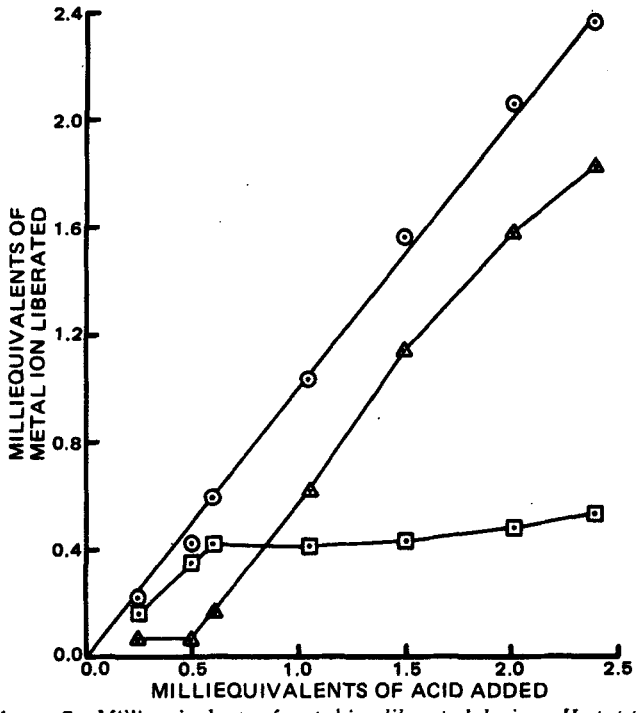

Figure 7—*Milliequivalents of metal ion liberated during pH-stat titration at pH 3.0 of a 5:1 magnesium–aluminum molar ratio mixture of aluminum hydroxycarbonate gel and magnesium hydroxide gel. Key: △, milliequivalents of magnesium ion in solution; □, milliequivalents of aluminum ion in solution; and ○, total milliequivalents of magnesium and aluminum ions in solution.*

agglomeration in the gel mixtures. Treadwell and Bernasconi (19) proposed an adsorption bonding of this type. Thus, the amorphous aluminum hydroxycarbonate would form a coating on the crystalline brucite magnesium hydroxide gel. The aluminum hydroxycarbonate coating would prevent protons from reaching the highly reactive brucite until the coating dissolves due to acid neutralization of the aluminum hydroxycarbonate. As was observed in the pH-stat titrigrams of mixed aluminum hydroxycarbonate–magnesium hydroxide gels, the acid neutralization will occur more slowly than expected due to the coating of the faster reacting magnesium hydroxide gel by the slower reacting aluminum hydroxycarbonate gel.

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Simple Epoxide Analogs of Trichothecans

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Abstract □ To define clearly the epoxide grouping role in trichothecan biological activity, a series of hindered epoxides was prepared. They possessed α,α′-substitution reminiscent of the epoxide environment of the natural products. None of these analogs demonstrated biological activities similar to the natural toxins.

Keyphrases □ Trichothecans—epoxide analogs, structure–activity relationships, toxicity □ Fungistatic agents—trichothecans, epoxide analogs, structure–activity relationships, toxicity

In 1946, as part of a program to discover new antibiotics, a highly fungistatic principle was isolated from a culture filtrate of *Metarrhizium glutinosum* S. Pope (1). This principle was highly irritating to human skin. Similar agents were produced by various microorganisms, including *Trichothecium roseum* and species of *Fusaria* and *Trichoderma* (2). Continued work with these materials led to the isolation in pure form of one of these principles; it was named trichothecin (3). Since that time, many related compounds have been isolated and characterized and are collectively known as the trichothecans (I), a name coined for the ring system possessed by all of these materials (4).

BACKGROUND

All trichothecans contain a 12,13-epoxy group, a 9,10-double bond, and the 4-β-hydroxyl. The simplest of the group, trichodermin (II), contains an acetate ester and only functionalities characteristic of all trichothecans. The most complex materials contain a fifth, macrocyclic ring, which is formed *via* esterification of hydroxyls at positions 4 and 15 by a long chain diacid.

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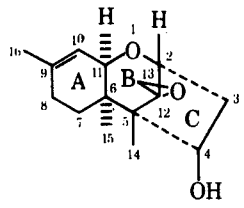
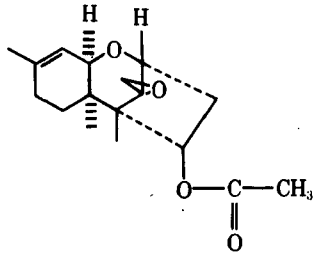


I



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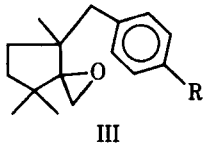


III

All trichothecans possess a high degree of biological activity. They also are very toxic to mammals and cause severe skin irritation on contact.

The chemistry and biology of this group of sesquiterpenoids were reviewed (5).

The trichothecans are interesting from several viewpoints. They seem to have great potential medicinal utility, particularly as antifungal, antibiotic, and antitumor agents. Although their toxicity has precluded extensive clinical use, their high activity warrants a search for active analogs that are less toxic. Since trichodermin is a potent antifungal agent and yet much less toxic than other trichothecans, high toxicity is not necessarily inherent in their basic structural features.

The trichothecans are also of likely agricultural significance. Elucidation of the features responsible for their toxicity to livestock could be useful in determining which trichothecans cause the various types of toxicity and could aid in the design of inhibitors or antidotes for their effects.

To elucidate the mechanism of action and the structural features necessary for the various types of activity possessed by the trichothecans, a series of compounds was proposed (III). This series is a model of the C ring of the trichothecan nucleus. It contains the epoxide, which is probably necessary for activity, plus heavy substitution on the adjacent carbon atoms. It has been proposed that lipophilicity is important for trichothecan activity (6); therefore, a benzyl group was attached to the cyclopentane ring, and the hydroxyl present at C-4 in the natural products was deleted.

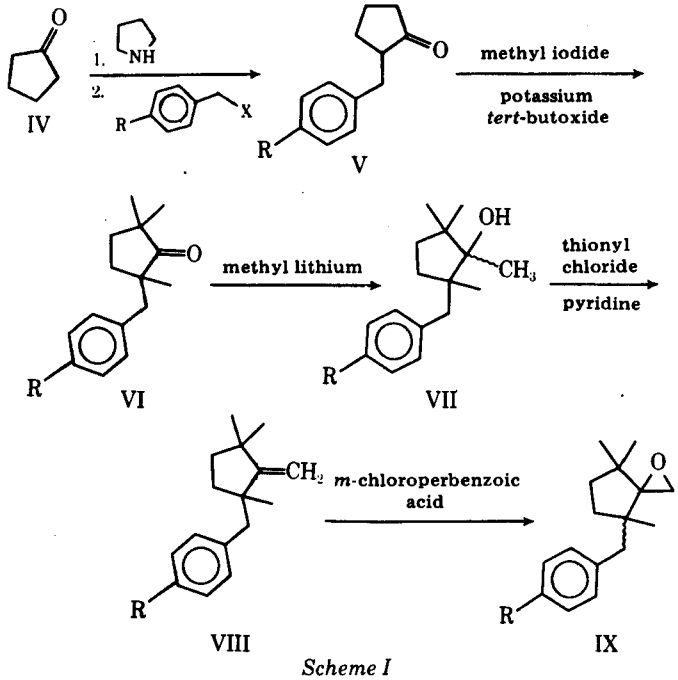
The compounds in the series are identical except for a varying substituent on the phenyl group *para*-position. Eventually, correlations may be attempted between activity, the Hammet σ value, and the partition coefficient; if such correlations exist, they would either lend support to or refute the hypothesis that lipophilicity is important. Also, making the epoxide even more hindered than it is in the natural product might produce a more selective agent.

DISCUSSION

The intermediates for the synthesis of the compounds were a series of 2-benzylcyclopentanones containing a variety of substituents in the phenyl ring *para*-position. Several 2-benzylcyclopentanones were synthesized using the appropriate benzyl halide and the pyrrolidine or morpholine enamine of cyclopentanone (7) (Scheme I).

The enamine alkylation was acceptable, except when a strong electron-withdrawing substituent was present on the phenyl ring. This effect is not easily rationalized; however, while many enamine alkylations proceed in yields of 45–55%, strong electron-withdrawing substituents decrease the yields. This alkylation has been used when the substituent is H, CH_3, OCH_3, OBz, Cl, NO_2, CN, or CO_2CH_3. In the *p*-nitrobenzyl halides, the yields are so low that the enamine alkylation is not synthetically useful[1].

The benzylic halides were commercially available, except for the methoxy derivative. This derivative was prepared from anise alcohol by



Scheme I

treatment with hydrobromic acid (8). Since this benzylic bromide is reported to be unstable, it was used immediately without purification.

The next step in the synthetic sequence was the conversion of the benzylcyclopentanones to the tetrasubstituted ketones. The reaction of all of the various 2-benzylcyclopentanones with potassium *tert*-butoxide in *tert*-butanol and excess methyl iodide resulted in the desired ketones in 72–81% yields.

It was anticipated that the tetrasubstituted ketones could be converted directly to the desired epoxides by treatment with either dimethylsulfonium methylide or dimethylsulfoxonium methylide (9). In no case would the highly hindered ketones react. An attempt also was made to effect a Wittig reaction with the ketones (10). As with the sulfur ylides, no reaction occurred and only starting material was recovered. This finding again shows the lack of reactivity of these tetrasubstituted ketones, a property that may best be explained by steric hindrance.

After direct conversion to the epoxide or olefin failed, the longer route of addition to the carbonyl, dehydration, and epoxidation was followed. Addition of the ketone, in ether, to an ethereal solution of excess methyl lithium followed by a reflux period led to a high alcohol yield (11). The use of less vigorous conditions, such as stirring at room temperature for 24 hr or refluxing for 6 hr, led to mixtures of starting material and the desired alcohol. No effort was made to separate the isomeric mixture of alcohols. The dehydration of the tertiary alcohols proceeded smoothly in yields of ~75%.

The final step in the synthesis was the epoxidation of the exocyclic olefins, which was performed both by peracid oxidation and by formation and base-catalyzed closure of an intermediate bromohydrin. The yield of epoxide was comparable in both procedures, and both procedures gave a mixture of isomers (~2:1 by GLC and NMR analysis). No attempt was made to separate the isomers. The peracid product was chromatographed on activated magnesium silicate[2] to yield the pure epoxide fraction.

The epoxides were assayed for antibiotic (12) and antimitotic (13) activity. None showed activity of ≥1% in the antimitotic screen of T-2 toxin, a naturally occurring trichothecan X. In the antibiotic screen of *Staphylococcus aureus, Escherichia coli, Salmonella gallinarum, Klebsiella, Pneumoniae, Mycobacterium smegmatis,* and *Candida albicans,* only *M. smegmatis* was inhibited by the simple epoxides prepared in this study (Table I). However, the activities were not sufficient to encourage further work.

Care was taken that all test media were near neutrality so that the epoxides would not be degraded by the medium. Apparently, the epoxide moiety of the model compounds does not meet the steric and/or electronic characteristics necessary for high activity if the epoxide group is the major pharmacophore of the trichothecans as proposed. It may well be that the

[1] Three explosions occurred while using *p*-nitrobenzyl bromide: twice while trying to distill the crude product mixture when the bath temperature reached 190° and once while stirring and refluxing a combination of *p*-nitrobenzyl bromide, 1-pyrrolidinocyclopentene, and dioxane. Since the dioxane was used immediately after distillation from lithium aluminum hydride, it is unlikely that peroxide formation was responsible.

[2] Florisil.

Table I—Minimum Inhibitory Concentration (MIC) against *Mycobacterium smegmatis* (ATCC 607)

Epoxide IX	MIC, μg/ml
R = H	100
R = Cl	50
R = CH_3	50
R = OCH_3	25

complete substitution of the α-carbons creates too high a steric hindrance for reactivity of the materials as alkylating agents of essential cellular components. These materials were not tested for skin irritation.

EXPERIMENTAL

Melting points[3] are uncorrected. All compounds gave satisfactory elemental analyses[4]. IR spectra[5] are reported in reciprocal centimeters. NMR spectra[6] were recorded with tetramethylsilane as an internal standard. NMR data are reported in parts per million (δ). Mass spectra[7] and GLC[8] data were obtained also. TLC employed aluminum oxide[9] and silica gel with fluorescent indicators. Column chromatography was done on silica gel[9] (70–325 mesh) and neutral alumina[10].

Benzylcyclopentanone Preparation—The procedure of Stork *et al.* was used (7). To a stirred solution of 1-pyrrolidinocyclopentene (1 mole equivalent) in dry dioxane, under nitrogen, was added benzyl halide (1.25 mole equivalent). The mixture was stirred and refluxed for 12 hr and cooled. Water was added, and the mixture was refluxed for an additional 3 hr. The solvent was removed *in vacuo*, and the residue was extracted three times with ether. The combined ethereal extracts were washed with 10% HCl, saturated sodium bicarbonate, water, and saturated brine and dried over sodium sulfate. Solvent removal and residue distillation yielded the benzylcyclopentanone.

2-Benzylcyclopentanone (*V, R = H*)—A 58% yield was obtained; bp 70–73°/0.2 mm [lit. (14) bp 108–110°/0.75 mm]; IR (neat): 1740; NMR ($CDCl_3$): 1.3–3.2 (9H, m, methylene and benzyl) and 7.23 (5H, s, ar); mass spectrum: *m/e* 174 (M^+) and 91 (base peak).

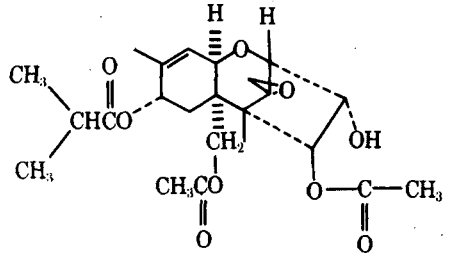
2-(p-Chlorobenzyl)cyclopentanone (*V, R = Cl*)—A 31% yield was obtained; bp 112–113°/0.1 mm; semicarbazone, mp 206–207° dec.; IR (neat): 1740; NMR ($CDCl_3$): 1.2–3.2 (9H, m, methylene and benzyl) and 7.1–7.25 (4H, m, ar); mass spectrum: *m/e* 208, 210 (M^+), and 126 (base peak).

Anal. (semicarbazone)—Calc. for $C_{13}H_{16}ClN_3O$: C, 58.87; H, 6.04; N, 15.85. Found: C, 58.69; H, 5.79; N, 15.63.

2-(p-Methoxybenzyl)cyclopentanone (*V, R = OCH_3*)—A 55% yield was obtained; bp 96–100°/0.05 mm; semicarbazone, mp 194–195° dec.; IR (neat): 1740 (CO), 1615, and 1585 (ar); NMR ($CDCl_3$): 1.4–3.2 (9H, m, methylene and benzyl), 3.8 (3H, s, OCH_3), and 6.5–7.0 (4H, m, ar); mass spectrum: *m/e* 204 (M^+) and 121 (base peak).

Anal. (semicarbazone)—Calc. for $C_{14}H_{19}N_3O_2$: C, 64.39; H, 7.28; N, 16.09. Found: C, 64.79; H, 7.41; N, 16.30.

2-(p-Methylbenzyl)cyclopentanone (*V, R = CH_3*)—A 52% yield was obtained; bp 68–70°/0.1 mm; semicarbazone, mp 211.5–212.5° dec.; IR (neat): 1740; NMR ($CDCl_3$): 2.3 (3H, s, ar CH_3), 1.5–3.2 (9H, m, methylene and benzyl), and 7.0 (4H, s, ar); mass spectrum: *m/e* 188 (M^+) and 105 (base peak).



X

Anal. (semicarbazone)—Calc. for $C_{14}H_{19}N_3O$: C, 68.57; H, 7.76; N, 17.14. Found: C, 68.84; H, 7.92; N, 17.31.

2,2,5-Trimethyl-5-benzylcyclopentanone Preparation—The McMurray procedure was used (11). A solution of potassium *tert*-butoxide was prepared by refluxing potassium metal in dry *tert*-butanol until the potassium had dissolved. About 1 mole equivalent of this solution was added slowly to a solution of the ketone in *tert*-butanol under nitrogen. The mixture was stirred for 10 min, and additional equivalents of potassium *tert*-butoxide and methyl iodide (sixfold excess) were added simultaneously at equal rates with cooling.

The mixture was stirred and heated at 40° for 48 hr. Filtration of the cooled mixture and subsequent removal of most of the *tert*-butanol *in vacuo* were followed by dilution with water and extraction three times with ether. The ethereal extracts were combined, washed with water and saturated brine, and dried with magnesium sulfate. Solvent removal and residue distillation afforded the respective fully methylated benzylcyclopentanones.

2,2,5-Trimethyl-5-benzylcyclopentanone (*VI, R = H*)—A 78% yield was obtained; bp 71–73°/0.05 mm; IR (neat): 1740 (CO); NMR ($CDCl_3$): 0.7 (3H, s, CH_3), 1.1 (6H, s, 2 CH_3), 1.3–2.0 (4H, m, methylene), 2.8 (2H, *AB* quartet, *J* = 14 Hz, benzylic), and 7.2 (5H, m, ar).

Anal.—Calc. for $C_{15}H_{20}O$: C, 83.33; H, 9.26. Found: C, 83.08; H, 9.24.

2,2,5-Trimethyl-5-(p-chlorobenzyl)cyclopentanone (*VI, R = Cl*)—A 72% yield was obtained; bp 83–85°/0.02 mm; IR: 1740 (CO); NMR ($CDCl_3$): 0.7 (3H, s, CH_3), 1.05 (6H, s, 2 CH_3), 1.2–2.0 (4H, m, methylene), 2.4 (2H, *AB* quartet, *J* = 14 Hz, benzylic), and 7.2 (4H, m, ar).

Anal.—Calc. for $C_{15}H_{19}ClO$: C, 72.00; H, 7.60; Cl, 14.00. Found: C, 71.75; H, 7.61; Cl, 13.78.

2,2,5-Trimethyl-5-(p-methoxybenzyl)cyclopentanone (*VI, R = OCH_3*)—An 81% yield was obtained; bp 95–99°/0.03 mm; IR (neat): 1740 (CO); NMR ($CDCl_3$): 0.72 (3H, s, CH_3), 1.08 (6H, s, 2 CH_3), 3.74 (3H, s, OCH_3), and 6.7–7.1 (4H, m, ar).

Anal.—Calc. for $C_{16}H_{22}O_2$: C, 78.05; H, 8.94. Found: C, 77.75; H, 8.82.

2,2,5-Trimethyl-5-(p-methylbenzyl)cyclopentanone (*VI, R = CH_3*)—A 75% yield was obtained; bp 72–76°/0.03 mm; IR (neat): 1740 (CO); NMR ($CDCl_3$): 0.72 (3H, s, CH_3), 1.05 (6H, s, 2 CH_3), 1.3–2.0 (4H, methylene), 2.3 (3H, aromatic CH_3), 2.7 (2H, *AB* quartet, *J* = 14 Hz, benzylic), and 7.0 (4H, s, ar).

Anal.—Calc. for $C_{16}H_{22}O$: C, 83.48; H, 9.57. Found: C, 83.25; H, 9.39.

1,2,2,5-Tetramethyl-5-benzylcyclopentanol Preparation—The McMurray procedure was used (11). The ketone in ether was added dropwise, with stirring, to an ethereal methyl lithium solution. The mixture was stirred and refluxed under nitrogen for 24 hr. Then the reaction mixture was cooled, water was added slowly to destroy the excess methyl lithium (cessation of gas evolution), and the reaction mixture was diluted with more water so that the volumes of water and ether were approximately equal. The layers were separated, and the aqueous layer was extracted with ether. The combined ethereal extracts were washed with water and saturated brine and dried over sodium sulfate. The alcohols were isolated by solvent removal *in vacuo* and subsequent distillation of the residue.

1,2,2,5-Tetramethyl-5-benzylcyclopentanol (*VII, R = H*)—A 98% yield was obtained; bp 85–87°/0.02 mm; IR (neat): 3500 (broad, OH) and 1603 (ar).

Anal.—Calc. for $C_{16}H_{24}O$: C, 82.74; H, 10.34. Found: C, 82.44; H, 10.35.

1,2,2,5-Tetramethyl-5-(p-chlorobenzyl)cyclopentanol (*VII, R = Cl*)—A 97% yield was obtained; bp 90–92°/0.02 mm; IR (neat): 3550 (broad, OH) and 1600 (ar).

Anal.—Calc. for $C_{16}H_{23}ClO$: C, 72.18; H, 8.65; Cl, 13.16. Found: C, 71.90; H, 8.68; Cl, 12.90.

1,2,2,5-Tetramethyl-5-(p-methoxybenzyl)cyclopentanol (*VII, R = OCH_3*)—A 95% yield was obtained; bp 120–122°/0.02 mm; IR (neat): 3600 (broad, OH), 1620, and 1590 (ar).

Anal.—Calc. for $C_{17}H_{26}O_2$: C, 77.86; H, 9.92. Found: C, 78.13; H, 9.69.

1,2,2,5-Tetramethyl-5-(p-methylbenzyl)cyclopentanol (*VII, R = CH_3*)—A 92% yield was obtained; bp 86–89°/0.02 mm; IR (neat): 3540 (broad, OH).

Anal.—Calc. for $C_{17}H_{26}O$: C, 82.83; H, 10.57. Found: C, 82.98; H, 10.29.

Tertiary Cyclopentanol Dehydration—The McMurray procedure

[3] Thomas-Hoover Unimelt.
[4] Analyses were performed by Midwest Microlab, Indianapolis, Ind., or on a 185B CHN analyzer, University of Kansas.
[5] Beckman IR 10 or IR 33 spectrometer.
[6] Varian Associates A-60-A or T-60 spectrometer.
[7] Varian Atlas CH5.
[8] Hewlett-Packard 5750 B gas chromatograph.
[9] E. Merck.
[10] Woelm.

was employed (11). The alcohol was dissolved in dry pyridine (15 ml/mmole of alcohol) and cooled to −5° under nitrogen. To the stirring solution was added thionyl chloride (0.34 ml/mmole of alcohol) at such a rate that the temperature did not rise above 5°. The mixture was stirred at 0° for 30 min; then water was added, with cooling, to destroy excess thionyl chloride.

After the exothermic destruction of thionyl chloride had ceased, the mixture was diluted with excess water, and the resulting aqueous mixture was extracted three times with ether. The combined ethereal extracts were washed with 6 *N* HCl (cold), saturated sodium bicarbonate, water, and saturated brine and dried over sodium sulfate. After solvent removal *in vacuo*, olefins were isolated by distillation.

2,2,5-Trimethyl-5-benzyl-1-methylenecyclopentane (*VIII*, *R* = *H*)—An 87% yield was obtained; bp 50–52°/0.01 mm; IR (neat): 3040, 3080 (vinyl), 1650 (vinyl), and 1605 (ar); NMR ($CDCl_3$): 0.69 (3H, s, CH_3), 1.07 (3H, s, CH_3), 1.10 (3H, s, CH_3), 1.2–1.9 (4H, m, methylene), 2.6 (2H, broad s, benzylic), 4.74 (1H, broad s, vinyl), 4.85 (1H, broad s, vinyl), and 7.2 (5H, broad s, ar).

Anal.—Calc. for $C_{16}H_{22}$: C, 89.72; H, 10.28. Found: C, 89.90; H, 10.19.

2,2,5-Trimethyl-5-(p-*chlorobenzyl*)*-1-methylenecyclopentane* (*VIII*, *R* = *Cl*)—A 79% yield was obtained; bp 63–66°/0.03 mm; IR (neat): 3070, 3100 (vinyl), 1660 (vinyl), and 1610 (ar); NMR ($CDCl_3$): 0.95 (3H, s, CH_3), 1.05 (3H, s, CH_3), 1.08 (3H, s, CH_3), 1.2–1.9 (4H, m, methylene), 2.63 (2H, broad s, benzylic), 4.7 (1H, broad s, vinyl), 4.90 (1H, broad s, vinyl), and 7.0–7.15 (4H, m, ar).

Anal.—Calc. for $C_{16}H_{21}Cl$: C, 77.42; H, 8.48; Cl, 14.10. Found: C, 77.22; H, 8.34; Cl, 13.93.

2,2,5-Trimethyl-5- (p-*methoxybenzyl*)*-1-methylenecyclopentane* (*VIII*, *R* = OCH_3)—A 76% yield was obtained; bp 83–86°/0.03 mm; IR (neat): 3050, 3090 (vinyl), 1645 (vinyl), and 1575 (ar); NMR ($CDCl_3$): 0.97 (3H, s, CH_3), 1.05 (3H, s, CH_3), 1.08 (3H, s, CH_3), 1.2–1.8 (4H, m, methylene), 2.59 (2H, broad s, benzylic), 3.72 (3H, s, OCH_3), 4.73 (1H, broad s, vinyl), 4.87 (1H, broad s, vinyl), and 6.8–7.05 (4H, m, ar).

Anal.—Calc. for $C_{17}H_{24}O$: C, 83.61; H, 9.84. Found: C, 83.87; H, 9.72.

2,2,5-Trimethyl-5-(p-*methylbenzyl*)*-1-methylenecyclopentane* (*VII*, *R* = CH_3)—A 62% yield was obtained; bp 71–72°/0.03 mm; IR (neat): 3040, 3090 (vinyl), and 1645 (vinyl); NMR ($CDCl_3$): 0.99 (3H, s, CH_3), 1.06 (3H, s, CH_3), 1.08 (3H, s, CH_3), 1.2–1.9 (4H, m, methylene), 2.31 (3H, s, ar CH_3), 2.61 (2H, broad s, benzylic), 4.68 (1H, s, vinyl), 4.82 (1H, s, vinyl), and 6.95 (4H, s, ar).

Anal.—Calc. for $C_{17}H_{24}$: C, 89.47; H, 10.53. Found: C, 89.22; H, 10.81.

Epoxidation and Purification of Epoxides—The olefin was dissolved in dry, acid-free methylene chloride. An equivalent of *m*-chloroperbenzoic acid (calculated as 85%) was dissolved in dry, acid-free methylene chloride and added slowly, with stirring, at room temperature. When TLC showed the disappearance of the starting olefin, freshly prepared 5% sodium hydrosulfite solution was added just to the disappearance of excess peracid (starch–potassium iodide paper).

The organic phase was separated and washed with water, 10% sodium bicarbonate, water, and saturated brine and dried over potassium carbonate. The solvent was removed *in vacuo*, and the residual oil was adsorbed onto an activated magnesium silicate column prepared in hexane (100:1) from a small volume of hexane. The column was eluted with hexane to remove unreacted olefin and then with 1% ether–hexane to elute the desired epoxide. This procedure gave products of sufficient purity for bioassay. Analytical samples were prepared by distillation.

1-Epoxymethylene-2,2,5-trimethyl-5-benzylcyclopentane (*IX*, *R* = *H*)—A 68% yield was obtained; bp 62–64°/0.02 mm; IR (neat): 3040 (CH, epoxide), 1600 (ar), and 830 (epoxide); NMR ($CDCl_3$); 2.4–3.0 (4H, m, benzylic and epoxide methylene); mass spectrum: *m/e* 230 (M^+) and 91 (base peak).

Anal.—Calc. for $C_{17}H_{24}O$: C, 83.48; H, 9.57. Found: C, 83.14; H, 9.94.

1-Epoxymethylene-2,2,5-trimethyl-5-(p-*chlorobenzyl*)*cyclopentane* (*IX*, *R* = *Cl*)—A 65% yield was obtained; IR (neat): 3040 (CH, epoxide), 1600 (ar), and 820 (epoxide); NMR ($CDCl_3$); 2.1–2.8 (4H, m, benzylic and epoxide methylene); mass spectrum: *m/e* 264, 266 (M^+), and 69 (base peak).

Anal. (by peak-matching mass spectrometry)—Calc. for $C_{16}H_{21}ClO$: 264.12795. Found: 264.12539.

1-Epoxymethylene-2,2,5-trimethyl-5-(p-*methoxybenzyl*)*cyclopentane* (*IX*, *R* = OCH_3)—A 73% yield was obtained; IR (neat): 3040 (CH, epoxide), 1610, 1580 (ar), and 820 (epoxide); NMR ($CDCl_3$): 2.1–2.8 (4H, m, benzylic and epoxide methylene); mass spectrum: *m/e* 260 (M^+) and 121 (base peak).

Anal.—Calc. for $C_{17}H_{24}O_2$: C, 78.46; H, 9.23. Found: C, 78.67; H, 8.95.

1-Epoxymethylene -2,2,5-trimethyl-5- (p-*methylbenzyl*)*cyclopentane* (*IX*, *R* = CH_3)—A 61% yield was obtained; IR (neat): 3050 (CH, epoxide) and 890 (epoxide); NMR ($CDCl_3$): 2.2–2.7 (4H, m, benzylic and epoxide methylene); mass spectrum: *m/e* 244 (M^+) and 105 (base peak).

Anal.—Calc. for $C_{17}H_{24}O$: C, 83.61; H, 9.84. Found: C, 83.46; H, 9.94.

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