Oxidation of *vic*-Diols to α-Dicarbonyl Compounds Using the Oxoammonium Salt Derived from 4-Acetamido-TEMPO and *p*-Toluenesulfonic Acid

Martin G. Banwell,* Vanessa S. Bridges, Joseph R. Dupuche, Sharon L. Richards, and Justine M. Walter

School of Chemistry, The University of Melbourne, Parkville, Victoria 3052, Australia

Received May 10, 1994®

Both open-chain and cyclic *vicinal*-diols are oxidized to the corresponding α-dicarbonyl compound by the oxoammonium salt derived from 4-acetamido-TEMPO and *p*-toluenesulfonic acid. With certain exceptions, yields are as high or higher than those obtained when Swern reagents are used to effect the same conversions.

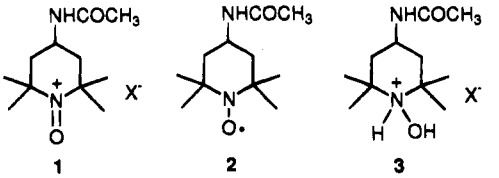
In 1987 we reported[1] that, in contrast to a number of other oxidants, the Swern reagent derived from trifluoroacetic anhydride and dimethyl sulfoxide provided an effective means for converting a range of *vic*-diols into the corresponding α-diketones. While we[2] and others[3] have subsequently employed this reagent in various closely related contexts, its use requires maintenance of both anhydrous conditions and low temperatures (−60 °C) for lengthy periods. As a result of these drawbacks we were intrigued by the recent report[4] that oxoammonium salts of the type **1**, which are derived by *in situ* acid-promoted disproportionation of 4-acetamido-TEMPO (**2**),[5] act as mild and selective oxidants which allow for the near-quantitative conversion of primary and secondary alcohols into the corresponding carbonyl compounds. The procedure is operationally simple, being run at 0 °C and then at room temperature, and furthermore, there is no need to maintain anhydrous conditions during the course of the reaction. The workup is also very straightforward, and the removal of the byproduct **3** does not present any problems. These attributes, coupled with the scattered reports[6] that stoichiometric amounts of various oxoammonium salts convert *vic*-diols into the corresponding acyloin, apparently without accompanying C—C bond cleavage, prompted us to investigate the title reaction. The results of our study are reported herein.

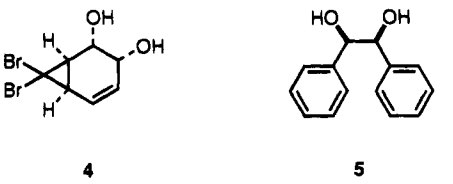
Preliminary experiments were conducted using the diols **4**[1] and **5** as test substrates, and several reaction parameters were varied (Table 1). The reaction conditions defined in entry 2 and detailed in the Experimental Section represent something approaching the optimum for oxidation of *vic*-diols to the corresponding α-dicarbonyl compounds. It is noteworthy that under these conditions higher yields of diketone **6** were obtained from diol **4** than when the previously reported[1] Swern reagent system was applied to the same substrate (89% *vs* 68%). In an effort to accelerate the rate of oxidation, higher reaction temperatures were examined (entries 4 and 7, Table 1). However, when the reaction mixtures were heated at reflux (40 °C) oxidation was no more rapid but product yield was reduced.

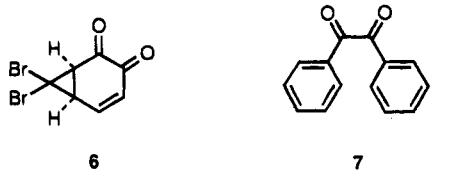
Table 1. Optimization of Reaction Conditions for Oxidation of Diols 4 and 5 with Oxoammonium Salt 1[a]

entry	substrate	solvent	reaction temp (°C)	equiv of 4-acetamido TEMPO (**2**)	time (h)	product (% yield)
1	**4**	CH_2Cl_2	18	4	24	**6** (81)
2	**4**	CH_2Cl_2	18	5	24	**6** (89)
3	**4**	CH_2Cl_2	18	6	16	**6** (89)
4	**4**	CH_2Cl_2	40	5	24	**6** (73)
5	**4**	$CHCl_3$[b]	18	5	24	**6** (78)
6	**5**	CH_2Cl_2	18	5	72	**7** (88)
7	**5**	CH_2Cl_2	40	5	72	**7** (80)
8	**5**	$CHCl_3$[b]	18	5	72	**7** (88)

[a] Reactions conducted using 50 mg of substrate and a total solvent volume of 4 mL. [b] Reactions run in ethanol-free chloroform.







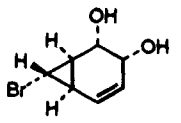
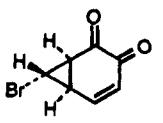
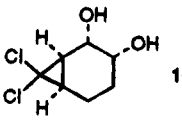
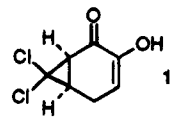
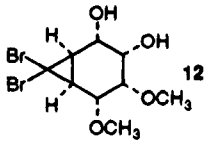
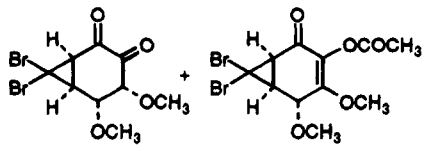
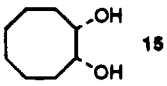
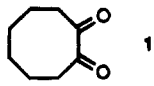
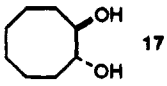
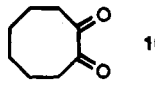
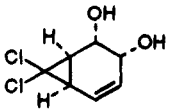
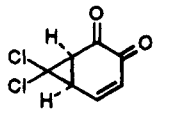
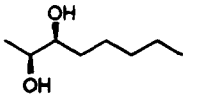
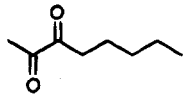
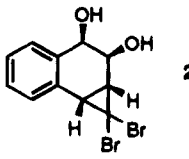
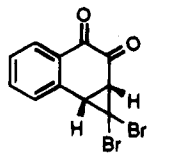
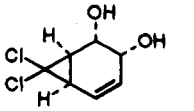
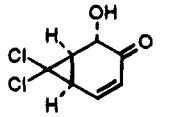
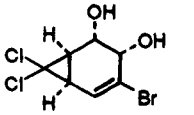
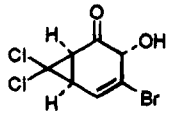
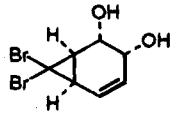
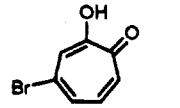
The near optimum conditions established for the oxidation of compounds **4** and **5** have been successfully applied to a range of substrates, and the results of this series of experiments are summarized in Table 2. In those cases where comparisons can be made (entries 1, 3, 4, and 7 in Table 2), the yields of product(s) are generally as high or higher than for the analogous

® Abstract published in *Advance ACS Abstracts,* September 1, 1994.

(1) Amon, C. M.; Banwell, M. G.; Gravatt, G. L. *J. Org. Chem.* **1987**, *52*, 4851.
(2) (a) Banwell, M. G.; Collis, M. P. *J. Chem. Soc., Chem. Commun.* **1991**, 1343. (b) Banwell, M. G.; Lambert, J. N.; Gulbis, J. M.; Mackay, M. F. *J. Chem. Soc., Chem. Commun.* **1990**, 1450.
(3) Braish, T. F.; Saddler, J. C.; Fuchs, P. L. *J. Org. Chem.* **1988**, *53*, 3647.
(4) Ma, Z.; Bobbitt, J. M. *J. Org. Chem.* **1991**, *56*, 6110.
(5) Available from Aldrich Chemical Co., Milwaukee, WI, and Fluka Chemie AG, Buchs, Switzerland.
(6) (a) Miyazawa, T.; Endo, T. *J. Org. Chem.* **1985**, *50*, 3930. (b) Anelli, P. L.; Banfi, S.; Montanari, F.; Quici, S. *J. Org. Chem.* **1989**, *54*, 2970. (c) Siedlecka, R.; Skarzewski, J.; Mlochowski, J. *Tetrahedron Lett.* **1990**, *31*, 2177.

0022-3263/94/1959-6338$04.50/0

Table 2. Oxidation of Some *vic*-Diols by the Oxoammonium Salt 1

Entry	Diol	Oxidation Product(s)	Reaction Time (h)	% Yield*
1	 **8**	 **9**	24	36 (66)
2	 **10**	 **11**	24	76
3†	 **12**	 **13** + **14**	48	54 (13) 30 (14) (0)
4	 **15**	 **16**	72	95 (95)
5	 **17**	 **16**	72	90
6	 **18**	 **19**	22	75
7	 **20**	 **21**	72	90 (87)
8	 **22**	 **23**	72	90
9§	 **18**	 **24**	22	80
10§	 **25**	 **26**	22	23
11§	 **4**	 **27**	24	30

* The yields in brackets are those obtained when trifluoroacetic anhydride 'activated' dimethyl sulfoxide was used as oxidant.

† The crude products from this oxidation reaction were subjected to treatment with acetic anhydride/pyridine prior to product isolation.

§ Reaction run using 1.0 equivalents of oxoammonium salt 1.

reactions carried out using the oxidant derived from trifluoroacetic anhydride and dimethyl sulfoxide. In the extreme (entry 3, Table 2), while the latter reagent system failed to give any characterizable products from substrate **12** oxidation using **1** (X = OTs) afforded, after acetylation of the crude reaction mixture, a 10:7 mixture of diketone **13** and the enol acetate **14** (84% combined yield). In the only case (entry 1, Table 2) where the Swern reagent provided higher yields of product it is assumed that this is because product **9** is sensitive to the acidic (?) conditions associated with the oxidation process and/or the subsequent chromatographic purification step.

Reagent **1** (X = OTs) does not seem to suffer from geometric constraints to the extent that it successfully converts both *cis*- and *trans*-related *vic*-diols (see entries 4 and 5, Table 2) into the corresponding α-dicarbonyl compound. Furthermore, open-chain diols (entry 7, Table 2) are also readily oxidized by the oxoammonium salt.

When 1.0 molar equiv of salt **1** (X = OTs) is used in the oxidation reaction then preferential conversion of diols into one of the two possible acyloins can be observed (entries 9 and 10, Table 2). For example, reaction of compound **18** (entry 9) under such conditions affords the product (**24**) in which it is the allylic, rather than homoallylic, hydroxyl group of the substrate that has been oxidized. The reverse selectivity is observed when diol **25** (entry 10) is oxidized under the same conditions, and the selective formation of acyloin **26** presumably arises because of the steric crowding of the allylic hydroxyl (in **25**) by the adjacent bromine. As testimony to this assertion, even when the "normal" oxidation stoichiometry (2.5 molar equiv of **1**) is employed, the title reagent does not convert diol **25** into the corresponding diketone. However, this conversion can be effected under Swern conditions (see Experimental Section), thus suggesting that the title reagent is the sterically more demanding one. The only product obtained from diol **4** when this substrate was oxidized with 1 molar equiv of **1** was the known[1] bromotropolone **27**. This product presumably arises *via* mono-oxidation to an intermediate acyloin which undergoes an enolization/electrocyclization/dehydrobromination sequence.[7] Some support for this proposal stems from the observation that both acyloins **24** and **26** are unstable and readily rearrange (see Experimental Section) to the corresponding α-tropolone (4-chloro-α-tropolone and 7-bromo-4-chloro-α-tropolone, respectively).

In summary, the salt **1** (X = OTs) is a readily generated, easily used, and effective reagent for the oxidation of *vic*-diols to α-dicarbonyls. The need to use 5.0 molar equiv of 4-acetamido-TEMPO (**2**) for every equivalent of diol,[8] coupled with the relatively high price of compound **2**, probably makes the title reagent most suitable for smaller scale work.

Experimental Section

General Procedures. 4-Acetamido-TEMPO (**2**) was purchased from Fluka Chemie AG, Buchs, Switzerland. Diols **5** and **17** were purchased from the Aldrich Chemical Co. and used as obtained while diols **4**,[1] **8**,[2a] **12**,[9] and **18**[2a] were prepared using the cited procedures. Diols **15**[1] and **20**[1] were prepared by standard *cis*-dihydroxylation[10] of the corresponding olefin. Compounds **10**, **22**, and **25** were synthesized by the methods detailed below. Unless otherwise specified, NMR spectra were recorded using deuteriochloroform as solvent.

(1α,2α,3α,6α)-7,7-Dichlorobicyclo[4.1.0]heptane-2,3-diol (10). A solution of (1α,6α)-7,7-dichlorobicyclo[4.1.0]hept-2-ene[11] (11.81 g, 73 mmol) and trimethylamine *N*-oxide (18.2 g, 242 mmol) in 2-methyl-2-propanol (300 mL) containing water (85 mL) and pyridine (13 mL) was treated in one portion with osmium tetraoxide (6 mL of a 2.5 wt % solution in 2-methyl-2-propanol). The reaction mixture was heated at reflux for 17.5 h and then cooled and concentrated under reduced pressure to give a dark brown oil. This material was dissolved in THF and the resulting solution filtered through a 4 cm deep pad of TLC grade silica gel contained in a sintered glass funnel. The filtrate was concentrated under reduced pressure to give a solid which was recrystallized ($CHCl_3$) to give the title compound **10** (10.2 g, 72%) as colorless crystalline masses: mp 118–119.5 °C; ν_{max} (KBr) 3408 cm^{-1}; ^1H NMR (300 MHz) δ 3.85 (m, 2H, H2 and 3), 2.10 (m, 1H), 1.93–1.50 (complex m, 6H), 1.48 (m, 1H); ^{13}C NMR (75 MHz) (d_6-acetone) δ 67.0, 66.7, 65.6, 33.4, 27.5, 25.8, 15.2; MS *m/z* (70 eV) 198 (0.3) 196 (0.4) ($M^{\bullet+}$), 182 (0.3) 180 (1.8) 178 (2.7) [$(M - H_2O)^{\bullet+}$], 163 (2.7) 161 (6.5) [$(M - Cl^{\bullet})^+$], 145 (6.4) 143 (19.3) [$(M - Cl^{\bullet} - H_2O)^+$], 71 (100) ($C_4H_7O^+$). Anal. $C_7H_{10}Cl_2O_2$: C, 42.7; H, 5.1; Cl, 36.0. Found: C, 42.8; H, 5.2; Cl, 35.6.

(1a*R*,2*S*,3*R*,7b*S*)-1,1-Dibromo-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-2,3-diol (22). *p*-Toluenesulfonic acid (1 crystal) was added to a solution of (1*R*,2*S*)-1,2-dihydronaphthalene-1,2-diol (5.0 g, 30.4 mmol) in 2,2-dimethoxypropane/acetone (65.5 mL of a 3:1 mixture), and the reaction mixture was stirred at room temperature for 30 min and then treated with NaOH (25 mL of a 10% aqueous solution). After being stirred for a further 10 min, the reaction mixture was diluted with ethyl acetate (50 mL) and the organic layer washed with brine (3 × 30 mL). The organic extract was dried ($MgSO_4$) and then filtered and concentrated under reduced pressure to give a yellow oil. Kugelrohr distillation (200 °C/0.5 mmHg) of this material then gave (3a*R*,9b*S*)-2,2-dimethyl-3a,9b-dihydronaphtho[1,2-*d*]-1,3-dioxole (5.84 g, 95%) as a clear colorless oil: ν_{max} (NaCl) 1601 cm^{-1}; ^1H NMR (400 MHz) δ 7.42 (dm, *J* = *ca.* 7.1 Hz, 1H), 7.31 (td, *J* = 7.6 and 1.5 Hz, 1H), 7.26 (td, *J* = 7.1 and 1.7 Hz, 1H), 7.15 (dd, *J* = 7.6 and 1.5 Hz, 1H), 6.46 (d, *J* = 9.8 Hz, 1H), 5.90 (dd, *J* = 10.0 and 2.8 Hz, 1H), 5.04 (d, *J* = 6.8 Hz, 1H), 4.92 (ddd, *J* = 6.8, 3.2 and 1.5 Hz, 1H), 1.49 (d, *J* = 0.5 Hz, 3H), 1.39 (d, *J* = 0.5 Hz, 3H); ^{13}C NMR (100 MHz) δ 131.4, 130.9, 129.7, 129.0, 127.8, 127.4, 126.8, 126.6, 106.8, 73.4, 72.9, 27.1, 25.8; MS (70 eV) *m/z* 202 (9) ($M^{\bullet+}$), 187 (11) [$(M - CH_3^{\bullet})^+$], 145 (100), 144 (23) [$(M - CH_3COCH_3)^{\bullet+}$], 116 (42), 115 (36), 57 (68); $[\alpha]^{19}_D$ +232° (*c* 10.3, $CHCl_3$); $C_{13}H_{14}O_2$ requires $M^{\bullet+}$, 202.0994; found $M^{\bullet+}$, 202.0992.

Freshly prepared potassium *tert*-butoxide (9.4 mL of a 1.0 M solution in 2-methyl-2-propanol) was added dropwise over a period of 4 h to a chilled (ice–water bath) solution of (3a*R*,9b*S*)-2,2-dimethyl-3a,9b-dihydronaphtho[1,2-*d*]-1,3-dioxole (1.24 g, 6.13 mmol) and bromoform (1.56 g, 0.54 mL, 6.13 mmol) in 2-methyl-2-propanol (3 mL). The resulting mixture was stirred at room temperature overnight and then quenched with water (20 mL). Hexane (20 mL) was added to the reaction mixture, and the phases were then separated. The aqueous phase was extracted with hexane (2 × 20 mL), and the combined organic extracts were washed with water (1 × 20 mL) before being dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a yellow oil. Subjection of this material to MPLC (silica gel, CH_2Cl_2 elution) gave, after concentration of the appropriate fractions (R_f 0.6), the acetonide of (1a*R*,2*S*,3*R*,7b*S*)-1,1-dibromo-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[a]naphthalene-2,3-diol (440mg, 52% at 37%

(7) Banwell, M. G. *Aust. J. Chem.* **1991**, *44*, 1.

(8) Byproduct **3** from the title reactions can be readily reoxidized to **2**, and a modification of the procedure reported by Bobbit and Ma[4] is provided at the end of the Experimental Section.

(9) Banwell, M. G.; Corbett, M.; Mackay, M. F.; Richards, S. L. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1329.

(10) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

(11) Banwell, M. G.; Halton, B. *Aust. J. Chem.* **1979**, *32*, 849.

conversion[12]) as a white crystalline solid: mp 91–92.5 °C; ν_{max} (KBr) 3024, 2981 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.35 (m, 2H), 7.26 (m, 2H), 4.93 (d, J = 6.1 Hz, 1H), 4.64 (broadened d, J = 6.1 Hz, 1H), 2.99 (d, J = 10.0 Hz, 1H), 2.49 (dd, J = 10.0 and 1.5 Hz, 1H), 1.39 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (100 MHz) δ 132.5, 130.7, 130.0, 129.4, 128.3, 128.1, 109.5, 73.2, 71.2, 32.7, 32.4, 31.8, 27.6, 26.1; MS (70 eV) m/z 361 (0.5) 359 (1) 357 (0.5) [(M − CH_3•)$^+$], 318 (9) 316 (18) 314 (9) [(M − CH_3-$COCH_3$)•$^+$], 237 (7) 235 (8) [(M − CH_3COCH_3 − Br•)$^+$], 209 (18) 207 (19), 128 (100); [α]$^{21}_D$ −34.2° (*c* 10.0, $CHCl_3$). Anal. Calcd for $C_{14}H_{14}Br_2O_2$: C, 45.0; H, 3.8; Br, 42.7. Found: C, 44.9; H, 3.5; Br, 42.7.

A solution of the acetonide of (1a*R*,2*S*,3*R*,7b*S*)-1,1-dibromo-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-2,3-diol (5.03 g, 13.4 mmol) in THF (100 mL) was treated with HCl (80 mL of a 3 M aqueous solution). The reaction mixture was stirred at room temperature for 24 h after which time TLC analysis showed consumption of all of the starting material. The reaction mixture was poured into water (150 mL) and extracted with ether (3 × 150 mL). The combined ethereal phases were washed with water (2 × 150 mL) and then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a yellow solid. Recrystallization ($CHCl_3$/hexane) of this material gave the title diol **22** (3.74g, 84%) as fine white needles: mp 64–66 °C; ν_{max} (KBr) 3312 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.43 (dm, J = 7.1 H, 1H), 7.38 (td, J = 7.1 and 1.5 Hz, 1H), 7.31 (td, J = 7.1 and 1.5 Hz, 1H), 7.27 (dd, J = 7.1 and 1.5 Hz, 1H), 4.53 (s, 1H), 3.82 (s, 1H), 3.68 (m, 1H), 3.24 (s, 1H), 3.04 (d, J = 10.5 Hz, 1H), 2.27 (dd, J = 10.5 and 3.9 Hz, 1H); ^{13}C NMR (100 MHz) δ 137.0, 131.4, 130.6, 129.6, 129.3, 128.3, 70.9, 70.0, 36.5, 34.1, 32.9; MS (70 eV) m/z 318 (5) 316 (10) 314 (5) [(M − H_2O)•$^+$], 237 (6) 235 (6) [(M − H_2O − Br•)$^+$], 209 (21) 207 (21) [(M − H_2O − Br• − CO)$^+$], 128 (100), 127 (21), 115 (28); [α]$^{20}_D$ −52.5° (*c* 10, $CHCl_3$). Anal. Calcd for $C_{11}H_{10}Br_2O_2$: C, 39.6; H, 3.0; Br, 47.8. Found: C, 39.8; H, 2.7; Br, 47.9.

(1*R*,2*S*,3*S*,6*S*)-4-Bromo-7,7-dichlorobicyclo[4.1.0]hept-4-ene-2,3-diol (25). A magnetically stirred solution of (3a*S*,7a*S*)-4-bromo-2,2-dimethyl-3a,7a-dihydro-1,3-benzodioxole[14] (5.3 g, 23.0 mmol) and triethylbenzylammonium chloride (60 mg, 0.26 mmol) in sodium hydroxide (4.2 mL of a 50% w/v aqueous solution) was cooled to 0 °C then treated with $CHCl_3$ (4.2 mL). The resulting mixture was stirred vigorously at 0 °C for 30 min and then at room temperature for 18 h. After this time, the reaction mixture was poured into brine (100 mL) and the aqueous phases extracted with $CHCl_3$ (4 × 100 mL). The combined organic phases were dried ($MgSO_4$) and then filtered and concentrated under reduced pressure to afford a brown oil which solidified on standing. This material was washed with cold methanol and then recrystallized (methanol) to give (3a*S*,5a*S*,6a*R*,6b*S*)-4-bromo-6,6-dichloro-2,2-dimethyl-3a,6,6a,-6b-tetrahydro-5a*H*-cyclopropa[*e*]-1,3-benzodioxole (3.25 g, 45%) as white crystalline masses: mp 107–108 °C; ν_{max} (KBr) 3039, 2984 cm^{-1}; ^{1}H NMR (400 MHz) δ 6.37 (dt, J = 7.0 and 1.0 Hz, 1H), 4.75 (dt, J = 8.0 and 1.0 Hz, 1H), 4.35 (d, J = 7.0 Hz, 1H), 2.39–2.30 (complex m, 2H), 1.44 (s, 3H), 1.41 (s, 3H); ^{13}C NMR (100 MHz) δ 125.6, 124.1, 110.2, 74.0, 70.5, 62.3, 30.0, 29.0, 27.4, 26.0; MS m/z (70 eV) 300 (2) 298 (4) 296 (2.5) [M − CH_4)•$^+$], 177 (64) 175 (100) {[M − Br• − $(CH_3)_2CO$]$^+$}; [α]$^{17}_D$ −58° (*c* 1, $CHCl_3$). Anal. Calcd for $C_{10}H_{11}BrCl_2O_2$: C, 38.3; H, 3.5; Br, 25.5; Cl, 22.6. Found: C, 38.2; H, 3.0; Br, 25.2; Cl, 22.8.

A magnetically stirred solution of (3a*S*,5a*S*,6a*R*,6b*S*)-4-bromo-6,6-dichloro-2,2-dimethyl-3a,6,6a,6b-tetrahydro-5a*H*-cyclopropa[*e*]-1,3-benzodioxole (1.96 g, 6.5 mmol) in THF (200 mL) was treated with HCl (170 mL of a 3 M aqueous solution). Two further aliquots (80 mL each) of HCl were added after 24 and 48 h. After 72 h TLC analysis (1:1 ethyl acetate/hexane elution) indicated that no starting material remained (R_f 0.5). The reaction mixture was poured into water (100 mL), and the aqueous phase was extracted with Et_2O (3 × 100 mL). The combined organic phases were washed with water (2 × 100 mL) and then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford a pale-yellow solid. Recrystallization (CH_2Cl_2) of this material gave diol **25** (1.36 g, 81%) as fine white needles: mp 140–141 °C; ν_{max} (KBr) 3328 cm^{-1}; ^{1}H NMR (300 MHz) δ 6.40 (d, J = 4.5 Hz, 1H), 4.22 (s, 2H), 2.92 (s, 1H), 2.73 (s, 1H), 2.36 (dd, J = 10.0 and 4.5 Hz, 1H), 2.15 (dd, J = 10 and 2 Hz, 1H); ^{13}C NMR (75 MHz, d_6-acetone) δ 129.4, 126.2, 72.9, 68.3, 66.5, 32.8, 32.3; MS m/z (70 eV) 241 (0.8) 239 (3) 237 (2) [(M − Cl•)$^+$], 223 (4) 221 (16) 219 (12) [(M − Cl• − H_2O)$^+$], 203 (7) 201 (7) [(M − Cl• − HCl)$^+$], 179 (11) 177 (64) 175 (100) [(M − Br• − H_2O)$^+$]. Anal. Calcd for $C_7H_7BrCl_2O_2$: C, 30.7; H, 2.6; Br, 29.2; Cl, 25.9. Found: C, 30.7; H, 2.3; Br, 29.0; Cl, 25.9.

Generalized Procedure for the Oxidation of *vic*-Diols Using Salt 1 (X = OTs). A magnetically stirred suspension of the appropriate diol (1 mmol) and *p*-toluenesulfonic acid monohydrate (950 mg, 5 mmol) in CH_2Cl_2 (5 mL) maintained at 0 °C was treated with a solution of 4-acetamido-TEMPO (**2**) (1.07 g, 5 mmol) in CH_2Cl_2 (10 mL) in a dropwise fashion over a period of 30 min. The resulting solution was stirred at 0 °C for a further 1 h before being warmed to room temperature and allowed to stir until the reaction was complete, as determined by TLC analysis (see individual entries in Table 2 for specific reaction times). Ethanol (2 mL) was then added and the mixture allowed to stir for a further 30 min. The reaction mixture was treated with water (30 mL), and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL) and then put aside for later recycling (see below). The combined organic phases were washed with brine (1 × 30 mL) and then dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the crude reaction product which was generally obtained as an orange oil and which usually contained a small amount of unreacted 4-acetamido-TEMPO. Purification of the oxidation product was carried out in various ways as described below.

(1α,6α)-7,7-Dibromobicyclo[4.1.0]hept-4-ene-2,3-dione (6). The crude product obtained from oxidation of diol **4** was filtered through a short pad of TLC grade silica (CH_2Cl_2 elution) to afford, after concentration of the filtrate, a yellow solid. Recrystallization (CCl_4) of this material gave diketone **6** as fine yellow needles, mp 120–122 °C (lit.[1] mp 119–120.5 °C). This material was identical, in all respects, with an authentic sample.

Benzil (7). The crude reaction mixture obtained from the oxidation of diol **5** was subjected to preparative TLC (silica gel, CH_2Cl_2 elution) and afforded a single major and chromophoric band (R_f 0.9) which on extraction (CH_2Cl_2) gave benzil (**7**) as yellow/green needles, mp 95–96 °C (lit.[15] mp 95 °C). This material was identical, in all respects, with an authentic sample of benzil.

(1α,6α,7β)-7-Bromobicyclo[4.1.0]hept-4-ene-2,3-dione (9). The crude product obtained from oxidation of diol **8** was filtered through a short pad of TLC grade silica gel (CH_2Cl_2 elution) to afford, after concentration of the filtrate, diketone **9** as a bright-yellow crystalline solid, mp 74–76 °C (lit.[2a] mp 76–78 °C). This material was identical, in all respects, with an authentic sample.[2a]

(1α,6α)-7,7-Dichloro-3-hydroxybicyclo[4.1.0]hept-3-en-2-one (11). The crude reaction mixture obtained from the oxidation of diol **10** was filtered through a short pad of TLC grade silica gel (CH_2Cl_2 elution) to afford, after concentration of the filtrate, the title α-hydroxy enone **11** as a colorless crystalline solid. Recrystallization (CH_2Cl_2/hexane) of a portion of this material afforded an analytically pure sample of compound **11**: mp 115–116 °C (sealed tube); ν_{max} (KBr) 3417, 1646 cm^{-1}; λ_{max} ($CHCl_3$) 282 (log ε 3.68), 239 (3.33) nm; ^{1}H NMR (300 MHz) δ 5.91 (s, 1H), 5.86 (t, J = 4.4 Hz, 1H), 2.97

(12) Higher yields (70% at 100% conversion) of this product can be obtained when dibromocarbene is generated under phase transfer conditions (Makosa conditions[13]) but the material obtained is of poorer quality than that produced by the cited procedure.

(13) Banwell, M. G.; Reum, M. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press: Greenwich, CT, 1991; Vol. 1, p 19.

(14) Mahon, M. F.; Molloy, K.; Pittol, C. A.; Pryce, R. J.; Roberts, S. M.; Ryback, G.; Sik, V.; Williams, J. O.; Winders, J. A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1255.

(15) *The Dictionary of Organic Compounds*, 5th ed.; Chapman and Hall: New York, 1982; p B00241.

(ddd, J = 21.3, 9.0 and 4.4 Hz, 1H), 2.85 (ddd, J = 21.3, 4.4 and 1.5 Hz, 1H), 2.74 (dd, J = 9.0 and 1.5 Hz, 1H), 2.42 (broadened t, J = 9.0 Hz, 1H); ^{13}C NMR (75 MHz) δ 184.6, 145.9, 115.3, 59.9, 36.8, 31.5, 20.8; MS (70 eV) m/z 196 (2) 194 (12) 192 (19) ($M^{\bullet+}$), 159 (33) 157 (100) ([M − Cl$^{\bullet}$]$^+$), 131 (13) 129 (41) ([M − Cl$^{\bullet}$ − CO]$^+$). Anal. Calcd for $C_7H_6Cl_2O_2$: C, 43.6; H, 3.1; Cl, 36.7. Found: C, 43.3; H, 3.1; Cl, 37.0.

(1α,4α,5α,6α)-7,7-Dibromo-4,5-dimethoxybicyclo[4.1.0]-heptane-2,3-dione (13) and (1′α,5′α,6′α)-7′,7′-Dibromo-4′,5′-dimethoxy-2′-oxobicyclo[4.1.0]hept-3′-en-3′-yl Ethanoate (14). The crude product obtained from the oxidation of diol **12** was filtered through a 3 cm deep pad of TLC grade silica gel (1:9 Et_2O/CH_2Cl_2 elution), and the filtrate was concentrated under reduced pressure to give a yellow oil. This material was dissolved in CH_2Cl_2 (10 mL) and the resulting solution cooled to 0 °C and then treated with acetic anhydride (82 μL, 0.58 mmol, 2 equiv with respect to **12**) and pyridine (47 μL, 0.58 mmol, 2 equiv with respect to **12**). The reaction mixture was allowed to warm to room temperature and then stand for 16 h before being concentrated under reduced pressure. The residue was subjected to preparative TLC (silica gel, 1:9 Et_2O/CH_2Cl_2 elution), and two chromophoric bands, A and B (R_f 0.6 and 0.8, respectively), were thereby obtained.

Extraction (Et_2O) of band A afforded diketone **13**[9] which was identical, in all respects, with an authentic sample.

Extraction (Et_2O) of band B afforded a solid which was recrystallized ($CHCl_3$/hexane) to give enol acetate **14** as colorless plates, mp 120−122 °C (lit.[9] mp 120−122 °C). This material was identical, in all respects, with an authentic sample.

Cycloctane-1,2-dione (16). The crude reaction product obtained from the oxidation of either diol **15** or **17** was filtered through a short pad of TLC grade silica (CH_2Cl_2 elution) to afford, after concentration of the filtrate, dione **16** as a volatile yellow oil. This material was identical, in all respects, with an authentic sample.[1] A sample of diketone **16** obtained by the above procedure was converted into the corresponding quinoxaline derivative (acetic acid, *o*-diaminobenzene, reflux, *ca.* 45 min), mp 123−124 °C (lit.[16] mp 120.2−120.7 °C).

(1α,6α)-7,7-Dichlorobicyclo[4.1.0]hept-4-ene-2,3-dione (19). The crude product obtained from oxidation of diol **18** was filtered through a short pad of TLC grade silica (CH_2Cl_2 elution) to afford, after concentration of the filtrate, a yellow solid. Recrystallization (CCl_4) of this material gave diketone **19** as bright-yellow crystals: mp 116−117 °C; ν_{max} (KBr) 3034, 1713, 1664, 1630 cm^{-1}; λ_{max} ($CHCl_3$) 279 (log ϵ 3.95), 250 (sh, 3.69) nm; ^{1}H NMR (400 MHz) δ 7.28 (ddd, J = 10.0, 6.0, and 1.0 Hz, 1H), 6.57 (d, J = 10.0 Hz, 1H), 3.24 (dd, J = 8.0 and 1.0 Hz, 1H), 3.14 (dd, J = 8.0 and 6.0 Hz, 1H); ^{13}C NMR (100 MHz) δ 183.1, 177.5, 143.8, 133.6, 66.1 (C7), 42.1, 36.1; MS (70 eV) m/z 192 (0.3) 190 (0.4) ($M^{\bullet+}$), 166 (3) 164 (18) 162 (27) [(M − CO)$^{\bullet+}$], 138 (2) 136 (11) 134 (17) [(M − 2 × CO)$^{\bullet+}$], 129 (13) 127 (41) [(M − CO − Cl$^{\bullet}$)$^+$], 101 (32) 99 (100) [(M − 2 × CO − Cl$^{\bullet}$)$^+$]. Anal. Calcd for $C_7H_4{}^{35}Cl_2O_2$: C, 44.0; H, 2.1; Cl, 37.1. $M^{\bullet+}$, 189.9588). Found: C, 44.0; H, 1.7; Cl, 37.3; $M^{\bullet+}$, 189.9586.

Octane-2,3-dione (21). Subjection of the crude material obtained from the oxidation of diol **20** to preparative TLC (silica gel, 1:1 CH_2Cl_2/pentane elution) afforded a single major, yellow, and chromophoric band (R_f 0.7) which upon extraction (CH_2Cl_2) gave dione **21**[1] as a volatile and bright-yellow oil: ν_{max} (NaCl)1715 cm^{-1}; ^{1}H NMR (300 MHz) δ 2.71 (t, J = 7.3 Hz, 2H), 2.32 (s, 3H), 1.57 (m, 2H), 1.28 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz) δ 199.5, 197.6, 35.6, 31.2, 23.7, 22.7, 22.3, 13.8. This material was identical, in all respects, with an authentic sample.

(1a*R*,7b*S*)-1,1-Dibromo-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene-2,3-dione (23). The crude product obtained from the oxidation of diol **22** was filtered through a 5 cm deep pad of TLC grade silica (CH_2Cl_2 elution), and after concentration of the filtrate, the title compound **23** was obtained as a yellow crystalline solid. This material was recrystallized ($CHCl_3$/hexanes) to give an analytically pure sample of dione **23** which was obtained as bright-yellow needles: mp 150−153 °C; ν_{max} (KBr) 1716, 1690 cm^{-1}; ^{1}H NMR (400 MHz) δ 8.12 (dd, J = 7.8 Hz, 1H, H4), 7.74−7.65 (complex m, 2H), 7.54 (ddd, J = 8.5, 7.1 and 1.5 Hz, 1H), 3.62 (d, J = 8.8 Hz, 1H), 3.39 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100MHz) δ 185.0, 177.3, 137.5, 135.0, 133.2, 130.5, 129.6, 129.2, 41.0, 39.0, 30.4; MS (70 eV) m/z 304 (0.3) 302 (0.6) 300 (0.3) [(M − CO)$^{\bullet+}$], 251 (1) 249 (1) [(M − Br$^{\bullet}$)$^+$], 195 (86) 193 (89) [(M − 2 × CO − Br$^{\bullet}$)$^+$], 114 (100) [(M − 2 × CO − 2 × Br$^{\bullet}$)$^{\bullet+}$]; [α]$^{19}_D$ -342° (*c* 3.95, $CHCl_3$). Anal. Calcd for $C_{11}H_6Br_2O_2$: C, 40.0; H, 1.8; Br, 48.4. Found: C, 40.1; H, 1.6; Br, 48.6.

(1α,2α,6α)-7,7-Dichloro-2-hydroxybicyclo[4.1.0]hept-4-en-3-one (24). The crude product obtained from oxidation of diol **18** [using 1.0 molar equiv of **1** (X = OTs)] was filtered through a short pad of TLC grade silica gel (CH_2Cl_2 elution) to afford, after concentration of the filtrate, the title compound **24** as a colorless and crystalline solid: mp 56−58 °C; ν_{max} (KBr) 3418, 1682 cm^{-1}; ^{1}H NMR (300 MHz) δ 6.91 (ddd, J = 10.3, 4.3 and 1.7 Hz, 1H,), 6.27 (d, J = 10.3 Hz, 1H), 4.29 (m, 1H), 3.47 (d, J = 2.0 Hz, 1H), 2.56−2.45 (complex m, 2H); ^{13}C NMR (75 MHz) δ 196.0, 142.2, 130.2, 68.5, 65.1, 36.8, 28.9; MS (CI, isobutane) m/z 197 (8) 195 (25) 193 (40) [(M + H)$^+$], 159 (42) 157 (100) [(M − Cl$^{\bullet}$)$^+$].

On standing this material was found to rearrange to 4-chloro-α-tropolone [mp 73−75 °C (lit.[17] mp 79−80 °C)], and this facile conversion meant that satisfactory microanalytical data could not be obtained on compound **24**.

(1*R*,3*S*,6*S*)-4-Bromo-7,7-dichloro-3-hydroxybicyclo[4.1.0]-hept-4-en-2-one (26). Oxidation of diol **25** using 1.0 molar equiv of salt **1** (X = OTs) gave an orange oil on workup. This material was filtered through a 1.5 cm deep pad of TLC grade silica (CH_2Cl_2 elution), and after concentration of the filtrate, the title compound **26** was obtained as pale-yellow crystals: mp 99−100 °C; ν_{max} (KBr) 3453, 1707 cm^{-1}; ^{1}H NMR (300 MHz) δ 6.55 (ddd, J = 5.4, 2.7, and 1.0 Hz, 1H), 4.51 (broadened s, 1H), 3.41 (d, J = 2.7 Hz, 1H), 2.99 (dd, J = 8.6 and 1.0 Hz, 1H), 2.94 (ddd, J = 8.6, 5.4, and 1.5 Hz, 1H); ^{13}C NMR (75 MHz) δ 197.5, 125.8, 124.0, 73.4 , 63.6, 39.3, 38.9; MS m/z (70 eV) 238 (14) 236 (57) 234 (43) [(M − HCl)$^{\bullet+}$], 210 (23) 208 (91) 206 (71) [(M − HCl − CO)$^{\bullet+}$], 101 (20) 99 (100) ($C_5H_4Cl^+$).

Compound **26** was found to be thermally unstable and is converted into 7-bromo-4-chloro-α-tropolone on standing. This situation has precluded the acquisition of satisfactory microanalytical data. Conditions for the deliberate conversion of compound **26** into the corresponding α-tropolone have been established. Thus, a solution of compound **26** (55 mg, 0.21 mmol) in Et_2O (20 mL) was heated at reflux for 15 min and then cooled to room temperature. The precipitated acyloin **26** (20 mg, 36% recovery) was removed by filtration. After the filtrate stood for 2 days pale-brown crystals separated, and this material was identified as 7-bromo-4-chloro-α-tropolone (22 mg, 70% at 64% conversion): mp 117−118 °C; ν_{max} (KBr) 3047, 1598, 1554 cm^{-1}; ^{1}H NMR (400 MHz) δ 7.98 (d, J = 11.2 Hz, 1H), 7.49 (d, J = 2.2 Hz, 1H), 6.98 (dd, J = 11.2 and 2.2 Hz, 1H); ^{13}C NMR (75 MHz) δ 169.8, 163.6, 145.6, 140.4, 126.9, 126.1, 121.4; MS m/z (70 eV) 236 (79) 234 (61) ($M^{\bullet+}$), 210 (25) 208 (100) 206 (78) [(M − CO)$^{\bullet+}$], 101 (20) 99 (61) ($C_5H_4Cl^+$). Anal. Calcd for $C_7H_4BrClO_2$: C, 35.7; H, 1.7; Br, 33.9; Cl, 15.9. Found: C, 35.8; H, 1.4; Br, 33.9; Cl, 15.3.

(1*R*,6*S*)-4-Bromo-7,7-dichlorobicyclo[4.1.0]hept-4-ene-2,3-dione. A magnetically stirred solution of oxalyl chloride (270 μL, 2.6 mmol) in CH_2Cl_2 was cooled to −60 °C ($CHCl_3$/liquid N_2 bath) and then treated, dropwise, with DMSO (340 μL, 4.8 mmol). The resulting mixture was stirred at −60 °C for *ca.* 20 min, and then a solution of diol **25** (262 mg, 1 mmol) dissolved in a minimum volume of 1:1 DMSO/CH_2Cl_2 was added. The reaction mixture was stirred at −60 °C for 1 h and then treated, over a period of 20 min, with triethylamine (1.4 mL). The resulting yellow solution was warmed to *ca.* −20 °C and then poured into HCl (20 mL of a 2 M aqueous solution). The aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic phases were washed with

(16) Blomquist, A. T.; Liu, L. H. *J. Am. Chem. Soc.* **1953**, *75*, 2153.

(17) Takase, K. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 1298.

water (1 × 50 mL) and then dried ($MgSO_4$) filtered, and concentrated under reduced pressure to afford a bright orange oil. This material was filtered through a 3 cm deep pad of TLC grade silica gel (CH_2Cl_2 elution), and the bright yellow band was collected and concentrated under reduced pressure to give a yellow soild. Recrystallization (CCl_4) of this solid gave the title diketone (90 mg, 35%): mp 116–117 °C; ν_{max} 3042, 1717, 1690 cm^{-1}; ^1H NMR (300 MHz) δ 7.73 (dd, J = 6.0 and 1.0 Hz, 1H), 3.32 (d, J = 8.0 and 1.0 Hz, 1H), 3.12 (dd, J = 8.0 and 6.0 Hz, 1H); ^{13}C NMR (75 MHz) δ 180.0, 172.1, 144.2, 128.1, 65.9, 42.0, 36.2; MS m/z (70 eV) 271 (0.3) 269 (0.6) 267 (0.4) $[(M - H^{\bullet})^+]$, 243 (9) 241 (19) 239 (12) $[(M - HCO^{\bullet})^+]$ 137 (11) 135 (64) 133 (100) $[(M - Br^{\bullet} - 2 \times CO)^+]$. Found: C, 31.2; H, 0.9; Br, 29.7; Cl, 26.2. Anal. Calcd for $C_7H_3BrCl_2O_2$: C, 31.2; H, 1.1; Br, 29.6; Cl, 26.3.

4-Bromo-α-tropolone (27). The crude product obtained from the oxidation of diol **4** using 1.0 equiv of **1** (X = OTs) afforded a light-yellow solid on workup. Recrystallization (cyclohexane) of this solid then gave α-tropolone **27**, mp 85–87 °C (lit.[18] mp 86–87 °C). This material was identical, in all respects, with an authentic sample.

Procedure for the Recycling of 4-Acetamido-TEMPO. Concentration of the combined aqueous phases from workup of the oxidation reactions described above gave the hydroxyamine salt **3** (X = OTs) as an off-white crystalline solid (79% recovery based on 4-acetamido-TEMPO used). A magnetically stirred solution of this salt (26.6 g, 69 mmol) and K_2CO_3 (19 g, 138 mmol) in water (325 mL) was treated with H_2O_2 (25 mL of a 30% w/v aqueous solution). The resulting yellow solution was allowed to stir vigorously at ambient temperature for 24 h, by which time a color change to orange was observed. The reaction mixture was then extracted with CH_2Cl_2 (5 × 200 mL), and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford 4-acetamido-TEMPO (**2**) (13.4 g, 91%; overall recovery 72%) as an orange powder, mp 145-147 °C (lit.[4] mp 146–147 °C).

Acknowledgment. We thank the Australian Research Council for financial support. J.R.D., S.L.R., and J.M.W. are grateful recipients of Australian Post-Graduate Research Awards. Dr. Gregg Whited (Genencor International Inc., South San Francisco) is warmly thanked for providing generous samples of (1*R*,2*S*)-1,2-dihydronaphthalene-1,2-diol and (1*R*,2*S*)-3-bromocyclohexa-3,5-diene-1,2-diol.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for compounds **24**, **26**, and (3a*R*,9b*S*)-2,2-dimethyl-3a,-9b-dihydronaphtho[1,2-*d*]-1,3-dioxole (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(18) Banwell, M. G.; Onrust, R. *Tetrahedron Lett.* **1985**, *26*, 4543.