Ring-Opening Reactions. 18. Synthesis of Cyclic Thioenol Ethers[1]

Torbjörn Frejd,*[2] J. Olle Karlsson, and Salo Gronowitz

Division of Organic Chemistry 1, Chemical Center, University of Lund, Lund, Sweden

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Thioenol ethers, and especially the cyclic ones, have attracted increased attention due to their potential use as basic synthetic building blocks. Thus, Takei et al.[3] and Wenkert et al.[4] have succeeded in replacing the alkyl(or aryl)thio groups of alkyl or aryl thioenol ethers with carbon–carbon bonds by using transition-metal (Ni(0)) catalysts and Grignard reagents. On the other hand, Trost and Tanigawa have shown that cyclic thioenol ethers can be allylically acetoxylated with palladium acetate in tetrahydrofuran (THF), which thereafter made carbon–carbon bond formation with organo cuprates possible.[5] The same authors have also demonstrated that thioenol ethers can be regiospecifically phenylated under different palladium-catalyzed conditions.[6]

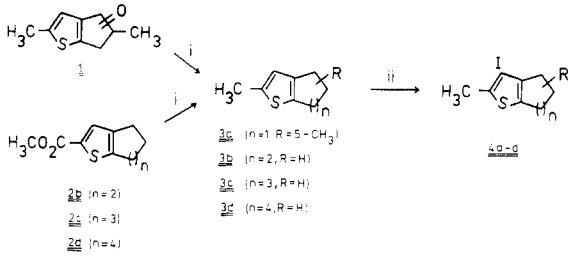
We now present our results on the synthesis of cyclic 2-propynyl thioenol ethers with special attention to regiospecificity by using the ring-opening reaction of suitably substituted [*b*]-annelated 3-thienyllithium derivatives.[7]

Results and Discussion

Since 3-iodothiophenes are the best precursors for the preparation of 3-thienyllithium derivatives with phenyllithium as the metal-introducing reagent,[8] some [*b*]-annelated 3-iodothiophenes were synthesized as shown in Schemes I and II by following essentially published procedures (see Experimental Section). It should be pointed out that the iodothiophenes **4e** and **4f** were obtained isomerically pure as checked by capillary column GC. This eliminates any rearrangement prior to cyclization of **5a** and **5b**.[9]

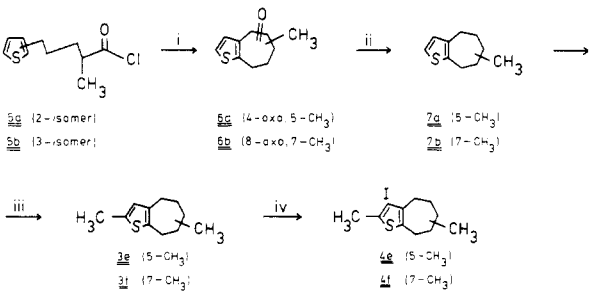
The general scheme for the syntheses of the 2-propynyl thioenol ethers is shown in Scheme III. The first step involves a halogen–metal exchange between the appropriate iodothiophene derivative (**4**) and phenyllithium to give the 3-thienyllithium derivatives **8**. The second step, i.e., the cleavage of the thiophene ring to give the cyclic enyne thiolates **9a–f**, occurred spontaneously at room temperature. The third step, the S-alkylation of **9a–f**, was accomplished in situ by the addition of a suitable alkylating reagent to the reaction mixture. Thus, **9a–f** were trapped with ethyl bromoacetate or benzyl chloride. In the reaction of **9a–d** with ethyl bromoacetate to give the ethyl esters of **10g–j**, it appeared important to quench the reaction after only a few minutes, since with a prolonged

Scheme I[a]



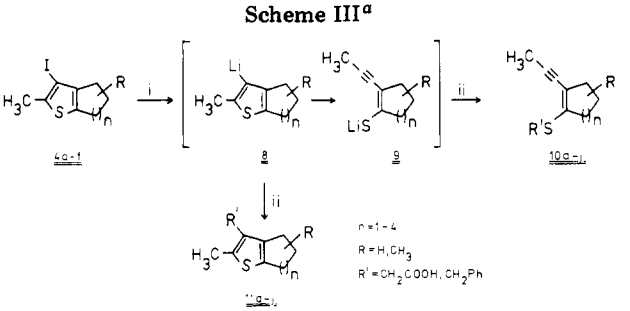
[a] (i) $LiAlH_4/AlCl_3$; (ii) I_2/HIO_3.

Scheme II[a]



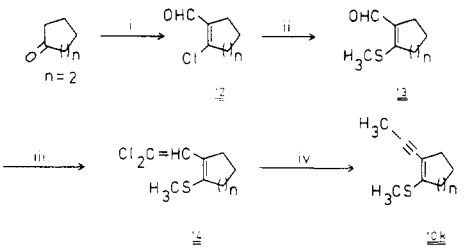
[a] (i) $SnCl_4$, CS_2, 0 °C; (ii) $LiAlH_4/AlCl_3$; (iii) BuLi, Me_2SO_4; (iv) I_2/HIO_3.

Scheme III[a]



[a] (i) PhLi, ether, 25 °C; (ii) R'X.

Scheme IV[a]



[a] (i) $POCl_3$, DMF; (ii) $Na^+SCH_3^-$; (iii) $Li^+(EtO)_2POC^-Cl_2$; (iv) (1) 2 equiv of BuLi, (2) CH_3I.

reaction time the reaction mixture darkened and the yields decreased considerably. The esters were hydrolyzed in situ to give the acids **10g–j**. Yields and physical data of the thioenol ethers **10a–j** are shown in Table I. Quite unexpectedly, **10e** and **10f** decomposed upon storage at room temperature, which was not the case with the other thioenol ethers. The reason for this remains obscure.

The thioenyne grouping can alternatively be introduced via thiolate substitution on a β-chlorovinyl aldehyde (**12**) to give a β-(alkylthio)vinyl aldehyde (**13**), followed by a Wittig–Horner reaction and subsequent elimination and alkylation steps to give **10k** (Scheme IV). However, this sequence does not give regiochemical control since, e.g., 3- and 4-methylcycloheptanone as well as 3-methylcyclo-

(1) Presented in part at the 2nd IUPAC Symposium on Organic Synthesis, Jerusalem-Haifa, 1978.
(2) Present address: Swedish Sugar Co. Ltd., PO Box 6, S-232 00 Arlöv, Sweden.
(3) Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* **1979**, 43.
(4) Wenkert, E.; Ferreira, T. W.; Michelotti, E. L. *J. Chem. Soc., Chem. Commun.* **1979**, 637.
(5) Trost, B. M.; Tanigawa, Y. *J. Am. Chem. Soc.* **1979**, *101*, 4413.
(6) Trost, B. M.; Tanigawa, Y. *J. Am. Chem. Soc.* **1979**, *101*, 4743.
(7) Cf.: Gronowitz, S.; Frejd, T. *Acta Chem. Scand., Ser. B* **1976**, *B30*, 485.
(8) The halogen–metal exchange between 3-bromothiophenes and phenyllithium is very slow or does not take place at all (T. Frejd, unpublished).
(9) Even though a previous statement in the literature about a rearrangement in a Friedel–Crafts cyclization of a thiophene derivative (Palmer, M. H.; Leitch, D. S.; Greenhalg, C. W. *Tetrahedron* **1978**, *34*, 1015) was proven erroneous (see ref 14), caution is recommended especially in cases where isomeric purity is important.

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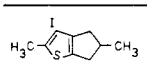
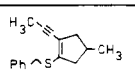
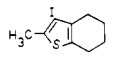
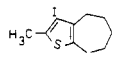
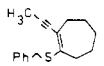
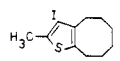
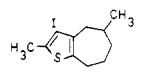
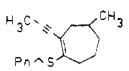
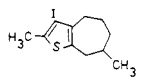
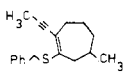
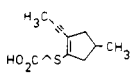
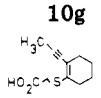
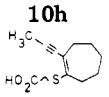
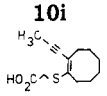
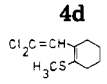
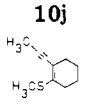
Table I. Yields and Physical Data of the Thioenol Ethers[a]

starting matl	product	yield, %	mp, °C (solvent)	^{1}H NMR ($CDCl_3$), δ [IR, cm^{-1}]
 4a	 10a	61	53.5-54 (EtOH)	0.98 (d, 3 H, 4-CH_3), 2.01 (s, 3 H, propargylic), 2.0-2.9 (m, 5 H, aliphatic), 4.08 (s, 2 H, benzylic), 7.3-7.4 (m, 5 H, aromatic); $J_{4\text{-}CH_3,4\text{-}H}$ = 6.0 Hz
 4b	 10b	63	75-76.5 (EtOH)	1.4-1.7 (m, 4 H, aliphatic), 1.99 (s, 3 H, CH_3), 2.0-2.3 (m, 4 H, allylic), 4.00 (s, 2 H, SCH_2), 7.2-7.5 (m, 5 H, aromatic)
 4c	 10c	52	chromatographed[b]	1.2-1.9 (m, 6 H, aliphatic), 2.03 (s, 3 H, CH_3), 2.2-2.5 (m, 4 H, SCH_2), 4.03 (s, 2 H, SCH_2), 7.2-7.5 (m, 5 H, aromatic)
 4d	 10d	63	chromatographed[b]	1.3-1.8 (m, 8 H, aliphatic), 2.03 (s, 3 H, CH_3), 2.2-2.6 (m, 4 H, allylic), 4.03 (s, 2 H, SCH_2), 7.2-7.5 (m, 5 H, aromatic)
 4e	 10e	53	chromatographed[b]	0.89 (d, 3 H, 4-CH_3), 1.0-1.9 (m, 5 H, aliphatic), 2.07 (s, 3 H, propargylic), 2.0-2.5 (m, 4 H, allylic), 4.07 (s, 2 H, SCH_2), 7.1-7.5 (m, 5 H, aromatic); $J_{4\text{-}CH_3,4\text{-}H}$ = 5.0 Hz
 4f	 10f	64	chromatographed[b]	0.83 (d, 3 H, 4-CH_3), 1.1-2.0 (m, 5 H, aliphatic), 2.05 (s, 3 H, propargylic), 2.1-2.5 (m, 4 H, allylic), 4.03 (s, 2 H, SCH_2), 7.2-7.5 (m, 5 H, aromatic); $J_{4\text{-}CH_3,4\text{-}H}$ = 5.0 Hz
4a	 10g	53	66-67.5 (hexane)	1.13 (d, 3 H, 4-CH_3), 2.06 (s, 3 H, propargylic), 2.0-3.0 (m, 5 H, aliphatic), 3.63 (s, 2 H, SCH_2), 9.60 (br s, 1 H, COOH) [IR (KBr) 1705 (COOH)]
4b	 10h	56	91-92.5 (hexane)	1.5-1.8 (m, 4 H, aliphatic), 2.03 (s, 3 H, CH_3), 2.1-2.4 (m, 4 H, allylic), 3.56 (s, 2 H, SCH_2), 10.0 (br s, 1 H, COOH) [IR (KBr) 1710 (COOH)]
4c	 10i	44	65.5-67 (hexane)	1.4-1.9 (m, 6 H, aliphatic), 2.03 (s, 3 H, CH_3), 2.3-2.6 (m, 4 H, allylic), 3.56 (s, 2 H, SCH_2), 8.95 (br s, 1 H, COOH) [IR (KBr) 1715 (COOH)]
4d	 10j	49	74.5-76 (hexane)	1.3-1.8 (m, 8 H, aliphatic), 2.03 (s, 3 H, CH_3), 2.2-2.6 (m, 4 H, allylic), 3.55 (s, 2 H, SCH_2), 9.95 (br s, 1 H, COOH) [IR (KBr) 1730 (COOH)]
 14	 10k	67	44-45 (hexane)	1.5-1.8 (m, 4 H, aliphatic), 2.03 (s, 3 H, propargylic), 2.0-2.4 (m, 4 H, allylic), 2.27 (s, 3 H, SCH_3)

[a] All thioenol ethers had satisfactory analytical data (±0.4% for C and H). [b] Hexane-ethyl acetate (95:5), silica gel.

pentanone give rise to isomeric mixtures of the corresponding β-chlorovinyl aldehydes.[10]

We have previously shown that thiophenes alkylated in the 3-position were formed as byproducts in ring-opening of 3-thienyllithium derivatives, particularly when the ring openings were slow.[11] In this case the alkylated thiophenes would have structures **11a–j**. Since these are isomeric with the ring-opening products, **10a–j**, it was necessary to establish the structures of the latter with a high degree of accuracy. IR and ^{1}H NMR spectroscopy proved essentially useless for this purpose. In the IR spectra of **10a–j** the carbon–carbon triple bond absorption was very weak, and their ^{1}H NMR (100 MHz) spectra lacked obvious characteristics. The mass and above all the ^{13}C NMR spectra proved to be of great value. Thus, in all of the thioenol ethers **10a–j** the molecular ion was the base peak, which is highly unlikely for the corresponding thiophenes **11a–j**.[12] Another feature of the mass spectra of **10a–f** and **10g–j** was the pronounced fragmentation of $SCH_2C_6H_5$ and SCH_2COOH groups, respectively, which has not been observed in thiophene derivatives of similar types.[12] The method of choice for the identification of **10a–j** is ^{13}C NMR spectroscopy (Table II). The acetylenic carbons show resonances in two distinct regions, i.e., at 91.6–93.4 ppm (relative to Me_4Si) and at 76.0–81.4 ppm, while the thiophene carbons have resonances at fields not higher than 120 ppm. This is quite clear from our data on the thiophenes with hydrogen in position 3 (**3a–d**) and the expected positive increment (i.e., to lower field) of the acetic acid and benzyl groups on C-3 resonances of thiophene derivatives.[13] Furthermore, the signals of the acetylenic methyl carbon (at 4.7–4.8 ppm) and the corresponding 2-methyl-group carbon of the thiophene ring (at 12–18 ppm) are sufficiently separated to be of diagnostic value.

It is clear from the ^{13}C spectra of the thioenol ethers that the substituent on the sulfur atom has a pronounced effect on one of the vinyl carbon resonances. Thus, while both of the vinyl resonances of **10a–d** appear in the interval 136.9–142.2 ppm, one of them appears at 134.8–137.7 ppm and the other at 116.0–124.4 ppm in **10g–k**. We therefore

(10) Karlsson, O.; Frejd, T., to be submitted for publication.
(11) Gronowitz, S.; Frejd, T. *Acta Chem. Scand., Ser. B* **1976**, *B30*, 287.
(12) Kinney, I. W.; Cook, G. L. *Anal. Chem.* **1952**, *24*, 1391.
(13) Benzyl and carboxy ethyl groups are expected to shift the resonance of the C-3 carbon of the thiophene ring toward lower field on the order of 10 and 7 ppm, respectively (cf.: Zetta, L.; Gatti, G. *Org. Magn. Reson.* **1972**, *4*, 585).

Table II. Comparison of the ^{13}C NMR Shifts of [*b*]-Annelated Thiophenes and the Corresponding Thioenynes[a] (For Simplicity, Carbon Atoms Are Numbered As Shown)

thiophenes **3**

thioenynes **10**

		R′ = CH_2Ph				R′ = CH_2COOH				R′ = CH_3			
compd	2,4,5-C	3-C	compd	2-C	4,5-C	compd	2-C	3-C	4,5-C	compd	2-C	3-C	4,5-C
3a	138.2, 141.8, 144.5	120.4	**10a**	76.0	137.9, 139.8	**10g**	80.1	93.4	120.7, 137.1				
3b	133.0, 134.8, 135.6	125.7	**10b**	79.6	136.9, 138.0	**10h**	79.4	92.6	121.0, 134.8	**10k**	81.2	91.8	116.0, 137.7
3c	133.4, 136.8, 140.2	128.8	**10c**	81.4	138.1, 142.2	**10i**	79.6	92.3	124.4, 137.4				
3d	134.5, 135.5, 138.1	127.1	**10d**	80.2	137.9, 139.8	**10j**	79.8	92.6	124.3, 137.4				

[a] $CDCl_3$ was used as solvent.

tentatively assign the high-field resonances of the latter to C-5.

The ^{13}C NMR spectrum of **10k** is very similar to those of **10b** and **10h**, which lends further support to the structural assignments of **10a–j**.

In conclusion, the presented work clearly shows the potential of the ring-opening route for regiospecific synthesis of unsymmetrically substituted cyclic thioenol ethers, not easily available by other methods.

Experimental Section

GLC analyses were performed on a Perkin-Elmer 900 gas chromatograph, NMR spectra were recorded with a JEOL MH 100 NMR spectrometer, and mass spectra were recorded with a Finnigan mass spectrometer. Capillary GLC analyses were performed on a Carlo Erba 4160-01 gas chromatograph equipped with a 27-m SE-52 column (gas flow rate 33 cm/s).

All reactions with organometallic reagents were performed in ether freshly distilled over sodium wire under a nitrogen atmosphere. Melting points are uncorrected.

Reduction of the Ketones. 4,5-Dihydro-2,5-dimethyl-6*H*-cyclopenta[*b*]thiophene (3a). A mixture of 4,5-dihydro-2,5-dimethyl-6*H*-cyclopenta[*b*]thiophen-6-one and 5,6-dihydro-2,5-dimethyl-4*H*-cyclopenta[*b*]thiophen-4-one (**1**;[14] 10.0 g, 0.060 mol) was reduced with $LiAlH_4/AlCl_3$ according to Brown and White.[15] The crude product was distilled: yield 5.7 g (62%); bp 58–60 °C (1.3 mm).

5-Methyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (7a) was prepared by reduction of 18.0 g (0.100 mol) of 5-methyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one (**6a**)[16] according to Brown and White.[15] The crude product was distilled: yield 12.3 g (74%); bp 101–105 °C (11 mm).

7-Methyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (7b) was prepared as in the preceding experiment from 18.0 g (0.100 mol) of 7-methyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]-thiophen-8-one (**6b**):[16] yield 12.3 g (74%); bp 101–103 °C (10 mm).

Reduction of Methyl Esters. Samples of 0.050 mol of appropriate [*b*]-annelated 2-thiophenecarboxylic esters (**2a–c**)[17] were treated with $LiAlH_4/AlCl_3$ according to Brown and White,[15] except that double equivalents of $LiAlH_4$ were used. The crude products were distilled.

2-Methyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (3b): yield 4.8 g (63% from **2a**); bp 50–51 °C (0.7 mm) [lit.[18] bp 101 °C (12.5 mm)].

2-Methyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (3c): yield 5.1 g (61% from **2b**); bp 63–65 °C (0.8 mm) [lit.[19] bp 110 °C (12 mm)].

2-Methyl-4,5,6,7,8,9-hexahydrocycloocta[*b*]thiophene (3d): yield 5.9 g (65% from **2c**); bp 77–78 °C (0.7 mm).

2,5-Dimethyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]-thiophene (3e) and 2,7-Dimethyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (3f). A sample of 8.3 g (0.050 mol) of the thiophene derivative (**7a** or **7b**) and 25 mL of dry ether were placed in a three-necked round-bottomed flask under a nitrogen atmosphere, and 40 mL (0.060 mol) of BuLi in hexane (1.5 M) was added. The mixture was then refluxed for 1 h. Thereupon it was cooled to −78 °C, and 7.6 g (0.060 mol) of dimethyl sulfate in 75 mL of dry ether was added. After 2 h the reaction mixture was allowed to reach room temperature, left for 1 h, treated with concentrated ammonium hydroxide, washed with water, dried ($MgSO_4$), evaporated, and distilled to give **3e** [6.3 g (70%), bp 115–117 °C (11 mm)] and **3f** [(6.2 g (69%), bp 113–116 °C (9 mm)], respectively.

General Procedure for the Iodination of the 2-Methyl [*b*]-Annelated Thiophenes 3a–f. The methylthiophenes **3a–f** were iodinated by the iodine–iodic acid method described in ref 7.

(14) Frejd, T.; Karlsson, O. *Tetrahedron* **1979**, *35*, 2155.
(15) Brown, B. R.; White, A. M. S. *J. Chem. Soc.* **1957**, 3755.
(16) Cagniant, P.; Merle, G.; Cagniant, D. *Bull. Soc. Chim. Fr.* **1970**, 322.
(17) Hauptmann, S.; Werner, E.-M. *J. Prakt. Chem.* **1972**, *314*, 499.
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4,5-Dihydro-2,5-dimethyl-3-iodo-6*H*-cyclopenta[*b*]thiophene (4a): yield 6.4 g (46% from **3a**); bp 96–98 °C (1.2 mm).

3-Iodo-2-methyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene (4b):[18] yield 9.0 g (65% from **3b**); bp 103–107 °C (0.8 mm) [lit.[18] bp 146–150 °C (12 mm)].

3-Iodo-2-methyl-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (4c): yield 10.7 g (73% from **3c**); bp 104–106 °C (0.5 mm); mp 40–41 °C (ethanol).

4,5,6,7,8,9-Hexahydro-3-iodo-2-methylcycloocta[*b*]thiophene (4d): yield 11.0 g (72% from **3d**); bp 113–114 °C (0.5 mm).

2,5-Dimethyl-3-iodo-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (4e): yield 10.0 g (65% from **3e**); bp 142–143 °C (2.5 mm).

2,7-Dimethyl-3-iodo-4,5,6,7-tetrahydro-8*H*-cyclohepta[*b*]thiophene (4f): yield 11.6 g (76% from **3f**); bp 142–143 °C (2.5 mm).

General Procedure for the Ring-Opening of the 3-Iodothiophenes. The 3-iodothiophenes **4a–f** (5.0 mmol) were each dissolved in 25 mL of anhydrous ether in a round-bottomed flask equipped with a rubber septum and a magnetic stirring bar. The flask was flushed with nitrogen, and the reaction was conducted under a nitrogen atmosphere. Phenyllithium (5.5 mmol) in ether was introduced with a syringe. The alkylating agent (5.5 mmol) was introduced after an appropriate period of time (15 min for the cyclopenta and tetrahydrobenzo derivatives, 2 h for the cyclohepta derivatives, and 1 h for the cycloocta derivative).

When ethyl bromoacetate was used as alkylating agent, the alkylation was allowed to proceed for 3–4 min only, in order to prevent resinification. Thereafter, the crude products were hydrolyzed by adding 25 mL of 5 M NaOH and 5 mL of ethanol and stirring for 2 h. The reaction mixture was then poured into water and washed with ether. The water phase was made acidic by hydrochloric acid and extracted with ether. The ether phase was washed with water, dried ($MgSO_4$), and evaporated.

When benzyl chloride was used as alkylating reagent, the reaction mixture was left 2 h before being quenched with water. The aqueous phase was extracted with ether, and the ethereal phase was washed with water, dried ($MgSO_4$), and evaporated.

From the crude products the following compounds were obtained in the pure state as indicated in Table I (together with yields and physical data): **1-(benzylthio)-4-methyl-2-(1-propynyl)cyclopentene (10a)**, **1-(benzylthio)-2-(1-propynyl)cyclohexene (10b)**, **1-(benzylthio)-2-(1-propynyl)cycloheptene (10c)**, **1-(benzylthio)-2-(1-propynyl)cyclooctene (10d)**, **1-(benzylthio)-4-methyl-2-(1-propynyl)cycloheptene (10e)**, **2-(benzylthio)-4-methyl-1-(1-propynyl)cycloheptene (10f)**, **[4-methyl-2-(1-propynyl)-cyclopenten-1-yl]thioacetic acid (10g)**, **[2-(1-propynyl)-cyclohexen-1-yl]thioacetic acid (10h)**, **[2-(1-propynyl)-cycloheptan-1-yl]thioacetic acid (10i)**, **[2-(1-propynyl)-cyclooctan-1-yl]thioacetic acid (10j)**.

2-(Methylthio)-1-formylcyclohexene (13). Sodium metal (7.4 g, 0.32 mol) was dissolved in 300 mL of absolute ethanol. The solution was then cooled to 0 °C, and 16 g (0.33 mol) of methanethiol was added, followed by 36 g (0.25 mol) of 2-chloro-1-formylcyclohexene.[17] After 15 min the mixture was heated, and reflux was maintained for 2 h. The ethanol was stripped off, and the residue was dissoved in ether, washed with water, dried ($MgSO_4$), and evaporated. The crude product was recrystallized from hexane: yield 32 g (65%); mp 46–47 °C; bp 141–143 °C (11 mm); IR (KBr) 1665 (C=O), 1580 cm^{-1} (C=C).

1-(Methylthio)-2-(2,2-dichloroethenyl)cyclohexene (14) was prepared according to Normant et al.[20] from 3.0 g (0.019 mol) of **13**. The crude product was chromatographed on silica gel by using hexane–ethyl acetate 95/5 as eluent; yield 2.2 g (50%). The compound was used in the next step without further characterization.

1-(Methylthio)-2-(1-propynyl)cyclohexene (10k) was prepared from 0.65 g (2.9 mmol) of **14** according to Normant et al.[20] The crude product was allowed to crystallize at −20 °C and was recrystallized from a small amount of hexane at −20 °C. For the yield and physical data see Table I.

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Registry No. 3a, 77416-12-7; **3b**, 40808-50-2; **3c**, 77416-13-8; **3d**, 77416-14-9; **3e**, 77416-15-0; **3f**, 77416-16-1; **4a**, 77416-17-2; **4b**, 77416-18-3; **4c**, 77416-19-4; **4d**, 77416-20-7; **4e**, 77416-21-8; **4f**, 77416-22-9; **7a**, 77416-23-0; **7b**, 77416-24-1; **10a**, 77416-25-2; **10b**, 77416-26-3; **10c**, 77416-27-4; **10d**, 77416-28-5; **10e**, 77416-29-6; **10f**, 77416-30-9; **10g**, 77416-31-0; **10h**, 77416-32-1; **10i**, 77416-33-2; **10j**, 77416-34-3; **10k**, 77416-35-4; **13**, 49571-45-1; **14**, 77416-36-5; 2-chloro-1-formylcyclohexene, 1680-73-5.

Supplementary Material Available: Table III showing elemental analyses and ^1H NMR data of compounds **3a–f**, **4a–f**, **7a–b**, **13**, and **14** (3 pages). Ordering information is given on any current masthead page.

C(15) Configuration of Isopimaren-15,16-diols and Sandaracopimaren-15,16-diols[1]

Ernest Wenkert* and Timothy D. J. Halls

Department of Chemistry, Rice University, Houston, Texas 77001

Paolo Ceccherelli* and Massimo Curini

Istituto di Chimica Organica della Facoltà di Farmacia, Università degli Studi, Perugia, Italy

Roberto Pellicciari*

Istituto di Chimica Farmaceutica e Tossicologica, Università degli Studi, Perugia, Italy

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The naturally occurring tricarbocyclic diterpenes of the pimarane skeletal type contain an increasing number of 15,16-diols (**1**). Whereas the stereochemistry of their rigid nuclear framework and of the substituents attached thereto could be determined readily by the spectral methods of analysis developed during the last three decades, the C(15) configuration has remained obscure in many cases in view of the nonrigid nature of the C(13)-attached dihydroxyethyl side chain. Recently there were introduced two procedures for the elucidation of the C(15) stereochemistry by ^{13}C NMR spectral analysis of cyclization products of the natural substances.[2,3] One of these new methods, developed for the analysis of pimaren-15,16-diols (**2**), was based on the isomerization of the olefinic diols into rigid (hydroxymethyl)tetrahydrofurans (**3**) and ^{13}C NMR spectral inspection thereof.[2] Since, in principle, this simple procedure is applicable also to sandaracopimaren-15,16-diols (**4**) and isopimaren-15,16-diols (**5**), its efficacy was investigated on diols derived from methyl sandaracopimarate (**6**) and virescenol B diacetate (**7**).

(1) Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances. 73. For the previous paper see: E. Wenkert, E. W. Hagaman, N.-y. Wang, G. E. Gutowski, and J. C. Miller, *Heterocycles*, **15**, 255 (1981).

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