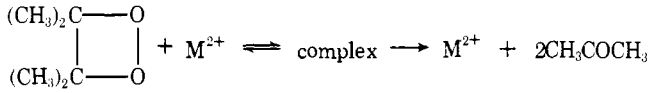
# Rearrangement of Tetramethyl-1,2-dioxetane by Boron Trifluoride in Aprotic Solvents

**P. D. Bartlett,* A. L. Baumstark, and M. E. Landis**

*Contribution from the Departments of Chemistry, Harvard University, Cambridge, Massachusetts 02138, and Texas Christian University, Fort Worth, Texas 76129.*
*Received August 26, 1976*

**Abstract:** The reaction of tetramethyl-1,2-dioxetane (TMD) in dichloromethane at −78 °C with boron trifluoride (followed by addition of methanol) produced 32–58% pinacolone, 20–28% cyclic pinacolone diperoxide, and 3–4% acetone. Iodometric titration showed 0.6–0.8 mol of active peroxide (exclusive of the cyclic diperoxide) per mole of pinacolone produced. The results are consistent with the initial rearrangement of TMD to pinacolone oxide, which is partly dimerized and partly hydrolyzed by water present in the system.

1,2-Dioxetanes decompose thermally to two carbonyl fragments, one of which may be produced in an excited state.[1] The thermal decomposition of tetramethyl-1,2-dioxetane (TMD, **1**) is sensitive to catalytic decomposition by trace im-



**1**

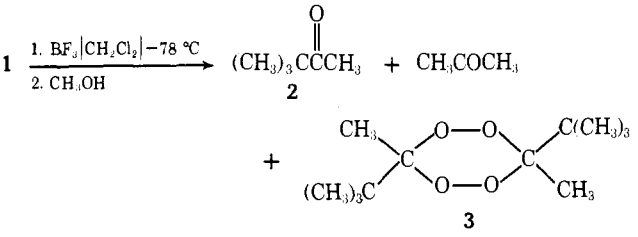
purities in solvents, probably transition metal ions, by a nonluminescent pathway.[2] Such catalysis by a series of metal dichlorides was observed[3] to be proportional to the Lewis acidity of the metal cation, measured independently toward a bidentate ligand. In the case of divalent metal ions such coordination could involve either one or two coordination sites, in the latter case with coordinate bonding to both oxygen atoms or even, in some cases, oxidative addition or reversible insertion of the metal between the two oxygen atoms. Since boron trifluoride in aprotic solvents is a strong Lewis acid with only a single site for coordination, we investigated its reaction with tetramethyl-1,2-dioxetane, with results quite different from those of the divalent metal ions.

## Results

Treatment of tetramethyl-1,2-dioxetane in carbon tetrachloride[4] (or other aprotic solvents) at room temperature with gaseous boron trifluoride for a few seconds resulted in rapid consumption of the dioxetane. The reaction mixture was quenched with $D_2O$ to allow NMR analysis. The major product was identified as pinacolone on the basis of its VPC retention time and its NMR (in $CCl_4$, *tert*-butyl, $\delta$ 1.17; methyl, 2.09) and IR spectra (in $CCl_4$, 2969 (m), 1700 (s), 1450 (w), 1355 (m), 1342 (m), 1190 (m), 1128 (s), 945 (w) $cm^{-1}$); variable amounts of acetone were also observed. Product loss (presumably to the $D_2O$ layer) was generally observed when the reaction was carried out at room temperature.

No molecular oxygen was evolved during the course of the conversion of TMD to pinacolone.[5] However, iodometric titration of the reaction mixture (carried out at room temperature) after complete conversion of the dioxetane indicated the presence of a small amount of peroxide (up to 10% based on dioxetane).

Product loss was minimized by carrying out the reaction at lower temperatures. Treatment of TMD in dichloromethane at −78 °C with boron trifluoride resulted in slow consumption of the dioxetane. After 30 min, methanol was added to quench the reaction. Under these conditions, total recovery of material was 68–88%, of which 4–7% was recovered TMD, 32–58% pinacolone, 20–28% cyclic pinacolone diperoxide, and 3–4%



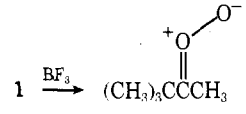
**2** **3**

acetone. Pinacolone diperoxide was isolated from the reaction mixture in 10% yield and identified by comparison of IR (in $CCl_4$, 3030 (s), 1485 (m), 1470 (w), 1460 (w), 1405 (m), 1380 (m), 1170 (m), 1120 (s), 1015 (w), 920 (m), 730 (s) $cm^{-1}$) and NMR spectra (in $CCl_4$, *tert*-butyl, $\delta$ 0.97; methyl, 1.66) with those of an authentic sample.

Iodometric titration of the reaction mixture (under conditions of high conversion of TMD to products) indicated the presence of active peroxide in substantial excess of recovered TMD (pinacolone diperoxide does not liberate iodine under the conditions). Table I shows the results of these experiments. Total product recovery was high enough (68–88%) to indicate that the active peroxide was not part of an unidentified organic species. Thus, this peroxide is presumably hydrogen peroxide and is titrated in 58–85% of the yield of pinacolone.

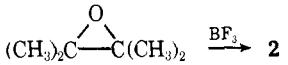
## Discussion

The formation of pinacolone from TMD represents a rearrangement of the carbon skeleton as well as a monodeoxygenation of the dioxetane. A reasonable first step in this transformation involves the initial coordination of $BF_3$ with TMD, followed by rearrangement of the complex to pinacolone oxide (**4**).[6] 2,3-Epoxy-2,3-dimethylbutane (**5**) is rearranged analo-



**4**

gously to pinacolone by the action of boron trifluoride in carbon tetrachloride. It has been reported that the ozonolysis of 2,3,3-trimethyl-1-butene[7] generated formaldehyde and pinacolone oxide, which subsequently dimerized to the dimeric



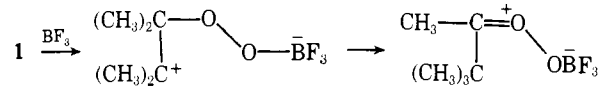
peroxide or rearranged to *tert*-butyl acetate. The latter compound is not stable under the conditions of these experiments.

Pinacolone formation can be accounted for by competitive hydrolysis of the intermediate carbonyl oxide by adventitious water. Formation of 0.55–0.85 equiv of hydrogen peroxide per

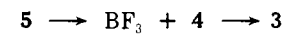
Table I. Products and Peroxide Titre for the TMD–Boron Trifluoride Reaction at −78 °C (millimoles)

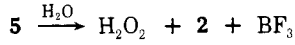
| Initial 1 | 1 recovered | 2 | 3 | Acetone | Total recovery | $P$ = titratable peroxide | $P - (1)$ = "$H_2O_2$" |
|---|---|---|---|---|---|---|---|
| 0.1146 | 0.0046 | 0.0367 | 0.0321 | 0.0046 | 0.0780 | 0.025 | 0.0204 |
| 0.0716 | 0.005 | 0.0394 | 0.0165 | 0.00215 | 0.0631 | 0.030 | 0.025 |
| 0.063 | 0.004 | 0.0365 | 0.0126 | 0.00189 | 0.0550 | 0.035 | 0.031 |

equivalent of pinacolone[8] indicates such a competitive hydrolytic process.

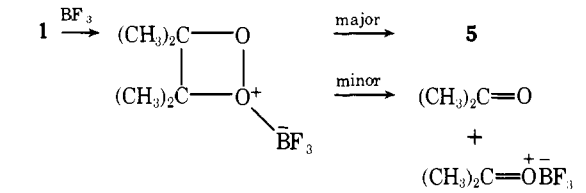


**5**

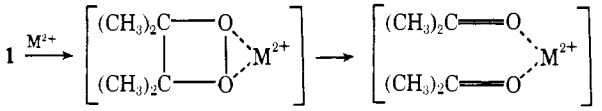




Concomitant with rearrangement of TMD is ring cleavage to acetone. Although acetone formation might be catalyzed by impurities[2,3] in boron trifluoride or in the solvents, it is also conceivable that acetone arises from a slower, competitive fragmentation of the initial monooxygen complex of TMD with the Lewis acid.



In conclusion, monooxygen coordination on TMD (by boron trifluoride) results predominantly in rearrangement rather than ring fragmentation. The decomposition of TMD catalyzed by transition metal salts,[2,3] however, produces no rearranged product. An attractive explanation for this difference in reaction mode is that complexation of TMD by transition



metal ions involves coordination at both oxygen atoms. Thus, it appears that one-oxygen coordination leads predominantly to rearrangement, whereas two-oxygen coordination catalyzes ring fragmentation.

## Experimental Section

**General.** $^1H$ NMR spectra were recorded on Varian T-60 and Varian HA-100 spectrometers. Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrometer. VPC analyses were performed on Varian Aerographs, Model A-700 or 90-P.

All solvents and compounds were of reagent grade. Carbon tetrachloride (Allied Chemicals) and dichloromethane (Eastman Organic Chemicals) were stored over molecular sieves type 4A (Fisher) until used. Sodium thiosulfate solutions were standardized by titration against iodine.

**Preparation of Tetramethyl-1,2-dioxetane (TMD).**[1a,9] Fresh silver acetate (1.7 g, 7.0 mmol) was added to 0.98 g (5.0 mmol) of freshly prepared 2-bromo-3-hydroperoxy-2,3-dimethylbutane[10] dissolved in 5 mL of anhydrous ether (Mallinckrodt). The heterogeneous solution was stirred at room temperature (in the dark) for 45 min. Silver bromide was filtered from the solution and washed with several 1-mL portions of pentane. The combined washings and the filtrate were washed with six separate 2-mL portions of 1.0 N NaOH and finally with 2 mL of water. The organic portion was dried over $MgSO_4$ and diluted to ca. 10 mL with pentane. The solution was filtered and cooled to −78 °C for 2 h, during which time yellow needles precipitated. The product was rapidly filtered while cold to yield 57 mg (10%) of TMD. The NMR spectrum displayed a sharp singlet at $\delta$ 1.45 in $CCl_4$ and 1.20 in benzene.

**Preparation of Pinacolone Diperoxide.**[11] Pinacolone (MCB, 50 g, 0.50 mol) was dissolved in 196 g of 70% $H_2SO_4$ (1.4 mol) and cooled to 4 °C. 30% $H_2O_2$ (72 g, FMC, 0.64 mol) was added to the solution (well stirred) over a 20-min period. The solution was stirred at 4 °C for an additional 1 h. The precipitate was filtered, washed with water, and recrystallized from benzene–ethanol (1:20), to yield 2.5 g of pinacolone diperoxide, mp 122.5–123.5 °C (lit. values: 121,[7] 123–124 °C[11]). The NMR spectrum ($CCl_4$) showed a singlet at $\delta$ 1.02 (9 H) and a singlet at $\delta$ 1.66 (3 H) in agreement with the reported spectrum.[12] The IR spectrum (KBr) showed absorptions at 2960 (w), 1480 (w), 1460 (w), 1441 (w), 1390 (w), 1378 (w), 1155 (w), 1120 (w), 1018 (w), 940 (vw), 905 (m), and 816 (w) $cm^{-1}$.

**Reaction of Tetramethyl-1,2-dioxetane with Boron Trifluoride at Room Temperature.** Tetramethyl-1,2-dioxetane (5.4 mg, 0.046 mmol) was dissolved in 0.4 mL of carbon tetrachloride in an NMR tube. Gaseous boron trifluoride (Matheson Gas) was bubbled through the solution (via a glass capillary tube) for ca. 3 s. The NMR spectrum of the dioxetane solution after treatment with boron trifluoride displayed three singlets: $\delta$ 1.20, 2.25, and 2.37 in the ratio of 3:1:1. The products were boron trifluoride complexes with acetone and pinacolone. The relative positions of these absorptions were dependent on the amount of added Lewis acid; for example, in another experiment with less dioxetane, the NMR signals for complexed pinacolone were observed at $\delta$ 1.37 (9 H) and 2.70 (3 H). After 5 min, 0.2 mL of $D_2O$ (Bio-Rad) was added to the reaction mixture; two products, pinacolone (*tert*-butyl, $\delta$ 1.17; methyl, 2.09) and acetone ($\delta$ 2.10) were observed in the NMR spectrum of the reaction mixture. The relative product composition, 80% pinacolone and 20% acetone, was determined by integration of product absorptions and represents the percentage of dioxetane that was converted to each product. Acetone yields were variable, attributable in part to its slow extraction into the $D_2O$ layer.

The carbon tetrachloride layer was separated from the $D_2O$ layer and was dried over a small amount of magnesium sulfate. VPC analysis (4 m × 6 mm 20% Carbowax 20 M on Chromosorb W, injection port 150 °C, column 75 °C, detector 190 °C, flow rate 55 ml/min) of the carbon tetrachloride solution indicated that the major product was pinacolone (retention time, 14 min) and that the minor product was acetone (retention time of 6.5 min). A trace amount of another product with the retention time of 1.4 min was also detected. Authentic *tert*-butyl acetate decomposed on the column to give a peak with the retention time of 1.4 min; thus, it is possible that a trace amount of *tert*-butyl acetate was also present in the reaction mixture. The infrared spectrum of the carbon tetrachloride solution (0.1 mm cell vs. $CCl_4$): 2969 (m), 1700 (s), 1450 (w), 1355 (m), 1342 (m), 1190 (m), 1128 (s), and 945 (w) $cm^{-1}$ was nearly identical with that of authentic pinacolone (Eastman Organic Chemicals).

In a typical experiment, 2.6 $\mu$L of dichloromethane was added to TMD (1.0 mg, 0.0086 mmol) in 0.4 mL of carbon tetrachloride. The NMR spectrum of the solution was recorded and the ratio of dichloromethane to TMD was determined. The solution was treated with boron trifluoride as previously described. The NMR spectrum of the reaction mixture after addition of $D_2O$ indicated a 78% recovery of material: 69% pinacolone and 9% acetone. The yield of pinacolone was increased to 83% if the reaction was carried out with a layer of $D_2O$ present before the addition of boron trifluoride.

**Isolation and Characterization of Pinacolone Diperoxide in the Low Temperature Reaction of Tetramethyl-1,2-dioxetane with Boron Trifluoride.** Ten separate small scale reactions of TMD with boron trifluoride at −78 °C in dichloromethane were carried out as follows:

TMD (12.3 mg, 0.106 mmol) was dissolved in dichloromethane (0.5

mL) with 0.1 mL of chloroform added as internal standard in an NMR tube. The NMR spectrum of the solution was recorded and the ratio of TMD to chloroform was determined. The mixture was cooled to −78 °C and gaseous boron trifluoride was bubbled through the solution for 10 s. The reaction mixture was allowed to stand at −78 °C for 30 min, and 50 μL of methanol was then added to dissociate complexes. The solution was allowed to warm quickly to room temperature, and the yields of products (average of ten experiments) were determined by integrations of product absorptions relative to that for internal standard ($CHCl_3$) in the ambient temperature NMR spectrum of the reaction mixture. Thus the product yields directly reflect the percentage of dioxetane that was converted to each product. Total recovery of material was 90%, of which 27% was recovered TMD. The remaining 63% of the material consisted of 70% pinacolone, 25% cyclic pinacolone diperoxide, and 5% acetone.

The combined reaction mixtures were washed with saturated aqueous sodium bicarbonate and dried over magnesium sulfate. Solvent and volatile products were removed at reduced pressure, yielding light yellow crystals. Recrystallization from ethanol (at −78 °C) gave 9 mg (10% based on TMD consumed) of white crystals of pinacolone diperoxide, mp 121.5–122.5 °C (mixed mp with an authentic sample). The IR spectrum (0.1 mm cell vs. $CCl_4$) 3030 (s), 1485 (m), 1470 (w), 1460 (w), 1405 (m), 1380 (m), 1170 (m), 1120 (s), 1015 (w), 920 (m), 730 (s) $cm^{-1}$; and the NMR spectrum ($CCl_4$) singlet at δ 0.97 (9 H) and singlet at 1.66 (3 H) were in agreement with those of an authentic sample.

**Determination of the Total Peroxide Content in the Low Temperature Reaction of TMD with Boron Trifluoride.** TMD (8.3 mg, 0.0716 mmol, purified by sublimation) was dissolved in 0.4 mL of dichloromethane and 0.1 mL of chloroform (internal standard). The NMR spectrum of the solution was recorded; the sample (in an NMR tube) was cooled to −78 °C and gaseous boron trifluoride was bubbled rapidly through the cold solution for 10 s. The NMR tube was then tightly capped and allowed to stand at −78 °C for 20–30 min. Methanol (45 μL) was added to the cold reaction mixture, and the resulting solution was allowed to warm quickly to room temperature (~5 min). The NMR spectrum of the reaction mixture was recorded and product composition was determined by integrations of product absorptions relative to that for chloroform (internal standard). Total peroxide content in the reaction mixture was determined by iodometric titration as described below.

Glacial acetic acid (5 mL) was added to 0.5 mL of saturated aqueous potassium iodide solution in an Erlenmeyer flask. Several lumps of dry ice were added to sweep out the air and the flask was loosely stoppered. The TMD–$BF_3$ reaction mixture was added to the acetic acid–KI solution, and the resulting solution was allowed to stand at room temperature for 15 min. The liberated $I_2$ was then titrated with 0.137 M $Na_2S_2O_3$. Under these conditions pinacolone diperoxide does *not* liberate iodine.

The results of this experiment and two others are shown in Table I.

**Acknowledgment.** This work was supported by the National Science Foundation and the National Institutes of Health at Harvard University and Texas Christian University, and by the Robert A. Welch Foundation at Texas Christian University.

## References and Notes

(1) (a) K. R. Kopecky, J. E. Filby, C. Mimford, P. A. Lockwood, and J. Y. Ding, *Can. J. Chem.*, **53**, 1104 (1975); (b) E. H. White, P. D. Wildes, J. Weicko, H. Doshan, and C. C. Wei, *J. Am. Chem. Soc.*, **95**, 7050 (1973); (c) N. J. Turro, P. Lechtken, N. E. Schore, G. Schuster, H. C. Steinmetzer, and A. Yekta, *Acc. Chem. Res.*, **7**, 97 (1974); (d) W. H. Richardson, F. C. Montgomery, M. B. Yelvington, and H. E. O'Neal, *J. Am. Chem. Soc.*, **96**, 7525 (1974); (e) W. Adam, G. A. Simpson, and F. Yany, *Tetrahedron Lett.*, 1757 (1971); (f) T. R. Darling and C. S. Foote, *J. Am. Chem. Soc.*, **96**, 1625 (1974); (g) T. Wilson and A. P. Schaap, *ibid.*, **93**, 4126 (1971); (h) H. E. Zimmerman and G. E. Keck, *ibid.*, **97**, 3257 (1975); (i) T. Wilson, D. E. Golan, M. S. Harris, and A. L. Baumstark, *ibid.*, **97**, 1086 (1975).
(2) T. Wilson, M. E. Landis, A L. Baumstark, and P. D. Bartlett, *J. Am. Chem. Soc.*, **95**, 4765 (1973).
(3) P. D. Bartlett, . L. Baumstark, and M. E. Landis, *J. Am. Chem. Soc.*, **96**, 5557 (1974).
(4) Treatment of TMD in methanol-$d_4$ with gaseous boron trifluoride resulted in the slow decomposition (complete conversion in 2 h) of the dioxetane to acetone. No additional products were observed (by NMR and VPC analyses).
(5) A. L. Baumstark, Ph.D. Thesis, Harvard University, 1974.
(6) For example, di-*tert*-butyl peroxide in the presence of $BF_3$ was found to produce the *tert*-butyl cation which was trapped by solvent. See D. Swern, Ed. "Organic Peroxides", Vol. III, Wiley, New York, N.Y., 1972, pp 21–23, and references cited therein.
(7) (a) R. Criegee, A. Kerekow, and H. Zinke, *Chem. Ber.*, **88**, 1878 (1955). (b) Carbonyl oxides in ozonolysis are trapped by methanol and by aldehydes. Such solvent trapping fails in the present case because oxygen-containing solvents bind the $BF_3$ and greatly reduce its rearranging action on **1**.[4]
(8) Mixtures of $BF_3$ and hydrogen peroxide are strong oxidizing reagents, capable of oxidizing aliphatic ketones to esters; see J. D. McClure and P. H. Williams, *J. Org. Chem.*, **27**, 24 (1962). Analogous reactions may be the source of product loss in the room temperature reactions of TMD with $BF_3$.
(9) K. R. Kopecky, J. H. van de Sande, and C. Mumford, Abstracts, 162nd National Meeting of the American Chemical Society, Washington, D.C., September 12–17, 1971, No. PETR-027.
(10) K. R. Kopecky, J. H. van de Sande, and C. Mumford, *Can. J. Chem.*, **46**, 25 (1968).
(11) (a) Monsanto Chemical Co. (H. A. Walter), U.S. Patent 2 591 645 (1952); (b) *Chem. Abstr.*, **47**, 3158 (1953).
(12) Y. Samitov, A. V. Aganov, A. I. Schreibert, and A. V. Sukharev, *Dokl. Akad. Nauk. SSSR*, **180**, 1122 (1968).

# Relative Energies of Diprotonation of Small Neutral Molecules

**Peter A. Kollman* and George L. Kenyon***

*Contribution from the Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California 94143.* *Received August 24, 1976*

**Abstract:** The proton affinities of a group of cations have been determined by ab initio molecular orbital calculations. For both first and second row bases, the proton affinity for diprotonation on the same atom is found to be negative; for diprotonation on neighboring atoms, the proton affinity is sufficiently large (and positive) to allow possible experimental determination in the gas phase. A simple electrostatic theory for estimating the difference between first and second proton affinities is surprisingly accurate when the results of such calculations are compared with the results of the ab initio calculations.

We have been intrigued by the fact that the cyclization of creatine (*N*-methylguanidinoacetic acid) to form creatinine (1-methyl-2-amino-2-imidazolin-4-one) occurs under very strongly acidic conditions (~9 N HCl),[1] an effective acidity far removed from the $pK_a$ of creatine's guanidinium group (~13).[2] One possibility is that the small amount of free guanidine base present in this highly acidic medium behaves as the nucleophile in the formation of the new C–N bond. Another