2-Chloromethyl-5-hydroxy-4-pyrone (3), mp 165–166 °C (lit.[30] mp 166–167 °C).

2-Hydroxymethyl-5-methoxy-4-pyrone (5), mp 119–120 °C (lit.[31] mp 119–121 °C).

2-Acetoxymethyl-5-acetoxy-4-pyrone (6). This material was prepared by acetylation of kojic acid, mp 100–102 °C (lit.[32] mp 102 °C).

Comenic Acid (7). This compound was prepared by catalytic oxidation of kojic acid, mp 220 °C dec (lit.[33] mp not specified).

Hydroxymaltol (2-hydroxymethyl-3-hydroxy-4-pyrone) (9), mp 149–151 °C (lit.[34] mp 152–153 °C).

Acknowledgment. Partial funds for the purchase of the Varian XL-100 NMR instrument were provided by NSF Grant GP-10293, which is gratefully acknowledged.

References and Notes

(1) T. Kotani, I. Ichimoto, and C. Tatsumi, *Hakko Kogaku Zasshi,* **51,** 66 (1973).
(2) M. J. Cook, A. R. Katritzky, and P. Linda, *Adv. Heterocycl. Chem.,* **17,** 256 (1974).
(3) (a) R. F. M. White and H. Williams, "Physical Methods in Heterocyclic Chemistry", Vol. IV, A. R. Katritzky, Ed., Academic Press, New York, N.Y., 1971, pp 228–232; (b) V. Herault and J. Gayoso, *C. R. Acad. Sci., Ser. C,* **269,** 298 (1969); (c) M. J. Cook, A. R. Katritzky, P. Linda, and R. Tack, *Chem. Commun.,* 510 (1970).
(4) F. Feist and E. Baum, *Ber.,* **38,** 3562 (1905).
(5) (a) J. Hirsch, *J. Heterocycl. Chem.,* **12,** 785 (1975); (b) M. A.-F. Elkashef and M. H. Nosseir, *J. Am. Chem. Soc.,* **82,** 4344 (1960). In other work on 4-pyrones, the ketonic oxygen is reported to form no hydrazone or oxime derivative; the molecule is resistant to heat, a fact that became associated with its name; the ketone group is resistant to reduction (A. A. Morton, "The Chemistry of Heterocyclic Compounds", McGraw-Hill, New York, N.Y., 1946, p 150).
(6) H. C. Smitherman and L. Ferguson, *Tetrahedron,* **24,** 923 (1968); this paper reviews all aspects of aromaticity in 4-pyrones.
(7) R. Zahradnik, C. Párkányi, and J. Koutecký, *Collect. Czech. Chem. Commun.,* **27,** 1242 (1962).
(8) R. J. Abraham and W. A. Thomas, *J. Chem. Soc. B,* 127 (1966); A. J. Jones, *Rev. Pure Appl. Chem.,* **18,** 253 (1968); J. A. Elvidge, *Chem. Commun.,* 160 (1965); G. M. Badger, "Aromatic Character and Aromaticity", Cambridge University Press, New York, N.Y., 1969, p 29. (a) N. Brown and P. Bladdon, *Spectrochim. Acta,* **21,** 1277 (1965); (b) J. Jonas, W. Derbyshire, and H. Gutowsky, *J. Chem. Phys.,* **69,** 1 (1965).
(9) (a) R. Mayo and J. H. Goldstein, *Spectrochim. Acta, Part A,* **23,** 55, (1967); (b) C. Mathis and J. H. Goldstein, *ibid.,* **20,** 871 (1964).
(10) R. C. Benson, C. Norris, W. H. Flygare, and P. Beak, *J. Am. Chem. Soc.,* **93,** 5591 (1971). See also H. J. Dauben, J. Wilson, and J. Laity, "Non-Benzenoid Aromatics", Vol. II, J. Snyder, Ed., Academic Press, New York, N.Y., 1971.
(11) K. Kakinuma, C. Hanson, and K. Rinehart, *Tetrahedron,* **32,** 217 (1976).
(12) G. C. Levy and J. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, N.Y., 1972, p 66.
(13) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972, p 183.
(14) J. B. Stothers and P. C. Lauterbur, *Can. J. Chem.,* **42,** 1563 (1964).
(15) Reference 13, p 294, gives data on quinones, for which the CO resonance is also abnormally shielded but not nearly as large as for **1.** See also C. Kingsbury and J. H. Looker, *J. Org. Chem.,* **40,** 1120 (1975).
(16) Reference 13, p 253; see, however, B. Hess Jr., L. Schaad, and C. Holyoke Jr., *Tetrahedron,* **28,** 3657, 5299 (1972) with regard to aromaticity of furan.
(17) Reference 12, p 114.
(18) Reference 12, p 115, shows that TFA causes much greater effect on the CO resonance of acetone (concentration of TFA not specified). See also G. E. Maciel and G. Natterstad, *J. Chem. Phys.,* **69,** 1030 (1965). In ^1H spectra, deshieldings of ca. 0.8 ppm for H-3 and ca. 0.5 ppm for H-2 of 4-pyrone have been reported (ref 3), on treatment with TFA.
(19) D. Martin, J. Weise, and H. J. Niclas, *Angew. Chem., Int. Ed. Engl.,* **6,** 318 (1967).
(20) I. Morishima, K. Yoshikawa, K. Okada, T. Yonezawa, and K. Goto, *J. Am. Chem. Soc.,* **95,** 165 (1973).
(21) The solution darkened, and new peaks appeared in the spectrum; the absorptions of the parent compound diminished.
(22) Reference 13, pp 183, 196.
(23) D. W. Mathieson, "Nuclear Magnetic Resonance for Organic Chemists", Academic Press, New York, N.Y., 1967, Chapter 5, suggests that for line separations of large magnitude, a first-order analysis should be adequate (thus for **5,** δ CH_2, 5.0 ppm; δ H-3, 6.56; and δ H-6, 7.99).
(24) Reference 13, p 343.
(25) (a) Y. Takeuchi and N. Dennis, *J. Am. Chem. Soc.,* **96,** 3657 (1974). (b) Roberts and Cristol, however, report small couplings through oxygen: *J. Am. Chem. Soc.,* **95,** 4392 (1973).
(26) For comparison data in benzenoid systems, see (a) F. J. Weigert and J. D. Roberts, *J. Am. Chem. Soc.,* **89,** 2767 (1976); (b) J. H. Goldstein, V. Watts, and L. Rattet, *Prog. Nucl. Magn. Reson. Spectrosc.,* **8,** 104 (1972); (c) K. Takahashi, T. Sone, and K. Fujieda, *J. Phys. Chem.,* **74,** 2765 (1970).
(27) C. Kingsbury, unpublished results; see also C.-J. Chang, *J. Org. Chem.,* **41,** 1881 (1976).
(28) J. L. Marshall and R. Seiwell, *J. Magn. Reson.,* **15,** 150 (1974), find larger values for $^3J_{CO-H}$.
(29) H. Ost, *J. Prakt. Chem.,* **2,** 19, 177 (1879).
(30) T. Yabuta, *J. Chem. Soc.,* **125,** 575 (1924).
(31) K. N. Campbell, J. F. Ackerman, and B. K. Campbell, *J. Org. Chem.,* **15,** 221 (1950).
(32) K. Maurer, *Chem. Ber.,* **63,** 32 (1930).
(33) C. Stephan, B. Tate, and R. P. Allingham, Belgian Patent 651 427; *Chem. Abstr.,* **64,** 9688e (1966).
(34) F. H. Stodola, *J. Am. Chem. Soc.,* **73,** 5912 (1951).

Reactions of Nitrogen Compounds with Ruthenium Tetroxide. 2. Oxidation of Tertiary Amines as a Convenient Alternative to von Braun Degradation[1]

Giancarlo Bettoni, Carlo Franchini, Flaviano Morlacchi, Nicola Tangari, and Vincenzo Tortorella*

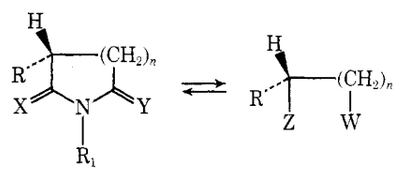
Institute of Pharmaceutical Chemistry, University of Bari, Bari, Italy

In the course of our previous work on the determination of the absolute configuration of cyclic amines, we correlated (*R*)-(−)-3-methylpiperidine (**1b,** n = 2) with (*R*)-(−)-2-methylglutaric acid (**8b,** n = 2) via (*R*)-(+)-1,5-dibromo-2-methylpentane (**7b,** n = 2), obtained from the benzoyl derivative (**2b,** n = 2) by the von Braun reaction.[2] This scheme could not be used with (*S*)-(+)-3-phenylpiperidine (**1d,** n = 2) and (*S*)-(+)-3-phenylpyrrolidine (**1d,** n = 1), the establishment of whose absolute configuration required much more laborious methods.[3,4]

von Braun's degradation fails with 3-arylamines (**1d**) because of drastic reaction conditions, low yields, and high boiling point of dibromo compound (**7d**). A possible alternative way to the von Braun reaction could be the direct oxidation of cyclic amines with ruthenium tetroxide. Among nitrogen compounds, it has been recently shown that amides[5,6] are oxidized by this reagent, but the few data reported in the literature indicate that only mixtures of intractable products are obtained when amines, without any acyl protection, are reacted with ruthenium tetroxide.[5,7]

In previous work in this field, we observed that ruthenium tetroxide has a low reactivity with the benzyl carbon attached to the nitrogen both in benzyllactams[8] and in *N*-acylamides having a phenyl group on the tertiary carbon adjacent to the nitrogen.[6] On the basis of this, we used ruthenium tetroxide to oxidize the *N*-benzyl derivatives of piperidines (**3a–d,** n = 2) and of pyrrolidines (**3a,d,** n = 1). This gave the corresponding imides (**6**), which were identified by their analytical and spectral characteristics, hydrolysis to the dicarboxylic acids (**8**), and by comparison with reference compounds prepared from the monoamides (**9**).

A very high optical yield was obtained in the oxidation of optically active amines. Hydrolysis of the imide *R*-(+)-**6b** (n = 2), obtained from *R*-(−)-**3b,** gave optically pure (*R*)-(−)-2-methylglutaric acid.[2] Analogously, the amines *S*-(−)-**3d** (n = 1, 2) gave the corresponding imides, which showed an optical rotation with the same sign as, but of a higher absolute



X = Y = H_2 R_1 = $C_6H_5CH_2$

1, R_1 = H
2, R_1 = C_6H_5CO
3, R_1 = $C_6H_5CH_2$
4, X = O; Y = CH_2
5, Y = O; X = CH_2
6, X = Y = O
7, Z = W = CH_2Br
8, Z = W = COOH
9, Z = COOH; W = $CONHCH_2C_6H_5$

a, R = H; **b,** R = CH_3; **c,** R = C_2H_5; **d,** R = C_6H_5 (n = 1, 2)

value than, that of the imides obtained by acidic cyclization of monobenzylamides (**9d**) obtained by the action of benzylamine on phenylglutaric and phenylsuccinic acid anhydrides belonging to the *S* series.

The oxidation was carried out at room temperature in a mixture of carbon tetrachloride and water containing an excess of sodium metaperiodate and a catalytic amount of ruthenium dioxide hydrate. After vigorous stirring for about 20 h, the *N*-benzylimides (**6**) were isolated in yields of around 50%. When the reaction time or the amount of sodium metaperiodate was reduced, the intermediate lactams (**4** and **5**) could be isolated from the reaction mixture.

The unsubstituted amines (**3a**) and the amines containing an alkyl group (**3b,c**) are oxidized much faster than the phenyl-substituted ones (**3d**). In fact, the reaction mixture of the latter contained monooxidized products even after a reaction for 80 h in the presence of an excess of sodium metaperiodate, these products being easily separated from the *N*-benzylimides by chromatography on a silica column.

These results show that *N*-benzylpiperidines and pyrrolidines having a substituent in the 3 position are oxidized by ruthenium tetroxide under very mild conditions, which permits their absolute configuration to be correlated with that of substituted glutaric and succinic acids. This reaction confirms the absolute configurations assigned before in a different manner[2-4] and therefore represents a convenient alternative to von Braun degradation of cyclic amines.

Experimental Section

Microanalyses were carried out by Dr. De Leonardis R., Istituto di Chimica Farmaceutica, Bari, with a Hewlett-Packard Model 185 C, H, N analyzer. The melting points, determined with a Buchi-Tottoli capillary melting point apparatus, are uncorrected. Optical rotations were determined on a Roussel-Jouan electronic micropolarimeter. Infrared, ^{1}H NMR, and mass spectra were determined with a Perkin-Elmer Model 257, a Varian HA-100, and a Perkin-Elmer Model 270 spectrometers, respectively. NMR chemical shifts are expressed in δ with Me_4Si as internal standard.

(*R,S*)-*N*-Benzyl-3-ethylpiperidine (3c, *n* = 2). 3-Ethylpiperidine[9] (obtained from catalytic reduction[10] of the corresponding pyridine) was refluxed with equimolecular amounts of benzyl chloride and triethylamine. Compound **3c** (n = 2) was obtained, bp 89 °C (0.8 mm), hydrochloride mp 146 °C (EtOH).

Anal. Calcd for $C_{14}H_{21}N$·HCl: C, 70.12; H, 9.25; N, 5.84. Found: C, 70.36; H, 9.17; N, 5.67.

(*S*)-(−)-*N*-Benzyl-3-phenylpiperidine (3d, *n* = 2). (*S*)-(+)-3-Phenylpiperidine (optical purity 97%),[3] treated as described above, gave the benzyl derivative: mp 53 °C (EtOH–H_2O); $[\alpha]_D$ −41° (MeOH); NMR ($CDCl_3$) δ 1.1–3.0 (9 H, m, alicyclic H), 3.49 (2 H, s, benzylic CH_2), 7.0–7.4 (10 H, m, aromatic H); mass spectrum *m/e* 251 (M^+).

Anal. Calcd for $C_{18}H_{21}N$: C, 86.01; H, 8.42; N, 5.57. Found: C, 85.84; H, 8.61; N, 5.52.

***N*-Benzylpiperidine-2,6-dione (6a, *n* = 2).** *N*-Benzylpiperidine (**3a**, n = 2, 1.90 g)[11] in CCl_4 (70 ml) was added with stirring to a solution of sodium metaperiodate (8.50 g) in water (100 ml) in the presence of ruthenium dioxide hydrate (0.10 g). After 24 h at room temperature, the aqueous layer was extracted several times with CCl_4 and the combined organic phases, after the elimination of RuO_4 with 2-propanol and filtration, were worked up in the usual way to give *N*-benzylpiperidine-2,6-dione (0.92 g, 41%), which was distilled under reduced pressure: ir (neat) 1725, 1675 cm^{-1}; NMR (CCl_4) δ 1.6–1.9 (2 H, m, 4-H), 2.44 (4 H, t, J = 6 Hz, 3,5-H), 4.74 (2 H, s, benzylic CH_2), 7.02–7.27 (5 H, m, aromatic H).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 71.23; H, 6.73; N, 6.71.

(*R*)-(+)-*N*-Benzyl-3-methylpiperidine-2,6-dione (6b, *n* = 2). Optically pure (*R*)-(−)-*N*-benzyl-3-methylpiperidine (**3b**, n = 2)[10] was oxidized as described above. The crude reaction mixture was purified by distillation under reduced pressure to give **6b** (n = 2) (70%), $[\alpha]_D$ +34.9° (CCl_4), which was shown to be identical with a sure sample obtained from 2-methylglutaric acid: ir (neat) 1725, 1675 cm^{-1}; NMR (CCl_4) δ 1.19 (3 H, d, J = 7 Hz, methyl H), 1.28–1.96 (2 H, m, 4-H), 2.18–2.72 (3 H, m, 3,5-H), 4.74 (2 H, s, benzylic CH_2), 7.0–7.3 (5 H, m, aromatic H).

Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45. Found: C, 71.91; H, 7.20; N, 6.33.

The hydrolysis of the imide **6b** (n = 2) with concentrated HCl under reflux (5 h) gave optically pure (*R*)-(−)-2-methylglutaric acid (100%).[2]

(*R,S*)-*N*-Benzyl-3-ethylpiperidine-2,6-dione (6c, *n* = 2). (*R,S*)-*N*-Benzyl-3-ethylpiperidine (**3c**, n = 2) was oxidized as described above. The crude reaction mixture (90%) was purified by distillation and compound **6c** (n = 2) was obtained (58%): bp 140–148 °C (1.2 mm); ir (neat) 1730, 1680 cm^{-1}; NMR (CCl_4) δ 0.91 (3 H, t, J = 8 Hz, methyl H), 1.05–2.0 (4 H, m, 4 and CH_2CH_3 H), 2.05–2.8 (3 H, m, 3,5-H), 4.78 (2 H, s, benzylic CH_2), 7.0–7.4 (5 H, m, aromatic H).

The hydrolysis of the imide, performed as described above, gave 2-ethylglutaric acid (92%).[12]

(*S*)-(−)-*N*-Benzyl-3-phenylpiperidine-2,6-dione (6d, *n* = 2). (*S*)-(+)-2-Phenylglutaric acid[13] (**8d**, n = 2) (optical purity 96%) was converted into the anhydride[14] which showed $[\alpha]_D$ +40.5° (absolute EtOH). By treatment of the anhydride with benzylamine in dry ether,[15] the benzylammonium salt of the acid (**9d**, n = 2) was obtained: mp 131 °C (EtOH–Et_2O); $[\alpha]_D$ +14.6° (absolute EtOH).

Anal. Calcd for $C_{25}H_{28}N_2O_3$: C, 74.23; H, 6.98; N, 6.93. Found: C, 74.25; H, 6.94; N, 6.64.

By treatment with 6 N HCl, the benzylammonium salt gave 2-phenyl-5-benzylamidoglutaric acid (**9d**, n = 2): mp 145–147 °C (EtOH–Et_2O); $[\alpha]_D$ +62° (absolute EtOH); ir (KBr) 3340, 1725 cm^{-1}; NMR (CD_3OD) δ 1.9–2.3 (4 H, m, 3,4-H), 3.50 (1 H, t, J = 7 Hz, 2-H), 4.24 (2 H, s, benzylic CH_2), 4.96 (exchangeable H), 7.08–7.34 (10 H, m, aromatic H).

The amide was dehydrated[16] by refluxing (30 min) with glacial acetic acid–concentrated sulfuric acid (9:1) to give the imide **6d** (n = 2): mp 69–70 °C (C_6H_6–*n*-C_6H_{14}): $[\alpha]_D$ −1.7° (absolute EtOH, *c* 7%); ir (KBr) 1720, 1670 cm^{-1}; NMR (CCl_4) δ 1.8–2.1 (2 H, m, 4-H), 2.3–2.5 (2 H, m, 5-H), 3.55 (1 H, t, J = 6 Hz, 3-H), 4.82 (2 H, s, benzylic CH_2), 6.8–7.4 (10 H, m, aromatic H).

In the same way from (*R,S*)-2-phenylglutaric acid, the racemic imide (**6d**, n = 2) having ir and NMR spectra identical with those of the optical isomer was obtained.

Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.61; H, 6.15; N, 4.93.

Compound **6d** (n = 2) was also obtained (25%) by oxidation (80 h) with ruthenium tetroxide of (*S*)-(−)-*N*-benzyl-3-phenylpiperidine (**3d**, n = 2), after chromatographic purification of the crude reaction mixture (67%) as described above: mp 59 °C (C_6H_6–*n*-C_6H_{14}); $[\alpha]_D$ −9.8° (absolute EtOH); ir and NMR spectra were identical with those shown by the same product obtained from **8d** (n = 2).

***N*-Benzylpyrrolidine-2,5-dione (6a, *n* = 1).** *N*-Benzylpyrrolidine (**3a**, n = 1)[17] was oxidized as described above. The crude reaction mixture (62%) was purified by chromatography on silica to give compound **6a** (n = 1) (32%): mp 98–99 °C (EtOH); ir (CH_3CN) 1775, 1705 cm^{-1};[18] NMR ($CDCl_3$) δ 2.6 (4 H, s, alicyclic H), 4.56 (2 H, s, benzylic CH_2), 7.16–7.34 (5 H, m, aromatic H).

(*S*)-(+)-*N*-Benzyl-3-phenylpyrrolidine-2,5-dione (6d, *n* = 1). (*S*)-(+)-2-Phenylsuccinic acid[19] (**8d**, n = 1) (optical purity 94%) was converted into the anhydride,[15] mp 81–82 °C, $[\alpha]_D$ +97.5° (Me_2CO), and then in the corresponding 2-phenyl-4-benzylamidosuccinic acid benzylammonium salt as described above: mp 155 °C (EtOH–Et_2O); $[\alpha]_D$ +62° (Me_2CO).

Anal. Calcd for $C_{24}H_{26}N_2O_3$: C, 73.82; H, 6.71; N, 7.18. Found: C, 73.53; H, 6.86; N, 6.80.

By treatment with 6 N HCl the salt gave the corresponding monobenzylamide (**9d**, n = 1): mp 135 °C (EtOH–Et_2O); $[\alpha]_D$ +88.6° (Me_2CO); ir (KBr) 1710, 1610 cm^{-1}.

Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.71; H, 6.02; N, 4.63.

The amide was dehydrated as described above to give the imide (**6d**, n = 1): mp 60 °C (EtOH); $[\alpha]_D$ +38° ($CHCl_3$);[20] ir (KBr) 1775, 1700 cm^{-1}; NMR ($CDCl_3$) δ 2.72 and 3.10 (2 H, AB part of ABX system, J_{AB} = 18 Hz, 4-H), 3.87 (1 H, q, X part, 3-H), 4.66 (2 H, s, benzylic CH_2), 7.0–7.5 (10 H, m, aromatic H).

Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.91; H, 5.71; N, 5.17.

Compound **6d** (n = 1) was also obtained from (*S*)-(−)-*N*-benzyl-3-phenylpyrrolidine (**3d**, n = 1)[4] having $[\alpha]_D$ −29° (MeOH, optical purity 74%) by oxidation (80 h) with ruthenium tetroxide as described above. The crude reaction mixture (70%), chromatographed on silica, gave the imide (26%): mp 65–67 °C (EtOH); $[\alpha]_D$ +34.5 °C ($CHCl_3$);[20] ir and NMR spectra identical with those shown by the same product obtained from **8d** (n = 1).

Registry No.—**1c** (n = 2), 59433-08-8; **1d** (n = 2), 59349-71-7; **3a** (n = 1), 29897-82-3; **3a** (n = 2), 2905-56-8; **3b** (n = 2), 37675-26-6; **3c** (n = 2), 59349-72-3; **3c** (n = 2) HCl, 59349-73-4; **3d** (n = 1), 59349-74-5; **3d** (n = 2), 59349-75-5; **6a** (n = 1), 2142-06-5; **6a** (n = 2), 42856-43-9; **6b** (n = 2), 59349-76-7; **6c** (n = 2), 59349-77-8; **6d** (n = 1), 59349-78-9; **6d** (n = 2), 59349-79-0; (±)-**6d** (n = 2), 59433-09-9; **8d**, (n = 1), 4036-30-0; **8d** (n = 2), 59349-80-3; **9d** (n = 1), 59349-81-4; **9d** (n = 1) $PhCH_2NH_2$, 59349-82-5; **9d** (n = 2), 59349-83-6; **9d** (n = 2) $PhCH_2NH_2$, 59349-84-7.

References and Notes

(1) For the previous article in this series, see ref 6.
(2) G. Bettoni, R. Perrone, and V. Tortorella, *Gazz. Chim. Ital.*, **102**, 196 (1972).
(3) F. Morlacchi, M. D'Ambruoso, and V. Tortorella, *Chim. Ind. (Milan)*, **56**, 465 (1974).
(4) G. Bettoni, C. Cellucci, and V. Tortorella, *Chim. Ind. (Milan)*, **56**, 465 (1974).
(5) J. C. Sheehan and R. W. Tulis, *J. Org. Chem.*, **39**, 2264 (1974).
(6) N. Tangari and V. Tortorella, *J. Chem. Soc., Chem. Commun.*, 71 (1975).
(7) L. M. Berkowitz and P. N. Rylander, *J. Am. Chem. Soc.*, **80**, 6682 (1958).
(8) Unpublished results obtained in our laboratory.
(9) H. Cottin, *Bull. Soc. Chim. Fr.*, 2729 (1966).
(10) G. Bettoni, E. Duranti, and V. Tortorella, *Gazz. Chim. Ital.*, **102**, 189 (1972).
(11) C. Schotten, *Ber.*, **15**, 421 (1882).
(12) M. F. Ansell and D. H. Hey, *J. Chem. Soc.*, 1683 (1950).
(13) L. Westman, *Ark. Kemi*, **11**, 431 (1957).
(14) K. Kawazu, T. Fujita, and T. Mitsui, *J. Am. Chem. Soc.*, **81**, 932 (1959).
(15) M. Naps and I. B. Johns, *J. Am. Chem. Soc.*, **62**, 2450 (1940).
(16) G. Casini, M. Ferappi, D. Misiti, and A. Schimberni, *Ann. Chim. (Rome)*, **49**, 1791 (1959).
(17) J. Schlinck, *Ber.*, **32**, 947 (1899).
(18) T. Matsuo, *Bull. Chem. Soc. Jpn.*, **37**, 1844 (1964).
(19) A. Fredga, J. P. Jennings, W. Klyne, P. M. Scopes, B. Sjoberg, and S. Sjoberg, *J. Chem. Soc.*, 3928 (1965).
(20) A less soluble racemate separates during crystallization; however, it is clear that a more extensive racemization occurs in the cyclization reaction.

Formation of Nitrate Esters by the Oxidation of Alkenes and Cyclopropanes with Thallium(III) Nitrate in Pentane[1]

Robert J. Ouellette* and Robert J. Bertsch

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

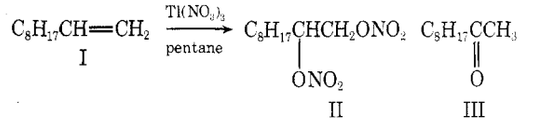
Received February 17, 1976

Nitrate esters are potentially useful synthetic intermediates for which few general methods of preparation are known. The corresponding alcohol may be esterified using nitric acid[2] alone or in a variety of cosolvents.[3-9] The corresponding halide can be metathetically converted to a nitrate ester using silver nitrate under heterogeneous[10-12] or homogeneous conditions.[13,14] More recently nitrates have been formed by mercury assisted solvolysis of alkyl halides.[15]

In our studies of the oxythallation and solvolytic dethallation of olefins by thallium(III) nitrate in methanol, we noted that nitrate esters are formed[16] in addition to the expected methyl ethers and carbonyl products.[17,18] As a result reaction conditions were sought under which the major product would be nitrate esters. Diethyl ether, dimethyl sulfoxide, sulfolane, and dimethylformamide all cause decomposition of the thallium(III) nitrate. Glyme, diglyme, and dioxane dissolve the thallium(III) nitrate to form stable solutions only if 1% nitric acid is added. Despite the fact that thallium(III) nitrate is very insoluble in pentane, the oxidation of the olefin does occur quite readily in this solvent.

In a typical reaction, a solution of the olefin in pentane is added to a stirred heterogeneous pentane–thallium(III) nitrate mixture maintained at room temperature. For most reactions a 10% excess of the oxidizing agent is used. Because of the relative instability of nitrate esters the reaction is terminated when it appears to be complete. The progress of the reaction can be qualitatively monitored by observing the change in the physical state of the thallium reagent.

Oxidation of 1-decene occurs in 1 h to give 1,2-decanediol dinitrate (II) in 85% yield. The remaining product is 2-decanone (III) which arises from a hydride shift in the dethallation



I II III

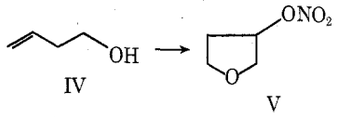
step. Thus a substantial decrease in rearranged product is observed compared to when methanol is the solvent in which yields of 34–40% 2-decanone are obtained.[16]

Reaction of *trans*-stilbene requires 72 h and leads to a mixture of *meso*- and *dl*-1,2-diphenyl-1,2-ethanediol dinitrate. Analysis of the mixture by using NMR resonances described earlier[16] indicates that the meso/*dl* ratio is 2:1. The reaction in methanol was found to be stereospecific.[16] There was no evidence of any rearranged products such as noted in the reaction in methanol.

Oxidation of cyclohexene in pentane occurs in 4 h to give *cis*- and *trans*-1,2-cyclohexanediol dinitrate (85%) and cyclopentanecarboxaldehyde (15%). The trans/cis ratio as determined by NMR is approximately 2/1. The resonance of the cis isomer (δ 5.10–5.55) and the trans isomer (δ 4.82–5.28) overlap somewhat and limit the accuracy of this method. The products contrast strongly with the results obtained in methanol where cyclopentanecarboxaldehyde is the major product.[17]

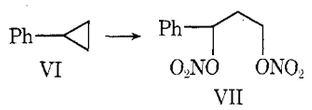
The *cis*- and *trans*-5-decenes react extremely slowly. After 11 days the cis isomer gave a mixture of *meso*- and *dl*-5,6-decanediol dinitrates in 64% yield with the remainder being 16% unreacted olefin, 9% 5-decanone, and 11% unidentified minor components. The trans isomer reacted more slowly. After 12 days a 38% yield of the *meso*- and *dl*-5,6-decanediol dinitrates was formed. The remaining material was 30% starting olefin, 17% 5-decanone, and 15% unidentified minor components. As the reaction time was increased, decomposition of product occurred with the evolution of NO_2. The exact percentages of the two dinitrate products were not determined.

3-Buten-1-ol (IV) reacts in 1 h to form exclusively 3-hydroxytetrahydrofuran nitrate ester (V). The product was isolated in 89% yield. There is no evidence of any open chain product.



IV V

Since we have noted similarities in the reaction of thallium(III) acetate with alkenes[19] and cyclopropanes[20] the oxidative cleavage of a cyclopropane by thallium(III) nitrate was examined. Phenylcyclopropane (VI) reacts in 12 h to give exclusively 1-phenyl-1,3-propanediol dinitrate (VII) which



VI VII

was isolated in 91% yield. There was no evidence of the symmetrically cleaved product, 2-phenyl-1,3-propanediol dinitrate.