Aromatic Substitution. 43. Perfluorinated Resinsulfonic Acid Catalyzed Nitration of Aromatics[1]

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Alkylbenzenes are nitrated in high yields with butyl nitrate or acetone cyanohydrin nitrate catalyzed by a perfluorinated resinsulfonic acid (Nafion-H) catalyst. The reactions are very clean and do not require any aqueous basic workup. Nitrations were also carried out with nitric acid, under azeotropic distillation conditions to remove water and thus prevent dilution of the acid, and with dinitrogen tetroxide.

Introduction of a nitro group into an aromatic ring is usually carried out via an electrophilic aromatic substitution using nitric acid, its metal salts, mixed anhydrides, and nitrate esters catalyzed by sulfuric acid.[2-5] Lewis acid catalysts have also been used in nitration.[2-5] All of these methods require subsequent aqueous basic workup. The use of solid acid catalysts in nitration is limited to a recent report[6] by Kameo, Nishimura, and Manabe on the use of polystyrenesulfonic acid catalysis in the nitration of aromatics with nitric acid.

Recently, we have studied electrophilic aromatic substitutions catalyzed by Nafion-H, a perfluorinated resinsulfonic acid. These studies have included alkylation,[7] aroylation,[8] and halogenation.[9]

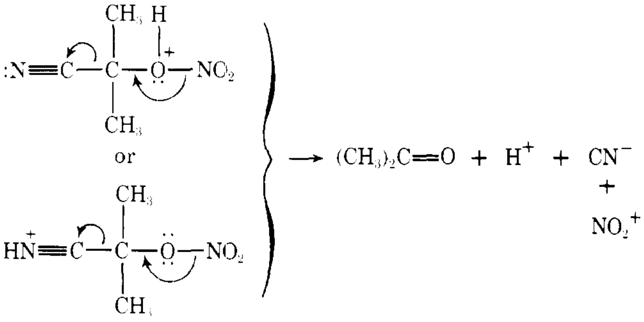
In a preliminary form, we have also reported the Nafion-H[10] catalyzed nitration of alkylbenzenes with *n*-butyl nitrate.[11] The unusual isomer distribution of the product nitroarenes and the limited range of reactivity have prompted us to study the reaction in detail and to also examine the reactivity of other nitrating agents under similar solid superacid-catalyzed conditions in order to define the scope and limitations of the method.

Results and Discussion

Nitration with *n*-Butyl Nitrate. Benzene and alkylbenzenes are nitrated in excellent yield with *n*-butyl nitrate at around 80 °C in the presence of solid Nafion-H acid catalyst. The reaction does not proceed at room temperature and is generally slow for preparative purposes at lower temperatures.

The reaction is very selective. Dinitro compounds are not formed in any significant amounts. The steric bulk of the solid acid complexed nitrating agent seems to play a significant role in determining the isomer distribution of products. Generally, a decreased amount of the more hindered isomer (ortho) is formed compared with conventional electrophilic solution reactions, thus increasing the selectivity of nitration at the less hindered (para) position (Table I).

Nitration with Acetone Cyanohydrin Nitrate (ACN). Acetone cyanohydrin nitrate (ACN) was previously used in the Lewis acid catalyzed nitration of alkylbenzenes.[5] ACN is more reactive than ordinary alkyl nitrates because of the greater ease of O–N bond cleavage in the intermediate O- or N-protonated ACN. Increase in entropy makes the cleavage of ACN very favorable.



The Nafion-H catalyzed nitration of deactivated aromatics with *n*-butyl nitrate gives only very low yields. Even nitration of chlorobenzene, for example, gave only 15% of chloronitrobenzenes (Table I). Due to the greater reactivity of ACN, we expected with its use to obtain higher yields of nitro compounds in the case of deactivated aromatics. As the data summarized in Table II show, nitration of alkylbenzenes with ACN gives the corresponding nitro compounds in good to moderate yield, with the nitration of chlorobenzene showing an improved 49% yield (as contrasted with 15% with butyl nitrate). The yields are not as high as we had expected. Although the yields increase somewhat with time, the isomer ratios remain the same. This may be due to the thermal decomposition of ACN at the needed reaction temperatures necessary for effective catalysis by Nafion-H.

The ortho–para ratio of nitrotoluenes obtained is lower (0.94) with ACN than with butyl nitrate (1.06), reflecting the somewhat larger bulk of the former reagent.

Azeotropic Nitration with Nitric Acid. While carrying out nitrations of alkylbenzenes with fuming nitric acid, the rate of reaction slows down with time. This is due to water produced in the reaction mixture which dilutes the nitric acid. In preparative nitrations, consequently, a large excess of nitric acid is needed, with much of the acid being wasted because of its dilution. It was, therefore, of interest to study the Nafion-H catalyzed nitration of aromatics with fuming and concentrated nitric acid under conditions of azeotropic removal of water.

Both fuming and concentrated nitric acid were found to be equally effective. The nitrations were carried out by heating the reaction mixture to reflux and azeotropically distilling off the water–aromatic mixture until no remaining nitric acid could be detected in the reaction mixture. The yields of nitro aromatics, however, vary to a large extent (Table III) depending upon the nature of the aromatic substrate. It thus seems indicated that part of the nitric acid also distills over in the form of a binary or ternary azeotrope. Further, nitric acid also undergoes some decomposition under the reaction conditions, liberating nitrous gases. The azeotropic nitration conditions are, however, somewhat more forcing than those with *n*-butyl nitrate and ACN, allowing to nitrate, for example, nitrobenzene to *m*-dinitrobenzene in 9% yield, whereas the former two systems gave no significant amount of *m*-dinitrobenzene.

Nitration with Dinitrogen Tetroxide. Aromatics have been nitrated with N_2O_4 in the presence of either BF_3[12] or concentrated sulfuric acid.[13] The ionic nitrations proceed through a nitronium ion complex $NO_2^+BF_4^-$ mixed with $NO^+BF_4^-$.[2] On the other hand, free-radical nitration of aromatics with N_2O_4 has also been carried out under UV irradiation.[14] It was of interest to determine how effective the

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Table I. Nitration of Aromatics with *n*-Butyl Nitrate over Nafion-H Catalyst

aromatic	registry no.	yield, %	registry no.	isomer distrubution (%)
benzene	71-43-2	77	98-95-3	
toluene	108-88-3	96	88-72-2	2-nitro (50)
			99-08-1	3-nitro (3)
			99-99-0	4-nitro (47)
o-xylene	95-47-6	98	83-41-0	3-nitro (47)
			99-51-4	4-nitro (53)
m-xylene	108-38-3	98	81-20-9	2-nitro (12)
			89-87-2	4-nitro (88)
p-xylene	106-42-3	95	89-58-7	2-nitro (100)
mesitylene	108-67-8	90	603-71-4	2-nitro (100)
1,2,4-trimethylbenzene	95-63-6	94	52414-96-7	3-nitro (8)
			610-91-3	5-nitro (92)
1,2,3,4-tetramethylbenzene	488-23-3	93	42887-62-7	
anisole[a]	100-66-3	86	91-23-6	2-nitro (32)
			100-17-4	4-nitro (68)
chlorobenzene	108-90-7	15		

[a] Some demethylation occurred under the reaction conditions.

Table II. Nitration with ACN over Nafion-H Catalyst

substrate	yield, %	isomer distribution (%)
benzene[a]	85	
toluene	79 (89[b])	2-nitro (47)
		3-nitro (3)
		4-nitro (50)
o-xylene	60	3-nitro (44)
		4-nitro (56)
m-xylene	61 (75[b])	2-nitro (11)
		4-nitro (89)
p-xylene	61	
mesitylene	36	
1,2,3,4-tetramethylbenzene	69	
chlorobenzene	49	2-nitro (28)[c]
		3-nitro (2)[d]
		4-nitro (70)[e]

[a] The temperature of the reaction mixture in this case was 80 °C. [b] Reaction continued for 24 h. [c] Registry no., 88-73-3. [d] Registry no., 121-73-3. [e] Registry no., 100-00-5.

Table III. Azeotropic Nitration with Fuming Nitric Acid over Nafion-H Catalyst

substrate	yield, %	isomer distribution (%)
benzene	77	
toluene	80	2-nitro (56)
		3-nitro (4)
		4-nitro (40)
o-xylene	47	3-nitro (45)
		4-nitro (55)
m-xylene	68	2-nitro (15)
		4-nitro (85)
p-xylene	60	
mesitylene	79	
chlorobenzene	87	2-nitro (38)
		3-nitro (1)
		4-nitro (61)
nitrobenzene[a]	9	

[a] Registry no., 99-65-0.

Table IV. Nitration with Dinitrogen Tetroxide over Nafion-H Catalyst

substrate	isomer distribution (%)
toluene	2-nitro (49)
	3-nitro (6)
	4-nitro (45)
o-xylene	3-nitro (41)
	4-nitro (59)
m-xylene	2-nitro (16)
	4-nitro (84)

Nafion-H catalyzed reaction also would be to effect electrophilic nitration.

When we nitrated alkylbenzenes with N_2O_4 in the presence of Nafion-H at 0 °C, nitration under these conditions was slow, thus rendering it unsuitable for preparative purposes. In general, solid acid catalysts are rather ineffective at such low temperatures. The isomer ratios of nitroarene products (Table IV), however, show that the products are obtained via typical electrophilic aromatic substitution. However, in addition to nitroarenes, products of side chain substitution were also obtained. Thus, for example, nitration of toluene with N_2O_4 provided, in addition to the three isomeric nitrotoluenes, significant amounts of phenylnitromethane and benzaldehyde. Phenylnitromethane could arise either via a free-radical pathway[15] or through ipso substitution in an electrophilic mechanism as illustrated in Scheme I. Similar formation of quinonoidal-type intermediates has been postulated before[16] to explain the side chain substitution in nitrations with acetyl nitrate.

We obtained phenylnitromethane only in the case of nitration with N_2O_4, in which NO_2 is always present in equilibrium with undissociated N_2O_4. On the other hand, formation of a quinonoid intermediate is quite likely in this sytem because NO_2^- is a good nucleophile that can capture the ipso Wheland intermediate, thus leading ultimately to phenylnitromethane.

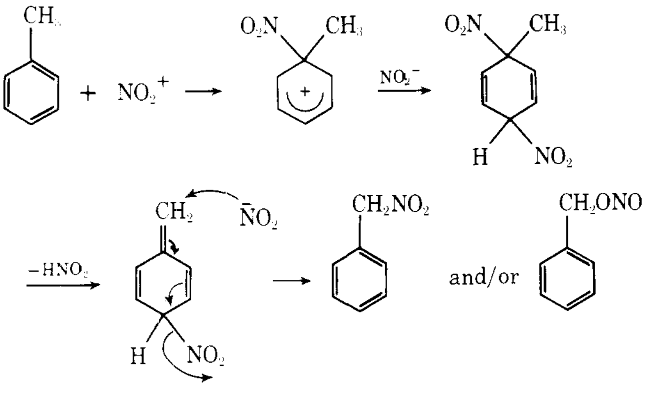
Formation of benzaldehyde can also occur by two different pathways: (a) by the Nef reaction of phenylnitromethane under the reaction conditions, and (b) by thermal decomposition of phenylnitromethane. Both pathways have been observed previously in the nitration of toluene with acetyl nitrate.[17] A somewhat larger than usual amount of *m*-nitrotoluene (6%) formed in N_2O_4 nitration of toluene indicates that the free-radical pathway may be to a limited degree concurrent also in the ring nitration with the electrophilic pathway.

Table V. Isomer Distribution in Nitration of Toluene

reagent	solvent	isomer ratio, % ortho	meta	para	ortho/para
$NO_2^+BF_4^-$ [a]	sulfolane	66	3	31	2.13[1]
HNO_3	CCl_4	53	3	44	1.20[1]
HNO_3/Nafion-H	toluene	56	4	40	1.40
N_2O_4/Nafion-H	CCl_4	49	6	45	1.09
n-butyl nitrate/Nafion-H	toluene	50	3	47	1.06
ACN/Nafion-H	toluene	47	3	50	0.94

[a] Homogeneous nitration; all other reactions were heterogeneous.

Scheme I



Conclusions

Preparative nitrations with *n*-butyl nitrate and ACN provide the cleanest method yet known for nitrations of aromatics. All of the byproducts are volatile organic materials. Nitro compounds can, therefore, be isolated simply by filtration of the catalyst, without the need of any aqueous basic washing or workup.

In the nitrations with *n*-butyl nitrate, ACN, and nitric acid over Nafion-H catalyst, on occasion small amounts of unexpected isomeric nitro compounds were also observed. These can be explained by the fact that alkylbenzenes themselves can undergo isomerization under the reaction conditions. However, these side reactions with proper choice of conditions remain minimal.

In all of the nitrations studied over the solid superacidic catalyst, there is a definite trend of the isomer ratios. For toluene, the more hindered *o*-nitrotoluene is formed in the following decreasing order by the different nitrating agents: nitric acid > *n*-butyl nitrate > dinitrogen tetroxide > ACN (Table V).

The low yield of nitromesitylene obtained in the nitration of mesitylene with ACN also reflects the relative bulkiness of the nitrating agent, as there is no alternative unhindered ring position available for nitration. It is thus indicated that the bulk of the Nafion-H complexed nitrating agent influences both isomer ratios of nitroarene products as well as overall yields of increasingly crowded aromatics.

Experimental Section

All solvents, fuming nitric acid, methyl nitrate, butyl nitrate, benzaldehyde, phenylnitromethane, aromatic substrates, and their nitro derivatives were commercially available highest purity materials and were purified by the usual methods before use. Acetone cyanohydrin nitrate was prepared from acetone cyanohydrin by the method of Freeman and Shepard.[18] The products were analyzed by gas–liquid chromatography as described previously.[4,17]

General Procedure for Nitration. (a) With *n*-Butyl Nitrate. A mixture of the corresponding aromatic (5 mL), *n*-butyl nitrate (2 g), and Nafion-H catalyst (500 mg) was heated at 80 °C for 6 h. The reaction mixture was then filtered while hot, and the solid residue was washed with chloroform (2 × 5 mL). Product nitroarenes were isolated by careful distillation of the filtrate.

(b) With ACN. A mixture of the corresponding aromatic (20 mL), acetone cyanohydrin (1.3 g, 10 mmol), and Nafion-H catalyst (500 mg) was heated at 110–120 °C for about 8 h. A trap containing anhydrous K_2CO_3 and acetone was used to absorb the HCN. The reaction mixture was worked up as above.

(c) With Nitric Acid. A mixture of the aromatic substrate (25 mL), fuming nitric acid (5.0 g) or an equivalent amount of concentrated nitric acid, and Nafion-H catalyst (500 mg) was heated under reflux using a Dean-Stark apparatus. Heating was continued until no nitrate ions could be detected in the reaction mixture. The reaction mixture was then worked up as described above.

(d) With Dinitrogen Tetroxide. A mixture of the aromatic substrate (5 mL), liquid dinitrogen tetroxide (1 g), and Nafion-H catalyst (500 mg) in carbon tetrachloride (10 mL) was stirred in the dark at room temperature for 1 h. The reaction mixture was then worked up by filtration, washing with water, aqueous sodium carbonate, and brine. The organic extract was dried over anhydrous magnesium sulfate and analyzed by GLC.

The sodium carbonate extract was neutralized with hydroxylamine hydrochloride (to pH 6.5) and extracted with ether. The ethereal layer was dried over anhydrous magnesium sulfate. Evaporation of the solvent gave phenylnitromethane identical with an authentic sample by IR, NMR, and GLC.

Benzaldehyde and phenylnitromethane were also detected in the original reaction mixture by ^1H NMR before workup.

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Registry No.—Nitric acid, 7697-37-2; dinitrogen tetroxide, 10544-72-6; butyl nitrate, 627-05-4; acetone cyanohydrin nitrate, 40561-27-1.

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