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Regioselective Nitration of Aromatic Hydrocarbons by Metallic Nitrates on the K10 Montmorillonite under Menke Conditions

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Aromatic hydrocarbons are nitrated with good regioselectivities by clay-supported cupric nitrate in the presence of acetic anhydride. The procedure commends itself by its simplicity and gives useful yields (75-98%). In each case, the predominant product can be predicted by consideration of the Hückel HOMO for the aromatic ring.

Whenever one considers electrophilic aromatic nitrations,$^{1)}$ the living fossil metaphor is well-nigh irresistible : the use of agressive sulfo-nitric mixtures, the frequent presence of numerous side products (polynitration, oxidation), the near statistical distribution of ortho and para ring-nitrated products, the oftentimes mediocre yields all conspire to give the reaction an archaic air. This was the challenge we opted to address. The present work follows earlier reports of the renovation of electrophilic nitration of both activated$^{2-3)}$ and deactivated$^{4)}$ aromatics, using as reagents metallic nitrates supported on montmorillonite clays.$^{5-7)}$

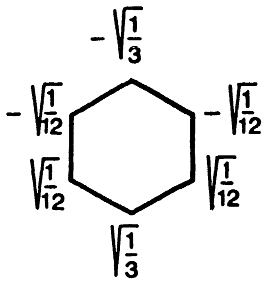
We report elsewhere$^{8)}$ a systematic investigation of the various reaction parameters (nature of the metallic nitrate; temperature; solvent; concentration) for nitration of a normally-activated aromatic hydrocarbon, taking toluene as a probe substrate. Here, we maintain constant these parameters, and we do the complementary study of structural variation in the hydrocarbon to be nitrated.

Let us set briefly the argument for the reaction conditions that were selected. One way of achieving regioselectivity is to put the reaction under orbital control$^{9)}$ with the predominant product arising from interaction of the frontier MO's. Aromatic hydrocarbons are rather soft Lewis bases.$^{10)}$ Since orbital control takes over, with respect to the competing charge control, in a soft-soft situation, the prescription is to use as soft a reagent as possible. Thus, we opted for "claycop" (clay-supported cupric nitrate$^{11-12)}$ because copper(II) is a relatively soft Lewis acid. A related choice was that of an auxiliary ligand : it is well known that the hard-soft character of a ligand modifies that of a Lewis acid or base. We elected the soft delocalized acetate anion for this purpose, and decided therefore to do the nitration in the presence of acetic anhydride, under what are known as Menke conditions:(13) there would be two other advantages in the presence of acetic anhydride, the soaking-up of excess humidity in order to maintain high the activity of the K10 montmorillonite support,(6) and the presence in the reaction medium of acetyl nitrate, well-known as a nitrating reagent.(1)

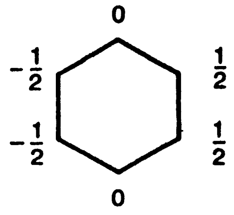
Our working mechanistic hypothesis is the scheme originally championed by Perrin(14) and more recently upheld by Kochi,(15) of the intermediacy of radical cations $ArH^{+\cdot}$ coupling with nitro radicals $NO_2^{\cdot}$ to form the Wheland intermediate. The $ArH^{+\cdot}$ species, we conjecture, would arise from oxidation of the aromatic hydrocarbon by copper(II); and covalent metallic nitrates -- such as anhydrous cupric nitrate -- are prone to decompose with formation of nitro radicals.(5)

This need not be the sole reaction path : especially under Menke conditions the reaction would be expected to have a hybrid character with a transition state along the continuum between the classical ($ArH + NO_2^{+}$) and the Perrin ($ArH^{+\cdot} + NO_2^{\cdot}$) descriptions. The nature of the main product does not allow to distinguish between these two descriptions, if one assumes identical coefficients for the atomic orbitals in the MO's for the neutral hydrocarbon and for the radical cation : the only difference is the lifting of the degeneracy in the Π^* MO's of bent $NO_2^{\cdot}$, in linear NO_2^{+} whose singly-occupied MO is lower in energy.

Turning now to the frontier MO's for the aromatic hydrocarbon, we consider the symmetric (S) and the antisymmetric (A) pair, degenerate in benzene, with the indicated coefficients :



S



A

Any substituent will lift the degeneracy of these A and S orbitals. Take the case of toluene. The methyl group is an electron donor. It will go to the site of least (unpaired) electron density : that with a zero coefficient in the A orbital, thus stabilizing the A state with respect to the S state. The latter becomes the frontier MO. Hence, the nitro electrophile -- and again whether this is $NO_2^{\cdot}$ or NO_2^{+} leads to the same prediction -- will go for the position of maximum electron density, C-4 where it is 1/3 rather than the positions with a 1/12 density. Para nitration should be dominant, as it indeed is (Table 1). A similar rationale holds for o-xylene. The two methyl groups stabilize more the S state than they do the A state : there is less electron density at C-2 and C-3 in the former (2/12) than at C-1 and C-2 in the latter (1/4). The A state becomes the frontier. Hence, a nitro electrophile will attack a position with 1/4 electron density, para to one of the substituents, in agreement with observation (Table 1). For m-xylene, again, the methyl donors stabilize the S state, and the A state thus becomes the frontier. The electrophile ought to prefer a position, ortho to one of the methyl groups, as it does (Table 1).

The reaction conditions are two hours reaction time, the substrate serves as its own solvent, and the reactions are run at room temperature. The preparation of "claycop" is as follows : K10 clay (30 g) is added to a solution of copper(II) nitrate trihydrate (28 g) in acetone (375 mL). The resulting suspension is placed in a rotary evaporator and the solvent is eliminated under reduced pressure (water jet aspirator) on a water bath at 50 °C. After 30 min, the dry solid crust adhering to the walls of the flask is flaked off with a spatula, ground to a powder, and evaporation is resumed for another 30 min in the same conditions, giving "claycop" as a light blue, free-flowing powder; yield : ≅ 58 g. The relative amounts of "claycop" and of acetic anhydride are 5 g and 5,1 g for each run consisting of 50 mL of the hydrocarbon to be nitrated. The isolated yields are 75-98%, based on the cupric nitrate introduced.

Table 1. Results for Selected Aromatic Hydrocarbons

Hydrocarbon $R-C_6H_5$ R=	Predicted major product	Regioselectivity[a)]	$HNO_3 + Ac_2O$ (homogeneous)[b)]
CH_3	4:obs.	2.6	0.33
C_2H_5	4:obs.	5.2	0.56
n-C_3H_7	4:obs	4.9	-
s-C_3H_7	4:obs.	11.9	1.17
n-C_4H_9	4:obs.	3.8	0.50
s-C_4H_9	4:obs.	11.9	-
t-C_4H_9	4:obs.	21.5	3.07
xylenes :			
1,2-	4:obs.	1.5	
1,3-	4:obs.	4.0	
naphthalene	1:obs.	10.0	

a) Corrected for statistical factors wherever necessary. b) Literature results : J. Chem. Soc., 1931, 1959 ; 1960, 4885 ; J. Am. Chem. Soc., 84, 3687 (1962).

Indeed, the regioselectivity in the nitration of naphthalene points to a mechanism which, while having a radical cationic component, is not a limiting radical cation mechanism.[16)] The regioselectivities obtained (Table 1) are rather impressive, improving in general upon earlier performances from the literature. They can be further improved, as indicated for the toluene case in another communication.[8)] In no case did we observe more than 2% of the meta isomer. Neither do we find polynitration nor oxidation products.

Finally, the dominant role of acetic anhydride appears to be that of an acid anhydride : of the drying agents $CaSO_4$, $MgSO_4$, silicagel, $CaCl_2$, P_2O_5, and Ac_2O, only the last two give non-zero (54 and 60% respectively) conversions after 22 h of reaction. Likewise, the K10 acidic montmorillonite is a far superior support to microporous solids, such as alumina or silica.

To sum-up : once more rational design has shown its worth, good yields and impressive selectivities are achieved.

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