with that obtained from the direct phenolic oxidative coupling of (±)-reticuline (1).

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**Registry No.** 1, 1699-46-3; 2a, 23979-21-7; 2b, 79970-49-3; 2c, 55781-26-5; 3, 5164-93-2.

## Aromatic Substitution. 50.[1] Mercury(II)-Promoted Azeotropic Nitration of Aromatics over Nafion-H Solid Superacidic Catalyst

George A. Olah,* V. V. Krishnamurthy, and Subhash C. Narang

*Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90007*

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In the course of our continued studies of nitration, we have previously reported[2] a new improved method of the nitration of aromatic compounds with nitric acid over a solid superacidic perfluorinated resin sulfonic acid (Nafion-H) catalyst.[3] We have subsequently also examined the nitration of aromatic compounds with a variety of other nitrating agents with Nafion-H catalysis.[2,4] With a solid superacid catalyst, the need for sulfuric acid (or other acids) can be eliminated, which also results in ease of workup. The catalyst can simply be separated, at the end of the reaction, by filtration. Further, one of the main problems with nitrations using nitric acid–sulfuric acid mixtures is that the nitration produces a molar equivalent of water, which causes dilution of the acid. Consequently, only a small portion of nitric acid is utilized during the reaction as the rate of nitration slows down considerably upon dilution. It is therefore highly desirable to remove water during the course of nitration with nitric acid. We have carried out Nafion-H-catalyzed nitrations both with concentrated and fuming nitric acid under conditions of azeotropic removal of water. It was thus possible to utilize nitric acid to a much larger degree than under conventional conditions of nitration.

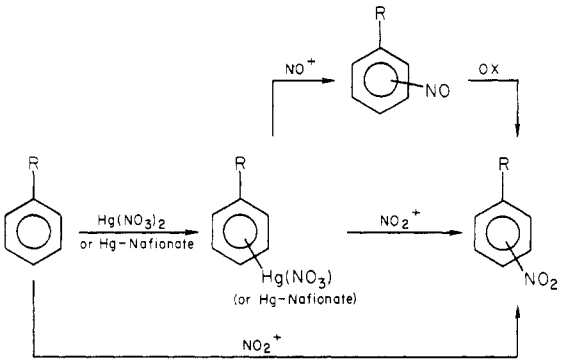
It is highly desirable in aromatic nitration to be able to change the obtainable isomer ratios of products from those obtained in conventional acid-catalyzed nitrations. One of the reported methods, in extension of similarly known effects in sulfonation,[5] is the nitration of aromatics with nitric acid in the presence of mercury(II) salts. Recently Stock has investigated in detail such nitrations in solution.[6,7] These nitrations provide isomer ratios significantly different from those obtained in the absence of mercury salts. It seemed, however, of interest to try to extend the scope of such nitrations by developing a catalytic method for mercury-promoted nitration.

Table I. $Hg^{2+}$-Promoted Nitrations of Aromatics over Nafion-H Catalyst

| substrate | yield,[a] % | isomer (distribution, %) |
|---|---|---|
| benzene | 71 | |
| toluene | 67 | 2-nitro (33), 3-nitro (7), 4-nitro (60) |
| ethylbenzene | 66 | 2-nitro (38), 3-nitro (5), 4-nitro (44), acetophenone (13) |
| *tert*-butylbenzene | 72 | 2-nitro (11), 3-nitro (17), 4-nitro (72) |
| *o*-xylene | 56 | 3-nitro (33), 4-nitro (67) |
| *m*-xylene | 48 | 2-nitro (11), 4-nitro (89) |
| chlorobenzene | 59 | 2-nitro (37), 3-nitro (2), 4-nitro (61) |
| bromobenzene | 76 | 2-nitro (44), 4-nitro (56) |
| naphthalene | 77 | 1-nitro (97), 2-nitro (3) |

[a] Yields are based on the amount of nitric acid.

Scheme I




## Results and Discussion

In continuation of our studies of the development of new nitration methods, we report now on the mercury(II)-impregnated Nafion-H-catalyzed nitration of aromatics with nitric acid under conditions of azeotropic removal of water.

Nitration of various aromatic substrates was carried out with concentrated nitric acid (70%) over Nafion-H catalyst in the presence of mercuric nitrate (20% by weight with respect to Nafion-H). The reactions were carried out under conditions of azeotropic removal of water. Table I summarizes the results of present study.

The yields of nitro aromatics (Table I) vary substantially. This is due to the fact that part of the nitric acid distills over in the form of binary and ternary azeotropes (which can be, however, reused if needed upon concentration). Further nitric acid also undergoes some decomposition under the reaction conditions, liberating nitrous gases. As the water formed is removed azeotropically from the reaction vessel, the catalyst (mercury-impregnated Nafion-H)[8] can be recovered without loss of activity and reused. The mercury(II) ion partly is bound to the acidic Nafion resin (Nafion-Hg) but is also soluble in the nitric acid layer. Regardless of this, under the azeotropic conditions of water removal the mercury salt is not removed, and the Nafion-H impregnated with $Hg^{2+}$ stays catalytic.

The function of the superacidic Nafion-H catalyst is to promote the formation of $NO_2^+$ from nitric acid. The

(1) For part 49, see: Olah, G. A.; Narang, S. C.; Olah, J. A. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 3298.
(2) Olah, G. A.; Malhotra, R.; Narang, S. C. *J. Org. Chem.* **1978**, *43*, 4628.
(3) Nafion is the trade name of Du Pont Co. for a commercially available perfluorinated resin sulfonic acid. The active H form was generated as described earlier.[2]
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(5) The mercury-promoted sulfonation of polycyclic aromatics is a well-recognized industrial process. For a discussion, see: Cerfontain, H. "Mechanistic Aspects in Aromatic Sulfonation and Desulfonation"; Interscience: New York, 1968; p 37.
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(7) Stock, L. M.; Wright, T. L. *J. Org. Chem.* **1979**, *44*, 3467.
(8) Any aqueous washing of the catalyst removes the mercury salt and regenerates Nafion-H without any loss of activity.

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Table II. Nitration over Nafion-H Catalyst with and without Mercury Promotion

| substrate | products | % isomer distribution: Nafion-H | % isomer distribution: Nafion-H/$Hg(NO_3)_2$ |
|---|---|---|---|
| toluene | 2-nitro | 56 | 33 |
| | 3-nitro | 4 | 7 |
| | 4-nitro | 40 | 60 |
| ethylbenzene | 2-nitro | 44.7 [a] | 43 |
| | 3-nitro | 2.0 | 6 |
| | 4-nitro | 53.3 | 51 |
| *o*-xylene | 3-nitro | 45 | 33 |
| | 4-nitro | 55 | 67 |
| chlorobenzene | 2-nitro | 38 | 37 |
| | 3-nitro | 1 | 2 |
| | 4-nitro | 61 | 61 |
| bromobenzene | 2-nitro | 45 | 44 |
| | 4-nitro | 55 | 56 |
| naphthalene | 1-nitro | 98 | 97 |
| | 2-nitro | 2 | 3 |
| *tert*-butylbenzene | 2-nitro | 18 | 11 |
| | 3-nitro | 11 | 17 |
| | 4-nitro | 71 | 72 |

[a] Results of $HNO_3/H_2SO_4$ nitration.[13]

Table III. Mercuration of Aromatics with Mercuric Trifluoroacetate[9]

| ArH | isomer distribution, % ortho | meta | para |
|---|---|---|---|
| toluene | 20.6 | 6.4 | 73.0 |
| ethylbenzene | 2.3 | 3.5 | 94.2 |
| isopropylbenzene | 0.6 | 5.4 | 93.9 |
| *tert*-butylbenzene | 0 | 8.4 | 91.6 |
| fluorobenzene | 27.6 | 0.2 | 72.2 |
| chlorobenzene | 27.3 | 0.1 | 72.6 |
| bromobenzene | 18.7 | 1.7 | 79.6 |

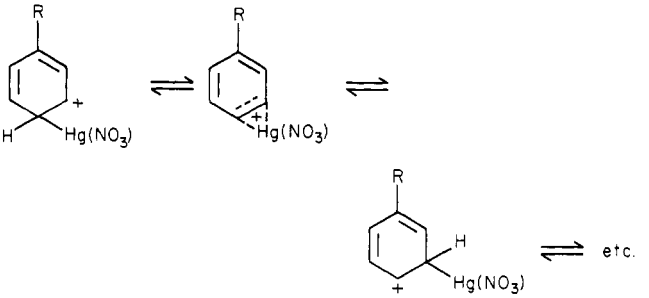
source of the unusual isomer distribution lies in the mercury(II) salt. In the absence of Nafion-H, mercuric nitrate still promoted nitration of toluene with 70% nitric acid, giving the same regioselectivity but in much lower yield, because the system without a strong acid catalyst is ineffective for nitration.

The nitroarenes are formed under the reaction conditions both by direct nitration (catalyzed by Nafion-H) and by nitrodemercuration[9] (or nitrosodemercuration–oxidation[7]) of initially formed arylmercuric nitrates (or surface arylmercuric Nafionates, Scheme I). Nitrodemercuration regenerates the mercuric nitrate (or Nafionate) which reenters the catalytic cycle.

The isomer distributions of Nafion-H-catalyzed nitrations of aromatics[2] and those obtained in the present study are summarized in Table II. The increased selectivity toward the formation of para-substituted and thus less hindered nitroarenes in the present study clearly indicates that at least in part the products are formed through the intermediacy of arylmercuric nitrate (or Nafionate). Mercuration of aromatics is well-known to be more selective[10] in forming para, and thus less hindered, arylmercuric products (Table III). Thus, the isomer distribution of the nitroarenes formed by nitrodemercuration should reflect the isomer distribution in mercuration.

Comparisons of Tables II and III indeed show similar trends but also some substantial differences (due obviously to direct electrophilic nitration).

The increased amount of meta isomer in the case of toluene, ethylbenzene, and *tert*-butylbenzene is another indication for the involvement of nitrodemercurative nitration. Not only is aromatic mercuration reversible, with the rates of ortho/para reversion greatly exceeding that of meta isomer, which thus builds up, but facile mercury shifts in arenemercurinium ions also were previously demonstrated in our studies under stable long-lived-ion conditions.[11] Both processes (inter- and intramolecular) increase the percentage of meta isomer in arylmercuration which is subsequently reflected in the nitrodemercuration products, i.e., nitroarenes.




It is interesting to reflect on the observed results in the case of ethylbenzene. Whereas attempted azeotropic nitration of ethylbenzene with nitric acid over Nafion-H catalyst gives only side-chain oxidation, yielding acetophenone,[12] the mercury(II)-promoted nitration over Nafion-H gives only 13% of side-chain oxidation. Thus, at least in this case, all the nitroethylbenzenes seem to be produced through nitrodemercuration.

Although the regioselectivity in the present study is increased toward the para and thus less hindered isomer, the isomer distributions do not parallel closely the isomer distributions of related mercuration. This is because direct elecrophilic nitration catalyzed by Nafion-H competes, at least to some extent, with demercurative nitration. The balance of the two competing paths will depend upon the relative reactivity of the specific aromatic toward mercuration vs. direct nitration. The observed isomer distributions reflect this competition. The differences in isomer distribution between mercuration and nitrodemercuration are probably due to the facile mercury shifts in arenemercurinium ions.

## Experimental Section

Nitric acid, mercuric nitrate, aromatic substrates, and their nitro derivatives were commercially available and were used as such without further purification. The products were analyzed by gas–liquid chromatography and by $^1H$ NMR with a Varian XL-200 superconducting NMR spectrometer.

The general procedure for nitration was as follows. A mixture of Nafion-H (500 mg) and mercuric nitrate (100 mg) in 70% nitric acid (8 mL) was stirred at room temperature for 1 h. The aromatic substate (25 mL) was added, and the reaction mixture was heated under reflux with the use of a Dean–Stark trap until no nitrate ion could be detected in the reaction mixture. (In the case of naphthalene, methylene chloride was used as a solvent.) The reaction mixture was then filtered while hot, and the solid residue

(9) Although Stock et al.[6,7] showed that mercury-catalyzed nitrations proceed through nitrosation–oxidation requiring a stoichiometric ratio of 2:1 between nitric acid and the arene, higher that 50% yields of nitroarenes (Table I), particularly in the case of ethylbenzene (vide infra), in the present study indicate that at least part of the products is formed by nitrodemercuration.

(10) Olah, G. A.; Hashimoto, I.; Lin, H. C. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 4121.

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(12) Olah, G. A.; Krishnamurthy, V. V.; Narang, S. C., unpublished results.

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was washed with diethyl ether. Product nitroarenes were isolated by careful distillation of the filtrate. The solid catalyst, after being washed with ether, was dried in air and could be reused.

**Acknowledgment.** Support of our work by the U.S. Army Office of Research is gratefully acknowledged.

**Registry No.** Benzene, 71-43-2; nitrobenzene, 98-95-3; toluene, 108-88-3; 1-methyl-2-nitrobenzene, 88-72-2; 1-methyl-3-nitrobenzene, 99-08-1; 1-methyl-4-nitrobenzene, 99-99-0; ethylbenzene, 100-41-4; 1-ethyl-2-nitrobenzene, 612-22-6; 1-ethyl-3-nitrobenzene, 7369-50-8; 1-ethyl-4-nitrobenzene, 100-12-9; acetophenone, 98-86-2; *tert*-butylbenzene, 98-06-6; 1-(1,1-dimethylethyl)-2-nitrobenzene, 1886-57-3; 1-(1,1-dimethylethyl)-3-nitrobenzene, 23132-52-7; 1-(1,1-dimethylethyl-4-nitrobenzene, 3282-56-2; 1,2-dimethylbenzene, 95-47-6; 1,2-dimethyl-3-nitrobenzene, 83-41-0; 1,2-dimethyl-4-nitrobenzene, 99-51-4; 1,3-dimethylbenzene, 108-38-3; 1,3-dimethyl-2-nitrobenzene, 81-20-9; 1,3-dimethyl-4-nitrobenzene, 89-87-2; chlorobenzene, 108-90-7; 1-chloro-2-nitrobenzene, 88-73-3; 1-chloro-3-nitrobenzene, 121-73-3; 1-chloro-4-nitrobenzene, 100-00-5; bromobenzene, 108-86-1; 1-bromo-2-nitrobenzene, 577-19-5; 1-bromo-4-nitrobenzene, 586-78-7; naphthalene, 91-20-3; 1-nitronaphthalene, 86-57-7; 2-nitronaphthalene, 581-89-5; isopropylbenzene, 98-82-8; 1-isopropyl-2-nitrobenzene, 6526-72-3; 1-isopropyl-3-nitrobenzene, 6526-74-5; 1-isopropyl-4-nitrobenzene, 1817-47-6; fluorobenzene, 462-06-6; 1-fluoro-2-nitrobenzene, 1493-27-2; 1-fluoro-3-nitrobenzene, 402-67-5; 1-fluoro-4-nitrobenzene, 350-46-9; mercuric nitrate, 10045-94-0; Nafion-H, 63937-00-8.

# *Communications*

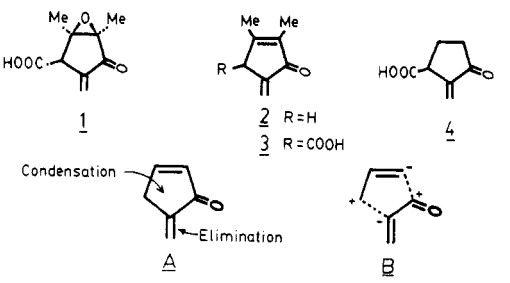
## Novel Route to α-Methylene Cyclopentenones. High-Yield Synthesis of Methylenomycin B

*Summary:* α-Methylenecyclopentenones were conveniently synthesized from the methyl acrylate–anthracene adduct, an α-methylene carbonyl equivalent.

*Sir:* Methylenomycin A (1) and B (2)[1] deepoxy-4,5-didehydromethylenomycin A (3)[2], and the related sarkomycin (4)[3] (see Chart I) were isolated from the culture broth of *Streptomyces* species and belong to a family of "cyclopentenoid antibiotics".[4] As a result of their interesting biological activities, total syntheses of these compounds have been accomplished.[5] These syntheses invariably involve two compulsory steps: the construction of the cyclopentenone ring and subsequent formation of the *exo*-methylene group via an elimination reaction (structure A). We now report a new approach to a short and high overall yield synthesis of α-methylenecyclopentenones as depicted in structure B. Construction of the desired bonds, a three-carbon annelation program, was achieved by reacting a propene unit with a masked α-methylene carbonyl function as illustrated in Scheme I. (See Table I for melting point and yield data).

The anion derived from the known ester adduct **5**[6] was alkylated with allyl halide [LDA, in THF/HMPA (10:1)] to give directly the product **6** (78–98% isolated yield).[7]

Chart I




Scheme I

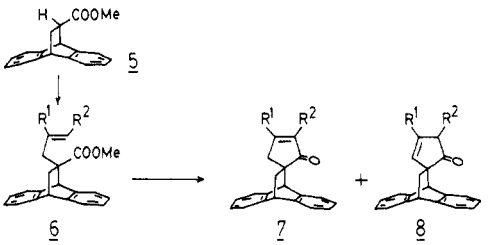



Table I

| | substituents | mp, °C 7 | mp, °C 8 | ratio of 7/8 | % yield |
|---|---|---|---|---|---|
| a | $R^1 = R^2 = Ph$ | 213[a] | | 1:0 | 92 |
| b | $R^1$ = Me; $R^2$ = Ph | 226.5[b] | | 1:0 | 93 |
| c | $R^1$ = H; $R^2$ = Ph | 210[a] | | 1:0 | 68 |
| d | $R^1$ = H; $R^2$ = *m*-OMe-$C_6H_4$ | 157–158[c] | | 1:0 | 70 |
| e | $R^1 = R^2$ = Me | 148[b] | see text | | |
| f | $R^1$ = Me; $R^2$ = H | 156–157[b] | 159[b] | 1:1 | 87 |
| g | $R^1 = R^2$ = H | 170–171[b] | 132–133[b] | 1:1.2 | 82 |

[a] From EtOH. [b] From $CH_2Cl_2$/hexane. [c] From $CCl_4$.

The allylic ester was then cyclized[8] by using LDA in THF/TMEDA (4:1) at room temperature overnight.[9]

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(7) We thank Miss Srisuthtiprut, Mrs. Poochaiwattananon, and Mrs. Udcharchon for spectroscopic, mass spectral, and analytical services.

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