from norcamphor in five steps in 73% overall yield. The transformation involves: (i) MCPBA (1.4 equiv), $(CH_2Cl)_2$, reflux, 2 h (96%); (ii) LDA (1.2 equiv), THF, −78 °C, 1 h; Me_3SiCl (2.1 equiv). −78 °C to −20 °C, 2 h; (iii) $PhSCH_2Cl$ (1.2 equiv), $ZnBr_2$ (0.01 equiv), 20 °C, 16 h [88% overall yield for (ii) and (iii)]; (iv) $NaIO_4$ (1.3 equiv), $MeOH/H_2O/PhH$, 20 °C, 16 h; (v) PhH, reflux, 2 h [86% overall yield for (iv) and (v)].

(7) This result is in accord with the low stereoselection normally observed for the condensation of ester enolates with carbonyl compounds. For a recent review on the subject, see: Petragnani, N.; Yonashiro, M. *Synthesis* **1982**, 521.