ethanol gave 165 g (97%) of **10** in two crops. An analytical sample was obtained by a second recrystallization, giving colorless crystals: mp 248°; ir (Nujol) 1640, 1620, 1590, 1530, and 1350 cm$^{-1}$; nmr (CDCl$_3$) 2.0 (m, 4 H), 2.6–3.4 (m, 4 H), 3.55 (m, 1 H, bridgehead), 7.3–7.8 (m, 3 H), and 8.0–8.6 (m, 3 H); mass spectrum *m/e* 383 (M$^+$).

*Anal.* Calcd for $C_{20}H_{15}ClFN_3O_2$: C, 62.59; H, 3.94; N, 10.95; Cl, 9.24; F, 4.95. Found: C, 62.40; H, 3.57; N, 10.90; Cl, 9.24; F, 5.10.

**12-Chloro-7,8-dihydro-8-(2-hydroxyethyl)-2-nitro-6*H*-benzo[*b*]indole[3,2,1-*d*,*e*]-1,5-naphthyridine (11).** A mixture of compound **10** (140 g) and potassium acetate (170 g) in diglyme (1 l.) was stirred and heated to reflux under argon for 3 hr. After cooling, water (600 ml) and concentrated HCl (300 ml) were added and the resulting mixture was heated on the steam bath for 4 hr. An additional 100 ml of concentrated HCl was then added and heating was continued for 1 hr. The mixture was then poured into excess aqueous $Na_2CO_3$ and extracted several times with methylene chloride. The combined extract was treated with charcoal, dried over sodium sulfate, and evaporated to leave a yellow solid. This was triturated with ethanol, chilled, filtered, washed with ethanol, and dried to give 58.2 g (42%) of compound **11**. Recrystallization from methylene chloride–ethanol gave light yellow needles: mp 219–220° dec; ir (Nujol) 3200, 1640, 1600, 1525, and 1330 cm$^{-1}$; nmr (TFA, external TMS) 2.1 (m, 4 H), 3.4–4.0 (m, 3 H), 3.50 (s, OH or NH$^+$), 4.22 (m, 2 H), 7.3–8.5 (m, 6 H), and 9.25 ppm (s, NH$^+$ or OH); mass spectrum *m/e* (rel intensity) 336 (40), 337 (100), and 381 (M$^+$).

*Anal.* Calcd for $C_{20}H_{16}ClN_3O_3$: C, 62.92; H, 4.22; N, 11.01. Found: C, 62.55; H, 4.23; N, 10.77.

If the reaction mixture was diluted with water, the acetate of **11** precipitated. This compound was difficult to crystallize but was characterized by ir (Nujol) 1735, 1640, 1590, 1520, and 1330 cm$^{-1}$ and mass spectrum *m/e* (rel intensity) 336 (30), 337 (100), and 423 (M$^+$).

**Acknowledgment.** We are indebted to Drs. W. Benz and F. Scheidl for mass spectra and elemental analyses.

**Registry No.**—**1**, 1193-65-3; **2**, 719-59-5; **3**, 21820-07-5; **4**, 784-38-3; **5**, 51230-56-9; **6**, 42471-56-7; **7**, 51230-57-0; **8**, 51230-58-1; **9**, 51230-59-2; **10**, 51230-60-5; **11**, 51230-61-6; **11** acetate, 51230-62-7.

## References and Notes

(1) D. R. Bender and D. L. Coffen, *J. Heterocycl. Chem.*, **8**, 937 (1971).
(2) D. L. Coffen, D. A. Katonak, and F. Wong, *J. Amer. Chem. Soc.*, in press.
(3) J. Angel, R. Michelot, and B. Tchoubar, *C. R. Acad. Sci., Ser. C*, **271**, 557 (1970).
(4) E. H. Fehnel, J. A. Deyrup, and M. B. Davidson, *J. Org. Chem.*, **23**, 1996 (1958); G. Kempter, D. Heilmann, and M. Mühlstädt, *J. Prakt. Chem.*, **314**, 543 (1972).
(5) Melting points are uncorrected. Nmr spectra were recorded on a Varian T-60 instrument and are reported in parts per million from internal tetramethylsilane. Infrared and mass spectra were recorded on Perkin-Elmer 137 and CEC-110B instruments, respectively.
(6) L. H. Sternbach, R. I. Fryer, W. Metlesics, G. Sach, and A. Stempel, *J. Org. Chem.*, **27**, 3781 (1962).
(7) D. W. Ockenden and K. Schofield, *J. Chem. Soc.*, 3440 (1953).

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# Ejection of the 19-Methyl Group in Tetracyclic Triterpenes

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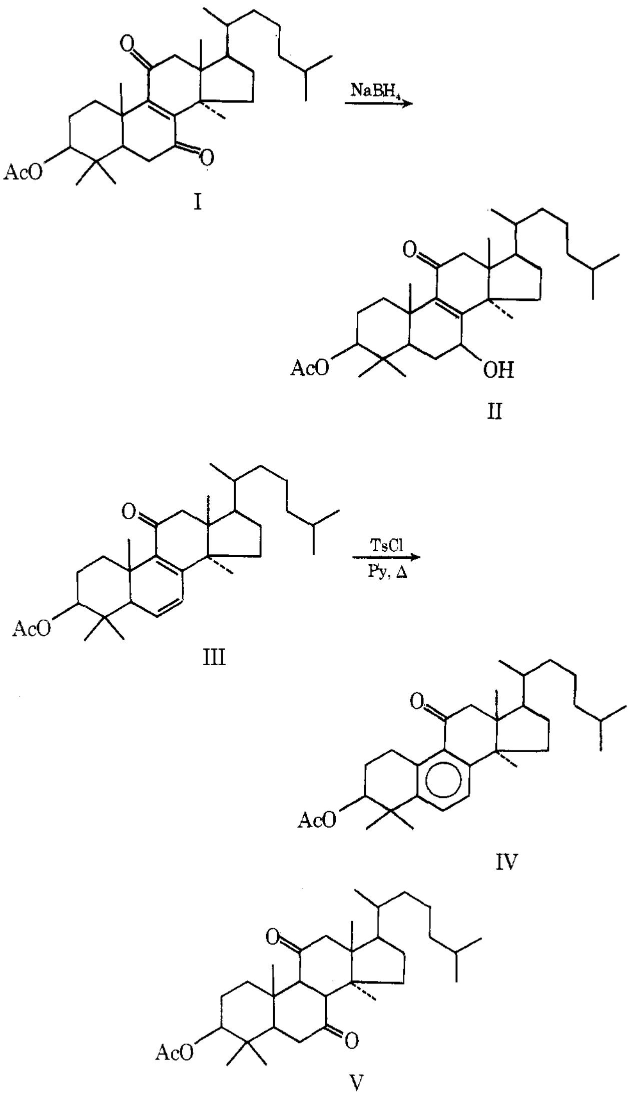
While ways to transform the lanostane skeleton to the cucurbitacin skeleton (a terpene family having potential antileukemic properties)[1] were being explored, a novel ejection of the 19-methyl group concurrently with B-ring aromatization (IV) was observed.[2] Only a few examples of B-ring aromatization of tetracyclic triterpenes have been cited.[3] This reaction (II or III to IV) seems to be unique from these other examples[3] in that it occurs under nonreducing conditions. Pyrolytic conditions led to a similar B-ring aromatization in a steroid system, but ionic conditions produced anthrasteroids instead.[4]

**Scheme I**



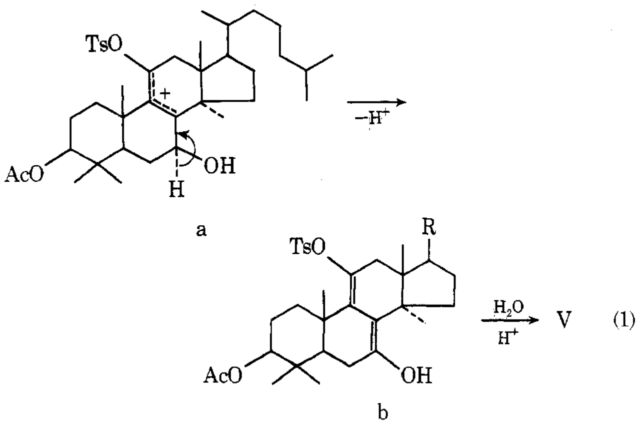
## Results

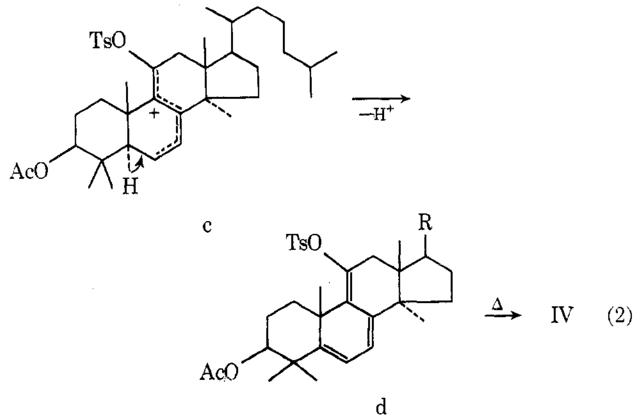
The enedione I was reduced (Scheme I) with sodium borohydride in the presence of ethyl acetate to give the $7\beta$-hydroxy II and $7\alpha$-hydroxy products in a 3:1 ratio. Reaction of II with excess gaseous $BF_3$ in carbon tetrachloride for 1 day or refluxing with a tenfold excess of *p*-toluenesulfonyl chloride (TsCl) in benzene for 3 hr yielded approximately a 1:3 mixture of III and V, respectively. Treatment of II with a tenfold excess of TsCl in pyridine (or collidine) first at 25° for 2 days and then subsequently at refluxing temperature for 2 days gave a 20–30% yield of IV and approximately a 30% yield of V; using benzene instead of pyridine as a solvent gave, under otherwise identical conditions, 16% of I, 11% of III, 11% of IV, and 56% of V. Reaction of II with 1.5 equiv of TsCl in pyridine under the above prescribed conditions produced 19% of I and 51% of V but *no* IV.

Treatment of the $7\alpha$-hydroxy isomer of II with a tenfold excess of TsCl in pyridine under identical conditions as above produced some V with unidentified products and no III or IV. When II or III was heated at reflux in pure pyridine or glacial acetic acid for 2 days, no reaction occurred. However, dienone III was converted quantitatively into IV by refluxing for 2 days in pyridine containing TsCl (Scheme I), thus confirming III as an essential intermediate in the generation of IV from II and that the transformation requires the presence of TsCl.

## Discussion

A mechanism in harmony with the above results follows. Reaction of $BF_3$ or TsCl with the 7β-hydroxy group in II produces III *via* a cis-E2 elimination.[5] Alternatively, reaction of these reagents with 11-oxo functional group followed by ejections of a 7β-hydrogen (a to b in eq 1) would generate V. Once the dienone III is formed, it too can react with toluenesulfonyl chloride concurrently with proton ejection (c to IV in eq 2), particularly in the presence of a base receptor, to generate an intermediate like *d* which could transform thermally[6] to IV. The loss of tosylate anion from the vinyl tosylate d in eq 2 is expected to be unfavorable; however, homolytic cleavage of the Ts–O bond would generate the benzyl-like tosyl radical and a resonance stabilized dienone radical which could subsequently eject a methyl radical to form IV.





## Experimental Section

**General.** All melting points were determined with a Fisher-Johns apparatus and are corrected. Infrared data, reported in kaysers (K = $cm^{-1}$), were obtained in KBr pellets; nmr data, reported in ppm (δ) from internal TMS, were determined in $CDCl_3$; and mass spectra were obtained at an ionization voltage of 70 eV with a Nuclide 12-90-G single focusing instrument having a resolution capability of 10,000. Carbon-hydrogen analysis was performed by Mr. Wayne Noell of Heterocyclic Chemical Corp., Harrisonville, Mo.

Column chromatography as performed using silica gel (MCB Grade 62) and tlc as performed on silica gel $HF_{254}$ (E. Merck). Hexane-ethyl acetate (4:1) was generally used as a solvent phase for tlc and development was effected by spraying with 2% ceric sulfate in 2 *N* sulfuric acid followed by brief heating; the characteristic colors observed after this development were red-orange for II, yellow-orange for III, gray-violet for IV, and orange-brown for V.

**3β-Acetoxy-7β-hydroxy-5α-lanost-8-en-11-one (II).** 3β-Acetoxy-5α-lanost-8-ene-7,11-dione[7] (I, 3.00 g) was dissolved in THF (6 ml) and methanol (8 ml) containing ethyl acetate (2 ml). Sodium borohydride (0.2 g) was slowly added to this stirred solution, which was maintained at ice bath temperature. After being stirred at room temperature for 1 hr, the reaction mixture was poured into ice–water which was subsequently extracted with ether. The cream-colored residue obtained after evaporation of the ether extracts was column chromatographed by gradient elution with benzene–hexane. The first fraction obtained (0.71 g) proved to be the 7α-hydroxy product: mp 217–218° (white needles from $CH_3OH$); $\lambda_{max}$ 3350 (O–H stretch), 1740 and 1250 (OAc), and 1645 and 1578 K (w) (enone); nmr 4.6 (humps, 2 p, 3α,7β-H's), 2.5 (m, 12-H's), 2.05 (s, 3 p, 3β-OAc), 1.40 (s, 3 p, C-19), 1.0 (s, 3 p, 14α-$CH_3$), 0.97 and 95 (s, 3 p each, 4,4-$CH_3$'s), and 0.9 (s, 3 p, C-18); mass spectrum 43 (100%), $M^+$ 500 (30), M − $CH_3$ 485 (12), and M − $H_2O$ 482 (17). The second fraction (1.94 g) was the desired 7β-hydroxy product (II): mp 213–215° (prisms from $CH_3OH$); $\lambda_{max}$ 3400 (O–H stretch), 1740 and 1250 (OAc), and 1645 and 1580 K (enone); pmr 4.6 (br t, 1 p, 3α-H), 4.4 (hump, 1 p, 7α-H), 2.6 (crude d, C-12), 2.05 (s, 3 p, 3β-OAc), 1.25 (s, 3 p, C-19), 1.08 (s, 3 p, 14α-$CH_3$), 0.92 (s, 6 p, 4,4-$CH_3$'s), & 0.80 (s, 3 p, C-18);[8] mass spectrum 43 (100%), $M^+$ 500 (52), M − $CH_3$ 485 (12), and M − $H_2O$ 482 (15).

**3β-Acetoxy-5α-lanosta-6,8-dien-11-one (III) and 3β-Acetoxy-5α-lanosta-7,11-dione (V).** A mixture of II (0.86 g) and TsCl (4.0 g) in dry benzene (25 ml) was heated at reflux until no starting material remained by tlc (3 hr). The cooled reaction mixture was diluted with ether, and the ethereal solution was washed with aqueous sodium bicarbonate. The sodium sulfate dried ethereal solution was concentrated, and the residue was column chromatographed through silica gel by gradient elution with benzene–hexane. The first fraction yielded 0.16 g of dienone III: mp 141.0–142.5° (plates from $CH_3OH$); $\lambda_{max}$ 1740 and 1240 (OAc), 1650, 1625 and 1530 K (dienone); nmr 6.2 (br s, 2 p, 6,7-H's), 4.6 (hump, 1 p, 3α-H), 2.9 (hump, 1 p, 5α-H long range coupled to C-19), 2.6 (crude d, 2 p, 12-H's), 2.06 (s, 3 p, OAc), 1.08 (d, $J$ = 4 Hz, C-19 long range coupled to 5α-H), 0.98, 0.96, and 0.94 (s, 3 p each, 4,4,14α-$CH_3$'s), and 0.85 (s, 3 p, C-18); mass spectrum 83 (100%), $M^+$ 482 (43), *m/e* 422 (64), 407 (37), 353 (30), 341 (32), and 328 (57). The second fraction yielded 0.53 g of dione V: mp 219–221° (white plates from $CH_3OH$);[9] $\lambda_{max}$ 1740 and 1245 (OAc), and 1700 K (C=O stretch); nmr 4.55 (br t, 1 p, 3α-H), 2.6 (m, 6 p, 6,8,9,12-H's), 2.06 (s, 3 p, OAc), 1.4 (d, $J$ = 2 Hz, C-19 long range coupled to 9α-H),[10] 1.21 (s, 3 p, 14α-$CH_3$), 0.91 (s, 3 p, 4β-$CH_3$), and 0.73 (s, 3 p, C-18);[8] mass spectrum $M^+$ 500.

**Reaction of II with Excess TsCl in Pyridine.** A mixture of II (0.56 g) and TsCl (2.0 g) was dissolved in pyridine (10 ml). After the mixture stood at room temperature for 5 days, tlc showed that no starting material remained and that a higher $R_f$ material had been formed. After being heated at reflux for 36 hr, the dark mixture was diluted with ether and then washed with water. Removal of the ether and subsequent column chromatography of the residue through silica gel using gradient elution (ethyl acetate–hexane) gave several products. Fraction 1 yielded 0.16 g of IV: mp 170–171° (needles from $CH_3OH$); $\lambda_{max}$ 1730 and 1250 (OAc), and 1670 (conjugated C=O stretch); nmr 7.25 (q, $J$ = 4 Hz, 2 p, C-6 and C-7), 4.38 (q, $J$ = 2 Hz, 1 p, 3α-H), 3.3 (m, 2 p, C-1), 2.74 (crude d, 2 p, C-12), 2.07 (s, 3 p, OAc), 1.32 (s, 6 p, 4,4-$CH_3$'s), 1.16 (s, 3 p, 14α-$CH_3$), 0.93 (s, 3 p, C-18), and 0.80 (d, $J$ = 6 Hz, 6 p, C-26 and C-27); mass spectrum 391 (100%), $M^+$ 466 (18), *m/e* 406 (54).

*Anal.* Calcd for $C_{30}H_{44}O_3$: C, 79.78; H, 9.93: O, 10.28. Found: C, 80.01; H, 9.62; O, 10.37.

The second fraction yielded 0.25 g of V: mp 218–220° (white plates from $CH_3OH$); the spectra was identical with that cited above.

**Reaction of II with TsCl in Pyridine.** A mixture of II (0.51 g) and TsCl (0.3 g) was dissolved in pyridine (10 ml). After the mixture stood at room temperature for 5 days, tlc indicated that little reaction had occurred.[11] After being heated at reflux for 37 hr, the cooled reaction mixture was diluted with ether and washed with water. Removal of the ether on a rotating evaporator and subsequent column chromatography through silica gel using gradient elution (ethyl acetate-hexane) gave 0.10 g of I and 0.26 g of V having identical spectra with that described above.

**Reaction of II with TsCl in Benzene.** The above experimental conditions were repeated except that the pyridine solvent was replaced by benzene; dissolution of II was incomplete at room temperature. Gradient elution chromatography through silica gel with ethyl acetate-hexane yielded 0.090 g of I in fraction 1, 0.062 g of IV in fractions 2, 0.060 g of III in fraction 3, and 1.32 g of V in fraction 4.

**3β-Acetoxy-19-norlanosta-5,7,9-trien-11-one (IV).** A mixture of III (0.084 g), pyridine (7 ml), and TsCl (0.15 g) was heated at reflux for 2 days. Tlc indicated that there was a quantitative conversion of III into IV. The pyridine was diluted with ether; the mixture washed well with water and then $NaHCO_3$ solution. Column chromatography of the residue obtained from evaporation of the ether through silica gel using ethyl acetate–hexane (1:40) as an eluent yielded 0.070 g of IV: mp 168–170°; the spectra was identical with that cited above.

**Acknowledgment.** I would like to express my appreciation to the UMKC Research Council for financial support of this research. In addition, I am extremely grateful to Dr. George R. Pettit at Arizona State University for providing me with a generous supply of isocholesterol.

**Registry No.**—I, 2115-49-3; II, 5168-22-9; II (7α-hydroxy), 51231-32-4; III, 51231-33-5; IV, 51231-34-6; V, 6593-12-0; TsCl, 98-59-9.

## References and Notes

(1) S. M. Kupchan, R. Smith, Y. Aynechi, and M. Maruyama, *J. Org. Chem.*, **35**, 2891 (1970).
(2) J. R. Dias, Abstracts, 9th Midwest Regional Meeting of the American Chemical Society, Lawrence, Kan., Oct. 1973, No. 330.
(3) K. Tsuda, E. Ohki, J. Suzuki, and H. Shimizu, *Chem. Pharm. Bull.* **9**, 131 (1961); H. de Nijs and W. N. Speckamp, *Tetrahedron Lett.*, 3631 (1973).
(4) A. Van der Gen, J. Lakeman, M. A. M. P. Gras, and H. Huisman, *Tetrahedron*, **20**, 2521 (1964).
(5) The reasons for the preferred eliminations of 7β-hydroxy group compared to the 7α-hydroxy group are presently under investigation.
(6) J. Loperfido, *J. Org. Chem.*, **38**, 399 (1973).
(7) G. R. Pettit, P. Hofer, W. Bowyer, T. R. Kasturi, R. Bansal, R. Kadunce, and B. Green, *Tetrahedron*, **19**, 1143 (1963).
(8) F. Hemmert, B. Lacoume, J. Levisalles, and G. R. Pettit, *Bull. Soc. Chim. Fr.*, 976 (1966).
(9) J. R. Dias, Ph.D. Thesis, Arizona State University, Tempe, Ariz. (1970).
(10) For an example and of a similar long-range C-19 coupling to a 1α-H, see N. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964, p 117.
(11) Apparently a large excess of TsCl is required for cis dehydration of II at room temperature.

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# A Study of the Diepoxidation of the Isomeric 2,4-Hexadienes

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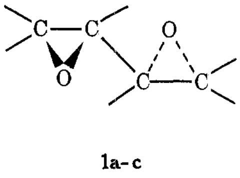
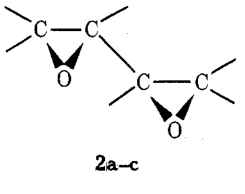
The literature contains little data on the conversion of conjugated dienes to diepoxides.[1] We recently had need to prepare and characterize the diepoxides arising from the *trans,trans-*, *cis,cis-*, and *cis,trans*-2,4-hexadienes.[2] We wish to report here the results of diepoxidation of each of these three dienes with three different peroxy acids and the infrared and proton nmr spectral properties of each of the diepoxide isomers.

## Results

The six possible diastereomeric 2,3,4,5-diepoxyhexanes are identified as follows: *trans,trans, meso*-(2*S*,3*R*,4*S*,5*R*)-, **1a**; *rac*-(2*S*,3*R*,4*R*,5*S*- or 2*R*,3*S*,4*S*,5*R*)-, **2a**; *cis,cis, meso*-(2*R*,3*R*,4*S*,5*S*)-, **1b**; *rac*-(2*R*,3*R*,4*R*,5*R*- or 2*S*,3*S*,4*S*,5*S*)-, **2b**; *cis,trans*, *rac*-(2*R*,3*R*,4*S*,5*R*- or 2*S*,3*S*,4*R*,5*S*)-, **1c**; *rac*-(2*R*,3*R*,4*R*,5*S* or 2*S*,3*S*,4*S*,5*R*)-, **2c**.



**1a-c**



**2a–c**

**Table I**
**Diepoxidation of the 2,4-Hexadienes**

| Peroxy acid[a] | Diene | 1a–c/2a–c[b] | Yield, % |
|---|---|---|---|
| MCPB | *trans,trans-* | 1.8 | 83 |
| PB | *trans,trans-* | 2.0 | 63 |
| PA | *trans,trans-* | 1.5 | 32 |
| MCPB | *cis,cis-* | 1.7 | 87 |
| PB | *cis,cis-* | 2.2 | 64 |
| PA | *cis,cis-* | 1.7 | 43 |
| MCPB | *cis,trans-* | 2.2 | 60 |
| PB | *cis,trans-* | 2.2 | 45 |
| PA | *cis,trans-* | 2.0 | 20 |

[a] MCPB = *m*-chloroperoxybenzoic acid, PB = peroxybenzoic acid; PA = peroxyacetic acid. [b] **1a** and **2a** from *trans,trans;* **1b** and **2b** from *cis,cis;* **1c** and **2c** from *cis,trans.*

Table I shows the ratios of diepoxides **1a–c** to **2a–c** and the yields obtained from treatment of each diene with three peroxy acids (peroxyphthalic acid was also studied but gave no significant yield with any diene). Each diene yielded two diepoxides which were readily separated by vpc, with isomers **1a–c** having a shorter retention time than isomers **2a–c** in each case.[3] Each isomer was isolated by preparative vpc and/or spinning band distillation. As expected, the reaction with peroxy acid was stereospecific; *i.e.*, each diene yielded two isomers which could be shown to be stereoisomerically pure by means of ir or nmr.

As shown in Table I, isomers **1a–c** are formed in larger amounts than **2a–c,** with the ratio of the two showing little variation for the three dienes and three peroxy acids. The substantially lower yield observed with peroxyacetic acid in each case is probably due to ring-opening reaction of diepoxide or monoepoxide with acetic acid. The aromatic acids (especially *m*-chlorobenzoic acid) precipitate from solution and are therefore not so readily available for further reaction. Significant amounts of monoepoxides were not present when the reactions were terminated.

The fact that isomers **1a–c** are formed in larger amounts than isomers **2a–c** can be explained by assuming that the first-formed monoepoxide exists in an essentially *s*-trans conformation (about the 3,4 bond) and that attack by peroxy acid anti to the epoxide oxygen is then sterically favored over syn attack. If the monoepoxide existed in both *s*-cis and *s*-trans conformations and if diepoxide were formed by anti attack on either conformation, then the ratio of diepoxides formed would be expected to show considerable variation between each of the three hexadienes. This is true because the *s*-cis forms of *cis,trans-* and (especially) *cis,cis*-2,4-hexadiene monoepoxides should be much less stable than that of the trans,trans isomer, because of greater steric repulsions from the methyl groups in the former cases. It has recently been reported[4] that epoxidation of 1,3-cyclohexadiene monoepoxide with *m*-chloroperoxybenzoic acid yields 95% trans and only 5% cis diepoxide. This result is in line with the above explanation, since peroxy acid should suffer greater steric hindrance by syn attack on 1,3-cyclohexadiene monoepoxide than on the *s*-trans form of the 2,4-hexadiene monoepoxides (the double bond and oxygen lone-pair electrons are closer together in the former).

## Experimental Section

**General.** Hexadienes were obtained from Chemical Samples Co. (*trans,trans-* and *cis,cis-*, 98%) and Aldrich (*cis,trans-*, 99%). *m*-Chloroperoxybenzoic acid (85%) and peracetic acid (40%) were commercial materials; peroxybenzoic acid was prepared by a standard procedure.[5] Infrared spectra were obtained with a Beck-