

## Nitroalkylation of Aromatic Hydrocarbons Promoted by Manganese(III) Acetate

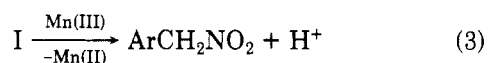
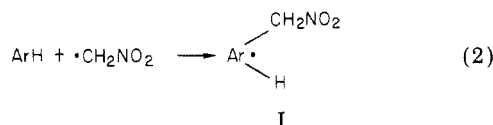
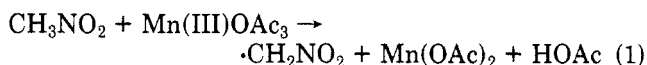
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Additional mechanistic and synthetic details concerning the formation of nitroalkylated aromatic products from the reaction of nitroalkanes with manganese(III) acetate and an aromatic compound are presented. A large isotope effect ( $k_H/k_D = 4.02-4.20$ ) was found for both manganese(III)- and cerium(IV)-promoted nitromethylations with nitromethane- $d_3$  while no isotope effect ( $k_H/k_D = 1.05$ ) was observed with benzene- $d_6$ . This indicated that deprotonation (most likely from an aci radical cation) to the nitromethyl radical is the slow step while subsequent rearomatization of a  $\sigma$ -radical complex occurs rapidly. Somewhat more convenient methods of activating the manganese(III) acetate promoter were found. However, attempts to find cooxidants or other additives which could improve this process met with only limited success. The reaction of either toluene or benzene with nitroethane or the nitropropanes and manganese(III) acetate in refluxing acetic acid gave much poorer yields (3-8%) of the corresponding nitroalkylated products. Incorporation of sodium acetate into these systems completely eliminated the aromatic substitution products and formed  $\alpha$ -nitroalkyl acetates instead. Implications of this finding on the mechanism for the generation of nitroalkyl radicals are discussed.

Aromatic nitromethylation can be carried out by heating a mixture of an aromatic, nitromethane, and manganese(III) acetate in acetic acid.<sup>1</sup> The reaction mechanism appears to involve interaction of the metal ion with nitromethane to produce nitromethyl radicals as key intermediates (eq 1).<sup>1</sup> These substitute onto the aromatic



hydrocarbon to produce radical  $\sigma$  complexes (I, eq 2), which are oxidatively converted to the products (eq 3). We were interested in taking a closer mechanistic look at the initial radical-forming step (eq 1), and to this end we carried out a series of kinetic isotope, solvent, and additive studies on the manganese(III)-promoted nitromethylation. Furthermore, we subjected other nitroalkanes to similar oxidative deprotonation conditions in the presence of aromatic compounds.

### Experimental Section

IR spectra were obtained with a Perkin-Elmer Model 710B spectrophotometer as thin films or KBr pellets. A 60-MHz Hitachi Perkin-Elmer Model R-24B spectrometer was used to run NMR spectra ( $\text{CDCl}_3$  solvent containing 1%  $\text{Me}_4\text{Si}$ ). GC analyses were made on a Hewlett-Packard Model 5840A gas chromatograph equipped with flame-ionization detectors and a capillary inlet system (split mode). Separations were performed with either a 10 m  $\times$  0.22 mm SP 2100 glass capillary column or a 15 m  $\times$  0.25 mm Carbowax 20M fused silica capillary column. Preparative gas chromatography was done on a GOW MAC Series 150 gas chromatograph equipped with a 4 ft  $\times$  0.25 in. SS 15% Carbowax 20M/Chrom P (80/100 mesh) column. Elemental analyses were performed by Micro Analysis Inc.

Manganese(III) acetate was prepared according to a literature procedure<sup>1,2</sup> and analyzed for purity by iodometry. Nitromethane- $d_3$  and benzene- $d_6$  (Aldrich, >99%) were checked by

NMR and used as is. The remaining reactants and solvents were commercially available in high purity and were used directly.

**Aromatic Nitroalkylation Promoted by Manganese(III) Acetate. General Procedure.** Manganese(III) acetate (10 mmol), aromatic hydrocarbon (10 mL), nitromethane (25 mL) or nitroalkane (5 mL) and acetic acid (25 mL) were refluxed together under nitrogen atmosphere with continuous stirring until the brown manganese(III) acetate was reduced to white manganese(II) acetate. After cooling, the reaction mixture was poured onto ethyl ether (25 mL) and water (50 mL). The resulting organic layer was separated, washed with water and aqueous sodium carbonate (5%), dried, and concentrated for subsequent analysis by GC. The same procedure was also used for reactions involving additional reagents (e.g.,  $\text{NH}_4\text{NO}_3$ , KOAc, KBr, acetic anhydride, and water) or propionic acid instead of acetic acid.

Products were isolated by preparative GC for nitroalkylations of benzene and toluene. The nitromethylation products from representative reactions were identified by comparison of their IR and NMR spectra and GC retention times with those of the authentic samples.<sup>1</sup> Other nitroalkylation products were identified on the basis of their spectra and in some cases elemental analysis.

$\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{NO}_2$ : IR (neat) 1570, 1410, 1390, 750, 690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.9 (d, 3 H), 5.6 (q, 1 H), 7.6 (s, 3 H). Mixture of *o*-, *m*-, and *p*- $\text{CH}_3\text{C}_6\text{H}_4\text{CH}(\text{CH}_3)\text{NO}_2$ : IR (neat) 1570, 1410, 1370, 800, 750, 690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.9, 2.0 (s, 3 H), 2.5, 2.6 (s, 3 H), 5.6 (q, 1 H), 7.4 (s, 4 H).  $\text{C}_6\text{H}_5\text{CH}(\text{NO}_2)\text{CH}_2\text{CH}_3$ : IR (neat) 1570, 1400, 750, 690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.0 (t, 3 H), 2.4 (m, 2 H) 5.7 (t, 1 H), 7.6 (s, 5 H). Mixture of *o*-, *m*-, and *p*- $\text{CH}_3\text{C}_6\text{H}_4\text{CH}(\text{NO}_2)\text{CH}_2\text{CH}_3$ : IR (neat) 1580, 1400, 850, 800, 760, 690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  0.9 (t, 3 H), 2.4 (m, 2 H), 2.5, 2.6 (s, 3 H), 5.8 (t, 1 H), 7.8 (s, 4 H).  $\text{CH}_3\text{CH}(\text{NO}_2)\text{O}_2\text{CCH}_3$ : IR (neat) 1775, 1570, 1370, 1220, 870  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.8 (d, 3 H), 2.2 (s, 3 H), 6.2 (q, 1 H). Anal. Calcd for  $\text{C}_4\text{H}_7\text{NO}_4$ : C, 36.09; H, 5.30; N, 10.53. Found (nitroethane reaction): C, 36.56; H, 5.30. Found (nitromethane plus  $\text{KO}_2\text{CCH}_3$  reaction): C, 35.81; H, 5.36; N, 10.71.  $\text{CH}_3\text{CH}_2\text{CH}(\text{NO}_2)\text{O}_2\text{CCH}_3$ : IR (neat) 1775, 1570, 1380, 1230, 1160  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.1 (t, 3 H), 2.2 (m, 2 H), 2.3 (s, 3 H), 6.2 (t, 1 H). Anal. Calcd for  $\text{C}_5\text{H}_9\text{NO}_4$ : C, 40.82; H, 6.17. Found: C, 42.05, 42.82; H, 6.17, 6.31.  $\text{CH}_3\text{CH}(\text{NO}_2)\text{O}_2\text{CCH}_2\text{CH}_3$ : IR (neat) 1765, 1570, 1360, 1125  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  1.2 (t, 3 H), 1.8 (d, 3 H), 2.5 (q, 2 H), 6.2 (q, 1 H).

Nitromethylation products from naphthalene, *p*-dimethoxybenzene and diphenyl ether were isolated by column chromatography (silica gel, mixed  $\text{CHCl}_3$ -hexanes as mobile phases) and identified by their NMR and IR. **2-(Nitromethyl)-1,4-dimethoxybenzene**: IR (neat) 1570, 1510, 1380, 1240, 1050, 815  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  3.8 (2 s, 6 H), 5.5 (s, 2 H), 7.0 (s, 3 H). **1-(Nitromethyl)naphthalene**: IR (neat) 1560, 1380, 790  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  7.6 (m, 7 H), 5.7 (s, 2 H). Mixture of **(nitromethyl)phenyl ether isomers**: IR (neat) 1600, 1570, 1500, 1380, 1250, 800, 750, 690  $\text{cm}^{-1}$ ; NMR ( $\text{CDCl}_3$ )  $\delta$  5.4, 5.6, 5.7 (s, 2 H) 7.2 (m, 9 H).

(1) M. E. Kurz and T. Y. R. Chen, *J. Org. Chem.*, **43**, 239 (1978).

(2) P. J. Andrusis, M. J. S. Dewar, R. Dietz, and R. L. Hunt, *J. Am. Chem. Soc.*, **88**, 5473 (1966).

Table I. Effect of Additives on the Nitromethylation of Aromatic Compounds with Nitromethane and Manganese Acetates

manganese salt (10 mmol)	aromatic (10 mL)	additive (amt)	products, <sup>a</sup> %	
			ArCH <sub>2</sub> NO <sub>2</sub> <sup>b</sup>	byproducts
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>		55	
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub>		14	
KMnO <sub>4</sub> + Mn(OAc) <sub>2</sub> <sup>c</sup>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>		60	
KMnO <sub>4</sub> + Mn(OAc) <sub>2</sub> <sup>d</sup>	C <sub>6</sub> H <sub>6</sub>		9	2, C <sub>6</sub> H <sub>5</sub> CHO
Mn(OAc) <sub>3</sub> <sup>e</sup>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>		54	
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	O <sub>2</sub> <sup>f</sup>	29	
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	NH <sub>4</sub> NO <sub>3</sub> <sup>g</sup> (50 mmol)	84	38, CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CHO
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub>	NH <sub>4</sub> NO <sub>3</sub> <sup>g</sup> (50 mmol)	9	11, C <sub>6</sub> H <sub>5</sub> CHO; 19, C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OAc
Mn(OAc) <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	NH <sub>4</sub> NO <sub>3</sub> <sup>g</sup> (50 mmol)	53	20, CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CHO
Mn(OAc) <sub>2</sub>	C <sub>6</sub> H <sub>6</sub>	NH <sub>4</sub> NO <sub>3</sub> <sup>g</sup> (50 mmol)	4	3, C <sub>6</sub> H <sub>5</sub> CHO
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub> or C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	KOAc (50 mmol)		6, CH <sub>3</sub> CH(NO <sub>2</sub> )OAc
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub> or C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	KBr (50 mmol)		some <sup>h</sup>
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	H <sub>2</sub> O (5 mL)	<1	
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	AcOAc (25 mL)	47	
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub>	AcOAc (25 mL)	22	
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub> CO <sub>2</sub> H (25 mL) <sup>i</sup>	5	8, CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CHO
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub> CO <sub>2</sub> H (12.5 mL) <sup>j</sup>	25	5, CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CHO
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub>	C <sub>2</sub> H <sub>5</sub> CO <sub>2</sub> H (25 mL) <sup>i</sup>	<1	4, C <sub>6</sub> H <sub>5</sub> CHO
Mn(OAc) <sub>3</sub>	C <sub>6</sub> H <sub>6</sub>	C <sub>2</sub> H <sub>5</sub> CO <sub>2</sub> H (12.5 mL) <sup>j</sup>	18	7, C <sub>6</sub> H <sub>5</sub> CHO

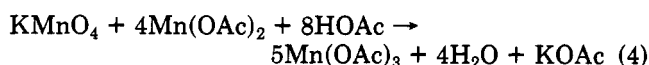
<sup>a</sup> Acetic acid (25 mL), nitromethane (25 mL), reflux; yield based on 1 mol of product/2 mol of manganese(III). <sup>b</sup> Mixture of ~55/20/25 ortho/meta/para from toluene. <sup>c</sup> KMnO<sub>4</sub> (2 mmol) and Mn(OAc)<sub>2</sub> (8 mmol) were heated together in acetic acid, and then other reactants were added. <sup>d</sup> KMnO<sub>4</sub> (2 mmol) and Mn(OAc)<sub>2</sub> (8 mmol) heated in presence of other reactants. <sup>e</sup> Recovered Mn(OAc)<sub>3</sub> reoxidized by KMnO<sub>4</sub> in the usual manner. <sup>f</sup> Constant oxygen purge. <sup>g</sup> Brown color of the Mn(III) salt had not been discharged at the end. <sup>h</sup> Unidentified. <sup>i</sup> No acetic acid used. <sup>j</sup> CH<sub>3</sub>CO<sub>2</sub>H (12.5 mL) was used as cosolvent.

For quantitative analysis, a known amount of an internal standard (usually *p*-nitrotoluene) was added to the reaction mixtures, and product peak areas were compared to that of the internal standard. Yield percentages were based on 1 mol of product/2 mol of manganese(III) salt promoter<sup>1</sup> and are the average of two or more runs in good agreement.

**Isotope Effect Studies.** For the nitromethane isotope study, manganese(III) acetate (2.5 mmol), benzene (2.5 mL), nitromethane (2 mL), and nitromethane-*d*<sub>3</sub> (2 mL) were refluxed in glacial acetic acid (5 mL) under nitrogen until the brown manganese(III) acetate color was discharged. The reaction mixture was worked up as above and analyzed by gas chromatography to make sure that very little of the nitromethylated products had been converted to benzaldehyde. The isolated nitromethylated benzene was analyzed quantitatively by NMR, and the relative rates,  $k_H/k_D$  (Table I), were determined from the ratio of C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NO<sub>2</sub> to C<sub>6</sub>H<sub>5</sub>CD<sub>2</sub>NO<sub>2</sub>. Control studies showed that nitromethane-*d*<sub>3</sub> did not undergo deuterium exchange under the reaction conditions and that only C<sub>6</sub>H<sub>5</sub>CD<sub>2</sub>NO<sub>2</sub> was obtained when benzene was nitromethylated with nitromethane-*d*<sub>3</sub> and manganese(III) acetate in acetic acid. A similar procedure was used in the benzene isotopic studies with the following reactant quantities: benzene (1 mL), benzene-*d*<sub>6</sub> (1 mL), nitromethane (5 mL), manganese(III) acetate (2.5 mmol), and acetic acid (5 mL). After the workup the relative rate,  $k_H/k_D$ , was obtained by comparing the ratio of C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NO<sub>2</sub> to C<sub>6</sub>D<sub>5</sub>CH<sub>2</sub>NO<sub>2</sub> by NMR. A control study showed that benzene-*d*<sub>6</sub> did not undergo deuterium exchange under simulated reaction conditions.

## Results

**Aromatic Nitromethylations.** One of the drawbacks cited earlier<sup>1</sup> in manganese(III) acetate promoted nitromethylations was the need to synthesize and isolate the desired salt. Heiba<sup>3</sup> had earlier reported that manganese(III) acetate could be generated stoichiometrically (eq 4) and used to oxidize carboxylic acids without isolation.



A similar procedure was used to synthesize manganese(III)

acetate in glacial acetic acid. This solution was then used without isolation by adding toluene and nitromethane and refluxing under a nitrogen atmosphere until all of the manganese(III) was reduced. By use of this approach, a 60% yield of nitromethylated toluenes (based on KMnO<sub>4</sub> as limiting reagent) was realized (Table I). No side products were observed.

An attempt was made to generate manganese(III) in situ by refluxing a mixture of nitromethane, the aromatic, manganese(II) acetate, and potassium permanganate (limiting reagent) in glacial acid. This resulted primarily in the formation of the byproducts, benzaldehyde and tolualdehyde from toluene and a lower yield of  $\alpha$ -nitrotoluene from benzene (Table I).

The manganese(II) acetate byproduct from typical nitromethylation reactions (eq 1) was able to be recovered in >85% yield and reoxidized quantitatively to an effective promoter by the standard procedure (Table I).

**Effect of Additives on Aromatic Nitromethylation.** Refluxing the usual reactants (nitromethane, manganese(III) acetate, and toluene) in acetic acid under an oxygen purge instead of the usual nitrogen blanket resulted in a substantial decrease in the nitromethylated product (Table I).

Ammonium nitrate had been reported to increase yields of nitromethylation.<sup>4</sup> Addition of ammonium nitrate (5:1 molar ratio to the manganese(III) acetate) to the usual reactants with toluene gave rise to an 84% yield of the nitromethylated products (Table I) and a 20% yield of the isomeric tolualdehydes as byproducts. Ammonium nitrate had less of an effect on the nitromethylation of benzene (9% yield of nitromethylated product) but produced significant amounts of byproducts, benzaldehyde (11%) and benzyl acetate (19%, Table I).

Earlier Bellamy had shown that ammonium nitrate could create an active nitromethylation promoter with manganese(II) acetate.<sup>4</sup> A similar study in which manganese(III) acetate and ammonium nitrate were refluxed in glacial acetic acid in the presence of an aromatic resulted

(3) E. I. Heiba, R. M. Dessau, and P. G. Rodewald, *J. Am. Chem. Soc.*, **96**, 7977 (1974).

(4) A. J. Bellamy, *Acta Chem. Scand., Ser. B*, **B33**, 208 (1979).

Table II. Nitromethylation of Other Aromatics Promoted by Manganese(III) Acetate

aromatic	% yield <sup>a</sup>	aromatic	% yield <sup>a</sup>
naphthalene	74	<i>p</i> -CH <sub>3</sub> OPhOCH <sub>3</sub>	71
PhPh	71 <sup>b</sup>		

<sup>a</sup> Based on 1 mol of product/2 mol of manganese(III) acetate. Single isomer only. Yields obtained from the comparison of the peak area of products to that of the internal standard without correction. Only a single run. Similar yields were obtained for the reaction promoted by Ce(IV) acetate.<sup>6</sup> <sup>b</sup> Three isomeric products were found.

in a color change to brown, indicating that manganese(III) acetate was formed. Nitromethylated aromatics were found in yields (4% with benzene and 53% with toluene) similar to those with manganese(III) acetate alone (Table I).

Potassium acetate and potassium bromide were also tried as additives in these reactions, and both salts completely inhibited nitromethylations (Table I). In the reaction with potassium acetate, a byproduct identified as  $\alpha$ -nitroethyl acetate was formed to the extent of about 6%.

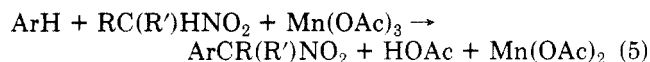
The deliberate addition of water to a typical reaction of toluene–nitromethane–manganese(III) acetate in acetic acid was also found to quench nitromethylation. On the other hand, when the dehydrating agent, acetic anhydride, was added to the standard reaction setup, a reasonable increase was observed in the nitromethylated benzenes but not in the toluene products (Table I).






**Solvent Studies.** Nitromethylations of toluene promoted by manganese(III) acetate were attempted in a number of different solvents besides acetic acid: acetonitrile, dimethyl sulfoxide, dimethyl formamide, and in excess nitromethane alone as solvent. Small amounts (5%) of  $\alpha$ -nitroxyls were found in acetonitrile; essentially no nitromethylated toluenes were found in any of the others. The use of propionic instead of acetic acid caused yield dropoffs in aryl nitromethanes from both benzene and toluene (Table I).

**Kinetic Isotope Studies.** In hopes of learning more about the details of the nitromethylation reaction, we performed a series of competition experiments. Benzene and manganese(III) acetate were reacted with a mixture of nitromethane and nitromethane-*d*<sub>3</sub> under the usual conditions, and the ratio of C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NO<sub>2</sub> to C<sub>6</sub>H<sub>5</sub>CD<sub>2</sub>NO<sub>2</sub> was determined. An isotope effect ( $k_H/k_D$ ) of 4.20 ± 0.12 was found. In a second set of competitions, a mixture of benzene and benzene-*d*<sub>6</sub> were reacted with nitromethane and manganese(III) acetate. In this case no apparent rate effect was observed ( $k_H/k_D = 1.05 \pm 0.03$ ).

**Other Aromatics.** A number of other electron-rich aromatic compounds (naphthalene, diphenyl ether, and *p*-dimethoxybenzene) were subjected to nitromethylation by using the standard procedure.<sup>1</sup> High yields of essentially a single nitromethylated *p*-dimethoxybenzene and naphthalene ( $\alpha$  isomer) and an isomeric mixture of nitromethylphenyl phenyl ethers were found (Table II).






**Other Nitroalkylations.** A more thorough investigation was undertaken to determine how general this nitroalkylation reaction was. Nitroethane, 1-nitropropane, 2-nitropropane, and 2-nitroethyl acetate were reacted with aromatics and manganese(III) acetate in refluxing acetic acid. The results of these nitroalkylations with benzene and toluene are shown in Table III and IV, respectively. The nitroalkylated products corresponding to the stoichiometry indicated in eq 5 were obtained in low yields

Table III. Nitroalkylation of Benzene Promoted by Manganese(III) Acetate<sup>a</sup>

		% yield		
		without additive	with KOAc, <sup>e</sup>	
				
R	R'			
H	H	14		6 <sup>b</sup>
CH <sub>3</sub>	H	5	9	30
C <sub>2</sub> H <sub>5</sub>	H	4	15	40
CH <sub>3</sub>	CH <sub>3</sub>	1 <sup>c</sup>	<i>d</i>	

<sup>a</sup> Yields based on 1 mol of product/2 mol of manganese(III) acetate; average of at least two runs in good agreement. <sup>b</sup> Nitroethyl acetate rather than nitromethyl acetate. <sup>c</sup> For a tentative identification, see the Experimental Section. <sup>d</sup> A number of unidentified byproducts were present. <sup>e</sup> No ArC(R)(R')NO<sub>2</sub> obtained.

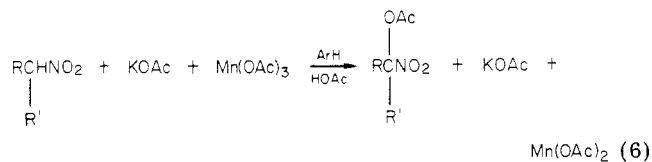
Table IV. Nitroalkylation of Toluene Promoted by Manganese(III) Acetate<sup>a</sup>

		% yield		
		without additive	with KOAc <sup>b</sup>	
				
R	R'			
H	H	55 (57/20/23)		6 <sup>c</sup>
CH <sub>3</sub>	H	11 (49/51) <sup>d</sup>	7	30
CH <sub>3</sub>	H		2	22 <sup>e</sup>
CH <sub>3</sub>	H		3	17 <sup>f</sup>
C <sub>2</sub> H <sub>5</sub>	H	7 (22/26/51)	12	40
CH <sub>3</sub>	CH <sub>3</sub>	1 <sup>g</sup> (22/22/56)	<i>h</i>	

<sup>a</sup> Yields based on 1 mol of product/2 mol of manganese(III) acetate; average of at least two runs in good agreement; nitroalkane (5 mL), manganese(III) acetate (10 mmol), and toluene (10 mL) in acetic acid (25 mL). <sup>b</sup> 25 mmol. <sup>c</sup> Nitroethyl acetate instead of nitromethyl acetate. <sup>d</sup> The meta and para isomers were not resolved. <sup>e</sup> KOAc, 20 mmol. <sup>f</sup> KOAc, 10 mmol. <sup>g</sup> For a tentative identification, see the Experimental Section. <sup>h</sup> A number of unidentified byproducts were present. <sup>i</sup> Ortho/meta/para ratio is given in parentheses.

from nitroethane and 1-nitropropane. In addition, byproducts identified as  $\alpha$ -nitroethyl acetate and  $\alpha$ -nitropropyl acetate were found, respectively, on the basis of IR, NMR, and elemental analysis. An unidentified product, which likely was 2-nitro-2-propyl acetate, was produced in trace amounts in the reaction involving 2-nitropropane. No aromatic substitution product was found in the reaction of 2-nitroethyl acetate; an unidentified product, not dependent on the involvement of the aromatic, was found.

The effect of introducing potassium acetate (25 mmol) in the nitroethylation and nitropropylation was to substantially increase the amount of  $\alpha$ -nitroalkyl acetates (eq 6) and to wipe out the nitroalkylated aromatic products



(Tables III and IV). Addition of lesser amounts of po-

Table V. Nitroethylation of Benzene in Propionic Acid<sup>a</sup>

solvent <sup>b</sup> ratio, HO <sub>2</sub> CCH <sub>3</sub> / HO <sub>2</sub> CC <sub>2</sub> H <sub>5</sub>	product yield, %		
	ArCH- (NO <sub>2</sub> )CH <sub>3</sub>	CH <sub>2</sub> CH- (NO <sub>2</sub> )O <sub>2</sub> CCH <sub>3</sub>	CH <sub>2</sub> CH- (NO <sub>2</sub> )O <sub>2</sub> CC <sub>2</sub> H <sub>5</sub>
1:0	5	9	
3:2	2	7	4
1:1	3	6	5
2:3	3	5	7
0:1	2		19

<sup>a</sup> Manganese(III) acetate (10 mmol), benzene (10 mL), nitroethane (10 mL), reflux; yields are based on 1 mol of product/2 mol of manganese(III). <sup>b</sup> Total solvent volume was 25 mL.

Table VI. Nitroethylation of Toluene in Propionic Acid<sup>a</sup>

solvent <sup>b</sup> ratio, HO <sub>2</sub> CCH <sub>3</sub> / HO <sub>2</sub> CC <sub>2</sub> H <sub>5</sub>	product yield, %		
	ArCH- (NO <sub>2</sub> )CH <sub>3</sub>	CH <sub>2</sub> CH- (NO <sub>2</sub> )O <sub>2</sub> CCH <sub>3</sub>	CH <sub>2</sub> CH- (NO <sub>2</sub> )O <sub>2</sub> CC <sub>2</sub> H <sub>5</sub>
1:0	11	7	
3:2	6	7	4
2:3	4	5	4
0:1	44		18

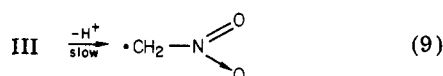
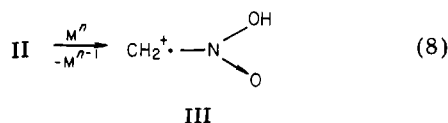
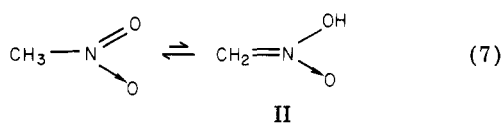
<sup>a</sup> Manganese(III) acetate (10 mmol), toluene (10 mL), nitroethane (10 mL), reflux; yields are based on 1 mol of product/2 mol of manganese(III). <sup>b</sup> Total solvent volume was 25 mL.

tassium acetate (10–20 mmol) in the toluene nitroethylations (Table IV) led to intermediate levels of both nitroethylated toluenes and  $\alpha$ -nitroethyl acetate.

When either benzene or toluene was nitroethylated in propionic instead of acetic acid, lower yields of the nitroethylated aromatics and substantial amounts of  $\alpha$ -nitroethyl propionate were observed in both cases (Tables V and VI). With acetic–propionic acid solvent mixtures  $\alpha$ -nitroethyl acetate and  $\alpha$ -nitroethyl propionate were obtained competitively (Tables V and VI).

## Discussion

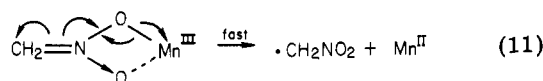
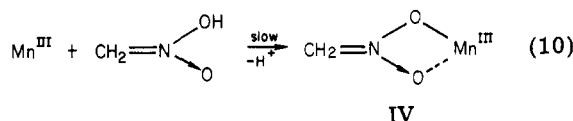
**Mechanism.** Previously a scheme involving the production of nitromethyl radicals (eq 1) and their attack on aromatic hydrocarbons (eq 2) had been proposed.<sup>1</sup> More details concerning the formation and substitution of the nitromethyl radical emerge from the kinetic isotope effect studies. The observance of a primary isotope effect ( $k_H/k_D = 4.2$ ) with manganese(III) acetate and deuterated nitromethane is consistent with a scheme involving the formation of a radical cation as a fast reversible process (eq 8) from the aci tautomer of nitromethane (eq 7), followed



by a slow proton loss (eq 9) to give the nitromethyl radical. An analogous scheme has been proposed to account for the manganese(III)-promoted oxidation of *p*-methylanisole to the methoxybenzyl radical.<sup>5</sup> The resulting nitromethyl

radical then substitutes onto the aromatic ring as before (eq 2) to give a  $\sigma$ -radical complex I. The results of the other isotopic study in which benzene and deuterated benzene reacted at virtually the same rate indicates that oxidative deprotonation of this complex (eq 3) occurs as a rapid step after the rate-determining process. Trapping of the aci radical cation III by acetate (or propionate) followed by oxidative deprotonation could account for the nitroalkyl acetate or propionate byproducts.

An alternate mechanism might involve coordination of the aci form with the metal ion in a slow step (eq 10).



Rapid electron transfer within the ligand–metal complex IV would produce the nitromethyl radical (eq 11). Using this scheme, one can better account for nitroalkyl acetates, preferentially found in nitroalkylations in the presence of acetate ion (Tables III and IV), as resulting from nucleophilic attack onto the coordinated ligand (IV) by acetate. This process would be expected to compete with nitroalkyl radical formation (eq 11) and would explain the absence of nitroalkylated aromatics (Tables III and IV) in reactions run in the presence of excess acetate. Larger amounts of nitroalkyl acetate byproducts were found in reactions with nitroethane and nitropropane. We have no explanation for the formation of the byproduct  $\alpha$ -nitroethyl acetate from the reaction of aromatic–nitromethane–manganese(III) acetate–potassium acetate.

This more complete investigation as to the scope of nitroalkylations of aromatics confirms the synthetic limitations with larger nitroalkanes.<sup>1</sup> As had been noted earlier, much smaller nitroalkylation yields (<10%) were obtained with nitroethane, 1-nitropropane, and 2-nitropropane, suggesting a possible steric factor. The isomer distribution is also affected by steric factors of the substituting entity as less ortho and more para substitution was found with the bulky 2-nitropropyl radical (Table IV).

Efforts to make the nitromethylation procedure catalytic in Mn(III) or to start with Mn(II) salts have been unsuccessful to date. However, more convenient ways of utilizing manganese(III) acetate have been found. Though the use of NH<sub>4</sub>NO<sub>3</sub> as a cooxidant increased nitromethylation yields (Table I), it also led to more side products. Many other additive effects were observed, most notably the deleterious effects on aromatic nitromethylation by KOAc, KBr, and water.

The electrophilic behavior of the nitromethyl radical<sup>1,6</sup> is conducive to its reacting readily with electron-rich substrates. A variety of these types of aromatics did undergo nitromethylation in high yield (Table II), suggesting possible synthetic utility.

**Registry No.** Naphthalene, 91-20-3; diphenyl ether, 101-84-8; *p*-dimethoxybenzene, 150-78-7; 1-(nitromethyl)naphthalene, 74631-02-0; *o*-(nitromethyl)phenyl phenyl ether, 79101-73-8; *m*-(nitromethyl)phenyl phenyl ether, 79101-74-9; *p*-(nitromethyl)phenyl phenyl ether, 79101-75-0; 2-(nitromethyl)-1,4-dimethoxybenzene, 79101-76-1; nitromethane, 75-52-5; nitroethane, 79-24-3; 1-nitro-

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propane, 108-03-2; 2-nitropropane, 79-46-9; benzene, 71-43-2;  $\alpha$ -nitrotoluene, 622-42-4; (1-nitroethyl)benzene, 7214-61-1; (1-nitropropyl)benzene, 5279-14-1; 2-nitroethyl acetate, 18942-89-7;  $\alpha$ -nitropropyl acetate, 79101-77-2; toluene, 108-88-3;  $\alpha$ -nitro-*o*-xylene, 38362-89-9;  $\alpha$ -nitro-*m*-xylene, 38362-90-2;  $\alpha$ -nitro-*p*-xylene, 29559-

27-1; *o*-(1-nitroethyl)toluene, 79101-78-3; *m*-(1-nitroethyl)toluene, 29342-32-3; *p*-(1-nitroethyl)toluene, 5437-59-2; *o*-(1-nitropropyl)toluene, 79101-79-4; *m*-(1-nitropropyl)toluene, 79101-80-7; *p*-(1-nitropropyl)toluene, 79101-81-8;  $\text{CH}_3\text{CH}(\text{NO}_2)\text{O}_2\text{CCH}_3$ , 24342-21-0;  $\text{CH}_3\text{CH}(\text{NO}_2)\text{O}_2\text{CC}_2\text{H}_5$ , 79101-82-9;  $\text{Mn}(\text{OAc})_3$ , 993-02-2.

## Free-Radical Aromatic Nitromethylation Promoted by Cerium(IV)

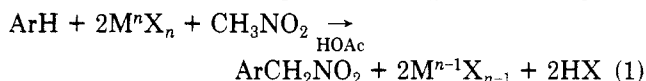
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A search for metal salt oxidants, other than manganese(III) acetate, capable of effecting aromatic nitromethylation with nitromethane was undertaken. Of the many screened, cerium(IV) salts showed the most promise. Cerium(IV) ammonium nitrate gave high, though initially erratic, yields (essentially 100% yield of isomeric  $\alpha$ -nitroxylens from toluene and  $\alpha$ -nitrotoluene from benzene). However, nitration products and aromatic aldehydes were generated as well. Product formation was followed as a function of time in these reactions, and nitromethylation products were shown to be converted to the corresponding isomeric tolualdehydes or benzaldehyde upon prolonged heating. Cerium(III) nitrate was shown to be primarily responsible for promoting this side reaction. Cerium(IV) acetate, generated in solution by ozonolysis of either cerium(III) nitrate or a mixture of cerium(III) acetate and cerium(III) nitrate in acetic acid, also was shown to promote high yields of nitromethylation products. Furthermore, this reaction was free of side products. Isomer studies and relative rates for nitromethylation were determined for both cerium(IV) salts in comparison with manganese(III) acetate. A Hammett treatment in each case gave similar  $\rho$  values (vs.  $\sigma^+$ ): -2.3 from manganese(III) acetate, -2.0 from cerium(IV) ammonium nitrate, and -1.9 from cerium(IV) acetate, indicating a common intermediate in each case. The nitromethyl radical, believed to be the substituting entity, exhibits marked electrophilic properties.

Recently we reported that aromatic nitromethylation could be accomplished by refluxing a mixture of the aromatic, nitromethane, and manganese (III) acetate in acetic acid.<sup>1</sup> This reaction (eq 1 with  $M^nX_n = \text{Mn}(\text{OAc})_3$ ) was



felt to involve the generation of nitromethyl radicals (by oxidative deprotonation of nitromethane) and their subsequent substitution onto the arene.<sup>1,2</sup> While this reaction provides a more direct route to aryl nitromethanes than existing methods,<sup>3,4</sup> it suffers the drawback that the manganese(III) salt must be synthesized by the chemical<sup>5</sup> or electrochemical<sup>6</sup> oxidation of manganese(II) acetate and is not able to be regenerated during the reaction.<sup>1</sup> Consequently, we were interested in finding other oxidants capable of promoting this reaction and herein report on our studies with other metal salt promoters, particularly in comparison to manganese(III) acetate.

### Experimental Section

**General Methods.** IR spectra were obtained with a Perkin-Elmer Model 710B spectrophotometer as thin films or KBr pellets. A 60-MHz Hitachi Perkin-Elmer Model R-24B spectrometer was used to run NMR spectra ( $\text{CDCl}_3$  solvent containing 1%  $\text{Me}_4\text{Si}$ ). GC analyses were made on a Hewlett-Packard Model 5840A gas chromatograph equipped with flame-ionization detectors and a

Table I. Nitromethylation of Benzene and Toluene Promoted by Metal Salts

metal salt	% nitromethylation product <sup>a</sup>		byproducts
	benzene	toluene	
$\text{Ce}(\text{NH}_4)_2(\text{NO}_3)_6$	55	100	many
$\text{Ce}(\text{OAc})_4$		58	none
$\text{CeK}_2(\text{NO}_3)_6$ <sup>b</sup>	17	36	some
$\text{CeH}_4(\text{SO}_4)_4$ <sup>b</sup>		23	some
$\text{Ce}(\text{NH}_4)_4(\text{SO}_4)_4 \cdot 2\text{H}_2\text{O}$ <sup>b</sup>		15	some
$\text{Ce}(\text{NO}_3)_3(\text{OH})$	6	10	some
$\text{Co}(\text{OAc})_3$		3	some
$\text{Mn}^{\text{III}}(\text{C}_5\text{H}_7\text{O}_2)_3$ <sup>c</sup>		1	some

<sup>a</sup> Based on 1 mol of product/2 mol of metal salt; average of at least two runs in good agreement. <sup>b</sup> In the presence of  $\text{Cu}(\text{OAc})_2$ . <sup>c</sup> The following metal salts gave no nitromethylation products at all:  $\text{Ce}(\text{OH})_4$ ,  $\text{Cu}(\text{BF}_4)_2$ ,  $\text{Cu}(\text{NO}_3)_2$ ,  $\text{CuCl}_2 \cdot \text{LiCl}$ ,  $\text{Cu}(\text{OAc})_2$ ,  $\text{Cu}(\text{OAc})_2 \cdot \text{LiCl}$ ,  $\text{FeCl}_3$ ,  $\text{Hg}(\text{NO}_3)_2$ ,  $\text{Hg}(\text{OAc})_2$ ,  $\text{MnCl}_3$ ,  $\text{MnO}_2$ ,  $\text{NH}_4\text{VO}_3$ ,  $\text{Pb}(\text{OAc})_4$ ,  $\text{Ti}(\text{OAc})_3$ ,  $\text{UO}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ .

capillary inlet system (split mode). Separations were performed with either a 10 m  $\times$  0.22 mm SP2100 glass capillary column or a 15 m  $\times$  0.25 mm Carbowax 20M fused silica capillary column. Preparative gas chromatography was done on a GOW MAC Series 150 gas chromatograph equipped with a 4 ft  $\times$  0.25 in. SS 15% Carbowax 20M/Chrom P (80/100 mesh) column. Ozonolyses were carried out with the use of a Purification Sciences Inc. Model LOA-1 ozone generator.

Cerium(IV) acetate was synthesized<sup>7</sup> and generally used without isolation. Cobalt(III) acetate was made by the oxidation of cobalt(II) acetate.<sup>8</sup> The remaining metal salts and organic reactants

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