Oxidative Cyclization of Dioximes and Bis(hydrazones) of 2-Unsaturated 1,4-Diketones

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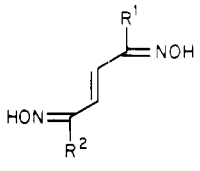
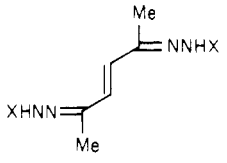
Received March 26, 1979

Oxidation of 1,4-disubstituted 2-butene-1,4-dione dioximes (1) with lead tetraacetate or phenyliodoso bis(trifluoroacetate) afforded the corresponding disubstituted pyridazine 1,2-dioxides (3) and dihydroisoxazoloisoxazoles (2). The compound which had been assigned to 3,6-diphenylpyridazine 1,2-dioxide (**3c**) by other authors was in fact proved to be **2c**. Lead tetraacetate was found to be the applicable reagent for the preparation of **3** from 1. Bis(iminoxyl) radicals (**13**) were postulated as the intermediates in these reactions. Preparation of 1,2-diiminopyridazinium bis(ylides) (**18**) and dihydropyrazolopyrazoles (**19**) has failed. Oxidation of 1,4-dimethyl-2-butene-1,4-dione bis(arylhydrazones) (**4c** and **4d**) with lead tetraacetate yielded 1,4-bis(arylazo)-1,4-dimethyl-1,3-butadienes (**22c** and **22d**). The structure of 1,4-bis(phenylazo)-1,4-dimethyl-1,3-butadiene (**22c**) was examined by X-ray crystallography.

A previous communication[1] described the reaction of 2-butene-1,4-dione dioximes (**1**) with some oxidizing reagents to give dihydroisoxazoloisoxazoles (**2**) together with pyridazine 1,2-dioxides (**3**). This paper describes details of this reaction and the oxidation of some 1,4-dimethyl-2-butene-1,4-dione bis(hydrazones) (**4**).



1a, $R^1 = R^2 = Me$
b, $R^1 = Me$; $R^2 = Ph$
c, $R^1 = R^2 = Ph$



4a, X = COMe
b, X = COPh
c, X = Ph
d, X = Ph(*p*-NO_2)

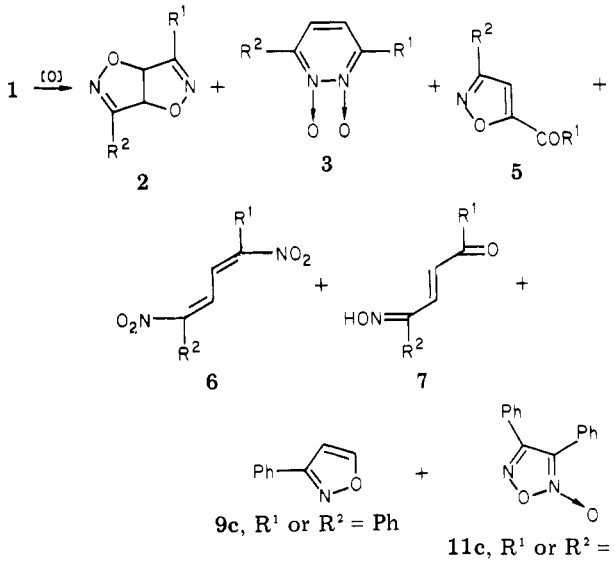
Results and Discussion

Oxidation of Dioximes 1. The oxidation of 1,4-dimethyl-2-butene-1,4-dione dioxime (**1a**) with lead tetraacetate (LTA) in methylene chloride gave 3,6-dimethyl-3a,6a-dihydroisoxazolo[5,4-*d*]isoxazole (**2a**), 3,6-dimethylpyridazine 1,2-dioxide (**3a**), 5-acetyl-3-methylisoxazole (**5a**), and 2,5-dinitrohexa-2,4-diene (**6a**) (Scheme I). When **1a** was treated with phenyliodoso bis(trifluoroacetate) (PITFA) in methylene chloride, **2a**, **3a**, and **6a** were obtained although Spyroudis et al.[2] have reported **3a** as the sole product of the oxidation of **1a** under similar conditions. The reaction of **1a** with ceric ammonium nitrate (CAN) in aqueous acetic acid afforded **5a**, **6a**, and monooxime **7a** in low yields as shown in Table I. The results of the oxidation of 1-methyl-4-phenyl-2-butene-1,4-dione dioxime (**1b**) and 1,4-diphenyl-2-butene-1,4-dione dioxime (**1c**) are also shown in Table I.

Oxidation of **1b** with LTA yielded **2b**, **3b**, and **5b**,[3] while the major product of the oxidation of **1c** with PITFA was identical (melting point and spectral data) with the compound regarded as the pyridazine 1,2-dioxide **3c**.[2] However, we have shown this assignment to be in error.

The NMR signal at δ 6.45 is at abnormally high field compared with the signals of the protons on the C-4 and C-5 of other pyridazine 1,2-dioxides, as those of **3a** and **3b** appeared around δ 7. The mass spectra of the compound showed strong ion peaks at *m/e* 264 (M^+) and 145 (M^+ – PhNCO) and a medium one at 119 (PhNCO). This fragment type is not common in those of **3** because the common fragment ions of pyridazine 1,2-dioxides are M^+

Scheme I



2 **3** **5**

6 **7**

9c, R^1 or R^2 = Ph

11c, R^1 or R^2 = Ph

Table I. Oxidation of 1 (Yields in %)[a]

compd	reagents	solvents	products			
			2a	**3a**	**5a**	**6a**
1a	LTA	CH_2Cl_2	8	33	tr	11
	PITFA	CH_2Cl_2	5	15 (10)[b]	0	2
	CAN	aq AcOH	0	0	3	10
			2b	**3b**	**5b**	**6b**
1b	LTA	CH_2Cl_2	10	19	3	*c*
			2c	**3c**	**5c**	**6c**
1c	LTA	CH_2Cl_2	60	15	*c*	2
	PITFA	CH_2Cl_2	51 (55)[b]	8	*c*	6
	CAN	aq AcOH	8	0	*c*	tr

[a] At room temperature for 1–2 h, for all runs. [b] See ref 2. [c] All attempts to isolate these compounds failed, although the formation of these compounds cannot be disproved.

(1) A. Ohsawa, H. Arai, and H. Igeta, *Heterocycles*, **9**, 1367 (1978).
(2) S. Spyroudis and A. Varvoglis, *Synthesis*, 837 (1976).
(3) 5-Benzoyl-3-methylisoxazole [mp 71–72 °C, S. D. Sokolov, L. P. Savochkina, and N. K. Kochetkov, *Zh. Obshch. Khim.*, **34**, 2207 (1964); *Chem. Abstr.*, **61**, 9486a (1964)] was not isolated.

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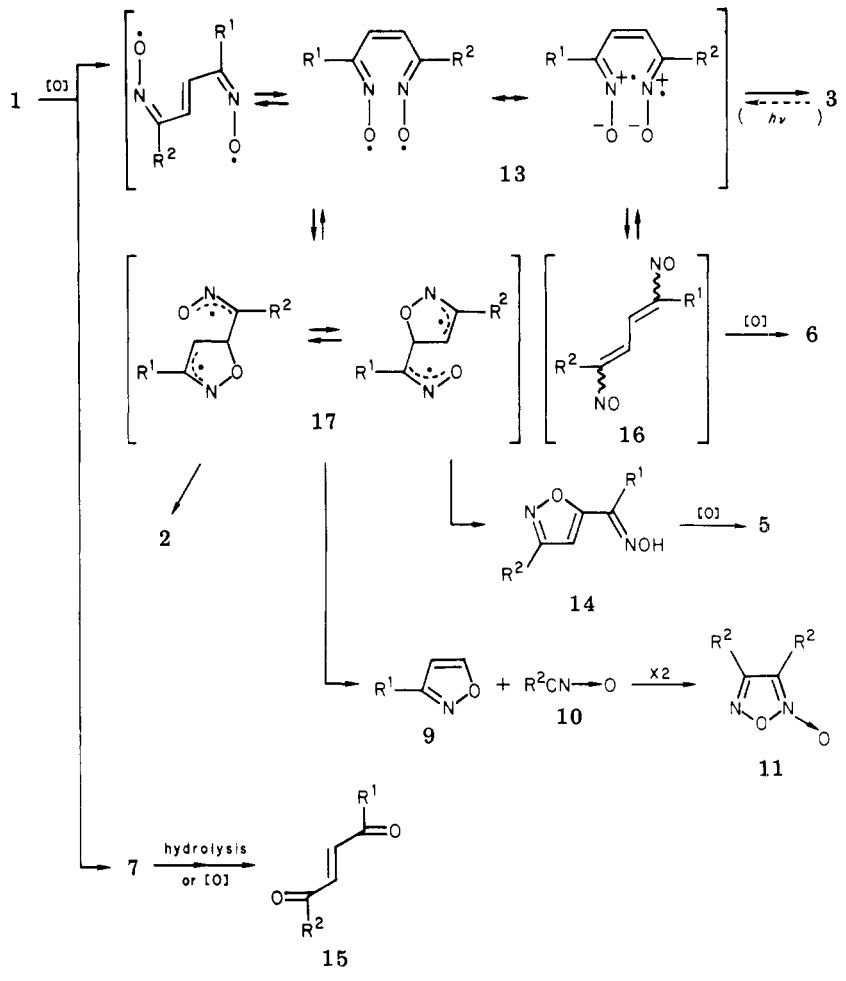
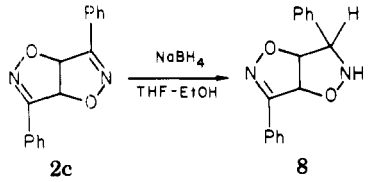
Scheme II



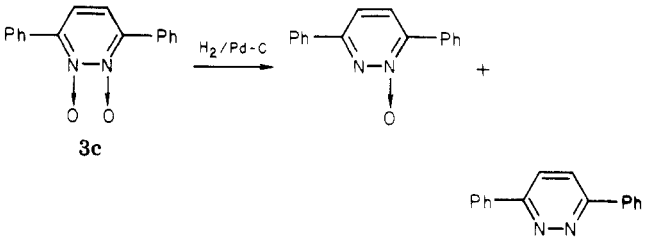
– 16 (O), M^+ – 30 (NO), and M^+ – 58 ($C_2H_2N_2$?) (see later). The compound showed the UV absorption at 259 nm (log ϵ 4.18, conjugated aryl). Furthermore, IR absorptions at 900 and 1343 cm^{-1} are not necessarily those of the N–O stretchings of the dioxide. Thus, the spectral data do not fit those expected of **3c**, but rather are characteristic of the dihydroisoxazoloisoxazole (**2c**) because known dihydroisoxazoloisoxazoles[4,5] show signals at δ 5.6–6.3 due to the protons in the 3a- and 6a-positions and some downfield shift due to the substituent effect of phenyl group would be expected for **2c**. The fragment mass peaks of M^+ – RNCO and $RNCO^+$ are also in agreement for **2c**.[4-6]

In addition, reduction of the compound with sodium borohydride in tetrahydrofuran–ethanol (10:1) yielded the dihydro compound **8**, similarly to other known dihydroisoxazoloisoxazoles.[4,5]



2c **8**

The oxidation of **1c** with PITFA yielded another product, whose NMR [δ 7.40–7.66 (6 H + 2 H, m) and 7.85–8.00 (4 H, m)], IR [(KBr) 825, 1350, 1398, and 1460 cm^{-1}], and mass spectra [*m/e* 264 (M^+), 248 (M^+ – O), 234 (M^+ – NO), 206 (M^+ – $C_2H_2N_2$?)] are characteristic for pyridazine 1,2-dioxides **3**. A strong UV absorption of the compound at 288 nm (log ϵ 4.35) is also characteristic for **3** (known pyridazine 1,2-dioxides show strong absorptions around 290 nm).[7,8] Furthermore, catalytic reduction of the compound on Pd–C in ethanol afforded 3,6-diphenylpyridazine 1-oxide and 3,6-diphenylpyridazine.



3c

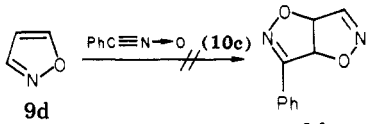
These facts show that this product is indeed pyridazine 1,2-dioxide **3c**, in contrast to Spyroudis' conclusion. The oxidation **1c** with LTA also afforded both **2c** and **3c**, and the yield of the latter was increased (approximately twice that obtained by oxidation with PITFA).

Thus, the oxidation of **1** with LTA is a more useful method for the preparation of pyridazine 1,2-dioxides than the oxidation of **1** with PITFA[2] and of pyridazines with 90% H_2O_2.[7,8]

(4) H. Arai, A. Ohsawa, K. Saiki, H. Igeta, A. Tsuji, T. Akimoto, and Y. Iitaka, *J. Chem. Soc., Chem. Commun.*, 856 (1977).
(5) A. Ohsawa, H. Arai, H. Igeta, T. Akimoto, A. Tsuji, and Y. Iitaka, *Tetrahedron*, **35**, 1267 (1979).
(6) H. Arai, A. Ohsawa, K. Saiki, and H. Igeta, *J. Chem. Soc., Chem. Commun.*, 133 (1977).
(7) Especially, the oxidation of arylpyridazines with 90% H_2O_2 did not yield practical amounts of the dioxides according to the method by Suzuki et al.[8]
(8) (a) I. Suzuki, M. Nakadate, and S. Sueyoshi, *Tetrahedron Lett.*, 1855 (1968); (b) M. Nakadate, S. Sueyoshi, and I. Suzuki, *Chem. Pharm. Bull.*, **18**, 1211 (1970).

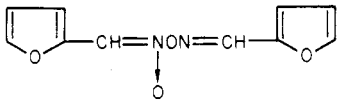
Although details of the effect of substituents and of the oxidizing reagents on the trend of the products is not obvious, an outline of the mechanism leading to the products is illustrated in Scheme II.

Regarding the formation of dihydroisoxazoloisoxazoles **2**, 1,3-dipolar cycloaddition between isoxazoles (**9**) and nitrile oxides (**10**) was disproved because isoxazole **9d** did not react with benzonitrile oxide (**10c**); only diphenylfuroxan (**11c**) was obtained.



9d **2d**

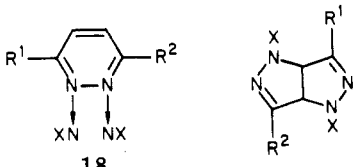
Although it is known that oximes of some five-membered heterocyclic compounds yield the unsymmetrical dimer, e.g., **12**[9] on the oxidation with LTA, no bicyclic product has previously been reported.



12

In our previous papers,[4,5] bis(iminoxyl) radicals **13** were postulated as the intermediates in the photoisomerization of the pyridazine 1,2-dioxides **3** into the dihydroisoxazoloisoxazoles **2**. The same intermediates **13** could be again assumed as the precursor of **2** in the oxidation of the dioximes **1** because oximes are known to generate iminoxyl radicals under some oxidative conditions,[10] and the biradical **13** might be the precursor of the pyridazine 1,2-dioxides **3** at the same time. The formation of acetylisoxazoles **5** may be explained by the oxidative C=N bond cleavage of their oximes **14**.[10] It was shown that **7a** gave the diketone **15a** instead of **5a** in the reaction under the described conditions. Dinitro compounds **6** may be formed via dinitroso compounds **16**. Oxidation of **1b** and **1c** afforded small amounts of 3-phenylisoxazole (**9c**) and diphenylfuroxan (**11c**). The former may arise from cleavage of the intermediate **17**, while the latter could be generated from benzonitrile oxide (**10c**),[11] which is the counterpart of **9c** in the postulated cleavage.

Oxidation of Bis(hydrazones) 4. Some *N*-acyliminopyridazinium ylides are stable enough to be isolated[12] and the results on the oxidation of **1** led us to expect the oxidation of **4** would yield 1,2-diiminopyridazinium bis(ylides) (**18**) or dihydropyrazolopyrazoles (**19**), both of which are unknown classes of compounds.



18 **19**

However, the oxidation of acylhydrazones (**4a** and **4b**) under the conditions described did not give any notable product, recovery of **4** or decomposition of the materials being observed depending upon conditions. We then investigated the reaction of 1,4-dimethyl-2-butene-1,4-dione bis(phenylhydrazone) (**4c**) and bis(*p*-nitrophenylhydrazone) (**4d**) (Table II). When **4c** was treated with PITFA or CAN, 5-acetyl-3-methyl-1-phenylpyrazole phenylhydrazone (**20c**) and 5-acetyl-3-methyl-1-phenylpyrazole (**21c**) were obtained, evidently resulting from the simple oxidative cyclization[10] and C=N bond cleavage. However, when **4c** was oxidized with LTA, a somewhat unstable compound (**22c**) was obtained as the major product, together with trace amounts of **20c** and **21c** (Scheme III). In a similar way, oxidation of **4d** using LTA or CAN afforded the corresponding compounds **20d**, **21d**, and **22d**, as shown in Table II.

Table II. Oxidation of 4 (Yields in %)

compd	reagents	solvents	conditions[a]	products		
				20c	**21c**	**22c**
4c	LTA	CH_2Cl_2	a	tr	tr	36
	PITFA	CH_2Cl_2	b	20	55	0
	CAN	aq AcOH	c	56	31	0
				20d	**21d**	**22d**
4d	LTA	CH_2Cl_2	a	tr	tr	17
	PITFA	CH_2Cl_2	a	10	59	0
	CAN	aq AcOH	c	tr	tr	69

[a] Condition a: at room temperature for 0.5 h. Condition b: the reagent was added at −20 °C, then stirred for 0.5 h at 0 °C. Condition c: the reagent was added at 0 °C, then stirred for 1 h at room temperature.

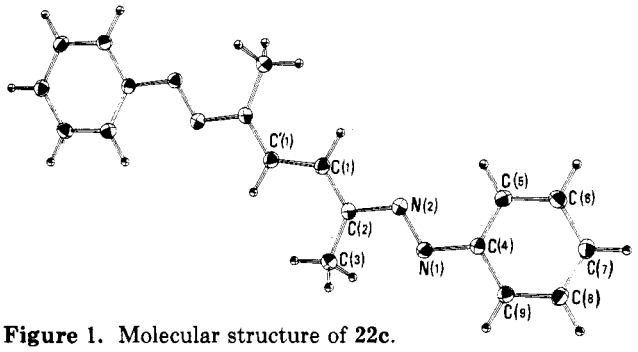
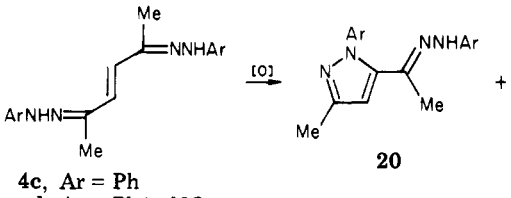


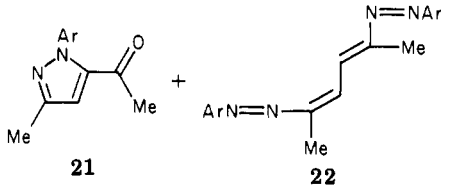
Figure 1. Molecular structure of **22c**.

Scheme III



4c, Ar = Ph
d, Ar = Ph(*p*-NO_2)

20

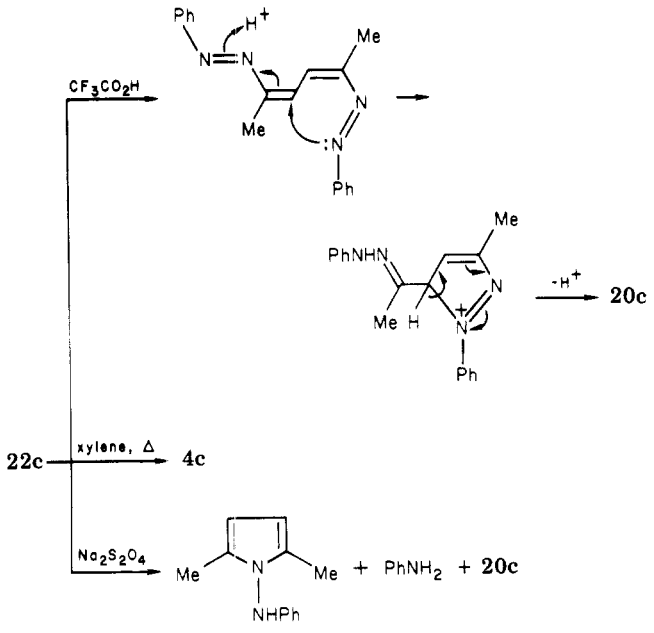


21 **22**

The compound **22c** crystallized as deep red needles (from EtOH–PhH, 1:5) which decomposed at 135 °C. It has the composition $C_{18}H_{18}N_4$ (elemental analysis) and showed a mass spectral peak at m/e 290 (M^+). Its NMR spectrum exhibited signals at δ 2.30 (6 H, s), 7.35–7.60 (6 H, m), 7.80–8.00 (4 H, m), and 7.80 (2 H, superimposed

(9) H. Kropf and R. Lambeck, *Justus Liebigs Ann. Chem.*, **700**, 18 (1966).
(10) (a) R. N. Butler, "Synthetic Reagents", Vol. III, J. S. Pizey, Ed., Wiley, New York, 1977, p 277, and references cited therein; (b) R. N. Butler, F. L. Scott, and T. A. F. O'Mahony, *Chem. Rev.*, **73**, 93 (1973), and references cited therein.
(11) T. Mukai, T. Oine, and A. Matsubara, *Bull. Chem. Soc. Jpn.*, **42**, 581 (1969).
(12) H. Hasegawa, H. Arai, and H. Igeta, *Chem. Pharm. Bull.*, **25**, 192 (1977), and references cited therein.

Scheme IV



singlet), and its UV spectrum showed absorptions at 245, 388, and 404 nm.

An X-ray analysis revealed that the compound has the structure of *all-trans*-1,4-bis(phenylazo)-1,4-dimethyl-1,3-butadiene (**22c**) as shown in Figure 1. The crystal data and its analysis are described in the experimental part; the structure was solved by the direct method.[13]

The compound **22c** yielded **20c** on treatment with trifluoroacetic acid and the mechanism of the transformation could be explained as shown in Scheme IV. Reduction of **22c** with $Na_2S_2O_4$ in aqueous ethanol afforded 2,5-dimethyl-1-phenylaminopyrrole, aniline, and **20c**, and in addition, **22c** yielded **4c** on refluxing in xylene, the mechanisms of these conversions being unclear.

Thus, the expectation of obtaining **18** and/or **19** was not fulfilled.[14]

Experimental Section

All melting points are uncorrected. IR spectra were measured with a Jasco IRA-1 spectrometer. Mass spectra were obtained on a Hitachi RMS-4 instrument. NMR spectra were run on Hitachi R-20 (60 MHz) and R-22 (90 MHz) spectrometers. UV spectra were run on a Hitachi EPS-3T instrument.

Preparation of 1,4-Disubstituted 2-Butene-1,4-dione Dioximes (1a–c). Compounds **1a–c** were obtained from corresponding diketones according to the usual procedure for the synthesis of oximes.

1,4-Dimethyl-2-butene-1,4-dione dioxime (1a): colorless plates (EtOH–H_2O, 2:3); mp 200 °C.[2]

1-Methyl-4-phenyl-2-butene-1,4-dione dioxime (1b): colorless needles (EtOH–H_2O, 2:3); mp 161–162 °C; IR (KBr) 3320, 1610, 1440, 1380, 1340, 1320, 1260, 1110, 1000, 940, 840 cm^{-1}; NMR (CD_3OD) δ 2.05 (3 H, s, CH_3), 6.08 (1 H, d, 2-H), 6.85 (1 H, d, 3-H), 7.42 (5 H, s, Ar-H), $J_{2,3}$ = 15.0 Hz. Anal. Calcd for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.79; H, 5.89; N, 13.78.

1,4-Diphenyl-2-butene-1,4-dione dioxime (1c): colorless plates (EtOH–H_2O, 2:3); mp 202–203 °C.[2]

Oxidation of 1 with Lead Tetraacetate. To a suspension of **1** (0.5 g) in 100 mL of CH_2Cl_2 was added LTA (1.5 molar equiv) in small portions with stirring at room temperature. After stirring for 1–2 h, the mixture was filtered and the solvent was distilled off under reduced pressure. The residue was subjected to a separation with silica gel column chromatography. Compounds **2**, **5**, **6**, **9**, and **11** were obtained from PhH elutions. Elution with CH_2Cl_2–MeOH (9:1) afforded **3**. The oxidation of **1a** yielded **2a** (8%) [mp 95–96 °C; mass spectrum *m/e* 140 (M^+, s), 124 (vw), 110 (s), 99 (m), 84 (s), 82 (base), 69 (m), etc.],[15] **3a** (33%) [mp 216 °C dec;[8] mass spectrum *m/e* 140 (M^+, base), 124 (w), 110 (s), 82 (m), etc.], **5a** (trace) (mp 73–75 °C)[16] and **6a** (11%) (mp 162–163 °C).[17] The oxidation of **1b** yielded **2b** (10%) [mp 102–103 °C; mass spectrum *m/e* 202 (M^+, base), 172 (vw), 145 (m), 144 (s), 119 (s), etc.],[15] **3b** (19%) [mp 181–182 °C; mass spectrum *m/e* 202 (M^+, s), 186 (w), 172 (w), 144 (base), 115 (m), etc.],[15] **5b** (3%) (mp 98–100 °C),[18] and **9b** (=**9c**, trace) [bp 70–77 °C (1 mmHg)].[19] The oxidation of **1c** gave **2c** (60%) [mp 176–177 °C; mass spectrum *m/e* 264 (M^+, base), 248 (vw), 234 (w), 145 (s), 144 (m), 119 (m), 103 (w), etc.; UV (EtOH) 259 nm (log ϵ 4.18)],[15] **3c** (15%) [mp 258 °C dec; mass spectrum *m/e* 264 (M^+, m), 248 (w), 234 (w), 206 (s), 128 (w), 102 (s), 77 (base); UV (EtOH) 288 nm (log ϵ 4.35)],[15] **6c** (2%) (mp 222 °C),[20] **9c** (trace), and **11c** (trace) (mp 113 °C).[21]

Oxidation of 1 with Phenyliodoso Bis(trifluoroacetate). To a suspension of **1** (0.5 g) in 100 mL of CH_2Cl_2, PITFA (1.2 molar equiv) was added in small protions with stirring at room temperature. After 1 h, the mixture was worked up in a manner similar to that above. The oxidation of **1a** yielded **2a** (5%), **3a** (15%), and **6a** (2%). The oxidation of **1c** gave **2c** (51%), **3c** (8%), **6c** (6%), **9c** (3%), an a trace of **11c**.

Oxidation of 1 with Ceric Ammonium Nitrate. A solution of CAN (1.3 molar equiv) in 80% AcOH (80 mL) was added dropwise to a solution of **1** (2 g) in 80% AcOH (20 mL) during 0.5 h with stirring at room temperature. The mixture was stirred for an additional 0.5 h, neutralized with aqueous $KHCO_3$, and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was subjected to silica gel column chromatography as mentioned above. The oxidation of **1a** gave **5a** (3%), **6a** (10%), and **7a** (6%): mp 109–111 °C; colorless needles from hexane–PhH; IR (KBr) 3280, 1675, 1620, 1365, 1270, 1255 cm^{-1}; NMR ($CDCl_3$) δ 2.05 (3 H, s, CH_3), 2.34 (3 H, s, CH_3), 6.42 (1 H, d, J = 17 Hz, C=CH), 7.22 (1 H, d, J = 17 Hz, C=CH), 9.75 (1 H, br s, NH). Anal. Calcd for $C_6H_9NO_2$: C, 56.69; H, 7.09; N, 11.02. Found: C, 56.60; H, 7.12; N, 11.2. The oxidation of **1c** yielded **2c** (8%), **6c** (trace), **9c** (trace), and **11c** (trace).

Reduction of 2c with $NaBH_4$. To a solution of **2c** (100 mg) in 100 mL of THF–EtOH (10:1), $NaBH_4$ (ca. 500 mg, large excess) was added in small portions with stirring at room temperature. After 4 h, the mixture was filtered, and then 10 mL of H_2O was added to the filtrate. The solution was extracted with CH_2Cl_2 and the extract was dried over $MgSO_4$ and evaporated. The residue was chromatographed over silica gel using CH_2Cl_2 as eluent. Aside from **2c** (20-mg recovery) and a trace amount of **9c**, 10 mg of 3,6-diphenyl-2,3,3a,6a-tetrahydroisoxazolo[5,4-*d*]-isoxazole (**8**) was obtained. Compound **8** had: mp 98–100 °C; colorless plates (MeOH); IR (KBr) 3400, 3200, 1600, 1500, 1450, 1420, 1360, 1250, 1135, 1040 cm^{-1}; NMR ($CDCl_3$) δ 4.56 (1 H, br dd, J = 13.0 and 4.0 Hz, 3-H), 5.45 (1 H, br d, J = 13.0 Hz, NH), 5.63 (1 H, dd, J = 4.0 and 6.4 Hz, 3a-H), 6.15 (1 H, d, J = 6.4 Hz, 6a-H), 7.35–7.55 (8 H, m, Ar-H), 7.80–7.95 (2 H, m, Ar-H). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.01; H, 5.35; N, 10.28.

Catalytic Reduction of 3c. The oxide **3c** (90 mg) was reduced in EtOH (30 mL) on 10% Pd-C until absorption of 7.6 mL of

(13) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971).

(14) Compounds **20c** and **20d** gave only **21c** and **21d**, respectively, as the major products on further oxidation with described oxidizing reagents, and the expected compounds **18** or **19** were not found in the reaction mixtures (see Experimental Section).

(15) Other spectral data are given in ref 5.

(16) Mp 75–76 °C: A. Quilico, L. Panizzi, and C. Epifani, *Gazz. Chim. Ital.*, **69**, 536 (1939); *Chem. Abstr.*, **34**, 1316 (1940).

(17) Mp 165–166 °C: J. A. Durden, Jr., D. L. Heywood, A. A. Sousa, and H. W. Spurr, *J. Agric. Food Chem.*, **18**, 50 (1970).

(18) Mp 104–105 °C: P. Grünanger and S. Mangiapan, *Gazz. Chim. Ital.*, **88**, 149 (1958); *Chem. Abstr.*, **53**, 13135f (1959).

(19) Bp 70–75 °C (1 mmHg): G. Bianchi and P. Grünanger, *Tetrahedron*, **21**, 817 (1965).

(20) Mp 219–211 °C: E. S. Lipina, V. V. Perekalin, and Y. S. Bobovich, *Zh. Obshch. Khim.*, **34**, 3640 (1964); *Chem. Abstr.*, **62**, 8989h (1965).

(21) Mp 113–115 °C: see ref 11.

H_2 was observed. The mixture was filtered and the filtrate was evaporated to dryness in vacuo. The residue was chromatographed over alumina. The first material (5 mg, 6%) obtained from CH_2Cl_2–PhH (1:1) elution was identical with 3,6-diphenylpyridazine.[22] The second material (75 mg, 89%) from CH_2Cl_2 elution was identical with 3,6-diphenylpyridazine 1-oxide.[23]

Attempted 1,3-Dipolar Cycloaddition of 9d with 10c. Benzonitrile oxide (**10c**) was generated in situ; to a solution of isoxazole (**9d**, 1 g) and benzohydroxamoyl chloride (1 g) in Et_2O (40 mL), a solution of Et_3N (0.7 g) in Et_2O (2 mL) was added with stirring at 5–10 °C. The mixture was allowed to stand for 2 h at room temperature. The mixture was evaporated in vacuo. The absence of 3-phenyldihydroisoxazoloisoxazole (**2d**)[5] in the residue was confirmed by TLC (silica gel). Diphenylfuroxan (**11c**) was obtained (300 mg) after silica gel column chromatography (PhH) of the residue.

Oxidation of 7a with LTA and CAN. LTA (350 mg) was added to a solution of **7a** (100 mg) in CH_2Cl_2 (30 mL) in small portions. The mixture was stirred for 2 h at room temperature, filtered, and evaporated. The residue was chromatographed over alumina using PhH as an eluent. Hex-3-ene-2,5-dione (**15a**, 40 mg, 45%) and **7a** (recovery, 40 mg) were obtained. A similar result was obtained on the oxidation of **7a** with CAN under the aforementioned conditions. Compound **5a** was not detected from the described mixtures (by NMR and TLC).

Preparation of Bis(hydrazones) (4a–d). Compounds **4a–d** were prepared from hex-3-ene-2,5-dione (**15a**) according to the common procedure for synthesis of hydrazones using a trace of acetic acid as a catalyst.

Compound 4a: yellow microneedles (50% EtOH); mp 257–259 °C. Anal. Calcd for $C_{10}H_{16}N_4O_2$: C, 53.57; H, 7.14; N, 25.00. Found: C, 53.57; H, 7.20; N, 24.74.

Compound 4b: yellow powder (50% EtOH); mp 231–232 °C. Anal. Calcd for $C_{20}H_{20}N_4O_2$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.69; H, 5.68; N, 16.40.

Compound 4c: yellow needles (AcOEt); mp 209–210 °C dec; NMR ($CDCl_3$–Me_2SO-d_6) δ 2.08 (6 H, s, $CH_3 \times 2$), 6.60 (2 H, s, C=CH), 6.70–7.40 (10 H, m, Ar-H), 9.00 (2 H, br s, NH). Anal. Calcd for $C_{18}H_{20}N_4$: C, 73.94; H, 6.90; N, 19.16. Found: C, 74.29; H, 7.30; N, 19.48.

Compound 4d: deep red microneedles (recrystallized from Me_2SO–H_2O, 1:1, below 100 °C); mp 252–255 °C dec; NMR (Me_2SO-d_6) δ 2.12 (6 H, s, $CH_3 \times 2$), 6.72 (2 H, s, C=CH), 7.30 (4 H, d, J = 8.2 Hz, Ar-H), 8.14 (4 H, d, J = 8.2 Hz, Ar-H), 10.3 (2 H, br s, NH). Anal. Calcd for $C_{18}H_{18}N_6O_4$: C, 56.54; H, 4.71; N, 21.99. Found: C, 56.23; H, 4.68; N, 21.84. The compound incorporates Me_2SO into its crystals (to give **4d**·$(Me_2SO)_{1.5-2.0}$; the Me_2SO could be eliminated on heating at ca. 150 °C (0.1 mmHg).

Oxidation of 4a and 4b. Compound **4a** was treated with LTA or PITFA and worked up as described below. TLC (silica gel and aluminum oxide) and NMR of the residue exhibited very complicated features of a mixture and no product was isolated despite careful chromatography (silica gel and aluminum oxide). When **4a** was treated with CAN, reaction did not take place, **4a** being recovered. Oxidation of **4b** with described reagents afforded similar results.

Oxidation of 4c with LTA. LTA (680 mg, 1.5 molar equiv) was added to a solution of **4c** (300 mg) in 80 mL of CH_2Cl_2 with stirring at ambient temperature. The mixture was stirred for 0.5 h at the temperature and filtered. The liquor was evaporated in vacuo below 30 °C. The residue was chromatographed over aluminum oxide using PhH as an eluent to give 108 mg (36%) of **22c**: dark red needles (EtOH–PhH, 1:5); mp 135–136 °C dec; IR ($CHCl_3$) 2990, 1600, 1480, 1460, 1420 cm^{-1}, etc.; NMR ($CDCl_3$) δ 2.30 (6 H, s, $CH_3 \times 2$), 7.35–7.60 (6 H, m, Ar-H), 7.80–8.00 (4 H, m, Ar-H), 7.80 (2 H, s, 2- and 3-H); UV (EtOH) 245, 388, 404, 428 (sh) nm; mass spectrum m/e 290 (M^+), 288, 262, 247, 185, 184 (base), 183, 170, 132, 115, 93, 91, 78, 77, etc. Anal. Calcd for $C_{18}H_{18}N_4$: C, 74.45; H, 6.25; N, 19.30. Found: C, 74.50; H, 6.20; N, 19.41. The elution with CH_2Cl_2 afforded a trace of **21c**: colorless needles (hexane); mp 56–57 °C; IR (KBr) 3060, 1682, 1600 cm^{-1}; NMR ($CDCl_3$) δ 2.31 (3 H, s, CH_3), 2.40 (3 H, s, CH_3), 6.73 (1 H, s, 4-H), 7.37 (5 H, s, Ar-H). Anal. Calcd for $C_{12}H_{12}N_2O$: C, 72.00; H, 6.00; N, 14.00. Found: C, 71.99; H, 6.29; N, 13.79. Next elution (CH_2Cl_2) gave a trace of **20c**: yellow prisms (hexane–PhH); mp 69–70 °C; IR (KBr) 3240, 1600, 1500 cm^{-1}; NMR ($CDCl_3$) δ 1.98 (3 H, s, CH_3), 2.30 (3 H, s, CH_3), 6.30 (1 H, s, 4-H), 6.40–7.30 (6 H, m, Ar-H and NH), 7.40 (5 H, s, Ar-H). Anal. Calcd for $C_{18}H_{18}N_4$: C, 74.45; H, 6.25; N, 19.30. Found: C, 74.25; H, 6.20; N, 19.11. When **20c** was kept in CH_2Cl_2 for a while at room temperature, it decomposed into a mixture where **21c** and $PhNHNH_2$ were major products. Further oxidation of **20c** with LTA, PITFA, and CAN afforded **21c** as the major product (68% with PITFA) and any other product was isolated. On treating **21c** (60 mg, in 0.5 mL of EtOH) with $PhNHNH_2$ (200 mg) and AcOH (20 mg) at 80 °C for 1.5 h, 75 mg (86%) of **20c** was obtained.

Oxidation of 4c with PITFA. To a suspension of **4c** (500 mg) in 40 mL of CH_2Cl_2, a solution of PITFA (1.5 g) in 50 mL of CH_2Cl_2 was added dropwise with stirring at −20 °C. The mixture was stirred further at 0 °C for 0.5 h. The solvent was evaporated in vacuo and the residue was chromatographed over aluminum oxide. Compounds **20c** and **21c** were obtained in the yields shown in Table II, while **22c** was absent.

Oxidation of 4c with CAN. A solution of CAN (2.4 g) in 50% AcOH (50 mL) was added to a suspension of **4c** (600 mg) in 50% AcOH (30 mL) dropwise with stirring at 0 °C. The mixture was stirred for 1 h at room temperature and neutralized cautiously with aqueous $KHCO_3$. The mixture was extracted with CH_2Cl_2 and dried over $MgSO_4$. The residue obtained after evaporation of the solvent was subjected to aluminum oxide column chromatography.

Oxidation of 4d with LTA. Compound **4d** was treated with LTA at room temperature as mentioned for **4c**. The deposited material (**22d**) was collected by filtration and washed with 50% AcOH, MeOH, and Et_2O, and dried in vacuo. Further purification (recrystallization) was difficult because of its insolubility and instability. The filtrate was handled as described before.

Oxidation of 4d with PITFA. Compound **4d** was treated with PITFA at room temperature. The mixture was worked up as described before. Compound **22d** was absent in this run.

Oxidation of 4d with CAN. Compound **4d** was treated with CAN as mentioned before. Compound **22d** was deposited from the reaction mixture, washed with 50% AcOH, and handled as described above. The filtrate was treated as described before. Compounds **20d** and **21d** were obtained in very low yields in this run. Compound **20d** had: mp 248–250 °C; dark yellow prisms (PhH–$CHCl_3$); IR (KBr) 3280, 1585, 1470, 1342, 1308 cm^{-1}; NMR (Me_2SO-d_6) δ 2.30 (6 H, s, $CH_3 \times 2$), 6.57 [2 H, d, J = 9.5 Hz, Ar-H), 6.70 (1 H, s, 4-H), 7.70 (2 H, d, J = 9.5 Hz, Ar-H), 7.88 (2 H, d, J = 9.5 Hz, Ar-H), 8.33 (2 H, d, J = 9.5 Hz, Ar-H), 10.22 (1 H, br s, NH); NMR (trifluoroacetic acid (TFA)) δ 2.40 (3 H, s, CH_3), 2.70 (3 H, s, CH_3), 6.52 (2 H, d, J = 9.5 Hz, Ar-H), 7.00 (1 H, s, 4-H), 7.90 (2 H, d, J = 9.5 Hz, Ar-H), 8.40 (2 H, d, J = 10.0 Hz, Ar-H), 8.62 (2 H, d, J = 10.0 Hz, Ar-H). Anal. Calcd for $C_{18}H_{16}N_6O_4$: C, 56.84; H, 4.21; N, 22.11. Found: C, 56.91; H, 4.09; N, 21.88. Compound **21d** had: mp 205–207 °C; pale yellow needles ($CHCl_3$); IR (KBr) 3120, 3090, 1683, 1597, 1500, 1440, 1350 cm^{-1}; NMR (Me_2SO-d_6) δ 2.28 (3 H, s, CH_3), 2.49 (3 H, s, CH_3), 7.16 (1 H, s, 4-H), 7.66 (2 H, d, J = 9.5 Hz, Ar-H), 8.28 (2 H, d, J = 9.5 Hz, Ar-H). Anal. Calcd for $C_{12}H_{11}N_3O_3$: C, 58.77; H, 4.49; N, 17.14. Found: C, 58.53; H, 4.45; N, 17.17. Compound **22d**: a very insoluble black powder which decomposed at 213–214 °C; IR (KBr) 1590, 1520, 1430, 1340 cm^{-1}; NMR spectrum of the compound in TFA was identical with that of **20d** because **22d** quantitatively changed into **20d** in TFA. Anal. Calcd for $C_{18}H_{16}N_6O_4$: C, 56.84; H, 4.21; N, 22.11. Found: C, 56.54; H, 4.33; N, 22.33.

When **20d** (150 mg) was treated with PITFA (200 mg) in CH_2Cl_2 (25 mL) at ambient temperature for 3 h, 50 mg (52%) of **21d** was obtained from the reaction mixture and no other isolable material was obtained despite careful column chromatography on aluminum oxide. On the other hand, when **21d** (30 mg) was refluxed with *p*-nitrophenylhydrazine (100 mg) in EtOH–AcOH (1:1, 1 mL) for 1 h, 30 mg (64%) of the hydrazone (**20d**) was obtained.

Reactions and Structure of 22c. A solution of **22c** (50 mg) was refluxed for 1 h in CH_2Cl_2 (20 mL). The solvent was evaporated in vacuo and the residue was chromatographed over

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(23) K. B. Tomer, N. Harrit, I. Rosenthal, O. Buchardt, P. L. Kumler, and D. Creed, *J. Am. Chem. Soc.*, **95**, 7402 (1973).

aluminum oxide to give 40 mg (80%) of **20c**. A solution of **22c** (70 mg) in PhH (10 mL) was added with 3 drops of TFA under cooling on an ice bath and the mixture was kept for 1 h at room temperature. The solvent was removed under reduced pressure at room temperature and the residue was found to contain 60 mg (86%) of **20c** (silica gel column chromatography). Compound **22c** (100 mg) was refluxed with xylene (5 mL) for 15 min. The deposited crystals were recrystallized from 50% EtOH to give 55 mg (55%) of **4c**.

A mixture of **22c** (200 mg) and $Na_2S_2O_4$ (202 mg) in 33% EtOH (40 mL) was stirred for 3 h at room temperature and acidified with 10% HCl. EtOH was removed in vacuo and saturated aqueous $NaHCO_3$ (1 mL) was added and the mixture was extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and the solvent was evaporated in vacuo. The residue was chromatographed over aluminum oxide with Et_2O–hexane (1:2) to give 20 mg (16%) of 2,5-dimethyl-1-phenylaminopyrrole (mp 89–90 °C, needles from hexane)[24] [IR (KBr) 3280, 3040, 2920, 1620, 1500 cm^{-1}; NMR (CCl_4) δ 2.06 (6 H, s, CH_3 × 2), 5.63 (2 H, s, 3- and 4-H), 6.13 (1 H, br s, NH), 6.32 (2 H, m, Ar-H), 6.78 (1 H, m, Ar-H), 7.11 (2 H, m, Ar-H)], together with 10 mg (17%) of $PhNH_2$ and 20 mg (10%) of **20c**. The crystal data of a single crystal of **22c** are as follows: space group $P2_1/n$, a = 11.062, b = 15.310, c = 4.642 Å, β = 93.612°, and Z = 2. Analysis was carried on 1074 independent reflections with $I > 3\sigma(I)$, within the limit $\theta < 70°$, which were obtained by a Philips automatic diffractometer using Cu Kα radiation. The structure was solved by the direct method[13] and the final R factor was 0.05 (refined by block diagonal least-squares method; see paragraph on supplementary material at the end of this paper).

(24) J. R. Kenneth, U.S. Patent 2725378; *Chem. Abstr.*, **51**, 910 (1957).

Acknowledgment. We thank a referee for his helpful suggestion on the mechanism of the conversion of **22c**.

Registry No. 1a, 68321-99-3; **1b**, 68322-00-9; **1c**, 25233-87-8; **2a**, 66252-15-1; **2b**, 68322-02-1; **2c**, 68322-03-2; **3a**, 19194-90-2; **3b**, 68322-01-0; **3c**, 62260-20-2; **4a**, 71118-25-7; **4b**, 71118-26-8; **4c**, 71118-27-9; **4d**, 71118-28-0; **5a**, 55086-61-8; **5b**, 2048-69-3; **6a**, 26331-58-8; **6c**, 61208-80-8; **7a**, 30829-18-6; **8**, 71118-29-1; **9b**, 30842-90-1; **9c**, 1006-65-1; **9d**, 288-14-2; **10c**, 873-67-6; **11c**, 5585-14-8; **15a**, 4436-75-3; **20c**, 71118-30-4; **20d**, 71118-31-5; **21c**, 71118-32-6; **21d**, 71118-33-7; **22c**, 71118-34-8; **22d**, 71118-35-9; 2,5-dimethyl-1-phenylaminopyrrole, 32570-25-5; 1-methyl-4-phenyl-2-butene-1,4-dione, 26480-56-8; 1,4-diphenyl-2-butene-1,4-dione, 4070-75-1; 3,6-diphenylpyridazine, 891-22-5; 3,6-diphenylpyridazine 1-oxide, 21111-33-1.

Supplementary Material Available: Tables of positional and thermal parameters, and interatomic distances and bond angles for the structure of the compound **22c** (2 pages). Ordering information is given on any current masthead page.

Acetolysis of the Isomeric 5,6-Dimethylnorbornyl *p*-Bromobenzenesulfonates[1a]

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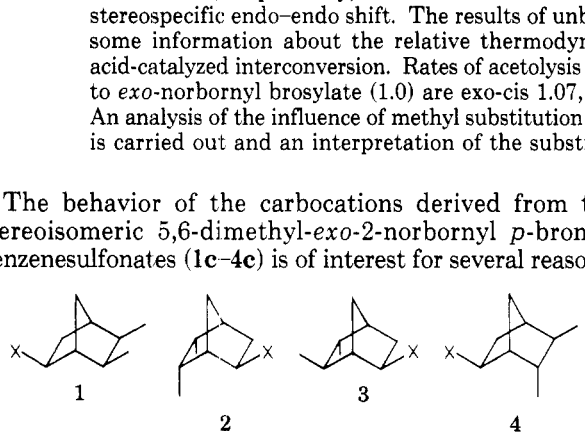
Received March 26, 1979

The products of acetolysis of the four stereoisomeric 5,6-dimethyl-*exo*-2-norbornyl brosylates and of acid-catalyzed addition of acetic acid to the three stereoisomeric 5,6-dimethylnorbornenes have been investigated. Acetolysis of the two Wagner–Meerwein (WM)-related *cis*-brosylates under kinetically controlled conditions led to identical product mixtures from which four acetates and one olefin, accounting for >99% of the products, were identified. Under similar conditions two different mixtures of known composition of the WM-related *trans*-brosylates also gave identical product mixtures, from which two acetates and one olefin, accounting for >99% of the products, were identified. The proportions of the total product arising from 6,2 hydride shift under these conditions are 93 and 57%, respectively, in the cis and trans series, these products arising almost exclusively from a single stereospecific endo–endo shift. The results of unbuffered acetolyses and acid-catalyzed olefin additions provide some information about the relative thermodynamic stabilities of the products and their relative rates of acid-catalyzed interconversion. Rates of acetolysis of the 5,6-dimethyl-*exo*-2-norbornyl brosylates at 25 °C relative to *exo*-norbornyl brosylate (1.0) are exo-cis 1.07, endo-cis 0.37, endo-5,exo-6 0.76, and exo-5,endo-6 <ca. 0.04. An analysis of the influence of methyl substitution at each of the four C5 and C6 positions on the rate of acetolysis is carried out and an interpretation of the substituent effects offered.

The behavior of the carbocations derived from the stereoisomeric 5,6-dimethyl-*exo*-2-norbornyl *p*-bromobenzenesulfonates (**1c**–**4c**) is of interest for several reasons.



1 2 3 4

a, X = OH; b, X = OAc; c, X = OBs

These systems provide one of the simplest tests of the stereospecificity of transannular (6,2) hydride shifts in norbornyl cations. A strong preference for endo–endo hydride migration has been demonstrated in solvolysis of more complex substrates[2,3] and in methyl- and dimethylnorbornyl cations in superacid media.[4] The products of the solvolyses of **1c**–**4c** are also of interest in relation to the influence of substitution on the relative rates of reaction of nucleophiles at WM-related sites[3d,5] and

(1) (a) Abstracted in part from the Ph.D. Thesis of Robert A. Reith, Carnegie-Mellon University. (b) Address correspondence to this author at the Department of Chemistry, University of Guelph.

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0022-3263/79/1944-3529$01.00/0