Ester-Directed Alkene Functionalization. A Potential Approach to Trichothecene Synthesis

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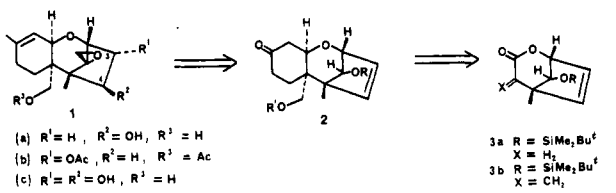
Construction of potential key intermediate **3b** for trichothecene synthesis is explored, on the basis of an ester-assisted alkene functionalization, which leads to a short synthesis of lactone **3a**. Evaluation of the directing effect of ester functionality on epoxidation of a neighboring double bond was carried out by using a number of cyclohexene and cycloheptene derivatives.

Trichothecenes exemplified by verrucarol (**1a**), calonectrin (**1b**), and scirpene-3,4,15-triol (**1c**), which show potent cytotoxicity have been extensively investigated in terms of their potential pharmacological application[1] and their total synthesis.[2] Considerable success for the latter has been achieved recently, on the basis of the realization[2b,c] that a suitable cyclopentanoid intermediate (C ring) can be converted to the tricyclic system present in 1. However, most of these approaches have been targeted toward a single natural product. Consequently, we have sought to develop a route which would allow introduction of oxygen functionality at C(3) and/or C(4) at an advanced stage, allowing the synthesis of **1a–c**, as well as more highly functionalized derivatives, from a common intermediate. A retrosynthetic analysis is shown in Scheme I, in which the C–ring unsaturation in **2** would allow introduction of the necessary hydroxy groups, as recognized in earlier approaches to the trichothecene family [see White et al. and Trost et al., ref 2a, 2b]. The intermediate **2** was expected to be available by manipulation of lactone **3a** by using the α-methylenation and cycloaddition sequences developed by others. Thus, our primary objective became the controlled and efficient construction of **3a** and its further manipulation. During the course of this study it became apparent that ester functionality exerts a significant stereochemical directing effect during reaction of a neighboring double bond with certain electrophiles. This paper describes an investigation of such directing power for a range of compounds and a short synthesis of the lactone **3a** which utilizes the observed stereocontrol.

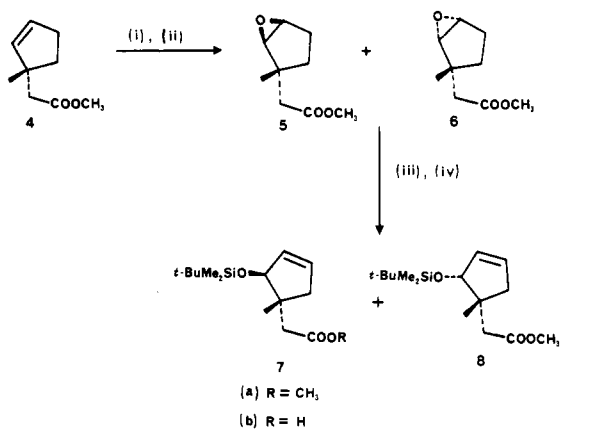
Results and Discussion

(A) Epoxidation of Unsaturated Esters. Evaluation of a Directing Effect from Ester Carbonyl Oxygen.

Scheme I



Scheme II[a]



[a] Reagents: (i) *N*-iodosuccinimide, Me_2SO, H_2O, 18 °C, 2 h; (ii) DBU, CH_2Cl_2, 20 °C, 15 h; (iii) *t*-$BuMe_2SiI$, CH_3CN, 0 °C, (iv) DBU, THF, reflux, 48 h.

Table I. Direct Epoxidation on 4[a]

compd	epoxidation conditions	ratio 5:6
4	MCPBA, Na_2HPO_4 CH_2Cl_2, 0 °C or 20 °C	1:1.5–2.0
4	$Mo(CO)_6$, *t*-BuOOH CH_3CN, reflux	1:4
4	PhCN, MeOH, $KHCO_3$ H_2O_2	1:1.8

[a] Yields are given in the Experimental Section.

For ease of manipulation of intermediates at several stages in the proposed sequence, it was essential to produce **3** with the stereochemistry depicted.[3] This required the conversion of the cyclopentene **4**, prepared from 3-methyl-2-cyclopentenyl acetate,[4] to epoxide **5**. Direct epoxidation of the alkene **4** with MCPBA in the presence of Na_2HPO_4 in CH_2Cl_2 resulted in a mixture of two epoxides, namely, α-epoxide **6** and the desired β-epoxide **5**, in a ratio of 1.5–2.0:1 (Scheme II). Molybdenum-catalyzed epoxidation[5a] led to a 4:1 ratio of **6** to **5**. Payne epoxidation[5b]

(1) Reviews: Tamm, Ch. *Fortsch. Chem. Org. Naturst.* **1974**, *31* 63. Bamburg, J. R.; Strong, F. M. *Microbial Toxins*, Vol. 7; Kadis, S., Ciegler, A., Ajl, S. J., Eds.; Academic Press: New York, 1971; pp 207–292. Doyle, T. W.; Bradner, W. T. *Anticancer Agents Based on Natural Product Models*, Cassady, J. M., Douros, J. D., Eds.; Academic Press: New York, 1980; pp 43–72.

(2) (a) Colvin, E. W.; Malchenko, S.; Raphael, R. A.; Roberts, J. S. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2069; **1978**, 658. Fujimoto, Y.; Yokura, S.; Nakanura, T.; Morikawa, T. *Ibid.* **1976**, 1691. Welch, S. C.; Wang, R. Y. *Ibid.* **1972**, 1853. Goldsmith, D. J.; Lewis, A. J.; Still, W. C. *Ibid.* **1973**, 4807. Trost, B. M.; Rigby, J. H. *J. Org. Chem.* **1978**, *43*, 2938. Anderson, W. K.; Lee, G. E. *Ibid.* **1980**, *45*, 501. Welch, S. C.; Rao, A. S. C. P.; Gibbs, C. G.; Wong, R. Y. *Ibid.* **1980**, *45*, 4077. Roush, W. R.; D'Ambra, T. E. *Ibid.* **1980**, *45* 3927. White, J. D.; Matsui, T.; Thomas, J. A. *J. Org. Chem.* **1981**, *46*, 3376. Goldsmith, D. J.; John, T. K.; Kwong, C. D.; Painter, G. R., III. *Ibid.* **1980**, *45*, 3989. Kodama, M.; Takahashi, T.; Kurahara, T.; Ito, S. *Tetrahedron Lett.* **1980**, *21*, 2811. Still, W. C.; Tsai, M.-Y. *J. Am. Chem. Soc.* **1980**, *102*, 3654. Pearson, A. J.; Ong, C. W. *Ibid.* **1981**, *103*, 6686. Koreeda, M.; Luengo, J. I. *J. Org. Chem.* **1984**, *49*, 2079. (b) Brooks, D. W.; Grothaus, P. G.; Mazdiyasni, H. *J. Am. Chem. Soc.* **1983**, *105*, 4472. Trost, B. M.; McDougal, P. G. *Ibid.* **1982**, *104*, 6110. Trost, B. M.; McDougal, P. G.; Haller, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 383. Kraus, G. A.; Roth, D.; Frazier, K.; Shimagaki, M. *Ibid.* **1982**, *104*, 114. (c) Schlessinger, R. H.; Nugent, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 116. Roush, W. R.; D'Ambra, T. E. *Ibid.* **1983**, *105*, 1058.

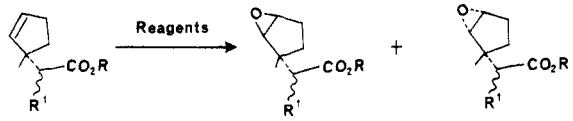
(3) This avoids unwanted cyclizations during the other stages should the protected alcohol be demasked and allows easier manipulation of the early intermediates to give the desired lactone.

(4) Full details for this conversion on a 20-g scale are given in: Pearson, A. J.; Chen, Y. S.; Han, G. R.; Hsu, S. Y.; Ray, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 267.

(5) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Carlson, R. G.; Behn, N. S. *J. Org. Chem.* **1967**, *32*, 1363.

0022-3263/86/1951-2505$01.50/0

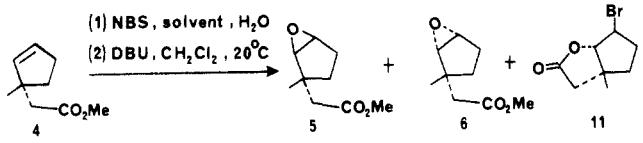
Table II. Direct Epoxidation on 9 and 10[a]



	product ratio	
	β-epoxide	α-epoxide
9, R = TBDMS, R^1 = H		
MCPBA, Na_2HPO_4 CH_2Cl_2, −10 °C	1	1.7
$Mo(CO)_6$, *t*-BuOOH PhH, reflux, 4 h	1	2.8
$Mo(CO)_6$, *t*-BuOOH CH_3CN, reflux, 8 h	1	4.7
10, R = CH_3, R^1 = CH_3		
MCPBA, Na_2HPO_4 CH_2Cl_2	1	2
$Mo(CO)_6$, *t*-BuOOH PhH, reflux	1	5

[a] Yields are given in the Experimental Section.

Table III. Indirect Epoxidation on 4 Using *N*-Bromosuccinimide[a]



		ratio		
solvent (temp, °C)	reactn time	5	6	11
Me_2SO (10)	0.5 h	1.4	1	none
Me_2SO (62)	5 min	1.6	1	0.2
CH_3CN (20)	3 d	1.8	1	0.8
CH_3COCH_3 (20)	8 d	2.6	1	0.3
THF (20)	6 h	1	1	1

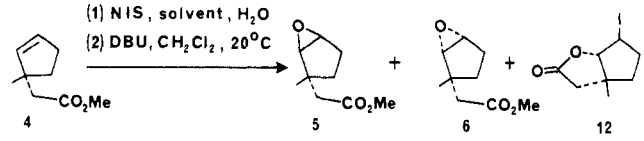
[a] Yields are given in the Experimental Section.

gave almost the same selectivity as MCPBA in favor of **6**. These results are summarized in Table I. An authentic sample of **6** was secured by the following transformations: (1) hydrolysis of **4** to the corresponding carboxylic acid (KOH, CH_3OH, H_2O), (2) iodo lactonization (I_2, saturated $NaHCO_3$ solution, THF/ether), (3) methanolysis of the lactone (K_2CO_3, CH_3OH).[6] The proton NMR spectra of **5** and **6** exhibit clear differences in chemical shifts for methylene (CH_2CO_2Me) and methyl group protons. Owing to a deshielding effect exerted by oxirane oxygen, a downfield shift was observed for the methyl protons of **5** and the methylene protons of the ester side chain on **6**. The same assignments were also made for the analogues of **5** and **6** in other cases.

Attempted alteration of the steric bulk of either the ester portion or the position α to the carbonyl in **4**, as in **9** and **10**, did not reverse the trend in favor of the formation of α-epoxides as shown in Table II. This implies that the ester carbonyl oxygen may have a directing effect on molybdenum-catalyzed epoxidation.

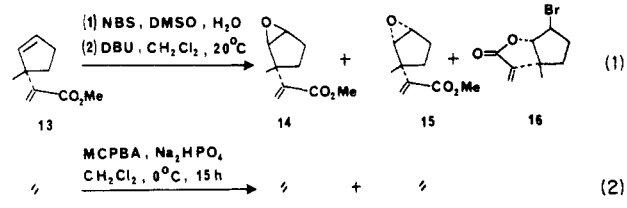
We then proceeded to pursue other alternatives such as indirect epoxidation via halohydrin formation, hopefully, to enhance selectivity toward β-epoxide. On treatment of the alkene **4** with *N*-bromosuccinimide (NBS) in wet Me_2SO,[7] followed by closure of the bromohydrin, the desired β-epoxide was indeed isolated as the major component with a 1.4:1 ratio. In some cases where various solvents were used, bromo γ-lactone was concurrently produced probably due to bromo lactonization which competed in the reaction (Table III). The use of *N*-iodosuccinimde (NIS) in this reaction turned out to be more rewarding. Using this reagent the desired β-epoxide **5** was obtained in a 4:1 ratio over **6** when the reaction was performed in Me_2SO, although other solvent systems failed to give satisfactory results (Table IV). A preliminary investigation of indirect epoxidation of α-methylene ester **13** via bromohydrin formation was equally encouraging, and the desired β-epoxide **14** was produced almost exclusively, accompanied by trace amounts of **15** and **16** (eq 1). In sharp contrast, on epoxidation of **13** with MCPBA, a similar result was obtained as before in which **15** was predominant over **14** (ratio of 2:1, eq 2).

Table IV. Indirect Epoxidation on 4 Using *N*-Iodosuccinimide[a]



		ratio		
solvent (temp, °C)	reactn time	5	6	12
Me_2SO (10)	20 min	4	1	none
CH_3CN (20)	1 h	2.3	1	1.7
CH_2Cl_2 (20)	1 h	1.7	1	2.3
CH_3COCH_3 (20)	3 h	1.2	1	1

[a] Yields are given in the Experimental Section.



Since the above results obtained for either direct or indirect epoxidation of various substrates were suggestive of a directing effect from the ester carbonyl oxygen, we were prompted to investigate similar reactions on a series of compounds designed to probe the effect further. The results are summarized in Table V.

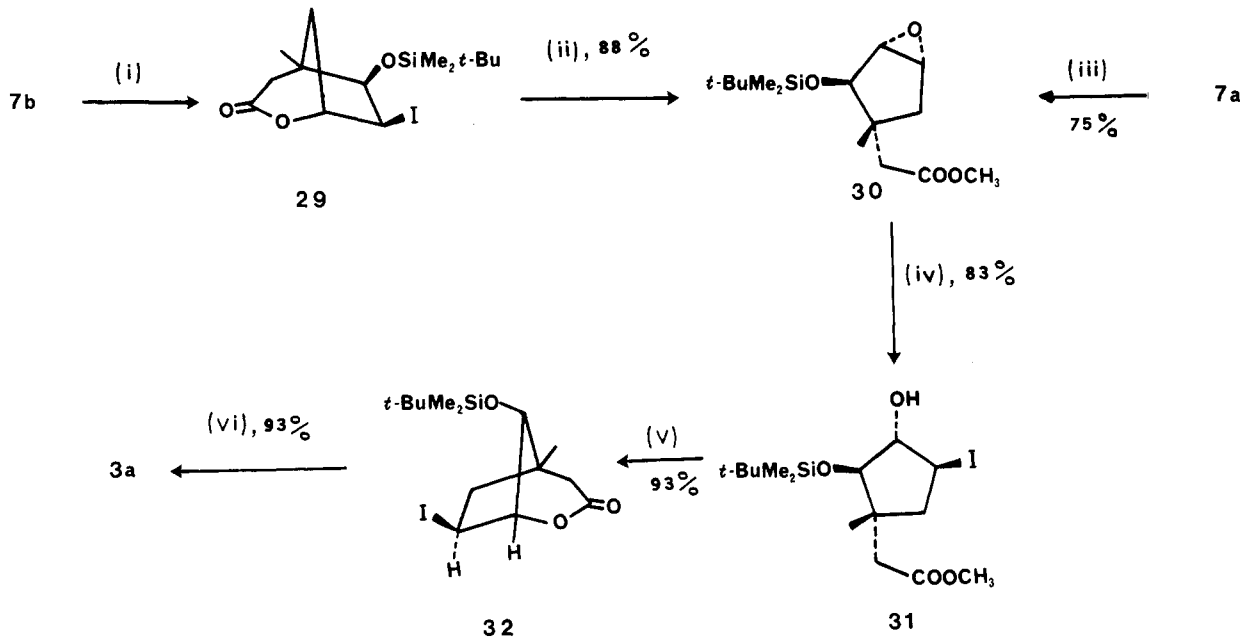
Direct epoxidation using MCPBA or *t*-BuOOH/$Mo(CO)_6$ was studied for compounds **17**, **18**, **19**, **23**, **24**, and **25** in which R = Et was chosen as the reference compound, assuming that the steric requirements of the ethyl substituent approximate to those of the CH_2CO_2Me group.

It is immediately apparent that the ester group has a significant directing effect during $Mo(CO)_6$-catalyzed epoxidation, and a rather variable effect during reaction with MCPBA. Owing to the pronounced chair shape of cycloheptene the stereocontrol from CH_2CO_2Me in **24** works against a strong conformational and steric bias, so the molybdenum-catalyzed reaction still gives predominantly anti epoxide, but less than the ethyl-substituted derivative **23**. The directing effect is more noticeable with the flatter cyclohexene derivative **18** (compared to **17**) which now gives a very high proportion of syn epoxide. The results obtained from allylic acetates **19** and **25** are extremely interesting, since it has been commonly assumed that acetylation of allylic alcohols leads to complete loss of stereodirecting power in these reactions.[8] Our results

(6) (a) Bartlett, P. A.; Myerson, J. *J. Am. Chem. Soc.* **1978**, *100*, 3950. (b) Chamberlin, A. R.; Dezube, M.; Dussault, P. *Tetrahedron Lett.* **1981**, *22*, 4611.

(7) Adapted from the bromohydrin procedure described in: Dalton, D. R.; Dutha, V. P.; Jones, D. C. *J. Am. Chem. Soc.* **1968**, *90*, 5498. There does appear to be a general directing effect from the ester group during iodohydrin formation, see also: Grieco, P. A.; William, E.; Sugahara, T. *J. Org. Chem.* **1979**, *44*, 2194. Metz, P.; Shafer, H. J. *Tetrahedron Lett.* **1982**, *23*, 4067. The origins of this effect are presently not understood and will be further investigated.

Scheme III[a]



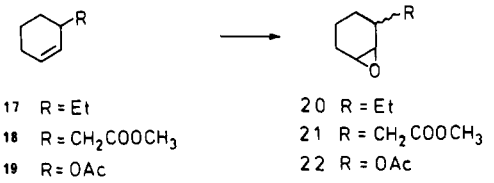
[a] Reagents: (i) I_2, Et_2O, THF, H_2O, $NaHCO_3$, 0 °C, 15 min; (ii) K_2CO_3, MeOH, 20 °C, 15 h; (iii) *t*-BuOOH (4 equiv), $Mo(CO)_6$ (5 mol), PhH, reflux, 5 h; (iv) Me_3SiI, DBN, CH_3CN, 0 °C; (v) *p*-TsOH·H_2O, C_6H_6, reflux, 1 h; (vi) DBN, DME, 105 °C, 64 h.

clearly show that the allylic acetoxy group is a very useful stereocontrol element, since epoxidation of **25** proceeds against the conformational bias, and we were unable to detect any anti epoxide from **19** in the 200-MHz ^1H NMR spectrum of crude products. These results are in contrast to those of Sharpless[8] but in agreement with the work of the Tolstikov group[9] who have reported that remote groups will direct the stereochemistry epoxidation (although allylic acetates were not studied).

In conclusion, the results of $Mo(CO)_6$-catalyzed epoxidation of compounds **17**, **18**, **19**, **23**, **24**, and **25** provides supporting evidence for a directive effect imposed by the ester moiety as previously observed for **4**, **9**, and **10**. The same effect might also account for the results obtained for indirect epoxidation of **4** and **13** via halohydrin intermediates, although more detailed studies are required before a full evaluation is possible.[7]

(B) Further Manipulation of Epoxide 5 To Give Lactone 3a. With a 4:1 mixture of **5** and **6** (Table V, entry 1) in hand, we were confronted with the problem of opening of the epoxides to give allylic alcohol derivatives. A number of standard procedures[10] for this conversion uniformly failed with **5** and **6**, but successful transformation of the mixture to protected alcohols **7** and **8** was accomplished by using *tert*-butyldimethylsilyl iodide, followed by base treatment of the intermediate iodo ether derivative[11] (Scheme II). The desired compound **7a** was easily separated from the mixture and we now required to convert this to the iodo lactone **32**.

Table V. Direct Epoxidation on 17, 18, 19, 23, 24, and 25



17 R = Et
18 R = CH_2COOCH_3
19 R = OAc

20 R = Et
21 R = CH_2COOCH_3
22 R = OAc

23 R = Et
24 R = CH_2COOCH_3
25 R = OAc

26 R = Et
27 R = CH_2COOCH_3
28 R = OAc

compd	epoxidtn condtns	product(s)	syn epoxide: anti ratio[a]	yield (%)[b]
4	MCPBA	**6:5**	1.5:1[c]	80
4	*t*-BuOOH/$Mo(CO)_6$	**6:5**	4:1[c]	70
17	MCPBA	**20**	1.0:0.9	92
18	MCPBA	**21**	2.3:1	98
19	MCPBA	**22**	1:1.5	90
17	*t*-BuOOH/$Mo(CO)_6$	**20**	1:6.5	63
18	*t*-BuOOH/$Mo(CO)_6$	**21**	15:1	66
19	*t*-BuOOH/$Mo(CO)_6$	**22**	100:0	45
23	MCPBA	**26**	1:1.5	85
24	MCPBA	**27**	1:1.2	95
25	MCPBA	**28**	1.6:1	92
23	*t*-BuOOH/$Mo(CO)_6$	**26**	1:4.2	85
24	*t*-BuOOH/$Mo(CO)_6$	**27**	1:2	82
25	*t*-BuOOH/$Mo(CO)_6$	**28**	5.2:1	72

[a] Determined by 200-MHz NMR. [b] Isolated yield. [c] Taken from Table I.

(8) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. These authors report a 40:60 syn:anti epoxide ratio on treatment of **6** with *t*-BuOOH/$Mo(CO)_6$. During the epoxidation of **19**, a sample was withdrawn from the reaction mixture at 0.5 h, 1.0 h, 2.0 h, and 4.0 h intervals. No anti epoxide was ever detected by 200-MHz NMR on the crude product after workup. However, in another experiment where a mixture of syn and anti epoxides was heated under reflux with a catalytic amount of $Mo(CO)_6$ and *t*-BuOOH, it was found that syn and anti epoxides both underwent decomposition and the latter appeared to proceed faster than the former. The acetoxy group has a directing effect, but the magnitude is difficult to evaluate.

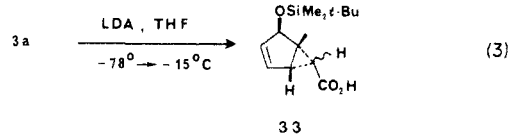
(9) Yurēv, V. P.; Gailyunas, I. A.; Spirikhin, L. V.; Tolstikov, G. A. *J. Gen. Chem. USSR* **1975**, *45*, 2269. Tolstikov, G. A.; Yurēv, V. P.; Gailyunas, I. A.; Rafikov, S. R. *Dokl. Akad. Nauk. USSR* **1974**, *214*, 120. Tolstikov, G. A.; Dzhemileu, D. M.; Yurēv, V. P.; Rafikov, S. R. *Ibid.* **1973**, *208*, 376.

(10) (a) Sharpless, K. B.; Lauver, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697. (b) Murata, S.; Suzuki, M.; Noyori, R. *Ibid.* **1979**, *101*, 2738. (c) Corey, E. J.; Marfat, A.; Falck, J. R.; Albright, J. O. *Ibid.* **1980**, *102*, 1433. (d) Rickborn, B.; Thummel, R. P. *J. Org. Chem.* **1969**, *34*, 3583.

(11) Detty, M. R. *J. Org. Chem.* **1980**, *45*, 924; *Tetrahedron Lett.* **1978**, 5087.

Surprisingly, direct iodo lactonization of the derived carboxylic acid **7b** (I_2, ether/THF, saturated $NaHCO_3$ solution, 0 °C, 15 h) gave *only* the undesired lactone **29** (Scheme III).[12] Consequently, **7a** was converted to epoxide **30** by using *t*-BuOOH/$Mo(CO)_6$,[5,13] and this epoxide was treated with trimethylsilyl iodide to afford a single iodohydrin, in which the silyl protection was not retained, and which was assigned the structure **31** by NMR spectroscopy and subsequent transformations. Direct conversion of **31** to the iodo lactone **32**, followed by dehydrohalogenation (DBN, DME, 105 °C, 64 h), provided the desired lactone intermediate **3a** in 93% yield.

Attempted methylenation of **3a** using various methods[2c,14] proved to be more problematic than anticipated. The enolate derived from **3a** by treatment with LDA in THF at −78 °C was found to rearrange, giving an approximately 1:1 mixture of stereoisomeric bicyclo[3.1.0]hexene derivatives **33** on warming from −78 °C to −15 °C (eq 3).[15] It is thus clear that introduction of α-methylene



33 (3)

functionality has to be effected at an early stage, prior to the formation of the [3.2.1] lactone system in order to avoid this unexpected rearrangement. Methylenation of **4** proceeded with no difficulty to afford **13** which was subjected to indirect epoxidation as described previously (eq 1) to provide the desired epoxide **14** as a major product. Further elaboration of **14** to the α-methylene lactone **3b** and thence to a variety of trichothecenes is currently under investigation and will be reported in due course.

Experimental Section

Infrared spectra were recorded with a Perkin-Elmer Model 1420 instrument and NMR spectra with Varian EM-360 or XL-200 spectrometers. Mass spectra were kindly provided by Professor H. Andrist, Cleveland State University, and by Dr. R. P. Lattimer, and BF Goodrich Company, Brecksville, OH. Melting points are uncorrected. All solvents used were freshly distilled under nitrogen as follows: tetrahydrofuran (THF) and benzene from Na/benzophenone; ether from $LiAlH_4$; acetonitrile from CaH_2. Compounds which were characterized by IR, NMR, and mass spectra data only were ascertained to be >95% pure by sharp melting point, TLC, and/or HPLC (Gilson 802 instrument) and 200-MHz NMR spectroscopy, unless otherwise stated.

Methyl (1-Methyl-2,3-epoxycyclopentyl)acetate (5 + 6). To a stirred solution of wet Me_2SO (30 mL containing 0.56 mL of H_2O) were simultaneously added through pressure-equalizing funnels 1.2 equiv of *N*-iodosuccinimide in Me_2SO (50 mL) (2 drops/s) and the alkene **4** (4 g, 0.026 mol) in Me_2SO (20 mL) (1 drop/s) at 18 °C (bath temperature) under Ar. After addition, the reaction mixture was stirred for 2 h. The resulting reddish solution was quenched with H_2O (20 mL) and extracted with ether (200 mL × 5). The combined ethereal layers were washed with H_2O (50 mL × 3) and brine (50 mL × 2), dried over $MgSO_4$, and concentrated. The residue was taken up by dichloromethane, followed by addition of 1.2 equiv of DBU. The solution was stirred at 20 °C for 15 h. The solvent was removed and replaced with ether (200 mL). The ethereal layer was washed with 2 M HCl (10 mL), saturated Na_2CO_3 solution (10 mL), H_2O (20 mL × 2), and brine (20 mL), dried $MgSO_4$, and concentrated. The residue was subjected to short-path distillation under reduced pressure. The epoxides were collected at 90–94 °C (13 mmHg) as a colorless liquid (1.7 g, 64%, based on recovered starting material; β-epoxide:α-epoxide = 4:1 by 200-MHz NMR) with recovery of the starting material (1.6 g): ν_{max} ($CHCl_3$) 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) (major product β-epoxide) δ 3.66 (s, 3 H, OCH_3), 3.43 (d, 1 H, epoxide H), 3.27 (br s, 1 H, epoxide H), 2.23 (2 H, CH_2CO_2Me), 2.04–1.94 (m, 2 × CH_2, CH_2 epoxide), 1.76–1.21 (m, 2 × CH_2), 1.20 (s, 3 H, CH_3). All the peaks of the minor α-epoxide **16** coincide with those of the major product except 2.45 (2 H, CH_2CO_2Me) and 0.99 (s, 3 H, CH_3); MS, *m/z* (rel intensity) (chemical ionization) 170 (M^+, 1.3), 171 (M + 1, 5.0), 199 (M + 29, 1.2), 138 (M − 31, 100), 111 (M − 59, 8.9).

Methyl (1-Methyl-2-((*tert*-butyldimethylsilyl)oxy)-3-cyclopentenyl)acetate (7a + 8). To a solution of the epoxides **5** and **6** (2.44 g, 14.4 mmol) in CH_3CN (15 mL) was dropwise added at 0 °C 1.5 equiv of *t*-$BuMe_2SiI$, generated by addition of 1.5 equiv of freshly prepared *t*-$BuMe_2SiSePh$ (5.84 g = 4.82 mL, 22 mmol) (aged *t*-$BuMe_2SiSePh$ would result in a poor yield of the final product) to a solution of 0.75 equiv of I_2 (2.73 g, 11 mmol) in CH_3CN (7 mL) at 20 °C. Immediately after the addition, the reaction mixture was quenched with saturated $NaHCO_3$ solution (20 mL) and extracted with ether (100 mL × 2). The ethereal extract was washed with 10% $Na_2S_2O_3$ solution to remove excess I_2 (if necessary), H_2O (20 mL × 3), and brine (20 mL), dried over $MgSO_4$, and concentrated. The residue was taken up by distilled THF (40 mL), followed by addition of 1.5 equiv of DBU (3.28 g, 22 mmol). The solution was refluxed for 48 h. After being cooled to room temperature, the reaction mixture was diluted with ether (200 mL), washed with 2 M HCl (20 mL), then with saturated $NaHCO_3$ solution (20 mL), dried over $MgSO_4$, and concentrated. The residue was subjected to HPLC (Whatman M 20, 10/25) eluted with 5% *tert*-butyl methyl ether in hexane (40 mL/min) to afford the allylic β-OTBDMS alkene **7a** (2.1 g) and α-OTBDMS alkene **8** (0.5 g) with a total yield of 63%.

7a (major product): ν_{max} ($CHCl_3$) 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.78–5.75 (m, 1 H, vinyl), 5.59–5.56 (m, 1 H, vinyl), 4.48 (s, 1 H, C*H*(OTBDMS)), 3.63 (s, 3 H, OCH_3), 2.35–2.33 (3 H, CH_2CO_2Me and one of allylic CH_2), 2.26 (1 H, m one of allylic CH_2), 1.03 (s, 3 H, CH_3), 0.88 (s, 9 H, $SiCMe_3$), 0.05 (s, 6 H, $SiMe_2$); MS, *m/z* (rel intensity) (chemical ionization) 284 (M^+, 5.1), 285 (M + 29, 20.3), 3.25 (M + 41, 12.8), 269 (M − 15, 100).

8: ν_{max} ($CHCl_3$) 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.84–5.80 (m, 1 H, vinyl), 5.66–5.63 (m, 1 H, vinyl), 4.28 (s, 1 H, CH(OTBDMS), 3.64 (s, 3 H, OCH_3), 2.49 (1 H, m, one of allylic CH_2), 2.46 and 2.38 (AB q, J_{AB} = 16 Hz, 2 H, CH_2CO_2Me), 2.06 (1 H, one of allylic CH_2), 1.10 (s, 3 H, CH_3), 0.86 (s, 9 H, $SiCMe_3$), 0.043 (s, 3 H, $SiMe_2$), 0.035 (s, 3 H, $SiMe_2$); MS, *m/z* (rel intensity) (chemical ionization) 284 (M, 19.3), 285 (M + 1, 95.0), 313 (M + 29, 100), 325 (M + 41, 50.3).

(1-Methyl-2-((*tert*-butyldimethylsilyl)oxy)-3-cyclopentenyl)acetic Acid (7b). The ester **7a** (0.1 g, 0.35 mmol) was hydrolyzed with methanolic KOH solution (0.55 g in 15 mL of methanol and 5 mL of H_2O) at 20 °C. After 15 h, ether (20 mL) was added and the pH of the solution was adjusted to 3 with oxalic acid. The mixture was then extracted with ether (100 mL). The organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated to furnish the carboxylic acid **7b** (0.95 g, 100%) as a colorless oil, which was used for iodo lactonization without further purification: ν_{max} ($CHCl_3$) 1708 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.80–5.75 (m, 1 H, vinyl), 5.61–5.56 (m, 1 H, vinyl), 4.52 (1 H, C*H*(OTBDMS)), 2.38 (s, 2 H, CH_2CO_2Me), 2.33 (1 H, allylic CH_2), 2.28 (1 H, allylic CH_2), 1.07 (s, 3 H, CH_3), 0.87 (s, 9 H, $SiCMe_3$), 0.05 (s, 6 H, $SiMe_2$).

Methyl α-(1-Methyl-2-cyclopentenyl)acrylate (13). To a solution of LDA in THF, derived from slow addition of 1.2 equiv of *n*-BuLi in hexanes (2.3 M, 1.7 mL) to diisopropylamine (0.6 mL, 4.29 mmol) in anhydrous THF (2 mL) at −2 °C under Ar, was dropwise added the ester **4** (500 mg, 3.25 mmol) at −78 °C. Five minutes after the addition, the reaction was quenched with

(12) Apparently the eclipsing of C–I and C–O bonds in the transition state leading to **23** is less unfavorable than the nonbonded interactions in that leading to **26** in which the iodide and trialkylsilyl groups are forced into close proximity (pseudo-1,3-diaxial interaction).

(13) The stereochemistry of direct epoxidation was confirmed by converting the iodo lactone **23** to epoxide **24** (K_2CO_3, MeOH, 20 °C, 15 h). Use of *m*-chloroperoxybenzoic acid on **7a** gave a 4:1 mixture of stereoisomeric epoxides in favor of **24**, in contrast to the single isomer obtained by the *t*-BuOOH/$Mo(CO)_6$ procedure.

(14) (a) Adapted for the preparation of **13**. (b) Roberts, J. L.; Borromeo, P. S.; Poulter, C. D. *Tetrahedron Lett.* **1977**, 1621.

(15) Consistent with the observation made by Roush et al.: Roush, W. R.; D'Ambra, T. E. *J. Org. Chem.* **1981**, *46*, 5045.

a solution of diphenyl diselenide (1.22 g, 3.9 mmol) in HMPA (0.7 mL) and THF (1 mL) at −78 °C. The resulting solution was stirred at −78 °C for another 0.5 h and warmed to −20 °C, then stirred for 0.5 h at that temperature. Brine was added, followed by dilution with ether (100 mL). The organic layer was washed with H_2O and brine, dried over $MgSO_4$, and concentrated to afford the crude α-phenylselenyl ester (1 g, ~100% yield), whose NMR spectrum indicated the absence of the starting ester. It was employed for the next transformation without further purification.

The second deprotonation of the α-phenylselenyl ester was effected in the same way as the first one and the corresponding enolate was treated with CH_3I. After workup, the residue was taken up with THF (10 mL) and the solution was cooled to 0 °C. To this solution was added hydrogen peroxide (30%) (4.1 mL). The solution was stirred for 2 h at 0 °C and worked up as usual to give **13** (300 mg, 63% from (**4**) after short-path distillation (bp 68 °C (9 mmHg)): ν_{max} ($CHCl_3$) 1720, 1624 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ 5.9 and 5.5 (s, 1 H each, 2 H, methylenic H), 5.7 (s, 2 H, vinyl), 3.8 (s, 3 H, OCH_3), 2.5–1.8 (m, 4 H, 2 × CH_2), 1.3 (s, 3 H, CH_3); MS, *m/e* (field desorption) 166 (M^+). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.3; H, 8.49. Found: C, 72.1: H, 8.63.

3-Ethylcyclohexene (17). To an ethereal solution of 3-bromocyclohexene (3 g, 0.0186 mol) was added dropwise 6.7 mL of freshly prepared ethylmagnesium bromide (3.34 M in ether) at 20 °C. The solution was stirred for 2 h and poured into ice–water, containing a few drops of concentrated H_2SO_4. The aqueous layer was extracted with ether (100 mL). The combined organic layers were washed with saturated NH_4Cl solution, H_2O, and brine, dried over $MgSO_4$, and concentrated. The residue was distilled under reduced pressure to afford the coupled product **17** (1.3 g, 65%) as a colorless liquid (bp 42–44 °C/(30 mmHg)): ν_{max} (CCl_4) 1650 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.72–5.54 (m, 2 H, vinyl), 2.0–1.10 (m, 9 H, 4 × CH_2 + methine CH), 0.91 (t, J = 7.2 Hz, 3 H, CH_3).

Methyl (2-Cyclohexenyl)acetate (18). To a solution of LDA, freshly generated by adding 1.6 M *n*-BuLi in hexanes (36 mL, 57.1 mmol) to diisopropylamine (8 mL, 57.1 mmol) in 20 mL of anhydrous THF at 0 °C, was added acetic acid (1.6 mL, 27.3 mmol) and HMPA (9.6 mL, 54.6 mmol) at 0 °C for 1 h. To this solution was added 3-bromo-1-cyclohexene (4 g, 0.025 mol) in 10 mL of anhydrous THF and the mixture was stirred for 2 h. The solution was quenched with H_2O, acidified to pH 1, and extracted with ether (200 mL). The organic layer was washed with dilute HCl solution, H_2O, and brine, dried over $MgSO_4$, and concentrated. The residue was taken up with acetone (50 mL) and treated with K_2CO_3 (4.4 g) and dimethyl sulfate (3 mL). The mixture was heated under reflux for 7 h, cooled to 20 °C, and diluted with ether (200 mL), and 50% NH_4OH solution (20 mL) was added to destroy any excess of dimethyl sulfate. The organic layer was washed with 50% NH_4OH solution, H_2O, and brine, dried over $MgSO_4$, and concentrated. The residue was distilled under reduced pressure to give the ester (**18**) (2.4 g, 63%) as a colorless liquid (bp 92–93 °C (16 mmHg)): ν_{max} (CCl_4) 1740, 1648 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.72 (ddd, J = 10, 4.2, 3.7 Hz, 1 H, vinyl), 5.53 (dd, J = 10, 2.0 Hz, 1 H, vinyl), 3.68 (s, 3 H, OCH_3), 2.69–2.49 (m, 1 H, methine CH), 2.32 and 2.26 (AB part of ABX, J = 12, 3.9, 2.4 Hz, 2 H, CH_2CO_2Me), 2.0–1.91 (m, 2 H, allylic CH_2), 1.90–1.24 (m, 4 H, 2 × CH_2).

3-Acetoxy-1-cyclohexene (19). 3-Hydroxy-1-cyclohexene was acetylated by the standard method (2 equiv of pyridine and 2 equiv of acetic anhydride in CH_2Cl_2 at 20 °C). After workup, the residue was distilled under reduced pressure to afford **19** (81%) as a colorless liquid (bp 77–78 °C (18 mmHg)): ν_{max} (CCl_4) 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.99–5.90 (m, 1 H, vinyl), 5.73–5.67 (br d, J = 10 Hz, 1 H, vinyl), 5.24 (br s, 1 H, C*H*(OAc)), 2.05 (s, 3 H, $COCH_3$), 2.10–1.45 (m, 6 H, 3 × CH_2).

3-Ethyl-1-cycloheptene (23). The title compound was prepared in exactly the same way as for **17** (yield, 71%): ν_{max} (CCl_4) 1605 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.88–5.66 (m, 1 H, vinyl), 5.54 (dd, J = 11.1, 3.4 Hz, 1 H, vinyl), 2.24–1.16 (m, 11 H, 5 × CH_2 and methine CH), 0.90 (t, J = 7.4 Hz, 3 H, CH_3); high resolution mass spectrum (M), calcd for C_9H_{16} 124.1253, found 124.1239.

Methyl (2-cycloheptenyl)acetate (24): preparation same as **18**; ν_{max} (CCl_4) 1743, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.77 (ddt, J = 11.3, 6.2, 2.2 Hz, 1 H, vinyl), 5.50 (dd, J = 11.3, 3.7 Hz, 1 H, vinyl), 3.68 (s, 3 H, OCH_3), 2.86–2.76 (m, 1 H, methine CH), 2.40 and 2.35 (ABX, J = 14, 4.1, 3.7 Hz, 2 H, CH_2CO_2Me), 2.22–1.18 (m, 8 H, 4 × CH_2); high resolution mass spectrum (M), calcd for $C_{10}H_{16}O_2$ 168.1151, found 168.1148.

3-Acetoxy-1-cycloheptene (25): preparation same as **19**; ν_{max} (CCl_4) 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.88–5.72 (m, 1 H, vinyl), 5.60 (dt, J = 12, 1.5 Hz, 1 H, vinyl), 5.46–5.30 (m, J = 7.4 Hz, 1 H, CH(OAc)), 2.03 (s, 3 H, $COCH_3$), 2.21–1.52 (m, 8 H, 4 × CH_2).

Direct Epoxidation on 17, 18, 19, 23, 24, and 25. (a) With MCPBA at 0 °C: A 0.12 M solution of organic substrate in dichloromethane was treated with MCPBA, Na_2HPO_4. (b) With *t*-BuOOH/$Mo(CO)_6$: *t*-BuOOH (2–4 equiv) and $Mo(CO)_6$ (0.05–0.1 equiv) were added to a 0.12 M solution of the organic substrate in benzene at room temperature. The stirred mixture was rapidly heated to boiling in a preheated bath (90 °C) and refluxed for 1–4 h. Product ratios were determined from 200-MHz ^1H NMR spectrum together with analytical HPLC where epoxides were separable; good agreement was obtained between the two methods. Pure samples of the isomeric epoxides were obtained where these were separable by HPLC, and authentic samples of syn epoxides were obtained from **18** and **24** by iodo lactonization followed by treatment with K_2CO_3 in methanol.

The results are tabulated in Table VI.

(1-Methyl-2-((*tert*-butyldimethylsilyl)oxy)-3-iodo-4-hydroxycyclopentyl)acetic Acid Lactone (29). To a solution of the carboxylic acid **7b** (114 mg, 0.42 mmol) in ether (4 mL) and THF (4 mL) was added saturated $NaHCO_3$ solution (8 mL). The mixture was stirred for 20 min and cooled to 0 °C and iodine (426 mg, 1.68 mmol) and added. The mixture was stirred at 0 °C for 15 h and then diluted with ether (100 mL). The organic layer was washed with $Na_2S_2O_3$ solution, H_2O, and brine, dried over $MgSO_4$, and concentrated. The residue was submitted to flash chromatography and eluted with 40% ethyl acetate in hexane to provide the δ-lactone **29** (130 mg, 78%) as a white solid (mp 116–118 °C): ν_{max} ($CHCl_3$) 1742 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 5.01 (d, J = 2 Hz, 1 H, CHO lactone), 4.76 (dd, J = 6, 2 Hz, 1 H, CHI), 3.47 (d, J = 6 Hz, 1 H, CHOSi), 2.55 and 2.45 (AB q, J_{AB} = 18 Hz, 2 H, CH_2CO_2R), 2.10 (d, J = 14 Hz, 1 H, bridge proton), 1.58 (d, J = 14 Hz, 1 H, bridge proton), 1.12 (s, 3 H, CH_3), 0.96 (s, 9 H, $SiCMe_3$), 0.07 and 0.06 (2 s, 6 H, $SiMe_2$); MS, *m/z* (rel intensity) (chemical ionization) 397 (M + 1, 53), 425 (M + 29, 5), 437 (M + 41, 1), 381 (M − 15, 6.8), 269 (M − 127, 12), 265 (M − 131, 85). Anal. Calcd for $C_{14}H_{25}O_3SiI$: C, 42.4; H, 6.36. Found: C, 42.5; H, 6.34.

Methyl (1-Methyl-2-((*tert*-butyldimethylsilyl)oxy)-3,4-epoxycyclopentyl)acetate (30). (a) From 7a. To a solution of the olefinic ester **7a** (251 mg, 0.88 mmol) in dry benzene (7 mL) was added a catalytic amount (5% molar equiv) of molybdenum hexacarbonyl (11.7 mg, 0.044 mmol) and 90% *tert*-butyl hydroperoxide (0.21 mL, 3.53 mmol). The reaction mixture was heated under reflux for 5 h. After cooling to room temperature, it was diluted with ether (100 mL), washed with 10% sodium bisulfite solution (5 mL × 2), water (10 mL × 2), and brine (10 mL), and dried over $MgSO_4$. The solvent was evaporated and the residue was subjected to HPLC (20% ethyl acetate in hexane, M20, flow rate: 30 mL/min) to afford the pure epoxide **30** (200 mg, 75%) as a colorless liquid.

(b) **From 29.** To a solution of the δ-lactone **29** (142 mg, 0.36 mmol) in methanol (5 mL) was added 2.1 equiv of K_2CO_3 (104 mg, 0.75 mmol). The reaction mixture was stirred at 20 °C for 15 h, diluted with ether (100 mL), washed with H_2O and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed (25% ethyl acetate in hexane) to afford **30** (95 mg, 88%) as a colorless liquid: ν_{max} ($CHCl_3$) 1733 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 4.09 (s, 1 H, C*H*(OTBDMS)), 3.63 (s, 3 H, OCH_3), 3.51 (bs, epoxide H), 3.34 (1 H, epoxide H), 2.43 and 2.35 (AB q, J_{AB} = 15 Hz, 2 H, CH_2CO_2Me), 2.07 (d, J_{gem} = 15 Hz, 1 H, one of CH_2), 1.64 (d, J_{gem} = 15 Hz, 1 H, one of CH_2), 0.91 (s, 9 H, $SiCMe_3$), 0.12 (s, 3 H, $SiMe_2$), 0.10 (s, 3 H, $SiMe_2$); high resolution mass spectrum (M − C_4H_9), calcd for $C_{11}H_{19}O_4Si$ 243.1053, found 243.1051.

Methyl (1-Methyl-3-iodo-4-hydroxy-5-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)acetate (31). To a stirred solution of the epoxide **30** (121 mg, 0.403 mmol) in dry CH_3CN (1.5 mL) containing 0.5 equiv of DBN (25 μL) was added 1.2 equiv of

Table VI.

compd	spectroscopic data
20a (as mixture)	^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.20–3.06 (m, 2 H, epoxide H), 1.90–0.70 (m, 12 H), 0.98 (t, J = 8 Hz, 3 H, CH_3)
20b (as mixture)	all the NMR signals coincide with or partly buried under those of **20** except, δ 2.87 (d, J = 3.9 Hz, 1 H, epoxide H), 2.14–1.98 (m, 2 H, CH_2), 0.97 (t, J = 8 Hz 3 H, CH_3)
21a (as mixture)	ν_{max} (CCl_4) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.70 (s, 3 H, OCH_3), 3.24–3.13 (m, 2 H, epoxide H), 2.57 and 2.38 (ABX, J = 18, 9, 8, Hz, 2 H, CH_2CO_2Me), 2.36 (m, 1 H, methine CH), 1.90–1.78 (m, 2 H, CH_2), 1.58–1.02 (m, 4 H, 2 × CH_2)
21b (as mixture)	all the NMR signals coincide with or partly buried under those of **21a** except, δ 3.71 (s, 3 H, OCH_3), 2.94 (d, J = 3.9 Hz, 1 H, epoxide H), 2.15–1.97 (m, 2 H, CH_2)
22a (obtained pure)	ν_{max} (CCl_4) 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.20–5.06 (m, 1 H, CHOAc), 3.30 (s, 2 H, epoxide H), 2.11 (s, 3 H, $COCH_3$), 1.91–1.77 (m, 2 H, CH_2), 1.69–1.18 (m, 4 H, 2 × CH_2).
22b (obtained pure)	ν_{max} (CCl_4) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.06 (t, J = 6.2 Hz, 1 H, CHOAc), 3.24 (br s, 1 H, epoxide H), 3.07 (d, J = 3.4 Hz, 1 H, epoxide H), 2.10 (s, 3 H, $COCH_3$), 2.10–1.70 (m, 3 H, CH_2) 1.56–1.21 (m, 3 H, CH_2)
26a (as mixture)	^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.18–2.98 (m, 2 H, epoxide H), 2.41–2.05 (m, 1 H, methine CH), 1.87–1.30 (m, 10 H, 2 × CH_2), 0.96 (t, J = 6 Hz, 3 H, CH_3)
26b (as mixture)	all the NMR signals coincide with or partly buried under those of **26a** except, δ 2.78 (t, J = 5 Hz, 1 H, epoxide H), 1.02 (t, J = 7 Hz, 3 H, CH_3)
27a (pure sample)	ν_{max} (CCl_4) 1742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.70 (s, 3 H, OCH_3), 3.13 (t, J = 4.8 Hz, 1 H, epoxide H), 2.96 (d, J = 4.8 Hz, 1 H, epoxide H), 2.64 and 2.57 (AB part of ABX, J = 16, 8, 4 Hz, 2 H, CH_2CO_2Me), 2.42–2.24 (m, 1 H, methine CH), 1.86–0.78 (m, 8 H, 4 × CH_2); high resolution mass spectrum (M), calcd for $C_{10}H_{16}O_3$ 184.1100, found 184.1099
27b (pure sample)	ν_{max} (CCl_4) 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.70 (s, 3 H, OCH_3), 3.17–2.93 (m, 1 H, epoxide H), 2.86 (dd, J = 6.7, 4.7 Hz, 1 H, epoxide H), 2.54 and 2.40 (AB part of ABX, J = 15, 7.8, 6.5 Hz, 2 H, CH_2CO_2Me), 2.67–2.35 (m, 1 H, methine CH), 2.31–2.03 (m, 2 H, CH_2), 1.77–1.18 (m, 6 H, 3 × CH_2); high resolution mass spectrum (M), calcd $C_{10}H_{16}O_3$ 184.1100, found 184.1129
28a (as mixture)	ν_{max} (CCl_4) 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.09 (dd, J = 10.7, 4.1 Hz, 1 H, CHOAc), 3.16–3.0 (m, 2 H, epoxide H), 2.38–0.74 (m, 8 H, 4 × CH_2), 2.06 (s, 3 H, $COCH_3$)
28b (as mixture)	ν_{max} (CCl_4) 1740 cm^{-1}; all the NMR signals coincide with or partly buried under those of **28a** except, δ 4.95–4.81 (m, 1 H, CHOAc), 2.05 (s, 3 H, $COCH_3$)

iodotrimethylsilane (69 μL, 0.483 mmol) (freshly opened) under N_2 at 0 °C. After 10 min, the reaction mixture was quenched with brine (5 mL) and diluted with ether (150 mL). The organic layer was washed once with H_2O (10 mL) and the second portion of H_2O (10 mL) was added. The biphasic mixture was allowed to stand for 1 h. The organic layer was again washed with another two portions of H_2O (10 mL × 2) and brine (10 ml), dried over $MgSO_4$, and concentrated. The residue was chromatographed (25% ethyl acetate in hexane) to afford the pure iodohydrin **31** (143 mg, 83%) [*Note*: (1) The amount of DBN added is crucial for a speedy reaction, otherwise the reaction either proceeds very slowly or does not take place. (2) In case of incomplete hydrolysis of the silyl group, the residue can be treated with oxalic acid in methanol for 0.5 h for a complete conversion of OTMS to OH.]: ν_{max} ($CHCl_3$) 3600, 1733 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.11 (q, 1 H, J = 8 Hz, CHI), 3.96 [q, 1 H, J = 8 Hz, CH(OH)], 3.67 (s, 3 H, OCH_3), 3.66 (d, J = 8 Hz, 1 H, CH(OTBDMS), 2.60 (dd, J = 16, 8 Hz, 1 H, CH_2), 2.30, 2 H, CH_2CO_2Me), 2.10 (dd, J = 16, 8 Hz, 1 H, CH_2), 1.09 (s, 3 H, CH_3), 0.90 (s, 9 H, $SiCMe_3$), 0.12 (s, 3 H, $SiMe_2$), 0.07 (s, 3 H, $SiMe_2$); high resolution mass spectrum (M – C_4H_9), calcd for $C_{11}H_{20}O_4SiI$ 371.0175, found 371.0172.

(1-Methyl-3-iodo-4-hydroxy-5-((*tert*-butyldimethylsilyl)oxy)cyclopentyl)acetic Acid Lactone (32). The iodohydrin **31** (21 mg, 0.05 mmol) was heated under reflux with a catalytic amount (3% molar equiv) of *p*-toluenesulfonic acid monohydrate in dry benzene for 1 h. After being cooled to room temperature, the reaction solution was diluted with ether (70 mL), washed with 50% brine (7 mL × 2), and dried over $MgSO_4$. The solvent was evaporated to afford the δ-lactone **32** (18 mg 93%) as a colorless liquid which was not further purified: ν_{max} ($CHCl_3$) 1745 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.71 (s, 1 H, CHO lactone), 4.28 (t, J = 8 Hz, 1 H, CHI), 3.98 (s, 1 H, CH(OTBDMS)], 2.59 (s, 2 H, CH_2CO_2Me), 2.41 (d, J = 8 Hz, 2 H, CH_2), 1.11 (s, 3 H, CH_3), 0.99 (s, 9 H, $SiCMe_3$), 0.21 (s, 3 H, $SiMe_2$), 0.16 (s, 3 H, $SiMe_2$); high resolution mass spectrum (M – C_4H_9), calcd for $C_{10}H_{16}O_3SiI$ 338.9913, found 338.9911.

(1-Methyl-4-hydroxy-5-((*tert*-butyldimethylsilyl)oxy)-2-cyclopentenyl)acetic Acid Lactone (3a). A solution of the iodo lactone **32** (12 mg, 0.03 mmol) in DME (0.5 mL) was sealed in an ampule under N_2 and heated to 105 °C for 64 h. The ampule was opened and the reaction solution was diluted with ether (50 mL), washed with H_2O and then brine, and dried over $MgSO_4$. The solvent was evaporated and the residue was chromatographed (flash chromatography, 25% ethyl acetate in hexane) to afford the olefinic lactone **3a** (7.5 mg, 93%) as a colorless liquid: ν_{max} ($CHCl_3$) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 6.14–6.07 (m, 2 H, vinyl), 4.72 (s, 1 H, CHO lactone), 3.96 (s, 1 H, CH(OTBDMS)), 2.58 and 2.68 (AB q, J_{AB} = 18 Hz, 2 H, CH_2CO_2R), 1.16 (s, 3 H, CH_3), 0.88 (s, 9 H, $SiCMe_3$), 0.10 (s, 6 H, $SiMe_2$); high resolution mass spectrum (M – C_4H_9), calcd for $C_{10}H_{15}O_3Si$ 211.0791, found 211.0793. Anal. Calcd for $C_{14}H_{24}O_3Si$: C, 62.7; H, 8.96. Found: C, 62.5; H, 8.98.

1-Methyl-2-((*tert*-butyldimethylsilyl)oxy)-6-carboxybicyclo[3.1.0]hex-3-ene (33) Formed during Attempted α-Methylenation of 3a. To a solution of LDA, generated by dropwise addition of *n*-BuLi in hexanes (2.6 M) (0.20 mmol, 77 μL) to a solution of diisopropylamine (0.22 mmol, 31 μL) in anhydrous THF (2 mL) at –4 °C and then cooled to –78 °C, was added the olefinic δ-lactone **3a** (45 mg, 0.17 mmol) in anhydrous THF (0.5 mL). The solution was stirred at –78 °C for 20 min to effect deprotonation and warmed to –15 °C when a stream of formaldehyde gas (cracked from 20 equiv of paraformaldehyde which was dried over P_2O_5 under high vacuum at 20 °C for 24 h prior to use) was passed over the solution surface with Ar as a carrier gas at a rate of 3 bubbles/s (measured from outlet) for a period of 0.5 h. At the end of this period, an additional 3 mL of anhydrous THF was added. The solution was warmed to 0 °C and allowed to remain at that temperature for 0.5 h and then warmed to 20 °C. The solution was left at 20 °C for 24 h and acidified with a dilute HCl solution (2 M). Ether (100 mL) was added and the organic layer was washed with H_2O and brine and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (preparative TLC, 40% ethyl acetate in hexane) to afford a 1:1 mixture of the cyclopropane derivatives **33** (28.8 mg, 80% corrected for the starting material recovered): mp 115–116 °C (chloroform) (None of the desired α-methylene lactone was obtained); ν_{max} ($CHCl_3$) 3300–2500, 1705 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 5.80–5.72 (m, 1 H, vinyl), 5.70–5.62 (m, 1 H, vinyl), 4.76 (br s, 1 H, CHOSi, collapsed into two singlets centered at δ 4.80 and 4.78 with equal intensity for two diastereomers when olefinic protons were decoupled), 2.27 (dt, 1 H, bridgehead H, collapsed into two doublets (J = 8 Hz) centered at δ 2.28 and 2.26 with equal intensity for two diastereomers when olefinic protons were decoupled), 2.01 (d, J = 8 Hz, 1 H, $CHCO_2H$), 1.31 (s, 3 H, CH_3), 0.89 (s, 9 H, $SiCMe_3$), 0.20 (s, 3 H, $SiMe_2$), 0.09 (s, 3 H, $SiMe_2$); high resolution mass spectrum (M – C_4H_9), calcd for $C_{10}H_{15}O_3Si$ 211.0791, found 211.0790. Anal. Calcd for $C_{14}H_{24}O_2Si$: C, 62.7; H, 8.95, found: C, 62.5; H, 8.92.

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Minor Products in Photoreactions of α-Diketones with Arenes. Abstraction of Hydroxylic Hydrogen by Triplet Carbonyl

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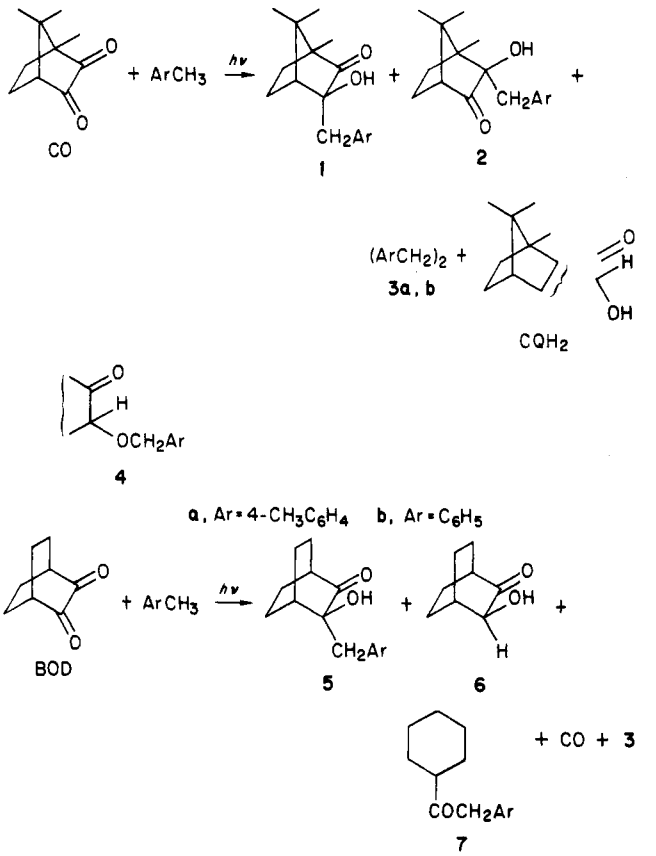
Photochemical reactions of cyclic saturated α-diketones in toluene or *p*-xylene produce 1:1 adducts as major products and smaller amounts of reduced diketone and bibenzyls, as expected from previous work. In addition, reaction of BOD gave 2% of the decarbonylation product, *p*-methylbenzyl cyclohexyl ketone; reaction of camphorquinone gave a mixture of decarbonylation products (10% total) including saturated and unsaturated monoketones. These compounds were secondary products arising from reaction of photoexcited diketone with the initially formed adducts; quenching and sensitization studies showed that triplet states of α-diketones were involved in both primary and secondary reactions. The decarbonylation products were also formed by reaction of benzophenone triplets or of *tert*-butoxy radicals with adducts. Deuterium labeling of the adducts was employed to demonstrate that the decarbonylation process involves abstraction of hydroxylic hydrogen.

One of the characteristic photoreactions[2] of α-dicarbonyl compounds is abstraction of a hydrogen atom from a wide variety of substrates to give semidione and substrate derived radicals which proceed to product(s) via coupling or disproportionation reactions. Some years ago we reported[3] a reaction of this type between camphorquinone (CQ) and substituted toluenes which gave about 70% of crystalline adducts[4] **1** and **2**, the appropriate bibenzyl (**3**), and about 10% of mixed hydroxycamphors (CQH_2). More recently it was shown[5] in a similar reaction of CQ or of bicyclo[2.2.2]octane-2,3-dione (BOD) with aromatic aldehydes that quantum yields and product compositions depended on experimental conditions and could be varied markedly, particularly by variations in light intensity. These results prompted a reinvestigation of the reactions of CQ and BOD with toluenes in order to determine if such a dependence on experimental conditions could be observed and to account for the unidentified 20% of reaction products. It was of particular interest to establish if O-benzylated products, such as **4**, were formed. While no evidence for **4** has been obtained, the new photocleavage reaction of α-hydroxy ketones observed forms the substance of this report. For convenience in NMR analysis, most of the work was performed with *p*-xylene.



Reaction Products

Initial experiments were performed with BOD since the symmetry of this diketone eliminates complications due to regio- and stereoisomerism of products. Irradiation of a solution of BOD in *p*-xylene under nitrogen at wavelengths longer than 380 nm furnished a mixture of the expected products: adduct **5a** (70%), reduced diketone **6** (17%), and bibenzyl **3a** (6%).[6] In addition gas chromatographic analysis showed the presence of about 2% of an additional product of relatively short retention time. Pure material corresponding to this peak was isolated by preparative scale TLC and shown, by spectroscopic properties and unexceptional synthesis (see Experimental Section), to be *p*-methylbenzyl cyclohexyl ketone (**7a**). The

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(6) Theoretically, yields of **3** and **6** should be equal. Control experiments showed that considerable **3** was lost by volatilization under the conditions of the workup.

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