J. Org. Chem. 1990, 55, 389-391

The Reaction between 7-Oxanorbornadienes and Tetraarylcyclopentadienones: A Short Synthesis of 1,2,3,4-Tetraarylbenzenes

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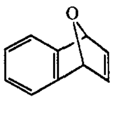
Received January 6, 1989

Highly arylated benzenes cannot generally be synthesized by sequences involving electrophilic aromatic substitution. On the other hand, cycloaddition reactions work quite well for the synthesis of such systems. One of the best-known examples of this strategy is the condensation between furan and benzyne to afford adduct 1, which then undergoes conversion to 1-naphthol upon treatment with acid.[1] A large number of variants upon this process have been reported; notable recent examples involve the use of bisarynes,[2] bisisobenzofurans,[3] and bisendooxides[2a,4] such as 2 and 3, or higher arynes such as naphthalyne[5] to construct more complex ring systems. Another type of cycloaddition, which has proved useful for the synthesis of highly arylated arenes, involves thermal condensation of tetraphenylcyclopentadienone (tetracyclone, 4a) with suitable alkynes[6] or arynes[7] to afford 1,2,3,4-tetraarylbenzenes (5) and 1,2,3,4-tetraarylnaphthalenes (6), respectively. A variety of methods are therefore available for the synthesis of highly substituted arenes. Some of them, however, are relatively limited in scope or involve intermediates requiring lengthy syntheses. In 1965 Fieser and Hadaddin reported a reaction which we found quite intriguing in this connection.[8] They found that heating a 2:1 mixture of 1 and 4a in refluxing diglyme (162 °C) leads to the formation of a mixture of 1,2,3,4-tetraphenylbenzene (7a) and the polycyclic substance 8 (as a mixture of stereoisomers). The reaction proceeds via a series of Diels–Alder and retro-Diels–Alder reactions, as shown in Scheme I. A few substituted analogues of 8 were prepared in like manner, and the intermediate 9 could be isolated by reaction between 1 equiv each of 1 and 4a at a lower temperature (80 °C). Fieser and Haddadin were mainly interested in proving that isobenzofuran (10) is an intermediate in this reaction, but we were intrigued by the formation of 7a in the penultimate step. An enormous number of substituted cyclopentadienones are known, usually prepared by the base-promoted double aldol reaction between a ketone and a 1,2-dione.[6] It appeared to us that the chemistry described in Scheme I could not only be made the basis of a very general route to highly substituted benzenes, but that this chemistry might be readily adaptable to the synthesis of other aromatic and heterocyclic systems as well.



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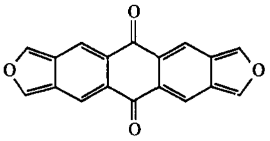

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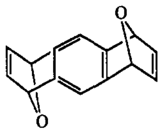

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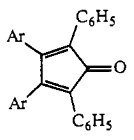
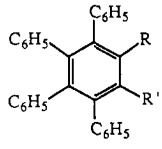


4a, Ar = C_6H_5
b, Ar = p-$MeOC_6H_4$
c, Ar = p-MeC_6H_4
d, Ar = p-$Me_2NC_6H_4$



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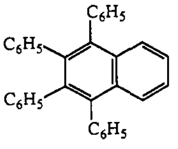

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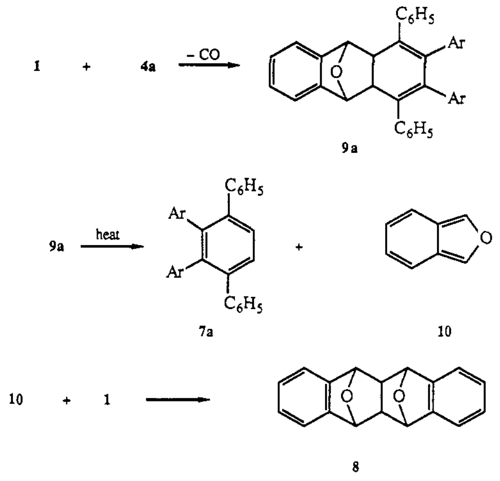
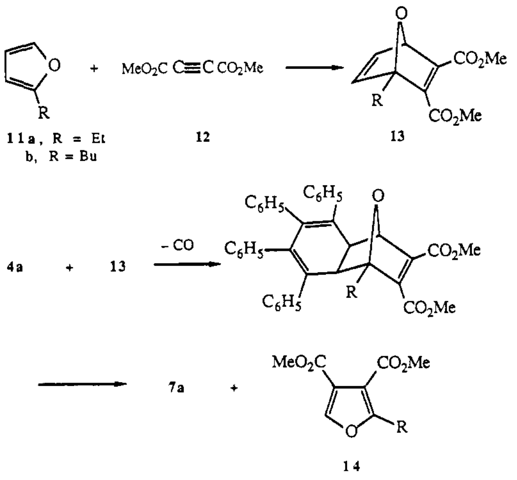
Scheme I



Scheme II



As an initial test of this conjecture, and in the interests of flexibility and convenience, we elected to replace 1 with a simpler derivative. Reaction of 2-ethylfuran (11)[9] with dimethyl acetylenedicarboxylate (12) at 90–100 °C afforded the 7-oxanorbornadiene 13a.[10] When 13a was heated with tetracyclone (4a) in diglyme under nitrogen at reflux (162 °C) for 12 h, it was converted smoothly and in good yield into a mixture of 1,2,3,4-tetraphenylbenzene (7a) and 2-ethyl-3,4-dicarbomethoxyfuran (14a). The reaction presumably proceeds as shown in Scheme II, with the initial Diels–Alder reaction occurring at the unsubstituted double bond of 13a. The substituted tetracyclones 4b–d were then synthesized by reaction between dibenzyl ketone and the

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[1] Wittig, G.; Pohmer, L. *Chem. Ber.* **1956**, *89*, 1334.

[2] (a) Luo, J.; Hart, H. *J. Org. Chem.* **1987**, *52*, 4833. (b) LeHoullier, C. S.; Gribble, G. W. *J. Org. Chem.* **1983**, *48*, 1682.

[3] Chiba, T.; Kenny, P. W.; Miller, L. L. *J. Org. Chem.* **1987**, *52*, 4327.

[4] Hart, H.; Meador, M. A.; Ward, D. L. *J. Org. Chem.* **1983**, *48*, 4357.

[5] LeHoullier, C. S.; Gribble, G. W. *J. Org. Chem.* **1983**, *48*, 2364.

[6] Ogliaruso, M. A.; Romanelli, H. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261.

[7] Campbell, C. D.; Rees, C. W. *Proc. Chem. Soc.* **1964**, 296.

[8] Fieser, L. F.; Haddadin, M. J. *Can. J. Chem.* **1965**, *43*, 1599.

[9] (a) Heid, J. V.; Levine, R. *J. Org. Chem.* **1948**, *13*, 409. (b) Fetizon, M.; Baranger, P. *Bull. Soc. Chim. Fr.* **1957**, 1311.

[10] Xing, Y. D.; Huang, N. Z. *J. Org. Chem.* **1982**, *47*, 140.

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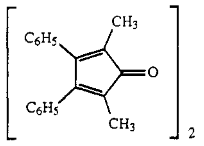
appropriate benzil. Reaction between **13a** and **4b–d** in refluxing diglyme occurred equally smoothly and afforded the substituted benzenes **7b–d** in good yields, together with furan **14a**, which is easily separated by flash chromatography.

It was found unnecessary to isolate and purify **13a** as a discrete intermediate in these reactions. Furan **11a** was heated overnight at 100 °C with **12** without solvent, and **4a** and diglyme were then added. After 18 h of reflux, the reaction had proceeded cleanly to a mixture containing only tetraphenylbenzene **7a** and the furan **14a**. The fact that the boiling point of **11a** is below the temperature required for the reaction between **13a** and **4a** prevented us from determining, without resorting to sealed tube reactions, whether **7a** could have been produced even more simply by heating a mixture of **12**, **4a**, and **11a** without preforming **13a**. However, the simple expedient of using the higher boiling 2-*n*-butylfuran (**11b**) (bp 140 °C) showed this to be possible; **7a** was formed in good yield (together with **14b**) by heating a 1:1: mixture of **12**, **4a**, and **11b** in refluxing diglyme. Somewhat different results were obtained when the 2,5-dimethyl-3,4-diphenylcyclopentadienone dimer[11] (**15**) was substituted for **4a** in these experiments. Thermolysis of a mixture of **15** and **13** (prepared in situ by the above procedure) afforded 1,4-dimethyl-2,3-diphenylbenzene (**16a**)[12] in good yield. Interestingly, heating a 1:1:0.5 mixture of **15**, **12**, and **11b** in refluxing diglyme resulted in formation primarily of 1,4-dimethyl-2,3-diphenyl-5,6-dicarbomethoxybenzene (**16b**), although thin-layer chromatography indicated the presence of a small amount of **16a**. Substance **16b** has previously been obtained by thermolysis of a mixture of **15** and **12**.[13] This demonstrates that the monomeric cyclopentadienone from thermal dissociation of **15**, even though negatively substituted as a result of bearing the carbonyl group, is still considerably more reactive than the electron-rich (but aromatic) furan.



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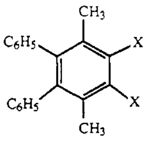

16a, X = H

b, X = CO_2CH_3

These reactions can be compared with related processes in the literature.[12] 3,6-Di(2′-pyridyl)-*s*-tetrazine reacts under mild conditions with both 7-oxanorbornadienes and norbornadienes to form furans and cyclopentadienes, respectively.[14] However, the reagent requires a lengthy synthesis, and the reaction is not adaptable to the synthesis of arenes. (The latter is also true for the reaction between oxazoles and alkynes to afford furans.[15]) Tetracyclones react with norbornadiene to afford compounds of type **7**,[12] but the 7-oxanorborbornadiene route described here has the advantage that the bicyclic dienophile need only be prepared in situ, and indeed frequently by simply heating a mixture of the three reaction components. Furthermore, the substitution pattern of the intermediate 7-oxanorborbornadiene, and hence that of the products, is readily controlled by proper choice of the initial furan and alkyne, and the reaction between 7-oxanorbornadienes and cyclopentadienones is adaptable in principle to the synthesis of a much wider range of aromatic systems. For example, since carbons 3 and 4 of the furan become carbons 5 and 6 of the final benzene, use of 3-substituted and 3,4-disubstituted furans should permit extension of the reaction to the synthesis of penta- and hexasubstituted benzenes, and the reaction should also be adaptable to the synthesis of furans substituted at the 3 and 4 positions with electronegative groups, which are otherwise difficult to obtain. We are exploring these possibilities.

Experimental Section

General Methods. NMR spectra were recorded in $CDCl_3$ on a Varian XL-400 spectrometer. Mass spectra were recorded on Hewlett-Packard Model 5988 gas chromatograph–mass spectrometer, equipped for direct solid sample insertion; the exact mass measurement on **7d** was carried out at the Yale University Instrumentation Center by fast atom bombardment. 1,2,3,4-Tetraphenylcyclopentadienone (**4a**),[16] 2-ethylfuran (**11a**),[9] and 2-butylfuran (**11b**)[17] were prepared according to literature directions.

3,4-Bis(*p*-methoxyphenyl)-2,5-diphenylcyclopentadienone (4b) was prepared according to a literature procedure.[18] The crude material, mp 214–216 °C, was suitable for further use. Flash chromatography afforded a sample of mp 222–222.5 °C (lit. mp 222–223 °C[18] and 226.8–227.2 °C[19]); ^{1}H NMR δ 3.75 (s, 6 H), 6.70 (d, 4 H), 6.84 (d, 4 H), 7.3 (s, 10 H).

3,4-Bis(*p*-methylphenyl)-2,5-diphenylcyclopentadienone (4c) was prepared according to a literature procedure.[18] The crude material, mp 215 °C, was suitable for further use. Flash chromatography afforded a sample of mp 218–219 °C (lit. mp 218–219 °C[18] and 221.8–222.6 °C[19]); ^{1}H NMR δ 2.2 (s, 6 H), 6.7 (d, 4 H), 6.9 (d, 4 H), 7.2 (s, 10 H).

3,4-Bis(*p*-(dimethylamino)phenyl)-2,5-diphenylcyclopentadienone (4d) was prepared according to a procedure provided by Dr. M. A. Ogliaruso of Virginia Polytechnic Institute.[6,20] Because the procedure is not readily available, it is repeated here. A mixture of 0.1 g (0.30 mmol) of 4,4′-bis(*p*-dimethylamino)benzil[21] [^{1}H NMR δ 3.05 (s, 12 H), 6.65 (d, 4 H), 7.85 (d, 4 H)] and 0.28 g (1.3 mmol) of dibenzyl ketone in 1 mL of 25% ethanolic potassium hydroxide was stirred magnetically for 150 h. It was then poured into 50 mL of water and extracted with a 9:1 benzene–cyclohexane mixture. The extracts were chromatographed over activated alumina, eluting with benzene. Evaporation of the eluates afforded 3,4-bis(*p*-(dimethylamino)phenyl)-2,5-diphenylcyclopentadienone (**4d**) as dark red needles, 0.105 g (68 %), mp 269–270 °C (lit.[6,20] mp 270–271 °C); ^{1}H NMR δ 2.9 (s, 12 H), 6.4 (d, 4 H), 6.75 (d, 4 H), 7.2 (br s, 10 H).

1-Ethyl-2,3-dicarbomethoxy-7-oxabicyclo[2.2.1]hepta-2,5-diene (13a). A mixture of 1.92 g (0.02 mol, 2.11 mL) of 2-ethylfuran (**11a**) and 2.84 g (0.02 mol, 2.46 mL) of dimethyl acetylenedicarboxylate (**12**) was heated under nitrogen at 100 °C for 19 h. Distillation afforded 1-ethyl-2,3-dicarbomethoxy-7-oxabicyclo[2.2.1]hepta-2,5-diene (**13a**) as a clear, viscous liquid: 3.68 g (77%); bp 104–110 °C (0.7 Torr); ^{1}H NMr δ 0.90 (t, 3 H, J = 8.0 Hz), 2.03–2.14 (m, 2 H (diastereotopic methylene protons)), 3.68 (s, 3 H), 3.75 (s, 3 H), 5.53 (d, 1 H, J = 4.0 Hz), 6.87 (d, 1 H, J = 5.6 Hz), 7.07 (dd, 1 H, J = 4.0 and 5.6 Hz). Anal. Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.11; H, 5.66.

1,2,3,4-Tetraphenylbenzene (7a) by the Reaction between 4a and 13a. A 0.570-g (2.4-mmol) sample of **13a** and 0.770 g (2.2 mmol) of **4a** were heated under nitrogen in diglyme at reflux for 2 days. The mixture was then poured into 125 mL of water. The

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[11] Fuchs, B.; Pasternak, M. *Chem. Commun.* **1977**, 537.

[12] Mackenzie, K. *J. Chem. Soc.* **1960**, 473.

[13] Allen, C. F. H.; Van Allan, J. *J. Am. Chem. Soc.* **1942**, *64*, 1260.

[14] Wilson, W. S.; Warrener, R. N. *Chem. Commun.* **1972**, 211.

[15] Lakhan, R.; Ternai, B. *Adv. Heterocycl. Chem.* **1974**, *17*, 99.

[16] Fieser, L. F.; Williamson, K. L. *Organic Experiments*, 6th ed.; Heath: Lexington, MA, 1987; p 348.

[17] Potts, K. T.; Robinson, R. *J. Chem. Soc.* **1955**, 2675.

[18] Dilthey, W.; Trösken, O.; Plum, K.; Schommer, W. *J. Prakt. Chem.* **1934**, *141*, 331.

[19] Coan, S. B.; Trucker, D. E.; Becker, E. I. *J. Am. Chem. Soc.* **1955**, *77*, 60.

[20] Ogliaruso, M. A., B. S. thesis, Polytechnic Institute of Brooklyn, 1960.

[21] Tüzün, C.; Ogliaruso, M. A.; Becker, E. I. *Organic Syntheses*; Wiley: New York, 1973, Collect. Vol. V, p 111.

resulting mixture was extracted with ether, and the ether extracts were washed with water and dried over Na_2SO_4. Flash chromatography over silica gel (elution with 80% hexane–20% ethyl acetate) afforded 1,2,3,4-tetraphenylbenzene (**7a**), 0.65 g (85%), mp 188–189 °C (lit.[8] mp 190 °C); ^{1}H NMR δ 6.75 (m, 4 H), 6.9 (m, 6 H), 7.08 (m, 4 H), 7.15 (m, 6 H), 7.3 (s, 2 H).

2,3-Bis(*p*-methoxyphenyl)-1,4-diphenylbenzene (7b). A 0.518-g (2.2-mmol) portion of **13a** and 0.879 g (2.0 mmol) of **4b** were reacted as described for the previous reaction between **13a** and **4a**. 2,3-Bis(*p*-methoxyphenyl)-1,4-diphenylbenzene (**7b**) was isolated by flash chromatography as a white crystalline solid: 0.80 g (90%); mp 186–189 °C (lit.[22] mp 185–186 °C); ^{1}H NMR δ 3.7 (s, 6 H), 6.5 (d, 4 H, J = 8 Hz), 6.7 (d, 4 H, J = 8 Hz), 7.1–7.3 (m, 10 H), 7.5 (s, 2 H).

2,3-Bis(*p*-methylphenyl)-1,4-diphenylbenzene (7c). **13a** (0.583 g, 2.4 mmol) and 0.825 g (2.0 mmol) of **4c** were reacted as described for the previous reaction between **13a** and **4a**. 2,3-Bis(*p*-methylphenyl)-1,4-diphenylbenzene (**7c**) was isolated by flash chromatography as a white crystalline solid: 0.472 g (58%); mp 204–206 °C; ^{1}H NMR δ 2.1 (s, 6 H), 6.65 (d, 4 H), 6.70 (d, 4 H), 7.0–7.1 (s, 10 H), 7.4 (s, 2 H). Anal. Calcd for $C_{32}H_{26}$: C, 93.62; H, 6.38. Found: C, 93.51; H, 6.29.

2,3-Bis(*p*-(dimethylamino)phenyl)-1,4-diphenylbenzene (7d). A 0.540-g (2-mmol) sample of **13a** and 1.1371 g (2.4 mmol) of **4d** were reacted as described for the previous reaction between **13a** and **4a**. 2,3-Bis(*p*-(dimethylamino)phenyl)-1,4-diphenylbenzene (**7d**) was isolated as a light brown solid, 0.46 g (49%), mp 234–236 °C; white solid, mp 236–237 °C after recrystallization from ethanol and flash chromatography; ^{1}H NMR δ 3.0 (s, 12 H), 6.55 (d, 4 H), 6.85 (d, 4 H), 7.3–7.4 (m, 10 H), 7.7 (s, 2 H); exact mass calcd for $(C_{34}H_{32}N_2 + H^+)$ 469.2644, found 469.2646.

Reaction of 13a (without Isolation) with 4a. 2-Ethylfuran (**11a**) (0.807 g, 8.40 mmol) and **12** (0.1.19 g, 8.38 mmol) were heated overnight at 100 °C under nitrogen. At that point, 30 mL of diglyme and 1.54 g (4.01 mmol) of **4a** were added. The mixture was refluxed overnight. TLC analysis of the resulting solution demonstrated the absence of **4a** and the presence of only **7a** and **13a**.

Reaction of a 1:1:1 Mixture of 11b, 12, and 4a. A mixture of 0.919 g (7.4 mmol) of **11b**, 1.05 g (7.4 mmol) of **12**, and 2.850 g (7.4 mmol) of **4a** ws refluxed in diglyme for 42 h under nitrogen. The mixture was then diluted with an equal quantity of water and extracted with benzene. The combined benzene extracts were dried over $MgSO_4$ and then evaporated in vacuum. Filtration afforded 1,2,3,4-tetraphenylbenzene (**7a**) as a white powder, mp 178–180 °C, together with a supernatant liquid. Recrystallization afforded 2.60 g (92%) of white crystalline material, mp 194 °C (uncorr.) (lit.[18] mp 190 °C). Flash chromatography of the supernatant liquid from the initial filtration afforded 3,4-dicarbomethoxy-2-*n*-butylfuran (**14b**): 1.07 g (61%); ^{1}H NMR δ 0.95 (t, 3 H), 1.37 (m, 2 H), 1.67 (m, 2 H), 2.90 (t, 2 H), 3.83 (s, 3 H), 3.87 (s, 3 H), 7.79 (s, 1 H). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 60.31; H, 6.40.

Reaction of 13b (without Isolation) with 15. A 0.479-g (3.86-mmol) portion of 2-*n*-butylfuran (**11b**) and 0.550 g (3.87 mmol) of **12** were heated overnight at 100 °C under nitrogen. At that point, 15 mL of diglyme and 1.0 g (1.92 mmol) of **15** were added. The reaction was allowed to reflux for 20 h. The reaction mixture was worked up as described for **7a** to afford 2.15 g of crude material, from which deposited ca 0.85 g (86%) of 1,4-dimethyl-2,3-diphenylbenzene (**16a**) as off-white crystals, mp 102 °C. Flash chromatography afforded white crystals, mp 110–112 °C (lit. 109 °C[13] and 113 °C[12]); ^{1}H NMR δ 2.2 (s, 6 H), 7.07 (dd, 4 H), 7.18 (m, 2 H), 7.24 (m, 4 H), 7.32 (s, 2 H).

Reaction of a 1:1:1 Mixture of 11b, 12, and 15. A mixture consisting of 0.481 g (3.88 mmol) of **11b**, 0.549 g (3.87 mmol) of **12**, and 1.02 g (1.96 mmol) of **15** in 15 mL of diglyme was refluxed for 3 days. The reaction was worked up as usual to afford a light brown viscous liquid, which slowly deposited 1,4-dimethyl-2,3-diphenyl-5,6-dicarbomethoxybenzene (**16b**) as an off-white crystalline material: mp 120–142 °C; 0.321 g (0.86 mmol, 22%); ^{1}H NMR δ 2.06 (s, 6 H), 3.90 (s, 6 H), 6.95 (dd, 4 H), 7.1–7.25 (m, 6 H). Flash chromatography over silica gel afforded material of mp 210–212 °C (lit.[13] mp 212 °C). TLC analysis demonstrated the absence of **16a** in this material but indicated the presence of a small amount of **16a** in the supernatant liquid, in addition to more **16b**.

Acknowledgment. Financial support by the National Science Foundation in the form of Grant no. 85-02078 to A.J.F. and a grant for partial support of the 400-MHz NMR spectrometer used in this work is gratefully acknowledged. Compound **4d** was synthesized in this laboratory by Peter C. Fox according to directions kindly provided by Dr. M. A. Ogliaruso of Virginia Polytechnic Institute and State University.

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[22] Abramov, V. S.; Shapshinskaya, L. A. *Zh. Obshch. Khim.* **1952**, 22 1450.

Crystal Structure Analysis of an Osmium(VI) Bisglycolate Produced by Reaction of a Sterically Hindered Chiral Nonracemic Alkene with Osmium Tetroxide

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Received July 11, 1989

Osmium tetroxide is widely recognized to be the premier reagent for accomplishing clean syn-dihydroxylation of carbon–carbon double bonds.[2] Since introduction of the process by Criegee in 1936,[3] several mechanistic investigations of stoichiometric level reactions have appeared.[4] More recently, Sharpless and his co-workers have attempted to gain detailed insight into the course of chiral-catalyzed asymmetric variants to this serviceable reaction.[5] A detailed kinetic study by Erdik and Matteson of OsO_4-catalyzed trimethylamine *N*-oxide oxidations has also just appeared.[6] *N*-Methylmorpholine *N*-oxide (NMO) constitutes an excellent alternative oxidizing agent.[7]

When amine oxides are present, the kinetics have been construed to require operation of the mechanistic sequence depicted in Scheme I, especially when hindered alkenes (e.g., α-pinene) are involved.[5b,6] Particularly noteworthy is the need to claim intervention of the osmium(VI) bisglycolate **3**. A direct consequence of the relatively substitution-inert character of such little known esters is that the step involving the conversion of **3** to **4** is rate-determining overall.

In those circumstances where the diol components to **3** are quite bulky, oxidation at osmium should be sterically retarded. Therefore, the concentration of **3** might be ex-

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(1) Author to whom queries concerning the X-ray crystallographic analysis should be directed.

(2) Schröder, M. *Chem. Rev.* **1980**, *80*, 187.

(3) Criegee, R. *Justus Liebigs Ann. Chem.* **1936**, *533*, 75. See also Criegee, R.; Marchand, B.; Wannowius, H. *Ibid.* **1942**, *550*, 99.

(4) (a) Subbaraman, L. R.; Subbaraman, J.; Behrman, E. J. *Inorg. Chem.* **1972**, *11*, 2621. (b) Clark, R. L.; Behrman, E. J. *Ibid.* **1975**, *14*, 1425. (c) Hartman, R. F.; Rose, S. D. *J. Org. Chem.* **1981**, *46*, 4340. (d) Deetz, J. S.; Behrman, E. J. *Ibid.* **1980**, *45*, 135. (e) Casey, C. P. *J. Chem. Soc., Chem. Commun.* **1983**, 126.

(5) (a) Jacobsen, E. N.; Markó, I.; Mungall, W. S.; Schröder, G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 1968. (b) Jacobsen, E. N.; Markó, I.; France, M. B.; Svendsen, J. S.; Sharpless, K. B. *Ibid.* **1989**, *111*, 737. (c) Wai, J. S. M.; Markó, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *Ibid.* **1989**, *111*, 1123.

(6) Erdik, E.; Matteson, D. S. *J. Org. Chem.* **1989**, *54*, 2742.

(7) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.