National Science Foundation is gratefully acknowledged. The Hewlett Packard 5993 GC–mass spectrometer used in this work was purchased, in part, with funds provided by the National Science Foundation (CHE 81-06056). We are grateful to A. M. van Leusen for providing a generous sample of *N*-nitroso-*N*-[(*p*-tolylsulfonyl)methyl]carbamate and to W. E. Buhro for his preliminary investigations of catalytic rearrangements.

Chemistry of *anti*- and *syn*-1,2:3,4-Naphthalene Dioxides and Their Potential Relevance as Metabolic Intermediates

Wing-Sum Tsang, Gary W. Griffin,* M. G. Horning, and W. G. Stillwell

Department of Chemistry, University of New Orleans, New Orleans, Louisiana 70148, and The Institute for Lipid Research, Baylor College of Medicine, Texas Medical Center, Houston, Texas 77030

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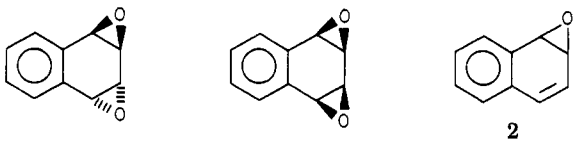
The reactivity, site of attack, and stereochemistry of reactions of a variety of nucleophiles with the *anti*- and *syn*-1,2:3,4-naphthalene dioxides have been explored. In most cases, substituted tetrahydronaphthalene products arising through attack at the C-1 and C-4 positions in the anti mode were obtained. These isomeric dioxides provide excellent precursors for a number of difficultly accessible 1,4-disubstituted naphthalene derivatives such as 1,4-diphenoxynaphthalene and 1,4-dicyanonaphthalene. Evidence is also presented that *anti*-naphthalene dioxide constitutes an intermediate metabolite in the rat.

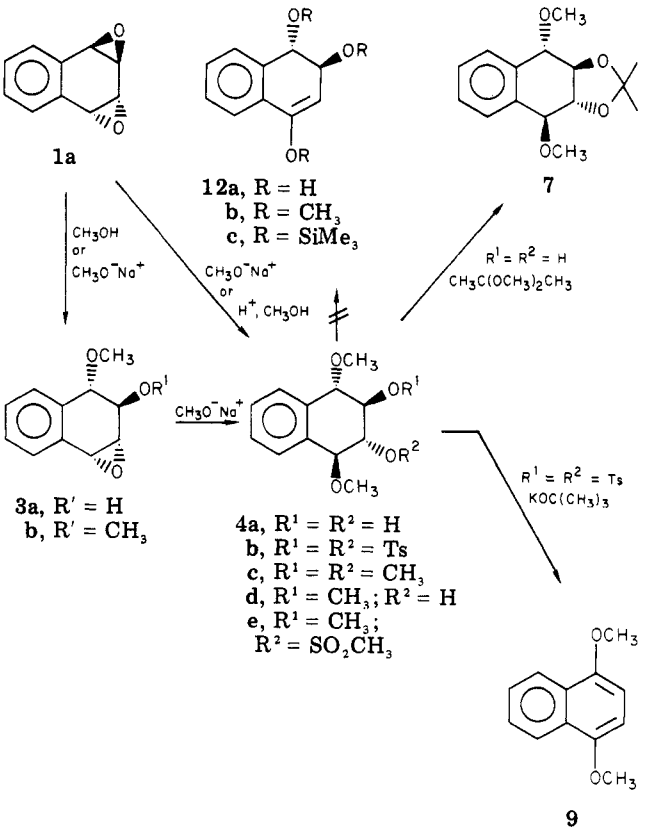
Our discovery of the direct oxidation of naphthalene to *anti*-1,2:3,4-naphthalene dioxide (**1a**)[1a,b] and the inde-



1a **1b** **2**

pendent initiation of a reinvestigation of naphthalene metabolism in rats by the Baylor group, while fortuitous, has led to a highly fruitful collaborative program.[2] As a result of these concurrent events, it became possible to characterize structurally a multitude of newly detected oxygenated and methylthio urinary metabolites of naphthalene and to define their stereochemistry. Of primary significance in this context was the revelation that the *anti*-1,2:3,4-naphthalene dioxide (**1a**), like the monoepoxide **2**,[3] is implicated as an intermediate in the metabolic processes. Heretofore, diepoxides have eluded detection as metabolites of polynuclear hydrocarbons. At this time, we report the synthetic details and structural elucidation of a number of precursors and metabolites synthesized in our laboratories, to which we have previously alluded.[2] It is our object to elaborate the conversions developed and to illustrate the potential utility of the isomeric naphthalene dioxides **1a** and **1b**[1c] for the synthesis of difficultly accessible disubstituted naphthalene derivatives. To avoid confusion, we have elected in this manuscript to employ

Scheme I



that nomenclature which has been adopted by the majority of investigators in the field of polynuclear aromatic hydrocarbon metabolism.[4]

Results and Discussion

Methanolysis of **1a** may be controlled to achieve opening of a single epoxy ring to give the monomethyl ether **3a**, which in turn may be converted to the diol diether **4a** by

(1) (a) K. Ishikawa and G. W. Griffin, *Angew. Chem.*, **89**, 181 (1977); *Angew Chem., Int. Ed. Engl.*, **16**, 171 (1977); (b) K. Ishikawa, H. C. Charles, and G. W. Griffin, *Tetrahedron Lett.*, 427 (1977); (c) E. Vogel, H.-H. Klug, and M. Schäfer-Ridder, *Angew Chem.*, **88**, 268 (1976); *Angew Chem., Int. Ed. Engl.*, **15**, 229 (1976).

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(4) W. S. Tsang and G. W. Griffin, "Metabolic Activation of Polynuclear Aromatic Hydrocarbons", Pergamon Press, Ltd., London, 1979, pp 1–125.

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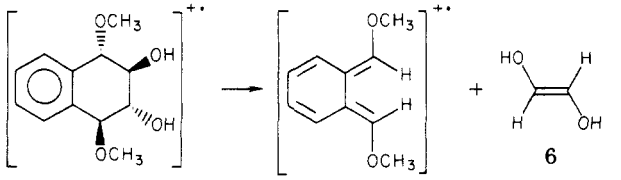
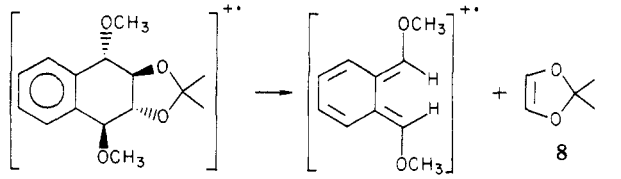
treatment with sodium methoxide (Scheme I). The diol **4a** may also be obtained directly from **1a** by allowing the bis oxide to react with sodium methoxide or, alternatively, with methanol under acidic conditions. The regiochemistry of the conversion of **1a** to **4a** was established by mass spectrometry. It is characteristic of such tetralins, e.g., **4a**, to undergo retro-Diels–Alder fragmentation to an *o*-xylylene ion and an alkene upon electron impact.[2] Despite insensitivity to configurational differences, this phenomenon is routinely used as a reliable diagnostic tool to differentiate positional isomers where the 1,4- and 2,3-substitution pattern on a tetralin nucleus is uncertain.[2] For example, the mass spectrum of **4a** shows a base peak at *m/e* 164, corresponding to the ion **5** (eq 1).



4a *m/e* 224 **5** *m/e* 164 **6** (1)

Conversion of **4a** to an acetonide assigned structure **7** provides verification that **4a** incorporates a vicinal diol moiety. The acetonide **7** is formed at room temperature upon stirring with 2,2-dimethoxypropane. That this acetonide is formed by cyclization of a vicinal rather than 1,3-diol is evident from mass spectral data presented in eq 2. The base peak (*m/e* 164) is identical with that of



7 *m/e* 264 **5** *m/e* 164 **8** (2)

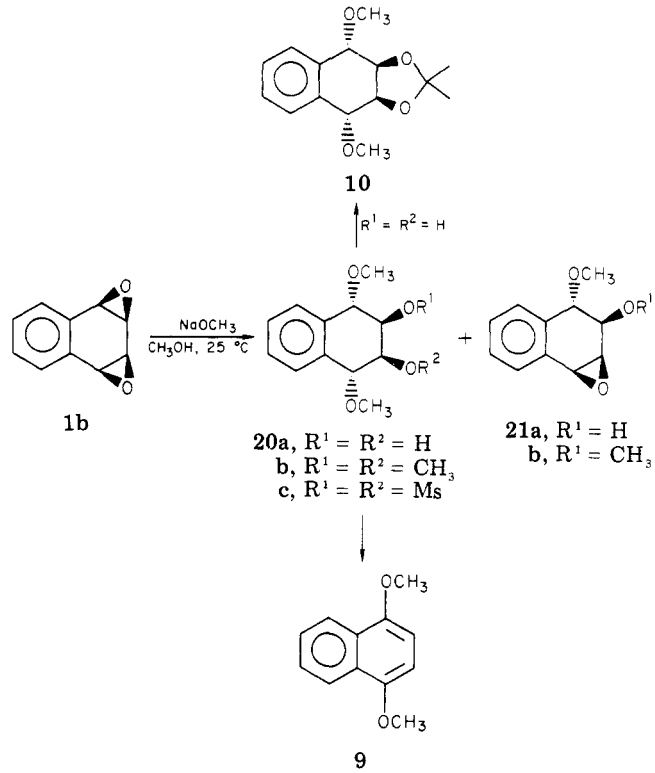
4a, while the molecular ion corresponds to that expected for **7**. No such retro-Diels–Alder fragmentation could occur if 1,3- or 1,4-bridging were implicated in the acetonide formation.

Further confirmation that attack of methoxide ion at the benzylic C-1 and C-4 positions of **1a** prevails to give **4a** was also obtained. The ditosylate **4b** was prepared from the diol **4a**, and the relevant NMR spectral features characteristic of the latter are retained. Upon treatment with potassium *tert*-butoxide, **4b** is converted to a dimethyl ether identical in all respects with an authentic sample of 1,4-dimethoxynaphthalene (**9**).

It is noteworthy that naphthalene oxide **2**, in contrast to **1a**, undergoes ring-opening at the 2-position by methoxide ion and other nucleophiles.[5] This may be attributed to the added allylic character at the C-2 position, which is absent in the case of **1a**.

The stereochemical aspects of the interconversion of **1a** to **4a** were also studied. It is not surprising that nucleophilic opening of the oxirane rings of **1a** by sodium methoxide should occur in an S_N2 manner with inversion at the 1,4-positions. That the transformation is highly regioselective may reflect the propensity for benzyl C–O weakening to precede methoxide binding; i.e., the addition

Scheme II



is nonsynchronous. These conclusions regarding stereochemistry based on mechanistic considerations are supported by NMR analysis (Table I). The NMR spectra of **4a**, the ditosylate **4b**, the tetramethyl ether **4c** (obtained by methylation of **4a** with methyl iodide and silver oxide),[6] as well as the acetonide **7**, all display AA'XX' signal splitting patterns, and this is consistent with the "all trans" stereochemistry assigned in this series of products derived from **1a**. Furthermore, the coupling constants for the vicinal 1,2-protons or stereochemically equivalent 3,4-protons are of such magnitude ($J_{1,2} = J_{3,4} = 6$ Hz) that they conform with vicinal diaxial proton splitting values observed in related systems.[7] It is also apparent from the 1,3-proton splitting pattern observed in the NMR spectrum of **4a–c** and **7** that a trans configuration must exist between the protons on C_2 and C_3; i.e., C_1H and C_3H, as well as C_2H and C_4H bear cis stereochemistry.

Verification of the "all trans" stereochemistry assigned to the products derived from **1a** was accomplished by comparing the NMR spectra of the acetonide **7** with that obtained in a similar manner from **1b** (vide infra). A singlet NMR signal (6 H) is observed for the methyl protons of the acetonide **7**. It is clear from inspection of molecular models that indistinguishable methyl protons would be anticipated for **7** as a result of the C_2 axis of symmetry inherent in this system. An isomeric *cis*-acetonide, assigned structure **10**, was obtained from the diol formed upon treatment of the *syn*-dioxide **1b** with sodium methoxide, which is discussed later. In this case, the methyl groups lie on opposite faces of the fused five-membered ring in the σ plane and are nonequivalent. It should be noted that the stereochemistry of the series of six parent isomeric 1,2,3,4-tetrahydroxy-1,2,3,4-tetra-

(5) (a) A. M. Jeffrey, H. J. C. Yeh, D. M. Jerina, R. M. DeMarinis, C. H. Foster, D. E. Piccolo, and G. A. Berchtold, *J. Am. Chem. Soc.*, **96**, 6929 (1974); (b) A. M. Jeffrey and D. M. Jerina, *ibid.*, **97**, 4427 (1975).

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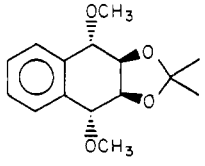

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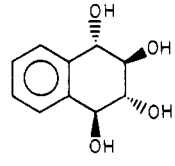


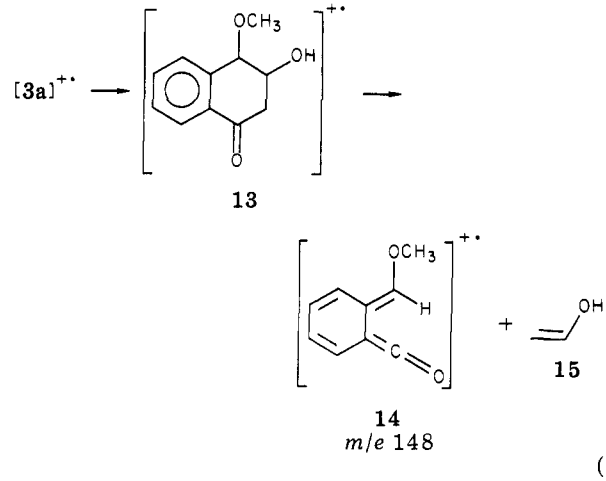
11

hydronaphthalenes has been established by independent synthesis, and the structural assignments of **4c** and **20b** (Scheme II) prepared from this series are secured. The NMR spectra of all other compounds described correlate in a self-consistent manner.[2d]

The facile formation of the trans acetonide **7** from **4a** is surprising. It is generally conceded that acetonides of cyclopentyl and cyclohexyl *cis*-1,2-diols are formed more readily than those of their trans counterparts.[8] This is attributed to the fact that less distortion and strain accrues during cyclization in the former case, which is clearly apparent from molecular models. The formation of acetonides of *trans*-1,2-diols of the type **7**, in which vicinal trans quasi-diequatorial hydroxyls are bridged, in fact, is rarely observed. If formed, rigorous conditions are generally required, and the yields are low.[8d] No such *trans*-acetonides are obtained, even in cases analogous to **4a**, which incorporates two trigonal centers in the diol ring.[9] That the acetonide **7** is formed by bridging a trans vicinal diol in this case, however, is supported by direct evidence and by comparison with reactions of related diols, as described later.

The tetramethyl ether obtained from **4a** and assigned structure **4c** was also synthesized in an alternate manner from the *anti*-dioxide **1a**. Acid-catalyzed hydrolysis of **1a** affords the tetraol **11**, which proved difficult to characterize by NMR and therefore was methylated to give **4c**, identical in all respects with the tetramethyl ether produced upon methylation of the diol **4a**. These convergent syntheses provide structural confirmation that **4c** and **11** embody the "all trans" stereochemistry characteristic of the diol **4a** and their derivatives **4** as independent synthesis showed.[2d] It is of interest that the tetraol **11** was identified as a major urinary metabolite of naphthalene in the rat.[2c,d]

The epoxy ether **3a** is the sole product obtained upon methanolysis of the anti dioxide **1a** and is also observed as a minor product upon treatment of the latter with sodium methoxide if the reaction time is limited (12 vs. 48 h). It is noteworthy that **3a**, unlike **1a**, is indefinitely stable to methanolysis at room temperature. Treatment of **3a**, however, with sodium methoxide gives a diol diether identical with **4a**, obtained in turn from **1a** directly. This confirms that nucleophilic ring-opening of **3a** with methoxide must occur exclusively at the benzylic position with inversion of configuration at that center. This correlation is not surprising since **3a** is the logical intermediate in the overall stepwise conversion of **1a** to **4a** with sodium methoxide. The mass spectrum of **3a** has a base peak at *m/e* 148 attributed to the retro-Diels–Alder cleavage shown in eq 3. Prior rearrangement of the molecular ion **3a** to **13** (eq 3) is invoked to rationalize the formation of the ion corresponding to **14** (*m/e* 148). Initial isomerization of **3a** to a ketone in the inlet port and subsequent ionization to



13

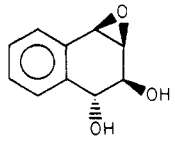
14
m/e 148

15

(3)

14 is rejected since thermolysis of **3a** should proceed with benzylic C–O bond cleavage and afford a β ketone with a base peak of *m/e* 134, upon fragmentation. Regardless of mechanistic details, the mass spectral data confirm that a methoxy group is present at the benzylic position in **3a**. Further support for the stereochemical assignment designated for **3a** was obtained from NMR coupling constant data, which indicate that trans substituents are present in the 1,2-positions.

The dimethyl ether **3b** was prepared by methylation of **3a**, for identification purposes, in anticipation of a search for the corresponding diol epoxide as a potential urinary metabolite of naphthalene in the rat.[2,10] The NMR coupling constants ($J_{1,2}$ = 3 Hz) obtained on the monomethyl ether **3a** are comparable to those observed for **17** and **19**,



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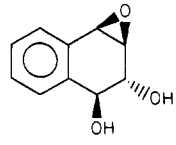

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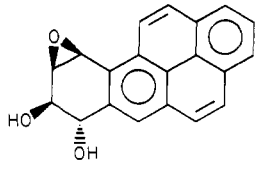

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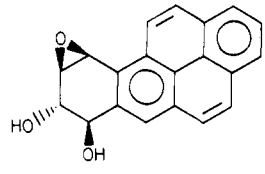

19

which complements the conclusion reached by Bruice[11] that, even in the absence of internal hydrogen bonding between a syn benzylic hydroxy group and the oxirane ring, the systems **3a** and **3b** adopt a conformation in which the vicinal 1,2-substituents are quasi-diaxial. Consequently, the differences in reactivity of **16** and **17** toward acid-catalyzed and noncatalyzed hydrolysis are attributed by Bruice[11] to conformational factors rather than internal hydrogen bonding.[12] In fact, internal hydrogen bonding may well be suppressed in aqueous media owing to the competitive hydrogen bonding of water to the oxirane ring. Indeed, a higher degree of anchimeric assistance to nucleophilic attack has been detected in both the naphthalene and benzo[*a*]pyrene series as the concentration of water is decreased in nonprotic solvents.[10,11]

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(12) P. B. Hulbert, *Nature (London)*, **256**, 146 (1975).

Table I. ^{1}H NMR Spectral Data of Nucleophilic Addition Products from Dioxides 1a and 1b[a]

	chemical shift						
	methine protons						
compds	C1	C2	C3	C4	coupling const	others	aromatic protons
3a[b]	4.27	4.50	3.78	3.91	$J_{1,2}$ = 2.65, $J_{2,3}$ = 2.5, $J_{1,3}$ = 1.5, $J_{3,4}$ = 4	3.40 (OMe), 1.74 (OH)	7.30-7.50
3b[b]	4.33	4.08	3.81	3.93	$J_{1,2}$ = 2.65, $J_{2,3}$ = 2.5, $J_{1,3}$ = 1.5, $J_{3,4}$ = 4	3.51 (OMe), 3.40 (OMe)	7.30-7.60
4a[b]	4.42	3.93	3.93	4.42	$J_{1,2}$ = $J_{3,4}$ = 6, $J_{1,3}$ = $J_{2,4}$ = 2.5	3.54 (OMe), 3.40 (OH)	7.30-7.42
4b	4.50	4.89	4.89	4.50	$J_{1,2}$ = $J_{3,4}$ = 6, $J_{1,3}$ = $J_{2,4}$ = 1.5	3.22 (OMe), 2.42 (Ar Me)	7.28-7.68
4c[b]	4.38	3.47	3.47	4.38	$J_{1,2}$ = $J_{3,4}$ = 6, $J_{1,3}$ = $J_{2,4}$ = 2	3.56 (OMe), 3.51 (OMe)	7.20-7.50
4d	4.47	3.65	3.87	4.35		3.60 (OMe), 3.46 (OMe)	7.20-7.50
4e	4.57	3.88	4.92	4.78		3.62, 3.66, 3.72 (OMe), 3.22 (OSO_2Me)	7.63 (br)
7	4.55	3.76	3.76	4.55	$J_{1,2}$ = $J_{3,4}$ = 6, $J_{1,3}$ = $J_{2,4}$ = 2.5	3.67 (OMe), 1.52 (Me)	7.20-7.70
10[c]	4.15-4.30					3.68 (OMe), 1.52, 1.38 (Me)	7.20-7.60
20a[b]	4.46	4.30	4.30	4.46	$J_{1,2}$ = $J_{3,4}$ = 5.5	3.45 (OMe)	7.30-7.43
20b	4.50	3.95	3.95	4.50	$J_{1,2}$ = $J_{3,4}$ = 6	3.53 (OMe), 3.48 (OMe)	7.20-7.50
20c[b]	4.68	5.35	5.35	4.68	$J_{1,2}$ = $J_{3,4}$ = 5.8	3.52 (OMe), 3.19 (OSO_2Me)	7.41
21a[b]	4.38	4.03	3.77	3.94	$J_{1,2}$ = 9, $J_{2,3}$ = 1.0, $J_{3,4}$ = 4.2, $J_{2,OH}$ = 4.4	3.72 (OMe), 3.25 (OH)	7.23-7.50
21b[b,e]	4.30	3.63	3.79	3.97	$J_{1,2}$ = 8.8, $J_{2,3}$ = 1.0, $J_{3,4}$ = 4.4	3.69 (OMe), 3.62 (OMe)	7.27-7.54
22a	5.40	4.10	4.10	5.40	$J_{1,2}$ = $J_{3,4}$ = 6, $J_{1,3}$ = $J_{2,4}$ = 2.5	2.90 (OH)	6.80-7.60
22b	5.76	5.20	5.20	5.76	$J_{1,2}$ = $J_{3,4}$ = 5.5, $J_{1,3}$ = $J_{2,4}$ = 2	3.00 (OSO_2Me)	6.80-7.52
23	5.38	3.95	3.95	5.38	$J_{1,2}$ = $J_{3,4}$ = 6.5, $J_{1,3}$ = $J_{2,4}$ = 2.5	1.50 (Me)	6.73-7.62
24							6.75-7.60, 8.15
25a	5.47	4.40	4.40	5.47	$J_{1,2}$ = $J_{3,4}$ = 5.5	2.60 (OH)	6.80-7.50
25b	5.75	5.48	5.48	5.75	$J_{1,2}$ = $J_{3,4}$ = 6	2.98 (OSO_2Me)	6.85-7.60
26	5.27	4.50	4.50	5.27	$J_{1,2}$ = $J_{3,4}$ = 5.8	1.52, 1.41 (Me)	6.75-7.60
27b	4.67	4.85-5.30		5.72		3.40 (OMe), 3.10, 2.99 (OSO_2Me)	6.80-7.55
28						3.96 (OMe)	6.60-7.68 8.05, 8.25
30a[b]	6.02	3.85	3.85	6.02	$J_{1,2}$ = $J_{3,4}$ = 5.9, $J_{1,3}$ = $J_{2,4}$ = 2.5	3.40 (OH), 2.17 (OAc)	7.07-7.32
31[b]	3.73	3.92	3.92	3.73	$J_{1,2}$ = $J_{3,4}$ = 5.6, $J_{1,3}$ = $J_{2,4}$ = 2.4	2.46 (Me)	7.20-7.49
32[b]	3.73	4.16	4.16	3.73	$J_{1,2}$ = $J_{3,4}$ = 5	2.44 (Me)	7.21-7.44
33a[b,c]		3.74-3.93				3.39 (OH), 1.86 (SMe)	7.78-7.86 7.27-7.35
34[c]		3.60-4.25				2.00 (SMe), 1.53 (Me)	7.75-8.05, 7.15-7.50
35[d]						2.57 (SMe)	7.63-7.77 (H_5,H_8), 7.57 (H_1,H_4), 7.34-7.48 (H_6,H_7)
36a[b]	4.02	4.42	4.42	4.02	$J_{1,2}$ = $J_{3,4}$ = 6	2.93 (OH), 2.04 (SMe)	7.23-7.56
37	3.85	4.60	4.60	3.85		2.22 (SMe), 1.37, 1.27 (Me)	7.15-7.53
40a[d,f]	4.67	3.54	5.93	6.58	$J_{1,2}$ = 4, $J_{2,3}$ = 5.4, $J_{3,4}$ = 9.5, $J_{1,OH}$ = 5, $J_{1,3}$ = 1, $J_{2,4}$ = 1	5.32 (OH), 1.89 (SMe)	7.00-7.40
42a[b,g]	4.12	4.34	4.29	4.78	$J_{1,2}$ = 4.9, $J_{2,3}$ = 2.3, $J_{3,4}$ = 6	2.15 (SMe)	7.38-7.60
45[b]	2.82	3.42	3.42	2.82	$J_{1,2}$ = $J_{3,4}$ = 7.1, $J_{1,3}$ = $J_{2,4}$ = 2.4, J_{1,CH_3} = 6.6	3.60 (OH), 1.47 (Me)	7.17-7.25
46	3.24	4.76	4.76	3.24	$J_{1,2}$ = $J_{3,4}$ = 6, $J_{1,3}$ = $J_{2,4}$ = 2.2, J_{1,CH_3} = 6.6	3.16 (OSO_2Me), 1.52 (Me)	7.23
47	3.15	3.46	3.46	3.15	$J_{1,2}$ = $J_{3,4}$ = 7.5, $J_{1,3}$ = $J_{2,4}$ = 2.4, J_{1,CH_3} = 6	1.48 (Me), 1.44 (Me)	7.22

Table I (*Continued*)

compds	chemical shift: methine protons C1	C2	C3	C4	coupling const	others	aromatic protons
49[d,f]	4.30	2.61	3.74	4.05	$J_{1,2}$ = 2.8, $J_{1,3}$ = 1.5, $J_{2,3}$ = 2.5, $J_{3,4}$ = 4, $J_{1,OH}$ = 9.3, J_{2,CH_3} = 7.2	3.73 (OH), 0.71 (Me)	7.30-7.62
51[d,h]	4.18	1.72	3.54	3.91	$J_{1,2}$ = 9.5, $J_{2,3}$ = 1, $J_{3,4}$ = 4.2, J_{2,CH_3} = 6.4	1.45 (Me)	7.22-7.63
54	~2.8-3.50 (H_{1a},H_{1b},H_{4a},H_{4b}), ~3.60-3.97 (H_2,H_3)					1.49 (Me)	7.14
56	4.80	2.18	4.37	2.95		2.90 (OH)	7.05-7.57
57	~2.84 (H_{1a},H_{1b},H_{4a},H_{4b}), ~4.58 (H_2,H_3)					1.30 (Me), 1.10 (Me)	7.15

[a] Spectra were recorded in $CDCl_3$ (unless stated otherwise) at 60, 90, or 200 MHz with Me_4Si as internal standard and are given as δ values with coupling constants (J) in hertz. [b] Spectra measured at 200 MHz. [c] Chemical shifts for H(1), H(2), H(3), and H(4) are so close that these protons cannot be assigned. [d] Spectra measured at 90 MHz. [e] In acetone-d_6. [f] In Me_2SO-d_6. [g] In D_2O. [h] In CD_3OD.

An attempt was made to synthesize the trimethyl ether, **12b**, of the dihydrotriol **11a** (Scheme I), the enol of a keto diol urinary rat metabolite of naphthalene, assigned this structure on the basis of mass spectral data. A base peak of m/e 191 is observed for the trimethylsilyl derivatized metabolite **12c**, corresponding to a loss of a $[(CH_3)_3SiO{=}CHOSi(CH_3)_3]^+$ fragment ion.[2c] This represents the anticipated fragmentation mode for such 1,2-dihydro-1,2-dihydroxynaphthalene derivatives. A mesylate precursor for **12b**, namely, **4e**, was prepared from the triether **4d**, which was obtained in turn by treatment of **3b** with sodium methoxide. Attempts to convert the monomesylate **4e** to the methylated metabolite **12b** by base-catalyzed elimination failed, and the sole product characterized was 1,4-dimethoxynaphthalene (**9**); i.e., elimination is accompanied by aromatization under these conditions. As noted earlier, 1,4-dimethoxynaphthalene (**9**) is also produced from the ditosylate **4b**. It is significant that syn eliminations are required in the conversions of the *p*-toluene- and methanesulfonate, **4b** and **4e**, respectively, to **9** and that they occur at 25 °C with potassium *tert*-butoxide as a base.

The isomeric *syn*-naphthalene 1,2:3,4-dioxide (**1b**), like the anti counterpart **1a**, gives two products, assigned structures **20a** and **21a**, respectively, upon treatment with sodium methoxide in methanol at 25 °C (Scheme II). The monomethyl ether **21a** was converted to the dimethoxy derivative **21b**, which is identical in all respects with that synthesized earlier by Bruice and co-workers from the *anti*-diol epoxide **16**.[11] This conversion correlates the configuration of **21a** with that of the diol epoxide **16** obtained by Jerina.[10] The hydroxy ether **21a**, like **16** and **21b**, has a coupling constant (J = 9 Hz) for the 1,2-methine protons, which is in accord with a conformation in which the trans hydroxy and methoxy groups are diequatorial.

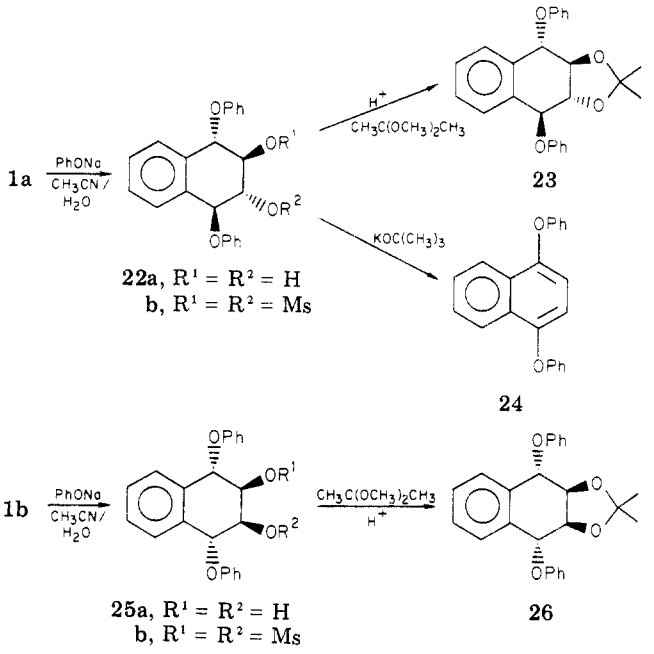
While complete conversion of **1b** to **20a** may be achieved in 72 h at ambient temperature, more control may be exercised on the relative product ratio of **21a** to **20a** than experienced with **1a**. This suggests that the intermediate epoxide **21a** is less reactive than the corresponding syn isomer **3a** derived from **1a**. In this context, Bruice and co-workers[11] compared the hydrolysis rates for the *anti*- and *syn*-diol monoepoxides **16** and **17**, respectively, as well as those for the dimethylated derivatives **21b** and **3b**. They established that the rate constants for the spontaneous hydrolysis of the syn diether and diol epoxides (**3b** and **17**, respectively) are comparable and higher than those found for the anti pair **21b** and **16**. Thus, it is clear that conformational effects are responsible for the rate phenomena.[11] Differential reactivities in this series arise from the inherent conformational dissimilarities, i.e., the 1,2-substituents in the syn series **3a,b** and **17** are trans diaxial, while those of **16**, **21a** and **21b** of the anti series are equatorial.[11] The enhanced reactivity observed in the former series reflects steric strain induced by unfavorable 1,3-diaxial interactions.

The NMR spectra of the diol **20a**, the tetramethyl ether **20b**, and the dimesylate **20c** all exhibit an AA'BB' or AA'XX' splitting pattern which is in full accord with the symmetry of the proposed structures. The absence of 1,3-proton splitting leads to the conclusion that the steric relationship between the 1,2,3,4-substituents is trans–cis–trans in **20a–c**. Further evidence to support the cis relationship between the 2- and 3-hydroxy groups in **20a** was obtained by treatment of this diol with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid. The *cis*-diol **20a**, like its trans counterpart, undergoes a facile transformation to give an acetonide, assigned structure **10**. Two signals of equal intensity are observed for the methyl group in the NMR spectrum of this product. The signal observed at higher field (δ 1.4) is assigned to the methyl group syn to the aromatic nucleus, which is shielded relative to the methyl protons syn to the 2,3-methine hydrogens at the ring juncture. The regioselectivity of addition of methoxides to **1b** was apparent from the mass spectrum of **20a**, which exhibits a base peak at m/e 164 anticipated for the retro-Diels–Alder *o*-xylylene ion **5**. This assignment was confirmed by conversion of **20a** to the dimesylate **20c**, which upon treatment with base undergoes transformation to 1,4-dimethoxynaphthalene (**9**) albeit in much lower than obtained from **4b**. A pair of sequential two-step syn eliminations are required in each case to effect the observed conversions.

In the present study, the reactions of two other nucleophilic oxy anions with **1a** and **1b** have also been examined. The nucleophilic addition of oxy nucleophiles to arene oxides is of synthetic, as well as biochemical interest. Enzymatic hydration of arene oxides to *trans*-dihydrodiols, for example, is a key step in metabolism of polynuclear aromatic hydrocarbons.[13] Both **1a** and **1b** are susceptible to attack by nucleophiles such as phenoxide and acetate ions. For example, when the *anti*-diepoxide **1a** is treated with sodium phenoxide in aqueous acetonitrile, a diphenyl ether assigned structure **22a** is formed in high yield

(13) (a) D. M. Jerina, H. Yagi, and J. W. Daly, *Heterocycles*, 1, 267 (1973); (b) D. M. Jerina and J. W. Daly, *Science*, 185, 573 (1974).

Scheme III



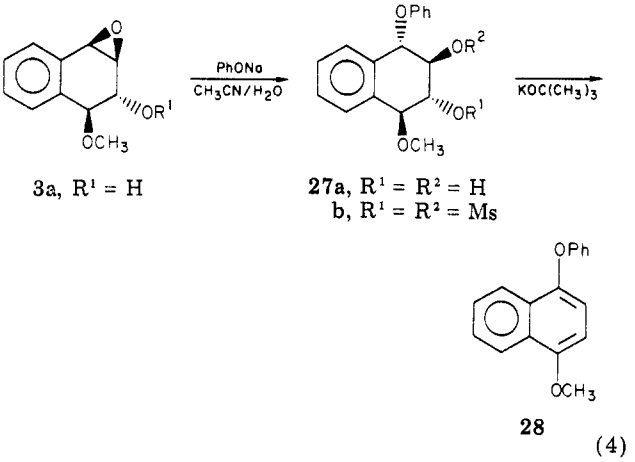
(Scheme III). As anticipated, opening of the epoxy rings occurs in the trans manner by attack at the C-1 and C-4 positions to afford the dihydroxy-substituted tetrahydronaphthalene **22a**. The conversion of **22a** to an acetonide derivative, **23**, with equivalent methyl groups is consistent with the structure proposed for the former incorporating a C_2 axis, and thus 1,4-regioselective additions of sodium phenoxide to **1a** occur in a trans manner at both sites. The NMR spectra of **22a** and **23** display AA'XX' splitting patterns typical of those exhibited by the corresponding dimethoxy derivatives **4a** and **7** assigned "all trans" stereochemistry. Furthermore, the magnitudes of the coupling constants ($J_{1,2}$ = 6 Hz and $J_{1,3}$ = 2 Hz) compare favorably with those observed for **4a** and **7**.

The absence of the characteristic retro-Diels–Alder fragmentation peaks in the mass spectra of **22a** and **23** is attributed to the facile, competitive cleavage of the phenoxy bonds. The ions $(M-94)^+$ and $(M-188)^+$, which correspond to loss of one and two molecules of phenol, respectively, comprise the secondary and base peaks in the mass spectrum of the diol diether **22a**. The crude dimesylate **22b**, prepared in turn from **22a** and mesyl chloride, when treated with potassium *tert*-butoxide gives an aromatized product, presumably the previously unknown 1,4-diphenoxynaphthalene (**24**). That this assignment is correct is evident from NMR spectral data. Zweig and co-workers[14] had established that a characteristic downfield shift from δ 7.6 to 8.2 is experienced by the aromatic protons in the 5,8-positions peri to 1,4-dimethoxy and methylthio substituents which may be used to differentiate 1,4- from 2,3-disubstituted naphthalene derivatives. This downfield shift of 0.6 ppm, absent in the spectra of 2,3-disubstituted naphthalenes, is attributed to a strong deshielding effect exerted by the 1,4-substituents on the proximal peri protons.[14] It is evident from inspection of the NMR spectrum of **24** that the characteristic "peri effect" observed for 1,4-dimethoxynaphthalene (**9**) is operative (δ 8.1).

Similarly, treatment of the *syn*-dioxide **1b** with phenoxide anion affords a diether diol assigned structure **25a** (Scheme III). The latter, like the stereoisomer **22a**, was readily converted to an acetonide, assigned structure **26**, which exhibits two distinct NMR methyl proton signals. The nonequivalent methyl signals, like those observed for **10**, arise from the anticipated differential electronic environments encountered by the methyl protons which lie on the molecular σ plane of **26**. As in the case of the "all trans" diol diether **22a**, mass spectrometry proved ineffective in defining the regioselectivity of attack by phenoxide ion on **1b**; i.e., loss of phenol occurred in place of retro-Diels–Alder fragmentation.

It should be noted that the base-induced conversion of the "all trans" diol dimesylate **22b**, obtained from the anti dioxide **1a**, occurs in higher yield than is observed for the dimesylate of the cis stereoisomer **25b**, although syn eliminations are required in both cases. These results parallel those observed with the corresponding methoxy analogues **4b** and **20c**.

The preparation of 1,4-diphenoxynaphthalene (**24**), which is clearly inaccessible by convenient, direct aromatic substitution reactions, provides an excellent example of the potential utility of arene oxides as synthetic precursors for other functionalized polynuclear systems, which we have begun to exploit. For example, the monoepoxide **3a**, formed from the *anti*-dioxide **1a** and methanol, reacts with phenoxide ion to give the unsymmetrical diol diether assigned structure **27a**, which was converted to the dimesylate **27b** without further purification (eq 4). The crude



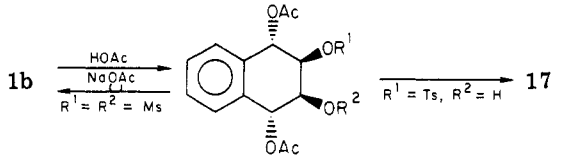
(4)

dimesylate, upon treatment with potassium *tert*-butoxide in tetrahydrofuran, is converted to 1-methoxy-4-phenoxynaphthalene (**28**). The signals for two aromatic protons in the NMR spectrum of **28** exhibit typical downfield "peri shifts",[14] albeit of differing magnitude [δ 8.05 (m) and 8.25 (m)], in accord with the structural assignment **28**.

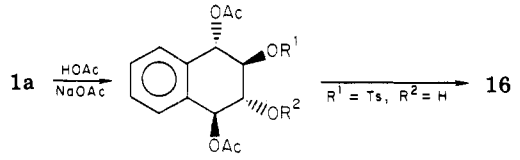
Treatment of **1b** with glacial acetic acid buffered with sodium acetate gives the diol diacetate **29a** (eq 5), which was prepared previously through a multistep synthesis devised by Schmidt and co-workers.[15] The dimesylate **29b** derived from **29a** was utilized by Schmidt as the key precursor in an alternate route to the *syn*-diepoxide **1b** first prepared by Vogel,[1c] while the monotosylate **29c** was converted with sodium carbonate in methanol to the *syn*-dihydrodiol epoxide **17** (eq 5).[10] We found that the *anti*-diepoxide **1a** is converted to the "all trans" isomeric diol diacetate **30a** upon reflux with buffered glacial acetic acid (eq 6) and was characterized by NMR by using criteria previously described for **4a** and **22a**. Treatment of the monotosylate **30b** derived from **30a** with sodium carbonate

(14) (a) A. Zweig, J. E. Lancaster, and M. T. Neglia, *Tetrahedron*, **23**, 2577 (1967); (b) A. Zweig, A. H. Maurer, and B. G. Roberts, *J. Org. Chem.*, **32**, 1322 (1967).

(15) R. R. Schmidt and R. Angerbauer, *Angew. Chem.*, **91**, 325 (1979); *Angew. Chem., Int. End. Engl.*, **18**, 304 (1979).



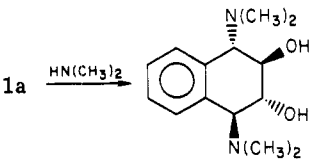
29a, $R^1 = R^2 = H$
b, $R^1 = R^2 = Ms$
c, $R^1 = Ts$; $R^2 = H$ (5)



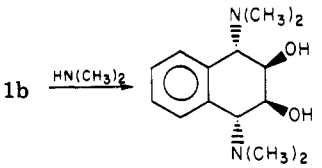
30a, $R^1 = R^2 = H$
b, $R^1 = Ts$; $R^2 = H$ (6)

in methanol affords the *anti*-diol epoxide **16**, providing an independent route to a structural affirmation for this biologically significant rat metabolite of naphthalene[2a] first prepared by Jerina and co-workers.[10]

It is maintained by Jerina that conventional nitrogen nucleophiles (e.g., ammonia and amide ion) are unreactive toward benzene oxide and naphthalene 1,2-oxide (**2**) in contrast to azide ion, which is more polarizable.[4a] Posner and Rogers,[16] however, found that **2** reacts at room temperature with weak nitrogen nucleophiles such as *n*-butylamine and aniline in the presence of basic alumina. It is proposed that the amine-doped alumina increases the rate of nucleophilic amine incorporation relative to aromatization of **2** to 1-naphthol.[16] On the basis of our experience, the isomeric dioxides **1a** and **1b** are much less susceptible to spontaneous ring-opening and aromatization than the naphthalene oxide **2** and thus perhaps more predisposed to sustain nucleophilic attack without accompanying aromatization. In fact, addition of dimethylamine to **1a** and **1b** in absolute ethanol proceeds under reflux to give adducts assigned structures **31** and **32**, respectively, in high yield (eq 7 and 8). The splitting patterns for the



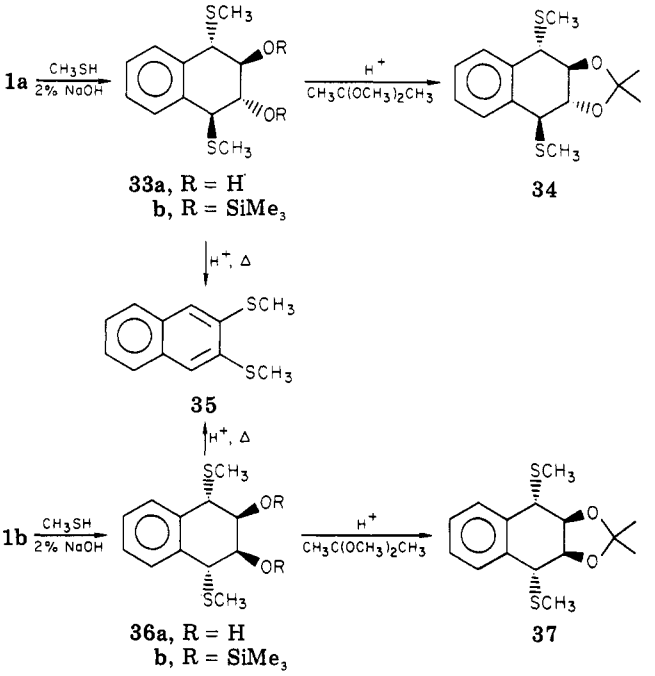
31 (7)



32 (8)

methine protons of these adducts (AA′BB′ and AA′XX′) are consistent with the assigned structures which would arise by 1,4-regioselective trans addition of dimethylamine to **1a** and **1b**, respectively. Also consistent is the fact that the chemical shifts for the methine protons on C_2 and C_3 which bear hydroxy groups (trans, δ 3.9; cis, δ 4.2) are identical within δ ±0.05 with those of the stereoisomeric adducts **4a** and **20a**, whose structures are securely established. Furthermore, it is also evident from the NMR spectra that regioselective addition of dimethylamine to

Scheme IV



the oxirane rings at the less hindered 2,3-positions in **1a** and **1b** to give a pair of symmetrical isomeric diol diamines with the hydroxy groups at the 1,4-benzylic positions may be excluded. No signals appear in the region δ 4.7, which is characteristic of a benzylic methine proton adjacent to the hydroxy group, such as that in 1,2,3,4-tetrahydro-1-naphthol. On the other hand, the chemical shift of the signals at δ 3.7 in the spectra of **31** and **32** corresponds closely to that of 1,2,3,4-tetrahydro-1-naphthylamine. Attempts, to date, to convert **31** or **32** to 1,4-bis(dimethylamino)naphthalene have proven unsuccessful.

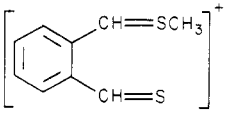
In mammals, the enzyme-catalyzed addition of glutathione to arene oxides to give a premercapturic acid precursor is recognized as a mechanism for the detoxification and excretion of a variety of xenobiotic aromatic substrates.[13] During the course of our studies on the metabolism of naphthalene in rats using GC and computerized GC/MS procedures, a series of methylthio derivatives were identified as urinary products.[2] Although many metabolites of naphthalene, including sulfur-containing conjugates, have been identified,[17] to our knowledge, no methylthio derivatives had previously been reported. It was subsequently established, by deuterium labeling experiments, that methionine or methionine derivatives are implicated as the source of the thiomethyl metabolites.[2b] While GC/MS techniques provide substantial information concerning the gross skeletal features of the derivatized naphthalene metabolites, complete structural characterization of the products, i.e., differentiation of positional isomers and elucidation of stereochemical details, necessitate extensive synthetic and spectroscopic effects, which could be facilitated as a consequence of the accessibility of the isomeric dioxides **1a** and **1b**. The reactions of these isomeric dioxides **1a** and **1b**, as well as the diol epoxides **16** and **17**, and naphthalene 1,2-oxide (**2**) with the sulfur nucleophile methanethiol were examined (Scheme IV) in an attempt to establish the structures and origin of urinary metabolites obtained in studies conducted with rats.

(16) G. H. Posner and D. Z. Rogers, *J. Am. Chem. Soc.*, **99**, 8214 (1977).

(17) (a) L. Young, *Biochem. J.*, **41**, 417 (1946); (b) E. Boyland, G. S. Ramsay, and P. Sims, *ibid.*, **78**, 376 (1961); (c) D. M. Jerina, J. W. Daly, B. Witkop, P. Zaltzman-Nirenberg, and S. Udenfriend, *Biochemistry*, **9**, 147 (1970).

Addition of sodium thiomethoxide to **1a** in an aqueous medium proceeds readily on stirring at 25 °C to give high yields (80%) of a bis(methylthio) derivative assigned structure **33a**. That ring opening occurs by attack at the C_1 and C_4 positions in a trans fashion, as observed for oxy and nitrogen nucleophiles, is once again evident from NMR data supplemented by mass spectral fragmentation patterns of trimethylsilyl derivatives. It is significant that **33a** corresponds to a major metabolite of naphthalene found in mouse and rat urine.[2a,b] Similar treatment of **1b** with thiomethoxide provides the methylthio adduct assigned structure **36a**, which was also identified as a urinary metabolite of naphthalene in rats.

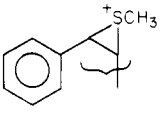
The regioselectivity of addition of methanethiol to **1a** was deduced from the mass spectrum of the Me_3Si derivative **33b** obtained from the diol adduct **33a**. An ion of m/e 181, assigned structure **38**, incorporating 1,4-sulfur



38

substituents, is evident in the spectrum of **33b** and is presumably formed in a process involving initial retro-Diels–Alder fragmentation.[2] The Me_3Si derivative **36b** of metabolite **36a** has a mass spectrum that closely resembles that of **33b**, suggesting that they are stereoisomers.[2] Acetonides **34** and **37** may also be formed readily from the diols **33a** and **36a**, respectively, which is also characteristic of other diols formed by 1,4-addition of nucleophiles to **1a** and **1b**. While the NMR spectrum of the acetonide **34** derived from the diol **33a**, obtained in turn from **1a**, is characterized by a sharp singlet for the methyl protons, nonequivalent signals are observed for the corresponding protons of the acetonide **37** derived from **1b**. Clearly, a consistent pattern of behavior toward nucleophiles is followed by both **1a** and **1b**.

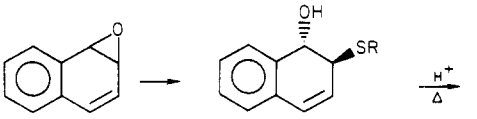
Both stereoisomeric diols **33a** and **36a** undergo rapid acid catalyzed dehydration (10% *p*-toluenesulfonic acid) upon heating under reflux in benzene with accompanying rearrangement to give 2,3-bis(methylthio)naphthalene (**35**) in high yield (90%). The structure of **35** was confirmed by comparison of the NMR spectral data and melting point reported for an authentic sample prepared in low yield (4%) by treatment of 2,3-dibromonaphthalene with cuprous methyl mercaptide.[14b] The rearrangement of **33a** and **36a** attending aromatization is assumed to proceed via sequential migration of the 1,4-thiomethyl groups to the 2,3-positions. Aromatization of such cyclic ions as **39**



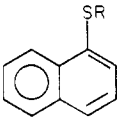
39

should occur with preferential cleavage of the C–S bond(s) adjacent to the benzylic position to give 2,3-bis(methylthio)naphthalene.

Treatment of naphthalene 1,2-oxide (**2**) with methanethiol gives *trans*-1-hydroxy-2-(methylthio)-1,2-dihydronaphthalene (**40a**, eq 9), identified as an additional urinary metabolite of naphthalene in rats.[2] The structural assignment **40a** is inferred from NMR coupling constants and chemical shift data which compare favorably with those reported by Jerina and co-workers[5a] for the corresponding ethylthio derivative **40b** prepared in a similar manner. The methylthio derivative **40a**, like its ethyl



2 **40a**, R = CH_3; **b**, R = CH_2CH_3

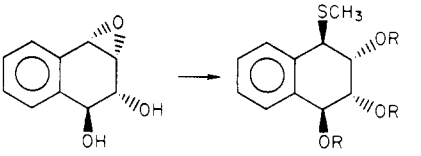


41a, R = CH_3; **b**, R = CH_2CH_3

(9)

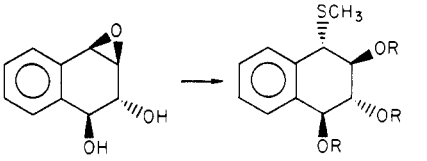
analogue, undergoes facile dehydration accompanied by methylthio migration under acidic conditions to give 1-(methylthio)naphthalene (**41a**). Since naphthalene 1,2-oxide (**2**) has been characterized as a primary metabolite in the microsomal oxidation of naphthalene, it is not surprising that both **40a** and **41a** were found as urinary metabolites of naphthalene in the rat.[2]

The two methylthio adducts **42a** and **43a**, synthesized from the diastereomeric dihydrodiol epoxide **16** and **17**, respectively (eq 10 and 11), were found to be identical with



(10)

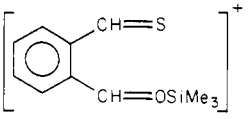
16 **42a**, R = H; **b**, R = $SiMe_3$



(11)

17 **43a**, R = H; **b**, R = $SiMe_3$

two sulfur metabolites detected in rat urine.[2] The mass spectra of the trimethylsilyl derivatives **42b** and **43b**, obtained from the triols **42a** and **43a**, respectively, show a prominent ion at m/e 223, assigned as structure **44**, which

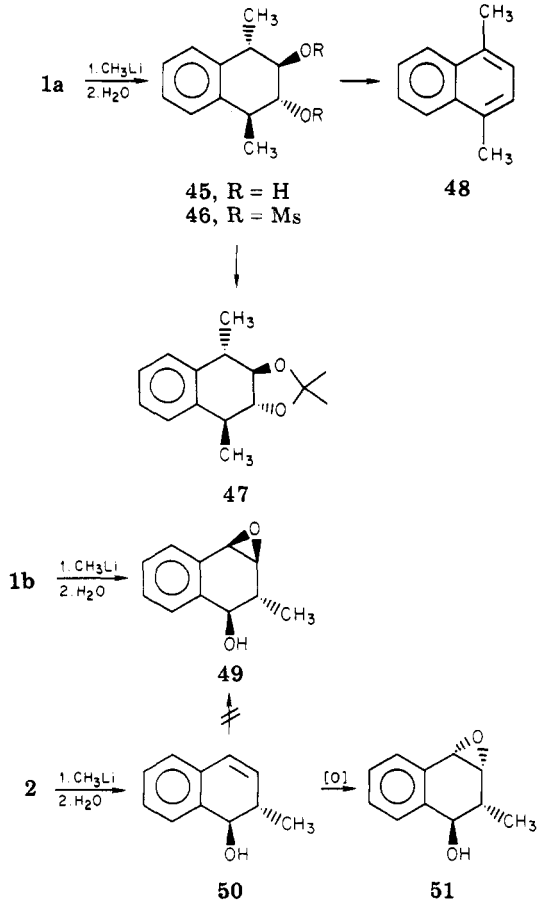


44

results from initial retro-Diels–Alder fragmentation. The stereochemical assignment of **42a** rests on previous generalizations developed for such systems with respect to C_2 and C_3 methine proton coupling constant data; i.e., the value of $J_{2,3}$ (2.3 Hz) is of such magnitude that the C_2 and C_3 OH groups must be cis.[10a,15] It is not insignificant that methylthio derivatives of a diepoxide are detected among the urinary metabolites of naphthalene in rats; this may be interpreted as evidence that di- or even polyarene oxides of polynuclear hydrocarbons could be intermediates in the metabolism of this class of compounds in vivo.

The reaction of **1a** and **1b** with typical organometallic reagents such as methyllithium and dimethyllithium cuprate has also been explored (Scheme V). Not unexpectedly, methyllithium in diethyl ether adds to **1a** to give as the sole product the tetrahydrodiol **45** formed by trans

Scheme V

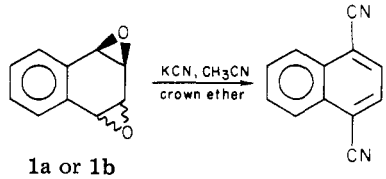


addition at the benzylic C_1 and C_4 sites of the diepoxide. The regioselectivity assigned to diol **45** was inferred from mass spectral data. A conspicuous peak is present in the mass spectrum of **45** at *m/e* 132, which corresponds to the anticipated retro-Diels–Alder fragment, incorporating methyl substituents at the original 1,4-positions of the parent ion. The conversion of the diol **45** to an acetonide **47** bearing equivalent methyl proton signals and having C_1–C_2 (C_3–C_4) and long range C_1–C_3 (C_2–C_4) methine proton coupling constant values ($J_{1,2}$ = 6 Hz, $J_{1,3}$ = 2 Hz, respectively) characteristic of other *trans*-2,3-diols in this series provides additional evidence to support the assignment. The dimesylate **46**, derived from **45**, upon treatment with base affords 1,4-dimethylnaphthalene (**48**) identical in all respects with an authentic sample; this supports the proposed gross structural assignment for the diol **45**. Acid-catalyzed dehydration of **45** to **48** was achieved (50%) upon treatment of the former with *p*-toluenesulfonic acid in toluene at reflux temperature for a period of 2 days. Under less drastic conditions, i.e., in benzene at reflux temperature, dehydration did not occur. No evidence for methyl migration or ring contraction accompanying dehydration was observed.

The reaction of **1b** with methyllithium, in direct contrast to that with **1a**, gives as a sole product **49**, formed by attack of methyllithium at the 2-position with trans opening of a single oxirane ring even when the reaction time is extended to longer periods than that employed with **1a** (Scheme V). That this monomethyl epoxide **49** has a hydroxy group which bears a syn configurational relationship to the residual epoxy group is clear from the NMR spectrum which resembles that of the *syn*-diol epoxide **17**; i.e., the benzylic hydroxy group at C_1 is intramolecularly hydrogen bonded in a transannular fashion to the oxygen of the epoxy ring.[10] Addition of methyllithium at C_2 rather than C_1 with inversion is evident from the chemical shift observed for the methyl group of **49** (δ 0.71) which appears at significantly higher field than that observed for the benzylic methyl substituent of **46a** (δ 1.45). The NMR coupling constant measured in Me_2SO-d_6 for the methine protons at C_1 and C_2 of **49** is approximately 3 Hz, which suggests that the hydroxy and methyl substituents at C_1 and C_2, respectively, designated as trans, are diaxial in this stereoisomer.

In contrast to expectations based on the relative size and proximity of the methyl substituent, peroxidation of the known *trans*-1-hydroxy-2-methyl-1,2-dihydronaphthalene (**50**)[5] with *m*-chloroperbenzoic acid gives **51** as the major product in addition to traces of **49**. The observed coupling constant (~9.5 Hz) is of such magnitude that it may be discerned that the C_1 and C_2 methine protons must occupy pseudodiaxial positions and that the C_1 benzylic hydroxy group is pseudoequatorial. This observation is consistent with the structural assignment **51**, in which intramolecular hydrogen bonding and accompanying conformational distortion are precluded by stereochemical relationships. It remains to be established why the *anti*-epoxide **51** is the predominant product formed upon peroxidation of **50** despite expectations to the contrary.

The reaction of **1a** and **1b** with cyanide anion has also been examined eq 12. Either of the oxides **1a** or **1b** upon

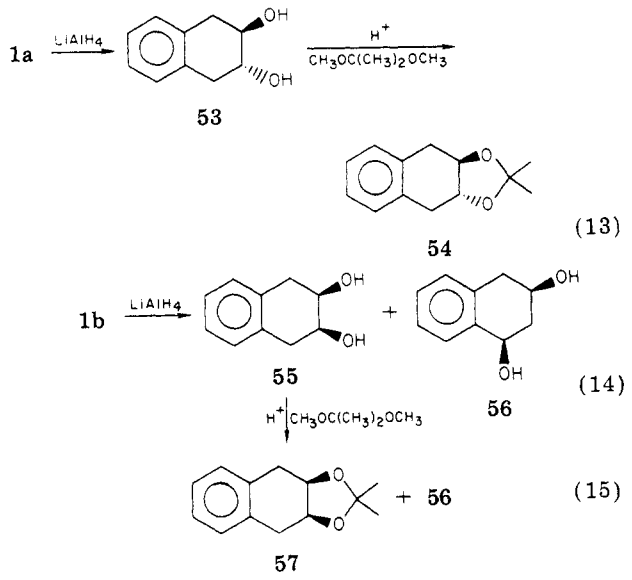


1a or 1b — 52 (12)

heating with potassium cyanide in acetonitrile in the presence of 18-crown-6[18] gives 1,4-dicyanonaphthalene (**52**), identical in all respects with an authentic sample prepared by treatment of 1,4-dibromonaphthalene with cuprous cyanide at elevated temperatures.[19] 1,4-Dicyanonaphthalene is a widely used electron-transfer agent,[19] and the synthesis of this useful reagent independently from **1a** and 1,4-dibromonaphthalene furnishes an excellent opportunity to compare the relative advantages of methods herein described for the synthesis of substituted aromatic systems with those of classical methods perhaps requiring more expensive and/or less accessible precursors such as the dibromide utilized here for the preparation of **52**.

Reduction of both **1a** and **1b** with lithium aluminum hydride has been examined (eq 13 and 14). The reaction of the *anti*-dioxide **1a** proceeds in ether to give a single product, **53**, derived by reduction of the benzylic C–O bonds from the least hindered side. The trans stereochemistry assigned to the reduction product **53** was confirmed by comparison with an authentic sample prepared from 1,4-dihydronaphthalene by the Prévost procedure followed by base hydrolysis of the diacetate.[11,20] Treatment of **53** with 2,2-dimethoxypropane and a trace of acid affords, as expected, the *trans*-acetonide **54**, whose NMR spectrum exhibits a sharp singlet signal for the methyl protons in accord with other 2,3-acetonides assigned trans stereochemistry. In contrast, two products designated **55** and **56** were obtained upon reduction of the isomeric dioxide **1b** with lithium aluminum hydride. The major product, assigned the *cis*-2,3-diol structure **55**, was pre-

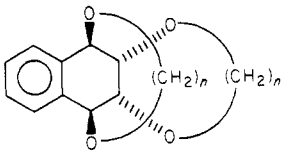
(18) F. L. Cook, C. W. Bowers, and C. L. Liotta, *J. Org. Chem.*, **39**, 3416 (1974).
(19) A. Albini, and D. R. Arnold, *Can. J. Chem.*, **56**, 2985 (1978).
(20) E. Ali and L. N. Owen, *J. Chem. Soc.*, 1066 (1958).



pared independently from 1,4-dihydronaphthalene by a modification of the Woodward procedure, in which potassium iodate and potassium acetate[21] were used rather than silver acetate.[20,22] It proved necessary to convert the *cis*-diol **55** in the crude mixture into the acetonide **57** in order to achieve the separation of the minor product **56**, which does not form an acetonide. On the basis of NMR data which indicate the presence of two different methine and methylene protons, respectively, the minor product **56** was assumed, but not proved, to be the *cis*-1,3-diol resulting from the attack of hydride anion at the C-1 and C-3 positions of the *syn*-dioxide **1b**. Considerable doubt remains regarding this stereochemical assignment, however, since Yang and co-workers[23] had found that a diacetonide could be formed by bridging two pairs of hydroxy groups in a cis 1,3 fashion.

syn-Benzene dioxide was found to exist in a state of equilibrium with its eight-membered-ring valence tautomer 1,4-dioxocin above 50 °C.[24] In the case of syn dioxide **1b**, however, the existence of a thermal equilibrium between **1b** and its 1,4-dioxocin valence tautomer could not be established, either by spectroscopic methods or by trapping reactions with dienophiles.[1c] This may be attributed to the fact that valence bond isomerization would accompany destruction of aromaticity in the adjacent ring. Thermolysis of the *syn*-dioxide **1b** in xylene at ~190 °C gives rise to 2,3-dihydroxynaphthalene (**58**), whose identity was established by comparison with an authentic sample. Both **1a** and **1b** have been found in preliminary studies to be photostable.

In summary, it is clear that the isomeric dioxides **1a** and **1b** are both susceptible to attack by nucleophiles, thus providing a useful synthetic entry into substituted tetrahydronaphthalene systems. The formation of **24** suggests that it may be possible to generate highly stable polyaryl ethers incorporating condensed ring units of potential utility as photo-sensitizers and electron-transfer sensitizers, as well as polymers of commercial significance. A host of unusual crown ethers, such as **59**, may be accessible from bis(oxiranes), of which **1b** is only representative and work in this area is in progress in collaboration with Prof. George Newkome and G. E. Kieffer, Louisiana State University in Baton Rouge.



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Experimental Section

Infrared spectra were recorded on Perkin-Elmer Model 257 and 283 spectrophotometers. Ultraviolet spectra were obtained on a Cary Model 17 spectrophotometer. Mass spectra were determined with a Hitachi Perkin-Elmer RMU-6E mass spectrometer.

The 60-MHz proton magnetic resonance spectra were obtained on a Varian A-60 or Hitachi Perkin-Elmer R-20B spectrometer. The 90-MHz spectra were recorded with a JEOL FX-900 spectrometer while 200-MHz spectra were recorded on a Bruker 200-MHz spectrometer, through the courtesy of Professor N. S. Bhacca (Louisiana State University, Baton Rouge). Deuteriochloroform was generally used as the solvent, and the chemical shift data are reported in parts per million (δ) downfield from tetramethylsilane used as an internal standard with coupling constants (J) given in hertz. The NMR spectral data are displayed in Table I and are therefore omitted from the Experimental Section.

Melting points were measured in capillary tubes on a Thomas-Hoover apparatus and are uncorrected. Silica gel G (PF 254; Brinkman Co.) on glass plates was used for thick- and thin-layer chromatography.

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Combustion analyses for C, H, and N all fall within acceptable limits of the theoretical values.

Preparation of *anti*-1,2:3,4-Naphthalene Dioxide (1a). The *anti*-naphthalene dioxide **1a** was synthesized from naphthalene and 85% *m*-chloroperbenzoic acid by using the procedure developed by Ishikawa and Griffin.[1a,b]

Preparation of *syn*-1,2:3,4-Naphthalene Dioxide (1b). The *syn*-naphthalene dioxide **1b** was prepared according to a modification of the original procedure.[1c,20] 1,4-Dihydronaphthalene (54.0 g, 0.42 mol),[25] glacial acetic acid (1200 mL), potassium iodate (21.0 g, 0.10 mol), water (5 mL), and iodine (51.0 g, 0.20 mol) were stirred at room temperature for 3 h and then heated under reflux with potassium acetate (28.0 g, 0.27 mol) for 4 h.[21] The mixture was allowed to cool, excess solvent removed under reduced pressure, and the residue dissolved in methanol (500 mL). The methanol solution was then treated with excess potassium hydroxide (20 g after neutralization) and allowed to stir for 2 h. The solution was then adjusted to pH 7 with acetic acid, water was added (200 mL), and the organic solvent was removed from the resulting mixture on a rotary evaporator. Continuous extraction of the residual aqueous phase with chloroform and subsequent concentration of this solvent gave the *cis*-diol **55** (30.0 g, 44%), which was crystallized from chloroform to give pure diol as white needles, mp 122–123 °C (lit.[20,22] mp 124–125 °C). The purified diol (4.0 g, 24 mmol) was then treated with trifluoroacetic anhydride (12 mL) in chloroform for 12 h at 0 °C to give the corresponding bis(trifluoroacetate). After repeated recrystallization from petroleum ether, this derivative (7.2 g, 20 mmol, 82%) was treated with *N*-bromosuccinimide (10.0 g, 56 mmol) in carbon tetrachloride (100 mL). Catalytic amounts of benzoyl peroxide were added initially, and the slurry was heated to 50–60 °C with stirring in a nitrogen atmosphere while simultaneously being irradiated with a G.E. sunlamp. Upon completion of the reaction (0.5 h), the resulting succinimide was collected on a filter and the filtrate concentrated under vacuum to give a dibromo bis(trifluoroacetate) as a yellow oil. Without further purification, this bromohydrin derivative was dissolved in dry tetrahydrofuran, and sodium methoxide (3.8 g, 70 mmol) was added at 0 °C while the

(21) L. Mangoni, M. Adinolfi, G. Barone, and M. Parrilli, *Tetrahedron Lett.*, 4485 (1973).
(22) P. E. Verkade, J. Coops, Jr., C. J. Maan, and A. Verkade-Sandbergen, *Justus Liebigs Ann. Chem.*, **467**, 217 (1928).
(23) S. K. Yang, D. W. McCourt, H. V. Gelboin, J. R. Miller, and P. P. Roller, *J. Am. Chem. Soc.*, **99**, 5124 (1977).
(24) H.-J. Altenbach and E. Vogel, *Agnew. Chem.*, **84**, 985 (1972); *Agnew. Chem., Int. Ed. Engl.*, **11**, 937 (1972).
(25) E. S. Cook and A. J. Hill, *J. Am. Chem. Soc.*, **62**, 1995 (1940).

nitrogen atmosphere was maintained. The resulting reaction mixture was stirred for 3 h and then partitioned twice between chloroform and water. The chloroform extracts were combined and dried over anhydrous potassium carbonate. Subsequent removal of the volatile solvent under reduced pressure afforded a residue containing the *syn*-diepoxide **1b**, which was subsequently recrystallized from ethyl acetate: 1.2 g (30%); mp 180 °C (lit.[1c] mp 178–180 °C). The NMR spectral data compared favorably with those reported for **1b** prepared earlier by Vogel and co-workers.[1c]

***r*-1-Methoxy-*t*-2-hydroxy-*c*,*c*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (3a).** A solution of 130 mg (0.81 mmol) of the bis(oxirane) **1a** in 20 mL of methanol was allowed to stand for 96 h at ambient temperature. Subsequent removal of the solvent under reduced pressure gave 150 mg (96%) of **3a** as an oily liquid which solidified upon standing in a freezer for 3 days: mp 89.5–90.5 °C; mass spectrum, *m/e* 192 (M^+), 174 ($M^+ - H_2O$), 160 ($M^+ - CH_3OH$), 148 ($M^+ - CH_3CHO$),[26] 145, 131, 115, 103, 91, 77. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.60; H, 6.30.

***r*,*t*-1,2-Dimethoxy-*c*,*c*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (3b).** The oxirane **3a** (210 mg, 1.10 mmol) was dissolved in 20 mL of DMF. Methyl iodide (620 mg, 4.40 mmol) and silver oxide (510 mg, 2.20 mmol) were added, and the mixture was stirred at ambient temperature for 72 h. Chloroform (50 mL) was added to the reaction mixture, and the resulting precipitate was removed by filtration. The filtrate was concentrated in vacuo at 100 °C, and the residual colorless oil was separated and purified by preparative TLC (silica gel) with ether–hexane (7:3, respectively) as the eluent mixture. The desired product was extracted from the silica gel by repeated washing with ether. The solvent was then removed under reduced pressure and the crude residual product purified by recrystallization from ether–hexane to give 160 mg of **3b** (72%) as a colorless crystalline solid: mp 105–106 °C (lit.[11] mp 115.7–117.0 °C); mass spectrum, *m/e* 206 (M^+), 191 ($M^+ - CH_3$), 175 ($M^+ - CH_3O$), 148.[26] Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 70.10; H, 7.02.

***r*,*t*-1,4-Dimethoxy-*t*,*c*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (4a). (a) Base-Catalyzed Reaction.** A solution of the bis(oxirane) **1a** (270 mg, 1.70 mmol) in 20 mL of methanol containing sodium methoxide (460 mg, 8.4 mmol) was stirred at ambient temperature for 48 h. To the resulting solution was added solid ammonium chloride (~100 mg), and stirring was continued for an additional 30 min. The resulting solids were collected on a filter and the filtrate concentrated in vacuo to give the crude product. The residue was then redissolved in methylene chloride (50 mL) and the residual solid removed by filtration. Subsequent removal of the solvent under reduced pressure gave a crystalline solid which was recrystallized from hexane–chloroform to give **4a**: 290 mg (78%); mp 130.5–131.5 °C; mass spectrum, *m/e* 206 ($M^+ - H_2O$), 192 ($M^+ - CH_3OH$), 174 ($M^+ - CH_3OH - H_2O$), 164,[26] 160 ($M^+ - 2\ CH_3OH$), 149. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.04; H, 7.06.

(b) Acid-Catalyzed Reaction. A mixture of the diepoxide **1a** (260 mg, 1.5 mmol) and *p*-toluenesulfonic acid monohydrate (30 mg, 0.15 mmol) in 20 mL of methanol was stirred at ambient temperature for 12 h. Powdered sodium bicarbonate (50 mg) was added and the reaction mixture stirred for another 30 min. The excess bicarbonate was removed by filtration, and the filtrate was concentrated under vacuum to give a solid, which was dissolved in 50 mL of methylene chloride. After collection of the residual insoluble material by filtration, the solvent was removed and the crude product recrystallized from chloroform–hexane to give pure diol **4a**: 260 mg (76%); mp 130.5–131.5 °C.

(c) Treatment of 3a with Sodium Methoxide. The oxirane **3a** (90 mg, 0.47 mmol) was treated with sodium methoxide (130 mg, 2.35 mmol) in methanol (20 mL) in a manner similar to that employed for **1a** with sodium methoxide to give **4a**: 84 mg (80%); mp 130.5–131.5 °C.

***r*,*t*-1,4-Dimethoxy-*t*,*c*-2,3-bis(tosyloxy)-1,2,3,4-tetrahydronaphthalene (4b).** A solution of the diol **4a** (410 mg, 1.81 mmol), tosyl chloride (1.38 g, 7.24 mmol), and pyridine (10 mL) was heated under reflux for 6 h. The resulting mixture was concentrated in vacuo and the residual oil purified by preparative TLC on silica gel by employing 50% ether–hexane as the eluent mixture to give 600 mg of **4b** (62%) as a colorless oil.

***r*,*t*,*c*,*t*-1,2,3,4-Tetramethoxy-1,2,3,4-tetrahydronaphthalene (4c). (a) Methylation of 4a.** The procedure outlined for the preparation of **3b** was followed. The diol **4a** (210 mg, 1.10 mmol) was treated with methyl iodide (620 mg, 4.4 mmol) and silver oxide (510 mg, 2.20 mmol) to give **4c** (180 mg, 62%) as a colorless oil: mass spectrum, *m/e* 252 (M^+), 220 ($M^+ - CH_3OH$), 189 ($M^+ - CH_3OH - CH_3O$), 164,[26] 149. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.38; H, 8.06.

(b) Methylation of 11. The procedure for the preparation of **11** will be described below. The tetraol **11** (200 mg, 1 mmol) was treated with methyl iodide (1.4 g, 10 mmol) and silver oxide (1.20 g, 5 mmol) in 20 mL of DMF to give 170 mg of **4c** (67%), which is identical in all respects with that obtained by methylation described above in method a.

***r*,*t*,*t*-1,2,4-Trimethoxy-*c*-3-hydroxy-1,2,3,4-tetrahydronaphthalene (4d).** The procedure outlined for the preparation of **4a** was followed. The oxirane **3b** (310 mg, 1.50 mmol) was allowed to react with sodium methoxide (410 mg, 7.60 mmol) in 20 mL of methanol. The crude product, obtained in 90% yield as a colorless oil, solidified after being allowed to stand for 5 days at ambient temperature to give crystals of **4d**: mp 55.5–56.5 °C; mass spectrum, *m/e* 206 ($M^+ - CH_3OH$), 174 ($M^+ - 2CH_3OH$), 164,[26] 149.

***r*,*t*,*t*-1,2,4-Trimethoxy-*c*-3-(mesyloxy)-1,2,3,4-tetrahydronaphthalene (4e).** A mixture of **4d** (170 mg, 0.71 mmol), methanesulfonyl chloride (250 mg, 2.20 mmol), and pyridine (2 mL) was stirred at ambient temperature for 3 days. Pyridine and excess methanesulfonyl chloride were removed under reduced pressure and separation, and purification of the residual oil were achieved by preparative TLC (silica gel) with ether–hexane (8:2) as the eluent mixture. A total of 170 mg (74%) of the mesylate **4e**, a colorless oil, was obtained which solidified after standing in a freezer for 3 days: mp 68–70 °C; mass spectrum, *m/e* 316 (M^+), 284 ($M^+ - CH_3OH$), 220 ($M^+ - CH_3SO_2OH$), 188 ($M^+ - CH_3SO_2OH - CH_3OH$), 164,[26] 149. Anal. Calcd for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37; S, 10.13. Found: C, 52.93; H, 6.37; S, 10.22.

***r*,*t*-1,4-Dimethoxy-*t*,*c*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (7).** A solution of **4a** (100 mg, 0.46 mmol) in 4 mL of 2,2-dimethoxypropane containing 5 mg of *p*-toluenesulfonic acid was stirred for 16 h at room temperature. Solid barium carbonate was then added, and the resulting mixture was allowed to stir for 15 min. The residual solid was removed by filtration, and the filtrate was concentrated to give the crude product which was separated and purified by preparative TLC on silica gel with ether–hexane (1:9, respectively) as the eluent mixture. The desired product was extracted from the silica gel band by repeated washing with ether. The solvent was removed under reduced pressure to yield 90 mg (74%) of **7** as colorless crystals which were recrystallized from hexane: mp 88 °C; mass spectrum, *m/e* 264 (M^+), 232 ($M^+ - CH_3OH$), 206 ($M^+ - CH_3COCH_3$), 189 [$M^+ - CH(OCH_3)_2$], 177, 174 ($M^+ - CH_3OH - CH_3COCH_3$), 164,[26] 146 ($M^+ - CH_3OH - CH_3COCH_3 - CO$), 131, 115, 103, 91. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.35; H, 7.55.

1,4-Dimethoxynaphthalene (9). A mixture of **4b** (530 mg, 1.0 mmol) and potassium *tert*-butoxide (450 mg, 4.0 mmol) in 20 mL of THF was stirred at the reflux temperature for 16 h. The reaction mixture was allowed to cool, solid ammonium chloride (~100 mg) was added, and stirring was reinitiated and continued for another 30 min. The resulting precipitate was removed by filtration, and the filtrate was concentrated under reduced pressure. The crude product was separated and purified by TLC on silica gel with 50% ether–hexane as the eluent mixture. Extraction of the chromatographic band with ether afforded 140 mg of **9** (75%) which was recrystallized from hexane; mp 85–86 °C (lit.[14b] mp 85 °C). The NMR data exhibited by **9** obtained in this manner were consistent with those reported earlier by Zweig and co-workers.[14a]

***r*,*t*,*c*,*t*-1,2,3,4-Tetrahydroxy-1,2,3,4-tetrahydronaphthalene (11).** A solution of the diepoxide **1a** (130 mg, 0.81 mmol) in 20 mL of 50% aqueous acetone was allowed to stand for 4 days at ambient temperature. Additional acetone (50 mL) was then added, and the solvent was removed under reduced pressure to

(26) This base peak is due to a retro-Diels–Alder decomposition.

afford a white solid which was recrystallized from methanol to give 11: 150 mg (94%); mp 180–185 °C.

Attempted Preparation of 1,2,4-Trimethoxy-1,2-dihydronaphthalene (12b). To the mesylate **4e** (820 mg, 2.60 mmol) dissolved in 30 mL of benzene was added 870 mg (7.80 mmol) of potassium *tert*-butoxide. The mixture was then stirred at reflux temperature for 17 h. Workup in the manner described for the preparation of **9** gave the crude product which was recrystallized from hexane to afford **9** as the sole product: 360 mg (73%); mp 84.5–86 °C.

***r*,*t*-1,2-Dihydroxy-*t*,*t*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (16).** The procedure of Yagi and co-workers[10] was modified as follows. To a solution of *trans*-1,2-dihydroxy-1,2-dihydronaphthalene[5a] (200 mg, 1.25 mmol) in freshly distilled THF (30 mL) was added 10-fold excess of *m*-chloroperbenzoic acid (~2.0 g). The reaction mixture was stirred under nitrogen at 0 °C for 1 h and then partitioned three times between ether (50 mL) and cold 10% sodium hydroxide solution (3 × 20 mL) as rapidly as possible. The ether solution was then washed with water and dried over potassium carbonate. Removal of the solvent under vacuum furnished yellow impure crystals which were recrystallized from chloroform to give white crystals of **16**, mp 154–155 °C (lit.[10] mp 153–155 °C). The NMR was consistent with that reported by Yagi and co-workers.[10]

***r*,*t*-1,2-Dihydroxy-*c*,*c*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (17).** The procedure of Bruice and co-workers[11] was employed to obtain the required sample of **17**.

Treatment of 1b with Sodium Methoxide. *r*,*c*-1,4-Dimethoxy-*t*,*t*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (20a) and *r*-1-Methoxy-*t*-2-hydroxy-*t*,*t*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (21a). A solution of 200 mg (1.25 mmol) of **1b** in 20 mL of warm methanol containing 400 mg (7.40 mmol) of sodium methoxide was stirred at room temperature for 24 h. Solid ammonium chloride was added, and the reaction mixture was allowed to stir for another 30 min. The resulting solids were collected on a filter, and the filtrate was concentrated under reduced pressure. The residue was then dissolved in chloroform (50 mL) and the remaining solid removed by filtration. The solvent was concentrated under vacuum, and the crude products were purified by thick-layer chromatography on silica gel with ether as the eluent to afford two products. The diol **20a** was eluted after the monooxide **21a**.

Fraction I, **21a**: 100 mg (42%); mp 66–67 °C; mass spectrum, *m*/*e* 160 ($M^+ - CH_3OH$), 131, 115, 103, 77. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.89; H, 6.24.

Fraction II, **20a**: 70 mg (25%); mp 96 °C; mass spectrum, *m*/*e* 224 (M^+), 206, 192, 174, 164,[26] 149, 131, 103, 91. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.39; H, 7.30.

***r*,*t*,*t*,*c*-1,2,3,4-Tetramethoxy-1,2,3,4-tetrahydronaphthalene (20b).** The procedure described for the preparation of **3b** was followed. The diol **20a** (150 mg, 0.67 mmol) was treated with methyl iodide (800 mg, 5.6 mmol) and silver oxide (650 mg, 2.8 mmol) to give **20b** (140 mg, 83%) as a colorless oil which was purified by distillation: bp 100–105 °C (0.2 mm); mass spectrum, *m*/*e* 220 ($M^+ - CH_3OH$), 189 ($M^+ - CH_3OH - CH_3O$), 164,[26] 149. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.47, H, 8.09.

***r*,*c*-1,4-Dimethoxy-*t*,*t*-2,3-bis(mesyloxy)-1,2,3,4-tetrahydronaphthalene (20c).** To a solution of 70 mg (0.31 mmol) of the diol **20a** dissolved in 5 mL of pyridine was added 250 mg (2.20 mmol) of methanesulfonyl chloride. The resulting reaction mixture was stirred at room temperature for 3 days. Subsequent workup and recrystallization from hexane gave 100 mg (84%) of **20c** as colorless crystals: mp 121 °C; mass spectrum, *m*/*e* 380 (M^+), 284 ($M^+ - MsOH$), 189 ($M^+ - MsOH - MsO$), 164,[26] 149, 131, 115, 103, 91. Anal. Calcd for $C_{14}H_{20}O_8S_2$: C, 44.21; H, 5.26; S, 16.84. Found: C, 44.10; H, 5.38; S, 16.62.

***r*,*t*-1,2-Dimethoxy-*t*,*t*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (21b).** The procedure utilized for the preparation of **3b** was applied to **21a** to obtain **21b**. The oxirane **21a** (50 mg, 0.26 mmol) was treated with methyl iodide (160 mg, 1.10 mmol) and silver oxide (130 mg, 0.55 mmol) to give **21b** (42 mg, 78%) as a colorless oil. The NMR spectrum was consistent with that of Bruice and co-workers.[11]

Treatment of 20c with Potassium *tert*-Butoxide. 1,4-Dimethoxynaphthalene (9). Conversion of **20c** to **9** was accomplished by using the procedure employed for the preparation of **9**. To a solution of 50 mg (0.13 mmol) of the dimesylate **20c** dissolved in 20 mL of dry THF was added 50 mg (0.52 mmol) of potassium *tert*-butoxide. The resulting mixture was stirred at reflux temperature for 16 h and worked up in the conventional manner to give **9** in low yield (10%).

***r*,*c*-1,4-Dimethoxy-*t*,*t*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (10).** The procedure outlined for the preparation of **7** was applied to **20a** to obtain the required sample of **10**. The crude product, obtained as a colorless oil, was recrystallized from cold hexane to give **10**: 102 mg (86%); mp 68 °C; mass spectrum, *m*/*e* 264 (M^+), 232 ($M^+ - CH_3OH$), 206 ($M^+ - CH_3COCH_3$), 189, 177, 174 ($M^+ - CH_3OH - CH_3COCH_3$), 164,[26] 146, 131, 115, 103, 91. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.27; H, 7.69.

***r*,*t*-1,4-Diphenoxy-*t*,*c*-dihydroxy-1,2,3,4-tetrahydronaphthalene (22a).** To a solution of **1a** (200 mg, 1.25 mmol) in 25 mL of acetonitrile were added 10 mL of 2% sodium hydroxide solution and 300 mg of phenol (3.19 mmol). The resulting solution was then heated under reflux for 24 h and allowed to cool. The excess phenol was then removed by addition of 20 mL of a 10% sodium hydroxide solution, and the products were extracted into chloroform. The combined organic phase was washed with water and saturated sodium chloride and then dried over potassium carbonate. The solvent was removed under reduced pressure and the residual crude product purified by preparative TLC on silica gel with ether as the eluent. After crystallization from dichloromethane–hexane, 400 mg (92%) of **22a** was obtained as a white crystalline solid: mp 154–156 °C; mass spectrum, *m*/*e* 348 (M^+), 254 ($M^+ - PhOH$), 160 ($M^+ - 2PhOH$). Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 76.00; H, 5.84.

1,4-Diphenoxynaphthalene (24). A 100-mg (0.29 mmol) sample of the diol **22a** was dissolved in 10 mL of pyridine to which was added 200 mg (1.75 mmol) of methanesulfonyl chloride. The resulting mixture was then stirred at ambient temperature for 3 days, and the pyridine and excess methanesulfonyl chloride were subsequently removed under reduced pressure. The residual mixture was separated and purified by TLC (ether) to give 130 mg (86%) of **22b** as a pale yellow oil.

A mixture of 130 mg of the crude dimesylate **22b** and 130 mg (1.20 mmol) of potassium *tert*-butoxide in 10 mL of dry THF was stirred at the reflux temperature for 16 h. Subsequent workup in the manner employed in the conversion of **4b** to **9** gave 50 mg (56% in two steps) of **24** as an off-white solid which was recrystallized from hexane: mp 99 °C; mass spectrum, *m*/*e* 312 (M^+), 235 ($M^+ - C_6H_5$). Anal. Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.40; H, 5.25.

***r*,*t*-1,4-Diphenoxy-*t*,*c*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (23).** A solution of the diol **22a** (100 mg, 0.29 mmol) in 6 mL of 2,2-dimethoxypropane containing 5 mg of *p*-toluenesulfonic acid was stirred overnight at room temperature. Subsequent workup in the manner described for the preparation of **7** and recrystallization from ether–hexane gave 90 mg (81%) of the desired *trans*-acetonide **23** as an off-white, crystalline solid: mp 153 °C, mass spectrum, *m*/*e* 388 (M^+), 295 ($M^+ - PhO$), 237 ($M^+ - PhO - CH_3COCH_3$), 209 ($M^+ - PhO - CH_3COCH_3 - CO$), 115. Anal. Calcd for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.15; H, 6.40.

***r*,*c*-1,4-Diphenoxy-*t*,*t*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (25a).** The procedure outlined for the preparation of **22a** was applied to **1b** without significant modification. The crude product obtained upon workup in the conventional manner was recrystallized from chloroform–hexane to give 380 mg (87%) of **25a** as white crystals: mp 137 °C; mass spectrum, *m*/*e* 348 (M^+), 254 ($M^+ - PhOH$), 160 ($M^+ - 2PhOH$). Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.92; H, 5.81

Conversion of the Diol 25a to 1,4-Diphenoxynaphthalene (24). To a solution of 100 mg (0.29 mmol) of **25a** in 10 mL of pyridine was added 200 mg (1.75 mmol) of methanesulfonyl chloride. The mixture was then stirred at room temperature for 3 days and worked up in the conventional manner to give 125 mg (80%) of **25b** as an oily residue.

The residual crude dimesylate **25b**, without further purification, was dissolved in 10 mL of dry THF and base elimination accomplished by addition of potassium *tert*-butoxide (130 mg, 1.20

mmol). The reaction mixture was heated under reflux for 16 h and worked up in the conventional manner to give 10 mg (11%) of **24** after recrystallization from hexane; mp 99 °C.

***r*,*c*-1,4-Diphenoxy-*t*,*t*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (26).** The acetalation procedure described for the preparation of the trans counterpart **23** was employed for the synthesis of **26** from **25a**. The crude product was recrystallized from hexane to give 100 mg (90%) of the desired acetonide **26** as a white crystalline solid: mp 154 °C; mass spectrum, *m*/*e* 388 (M^+), 295 (M^+ – PhO), 237 (M^+ – PhO – CH_3COCH_3), 209 (M^+ – PhO – CH_3COCH_3 – CO), 115.

1-Methoxy-4-phenoxynaphthalene (28). The oxirane **3a** (100 mg, 0.52 mmol) was allowed to react with sodium phenoxide, using the procedure outlined for the preparation of **22a**. The resulting diol **27a** was esterified with mesyl chloride in pyridine, and the crude product was separated and purified by TLC (ether) to give **27b** as a pale yellow oil.

The dimesylate **27b**, without further purification, was dissolved in 10 mL of dry THF and converted to the diether **28** by treatment with potassium *tert*-butoxide (150 mg, 1.40 mmol). The reaction mixture was allowed to stir at reflux temperature for 12 h and worked up in the conventional manner to give 25 mg (20% in three steps) of **28** as white needles after recrystallization from hexane: mp 87–88 °C; mass spectrum, *m*/*e* 250 (M^+), 235 (M^+ – CH_3), 219 (M^+ – OCH_3), 207, 179, 173 (M^+ – Ph). Anal. Calcd for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.40; H, 5.73.

***r*,*c*-1,4-Diacetoxy-*t*,*t*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (29a).** A solution of 100 mg (0.63 mmol) of **1b** in 10 mL of acetic acid containing 100 mg of sodium acetate was heated to 100 °C for 10 min. The solution was diluted with 100 mL of water and neutralized by the careful addition of 500 mg of sodium bicarbonate. The solution was extracted with ether and the extracts were dried over anhydrous potassium carbonate. The solvent was removed under reduced pressure, and the components of the residual mixture were separated and purified by TLC (ether) to give 84 mg (50%) of **29a**. The melting point (153–154 °C) and NMR spectral data for **29a** compare favorably with those described by Schmidt and co-workers.[15]

***r*,*t*-1,4-Diacetoxy-*t*,*c*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (30a).** The solvolysis procedure described above for the *cis*-diacetate **29a** was used for the conversion of **1a** to **30a**. Separation and purification of the residual organic mixture derived from **1a** (100 mg, 0.63 mmol) was achieved by preparative TLC with ether as the eluting solvent. Recrystallization of the separated product from ether yielded 60 mg (33%) of **30a** as colorless crystals, mp 164–165 °C.

Conversion of 30a to 16. The procedure described by Schmidt and co-workers[15] was employed without significant modification for this transformation. The diol **30a** (200 mg, 0.07 mmol) was allowed to react with tosyl chloride (13.3 mg, 0.07 mmol) in pyridine to give **30b** as colorless syrup (70%). Treatment of the resulting monotosylate with sodium carbonate in methanol afforded the *anti*-diol epoxide **16**. The melting point and NMR spectrum are consistent with those reported by Yagi and co-workers.[10]

***r*,*t*-1,4-Bis(dimethylamino)-*t*,*c*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (31).** Through a stirred solution of **1a** (200 mg, 1.25 mmol) in absolute ethanol (20 mL) was slowly bubbled dry dimethylamine (2 mL). The addition of dimethylamine was adjusted to last 0.5 h. The resulting mixture was heated under reflux for 1 h and allowed to cool, and the solvent was removed under reduced pressure. Recrystallization of the crude product from ether–hexane yielded 220 mg (75%) of **31** as colorless crystals: mp 124–126 °C; mass spectrum, *m*/*e* 232 (M^+ – H_2O), 205 (M^+ – $HN(CH_3)_2$), 187 (M^+ – H_2O – $HN(CH_3)_2$), 176, 157, 143, 131. Anal. Calcd for $C_{14}H_{22}N_2O_2$: C, 67.17; H, 8.86; N, 11.19. Found: C, 67.43; H, 9.08; N, 11.20.

***r*,*c*-1,4-Bis(dimethylamino)-*t*,*t*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (32).** The procedure described for the preparation of the trans isomer **31** was utilized to transform **1b** to **32**. Recrystallization of the crude product from benzene–hexane gave 250 mg (80%) of **32** as off-white crystals: mp 95–97 °C; mass spectrum, *m*/*e* 250 (M^+), 205 (M^+ – $NH(CH_3)_2$). Anal. Calcd for $C_{14}H_{22}N_2O_2$: C, 67.17; H, 8.86; N, 11.19. Found: C, 67.13; H, 8.68; N, 10.98.

***r*,*t*-1,4-Bis(methylthio)-*t*,*c*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (33a).** A mixture of 200 mg (1.25 mmol) of **1a**, 1.00 g of methanethiol, and 30 mL of 2% sodium hydroxide solution was stirred under nitrogen at room temperature for 1 h. The resulting precipitate was separated by filtration, washed with water, and then recrystallized from chloroform–hexane to give 260 mg (81%) of **33a** as white crystals: mp 143–144 °C; mass spectrum, *m*/*e* 238 (M^+ – H_2O), 223 (M^+ – H_2O – CH_3), 208 (M^+ – CH_3SH), 190 (M^+ – H_2O – CH_3SH), 161 (M^+ – CH_3SH – CH_3S), 131, 115, 103, 91, 77. Anal. Calcd for $C_{12}H_{16}O_2S_2$: C, 56.21; H, 6.29; S, 25.01. Found: C, 56.34; H, 6.31; S, 24.95.

***r*,*t*-1,4-Bis(methylthio)-*t*,*c*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (34).** A solution of **33a** (100 mg, 0.39 mmol) in 5 mL of 2,2-dimethoxypropane containing 5 mg of *p*-toluenesulfonic acid was stirred at room temperature for 16 h. A subsequent workup in the manner described for the preparation of **7** and recrystallization from hexane gave 72 mg (60%) of the desired *trans*-acetonide **34** as colorless crystals: mp 93–94 °C; mass spectrum, *m*/*e* 296 (M^+), 248 (M^+ – CH_3SH), 191 (M^+ – CH_3COCH_3 – CH_3S), 163 (M^+ – CH_3COCH_3 – CH_3S – CO), 115. Anal. Calcd for $C_{15}H_{20}O_2S_2$: C, 60.77; H, 6.80; S, 21.63. Found: C, 60.71; H, 6.86; S, 21.48.

***r*,*c*-1,4-Bis(methylthio)-*t*,*t*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (36a).** The procedure outlined for the conversion of **1a** to **33a** was employed in synthesizing the diol **36a**; however, in this case, the crude crystalline product was collected by vacuum filtration, washed with cold water, and then recrystallized from chloroform–hexane to give 200 mg (63%) of **36a** as white needles: mp 102–103 °C; mass spectrum, *m*/*e* 256 (M^+), 208 (M^+ – CH_3SH), 161 (M^+ – CH_3SH – CH_3S), 131, 115, 103, 91, 77. Anal. Calcd for $C_{12}H_6O_2S_2$: C, 56.21; H, 6.29; S, 25.01. Found: C, 56.45; H, 6.35; S, 25.05.

***r*,*c*-1,4-Bis(methylthio)-*t*,*t*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (37).** The procedure outlined earlier for the preparation of **34** was employed to convert **36a** to **37**. The crude product was obtained as a colorless oil and crystallized from hexane to give 80 mg (70%) of **37** as colorless prisms: mp 59–61 °C; mass spectrum, *m*/*e* 296 (M^+), 281 (M^+ – CH_3), 249 (M^+ – CH_3S), 221 (M^+ – CH_3 – CH_3COOH), 191 (M^+ – CH_3S – CH_3COCH_3), 174 (M^+ – CH_3 – CH_3COOH – SCH_3), 163 (M^+ – CH_3S – CH_3COCH_3 – CO), 144 (M^+ – $2CH_3S$ – CH_3COCH_3), 115. Anal. Calcd for $C_{15}H_{20}O_2S_2$: C, 60.77; H, 6.80; S, 21.63. Found: C, 60.83; H, 6.86; S, 21.44.

Acid-Catalyzed Dehydration of 33a and 36a. 2,3-Bis(methylthio)naphthalene (35). To a mixture of 20 mg of *p*-toluenesulfonic acid in 60 mL of benzene was added 50 mg (0.20 mmol) of either diol (**33a** or **36a**). The resulting mixture was heated under reflux for 4 h and then allowed to cool. Solid barium carbonate (~0.5 g) was added and stirring continued for 0.5 h. The excess carbonate was removed by filtration, and the filtrate was concentrated in vacuo to give a yellow oil. The crude product was purified by sublimation at 130–150 °C (0.1 mm) to afford 40 mg (93%) of **35** which was then recrystallized from methanol: mp 84–86 °C (lit.[14b] mp 86–87 °C); mass spectrum, *m*/*e* 220 (M^+), 172 (M^+ – CH_3SH).

***trans*-1-Hydroxy-2-(methylthio)-1,2-dihydronaphthalene (40a).** A mixture of 140 mg (0.97 mmol) of naphthalene oxide 2,[3d] 500 mg of methanethiol, and 15 mL of 2% aqueous sodium hydroxide was stirred under nitrogen at 5–10 °C for 2 h. The products were extracted into ether which was then dried over potassium carbonate. Removal of the solvent under reduced pressure and recrystallization of the residue from hexane afforded 80 mg (43%) of **40a** as white needles, mp 67–69 °C. A minor component (<10% in the crude product) shows absorptions at δ 4.00 (H_1), δ 4.38 (H_2) and the vinyl region and is assumed to derive from attack of the sulfur nucleophile at the C_1 position. The major component was assigned structure **40a** on the basis of NMR data which compare favorably with the corresponding ethylthio derivative **40b** prepared in a similar manner by Jerina and co-workers.[5a] The mass spectrum of **40a** showed the following: *m*/*e* 192 (M^+), 174 (M^+ – H_2O), 159 (M^+ – H_2O – CH_3), 145 (M^+ – CH_3S). Anal. Calcd for $C_{11}H_{12}OS$: C, 68.71; H, 6.29; S, 16.68. Found: C, 69.01; H, 6.34; S, 16.47.

1-(Methylthio)naphthalene (41a). A solution of **40a** (20 mg, 0.10 mmol) and *p*-toluenesulfonic acid (10 mg) in benzene (30 mL) was heated under reflux for 4 h. A subsequent workup in the

conventional manner afforded 1-(methylthio)naphthalene (**41a**) which is identical in spectral and other features with that obtained by methylation of 1-naphthalenethiol in methanol with diazomethane (ether solution).[2a] The mass spectrum of **41a** shows *m/e* 174 (M^+), 159 ($M^+ - CH_3$), and 115.

***r*-1-(Methylthio)-*t*,*t*,*c*-2,3,4-trihydroxy-1,2,3,4-tetrahydronaphthalene (42a).** A mixture of 67 mg (0.38 mmol) of *anti*-diol epoxide **16**, 200 mg of methanethiol, and 10 mL of 2% sodium hydroxide solution was stirred under nitrogen for 2 h. Ether was added to the reaction mixture. The organic layer was then separated and the aqueous phase extracted repeatedly with ether. The combined organic phase was washed with water and dried over anhydrous potassium carbonate. Removal of the solvent and recrystallization of the residue from chloroform afforded 50 mg (60%) of **42a** as colorless crystals: mp 132–133 °C; mass spectrum, *m/e* 226 (M^+), 208 ($M^+ - H_2O$), 160 ($M^+ - H_2O - CH_3SH$). Anal. Calcd for $C_{11}H_{14}O_3S$: C, 58.38; H, 6.24; S, 14.17. Found: C, 58.54; H, 6.40; S, 14.10.

***r*-1-(Methylthio)-*t*,*c*,*t*-2,3,4-trihydroxy-1,2,3,4-tetrahydronaphthalene (43a).** The procedure outlined above for the preparation of **42a** was employed for the synthesis of its counterpart **43a** from **17**. The crude product, obtained as a colorless oil, was converted to the trimethylsilyl ether derivative **43b** upon treatment with excess bis(trimethylsilyl)acetamide in pyridine (for the mass spectrum, see ref 2c).

***r*,*t*-1,4-Dimethyl-*t*,*c*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene (45).** To a solution of 200 mg (1.25 mmol) of **1a** in 35 mL of anhydrous ether maintained under nitrogen and at 0 °C was added 7 mL (10 mmol) of 1.4 M methyllithium in ether. The mixture was stirred at 0 °C for 4 h and then quenched with aqueous hydrochloric acid (10%). The organic phase was then separated and the aqueous phase extracted repeatedly with ether. The combined organic phase was washed with water and saturated sodium chloride and dried over potassium carbonate. Removal of the solvent under reduced pressure and recrystallization of the residue from ether–hexane afforded 150 mg (63%) of the diol **45**: mp 112–113 °C; mass spectrum, *m/e* 192 (M^+), 174 ($M^+ - H_2O$), 159 ($M^+ - H_2O, CH_3$), 145 ($M^+ - CH_3OH - CH_3$), 132,[26] 131, 117, 115, 105, 103, 91, 77, 60. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.08; H, 8.50.

***r*,*t*-1,4-Dimethyl-*t*,*c*-2,3-bis(mesyloxy)-1,2,3,4-tetrahydronaphthalene (46).** A mixture of 100 mg (0.52 mmol) of diol **46a**, 250 mg (2.20 mmol) of methanesulfonyl chloride, and 4 mL of pyridine was stirred at ambient temperature for 2 days. The excess solvent and methanesulfonyl chloride were subsequently removed under reduced pressure. Separation and purification of the residual organic mixture by preparative TLC with a mixture of ether–hexane (8:2) as the eluting solvent afforded the dimesylate **46** as a colorless oil.

***r*,*t*-1,4-Dimethyl-*t*,*c*-2,3-*O*-isopropylidene-1,2,3,4-tetrahydronaphthalene (47).** The acetalation procedure described for the preparation of **7** was applied to obtain **47** from **45**. The crude product, obtained in 70% yield as a colorless oil, was crystallized from hexane to give pure **47** as white crystals: mp 90–91 °C; mass spectrum, *m/e* 217 ($M^+ - CH_3$), 157 ($M^+ - CH_3 - CH_3COOH$). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.80; H, 8.58.

1,4-Dimethylnaphthalene (48). (a) Base-Catalyzed Reaction. The dimesylate **46** was dissolved in 20 mL of dry THF and elimination accomplished by addition of potassium *tert*-butoxide (225 mg, 2 mmol). The reaction mixture was heated under reflux for 16 h and worked up in the conventional manner to give 50 mg (62% in two steps) of **48**. The NMR spectral data for **48** compare favorably with those of an authentic sample obtained from Aldrich.

(b) Acid-Catalyzed Reaction. A solution of **45** (50 mg, 0.26 mmol) and *p*-toluenesulfonic acid (20 mg) in toluene (60 mL) was heated under reflux for 2 days. Subsequent workup in the manner described for the preparation of **35** gave 20 mg (50%) of **48** as a pale yellow syrup along with some unreacted starting material. Dehydration did not occur if benzene was used as the solvent.

***r*-1-Hydroxy-*t*-2-Methyl-*c*,*c*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (49).** The procedure outlined above for the preparation of **45** was applied to **1b**. The crude reaction product after separation from solvents was purified by preparative TLC on silica gel by using 50% ether–hexane as the eluent mixture. Recrystallizatioin of the separated product from hexane yielded 60 mg (27%) of **49** as colorless crystals: mp 62–63 °C; mass spectrum, *m/e* 176 (M^+), 158 ($M^+ - H_2O$), 130 ($M^+ - H_2O - CO$). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 75.16; H, 7.00.

***trans*-1-Hydroxy-2-methyl-1,2-dihydronaphthalene (50).** The procedure described by Jerina and co-workers[5a] was followed without much major modification to achieve a conversion of **2** to **50**. The crude product was purified by preparative TLC (ether) to give 100 mg (40%) of white crystalline solid which consisted of **50** and the *trans*-1-methyl-2-hydroxy isomer in the ratio of 9:1. Fractional crystallization of the separated product from hexane allowed isolation of 40 mg of **50** free of *trans*-1-methyl-2-hydroxy isomer: mp 68–69 °C; the NMR spectrum is consistent with that of Jerina and co-workers:[5a] mass spectrum, *m/e* 160 (M^+), 145 ($M^+ - CH_3$), 142 ($M^+ - H_2O$), 131. Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.68; H, 7.56.

***r*-1-Hydroxy-*t*-2-methyl-*t*,*t*-3,4-epoxy-1,2,3,4-tetrahydronaphthalene (51).** To a solution of **50** (40 mg, 0.25 mmol) in dry THF (30 mL) was added a 10-fold excess of *m*-chloroperbenzoic acid (400 mg). The reaction mixture was stirred under nitrogen at room temperature for 8 h and then partitioned twice between ether (100 mL) and 10% sodium hydroxide solution (2 × 20 mL). The organic phase was then washed with water and dried over potassium carbonate. Subsequent removal of the volatile solvent and recrystallization of the residue from chloroform–hexane afforded 25 mg (57%) of **51**: mp 136–138 °C; mass spectrum, *m/e* 176 (M^+), 161 ($M^+ - CH_3$), 158 ($M^+ - H_2O$), 147, 119.

1,4-Dicyanonaphthalene (52). A 162-mg (2.5 mmol) sample of dry potassium cyanide and 10 mL of an acetonitrile solution containing 100 mg (0.625 mmol) of either **1a** or **1b** and 1 drop of dibenzo-18-crown-6 were introduced into a 50-mL round-bottomed flask equipped with a magnetic stirring bar and a condenser fitted with a drying tube. The two-phase system was heated under reflux with vigorous stirring for 2 days. The reaction mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel with ether as the eluent. Recrystallization of the separate product from toluene yielded 45 mg (40%) of **52** which was identical in every respect with an authentic sample obtained by treatment of 1,4-dibromonaphthalene with cuprous cyanide.[19]

***trans*-2,3-Dihydroxy-1,2,3,4-tetrahydronaphthalene (53).** To a solution of 200 mg (1.25 mmol) of **1a** dissolved in 30 mL of anhydrous ether was added 250 mg (6.6 mmol) of lithium aluminum hydride. The reaction mixture was heated under reflux for 1 h, and the flask and contents were subsequently cooled in an ice bath. Excess ethyl acetate was added to quench the residual lithium aluminum hydride followed by sufficient dilute sulfuric acid (10%) to cause two distinct phases to appear. The organic layer was then separated, washed with water and saturated sodium chloride solution, and dried over potassium carbonate. The organic phase was concentrated under vacuum and the crude product recrystallized from benzene to give 102 mg (50%) of **53** as white plates: mp 133–134 °C (lit[20] mp 135–136 °C); the NMR spectrum was consistent with that of Bruice and co-workers.[11]

***trans*-2,3-*O*-Isopropylidene-1,2,3,4-tetrahydronaphthalene (54).** The acetalation procedure described for the preparation of **7** was applied to **53**. The crude product was recrystallized from methanol and water to give pure **54** as colorless crystals: mp 76–77 °C; mass spectrum, *m/e* 189 ($M^+ - CH_3$), 146 ($M^+ - CH_3COCH_3$). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.28; H, 8.06.

***cis*-2,3- and -1,3-Dihydroxy-1,2,3,4-tetrahydronaphthalene (55 and 56).** The reduction procedure outlined above for the preparation of **53** was applied to **1b**. Subsequent workup in the conventional manner gave a product mixture consisting of **55** and **56** in the ratio of 8.5:1.5. Comparison of the NMR spectrum of the crude product with that of an authentic sample of *cis*-2,3-dihydroxy-1,2,3,4-tetrahydronaphthalene[11,20] (see preparation of **1b**) established the structure of the major component as **55**. Conversion of *cis*-2,3-diol **55** to an acetonide derivative, **57**, allowed the separation of the minor product **56** which forms no acetonide. Recrystallization of the separated product from chloroform–hexane gave 20 mg of **56** as colorless crystals: mp 81–82 °C; mass

spectrum, m/e 164 (M^+), 146 ($M^+ - H_2O$), 128 ($M^+ - 2H_2O$), 91. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.07; H, 7.30.

***cis*-2,3-*O*-Isopropylidene-1,2,3,4-tetrahydronaphthalene (57).** The pure *cis*-2,3-diol **55** or the product mixture obtained above was treated with 2,2-dimethoxypropane and *p*-toluenesulfonic acid to give the desired acetonide **57** as an off-white solid which was recrystallized from aqueous ethanol: mp 76 °C; mass spectrum, m/e 204 (M^+), 189 ($M^+ - CH_3$), 129 ($M^+ - CH_3 - CH_3COOH$). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.60; H, 7.81.

2,3-Dihydroxynaphthalene (58). A sample of diepoxide **1b** (50 mg, 0.31 mmol) was dissolved in 5 mL of xylene and sealed in a thick-walled Pyrex tube. The tube was then heated inside a steel "bomb" at 190 °C for 1 day. The solvent was removed under vacuum, and the residue was purified by preparative TLC on silica gel with ether as the eluent. The melting point and NMR spectrum of the separated product (50%) were consistent with those of an authentic sample of 2,3-dihydroxynaphthalene (Aldrich).

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Registry No. **1a**, 58717-74-1; **1b**, 58692-14-1; **2**, 17180-88-0; **3a**, 83731-25-3; **3b**, 69153-87-3; **4a**, 83731-26-4; **4b**, 83731-27-5; **4c**, 83731-28-6; **4d**, 83731-29-7; **4e**, 83731-30-0; **7**, 83731-31-1; **9**, 10075-62-4; **10**, 83780-84-1; **11**, 76561-86-9; **16**, 69222-28-2; **17**, 69222-27-1; **20a**, 83731-32-2; **20b**, 83731-33-3; **20c**, 83731-34-4; **21a**, 83780-85-2; **21b**, 69483-35-8; **22a**, 83731-35-5; **22b**, 83731-36-6; **23**, 83731-37-7; **24**, 83731-38-8; **25a**, 83731-39-9; **25b**, 83731-40-2; **26**, 83780-86-3; **27a**, 83731-41-3; **27b**, 83731-42-4; **28**, 83731-43-5; **29a**, 69532-85-0; **30a**, 83731-44-6; **30b**, 83780-87-4; **31**, 83731-45-7; **32**, 83731-46-8; **33a**, 83731-47-9; **34**, 83731-48-0; **35**, 10075-76-0; **36a**, 83731-49-1; **37**, 83780-88-5; **40a**, 83731-50-4; **41a**, 10075-72-6; **42a**, 83780-89-6; **43a**, 83780-90-9; **43b**, 83731-51-5; **45**, 83731-52-6; **46**, 83731-53-7; **47**, 83731-54-8; **48**, 571-58-4; **49**, 83780-91-0; **50**, 54226-01-6; **51**, 83780-92-1; **52**, 3029-30-9; **53**, 41597-55-1; **54**, 83731-55-9; **55**, 35583-15-4; **55** bis(trifluoroacetate), 83731-56-0; **55** β,β-1,4-dibromobis(trifluoroacetate), 83731-57-1; **56**, 83731-58-2; **57**, 83731-59-3; **58**, 92-44-4; naphthalene, 91-20-3; 1,4-dihydronaphthalene, 612-17-9; *trans*-1,2-dihydro-1,2-dihydroxynaphthalene, 771-16-4.

Acid-Catalyzed Intramolecular C-Alkylation in β,γ-Unsaturated Diazomethyl Ketones. 2.[1] A Simple New Synthetic Route to Octahydro-4,10a-ethanophenanthren-12-ones and Octahydropentaleno[6a,1-*a*]naphthalen-4-ones

Gutta O. S. V. Satyanarayana, Subhas C. Roy, and Usha Ranjan Ghatak*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta-700 032, India

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The utility of acid-catalyzed intramolecular C-alkylation and alkylation–rearrangements of the rigid diazomethyl ketones **1a–c** pertaining to a new and simple efficient synthesis of the respective octahydro-4a-hydroxy-4,10a-ethanophenanthren-12-ones **7a–c** and 3a-methylhexahydropentaleno[6a,1-*a*]naphthalen-4-ones **8a–c** are described. The most thoroughly studied case was that of **1a**, which clearly revealed that in a polar solvent, nitromethane, and with strong protic acids or boron trifluoride etherate the hydroxycyclopentanone **7a** is the major product arising through the Wagner–Meerwein shifts of the initially generated respective cyclobutanone carbinyl cation. While strong protic acids (aqueous $HClO_4$ or aqueous HBF_4) in nonpolar solvents (benzene or chloroform containing ethanol stabilizer) exclusively produce the unsaturated cyclobutanone **3a**, solvents of intermediate polarities with HBF_4 or boron trifluoride etherate gave all three possible products, **3a**, **7a**, and **8a**. The structure of the products formed in the acid-catalyzed reactions of **1b,c** also depends upon the catalyst–solvent combinations as well as the reaction conditions and the nature of the substrates. The hydroxycyclopentanones **7a–c** underwent facile rearrangement with toluene-*p*-sulfonic acid or iodine in refluxing benzene, leading to the respective pentaleno-annulated ketones **8a–c** in excellent yields. These were also obtained from the respective unsaturated cyclobutanones **3b,c**. The benzylic ketone **15a**, prepared in good yield through oxidation of **7a**, rearranged to the respective enedione **16a** in excellent yield. Catalytic hydrogenolysis of the hydroxycyclopentanones **7a–c** afforded the respective bridged ketones **12a–c** exclusively. The stereochemistry of **12a** and **12b** has been established by the X-ray method. The unsaturated cyclopentanones **8a–c** undergo stereospecific hydrogenation to the respective cis AB cyclopentanones **13a–c** whereas lithium–liquid ammonia reduction of **8a,c** gives the respective diastereoisomeric cyclopentanones **13a,c** and **14a,c** in a ratio of ca. 1:9 from which the major isomers were easily separated. The ketone **8b** on similar reduction, however, gave an inseparable mixture of **13b** and **14b** in a ratio of ca. 1:2. The stereochemistries of the epimeric ketones **13a–c** and **14a–c** were assigned from the significant difference in the chemical shifts of the 3a-methyl group in these diastereoisomeric pairs. The cyclopentenone **8a** has been transformed into the parent hydrocarbon **18a**.

Intramolecular olefinic participation in the acid-induced decomposition of γ,δ-unsaturated α-diazomethyl ketones[2] has been extensively studied by Mander and his coworkers[3] and by ourselves[4] for simple elaboration of the

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