HETEROCYCLES, Vol 28, No 2, 1989

ELECTROPHILIC AMINATION. DIRECT PRIMARY AMINATION OF ARENES USING PHTHALIMIDE DERIVATIVES

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Abstract– Electrophilic primary amination of arenes has been achieved by the thermolysis or photolysis of N-sulfonyloxyphthalimide in the presence of trifluoromethanesulfonic acid or of 1-phthalimido-2,4,6-triphenylpyridinium tetrafluoroborate in the presence of CF_3CO_2H. The diacylnitrenium **10** was probably formed in the latter case. The structure of one of the byproducts, **7** was established by single crystal X-ray analysis.

The direct amination of arenes (replacement of H by NR_2) has received increasing attention in recent years,[1] but relatively few general methods have been developed. Electrophilic primary amination has been achieved using chloramines,[2a] hydroxylamine/$AlCl_3$,[2b] hydroxylamine-O-sulfonic acid/$AlCl_3$,[2c] hydrazoic acid/$AlCl_3$,[2d] and lately N-aminopyridinium salts.[2e] Electrophilic arylamination has been achieved using aryl azides/$AlCl_3$ (and a proton source),[3] and N-arylaminopyridiniums.[4] Aminations using trichloramine and $AlCl_3$ actually involve attack of a chlorobenzenonium cation by an amine anion equivalent.[5] Free-radical primary amination of arenes was effected using hydroxylamine and Ti^{3+} or NH_2OSO_3H and Fe^{2+},[6] or by photolysis of N-tosyloxyphthalimide.[7]

We now report some preliminary studies on the generation of the phthalimide cation. In the expection that protonation of N-sulfonyloxyphthalimides (1) would occur at sulfonyl oxygen and thus produce a good leaving group (the sulfonic acid) and a diacylnitrenium ion we have studied[8] the thermolysis and photolysis

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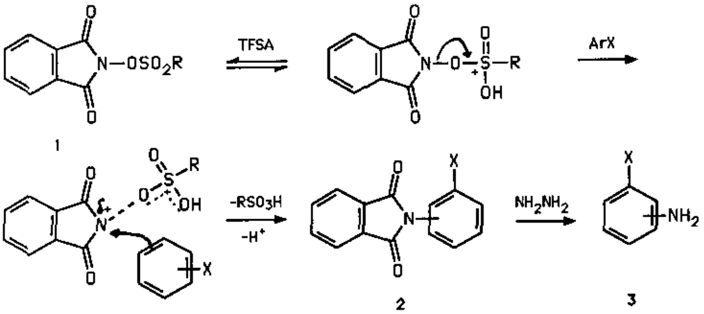
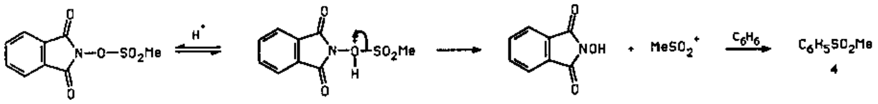
Dedicated to Prof. Sir Derek Barton in honor of his 70th birthday.

of 1 in arene solvents in the presence of acids (for the sake of comparison we also studied the decomposition in the absence of acid using Cadogan's conditions[7]). For quantitative analysis of yields and isomer ratios the phthalimides 2 were heated with hydrazine hydrate and the anilines 3 analyzed by g.l.c. The results are summarized in Table 1. We were unable to reproduce the high yields of anisidides reported.[7] The isomer ratios obtained suggest that products 2 are formed by attack of C_6H_5X by an electrophilic species, but that a free nitrenium ion is not formed. The results are more in accord with a concerted process, the transition state of which varies with the nature of the leaving group, substrate, and reaction conditions (quantity of acid, mode of decomposition). In the one case where products other than 2 were analyzed (C_6H_6, N-mesyloxyphthalimide) aniline and phthalic acid (hydrolysis of 2, R=H) were found, as well as methyl phenyl sulfone (**4**). This latter may arise by protonation of the oxygen attached to N, followed by heterolysis, to yield $CH_3SO_2^+$.



Scheme 1



In earlier work we developed a method of generation of aryloxenium ions from N-aryloxypyridiniums,[9] and have extended it to the formation of N-acyl-N-arylnitrenium ions under neutral conditions from 1-(N-acetyl-N-aryl)amino-2,4,6-triphenylpyridinium tetrafluoroborates.[4] We now describe a further extension to the generation of diacylnitrenium ions and aromatic substitution by these species.

Table 1. Decomposition of 1 in C_6H_5X in the presence of CF_3SO_3H

R in 1	TFSA (equiv.)	conditions(h)	X in C_6H_5X	yield of 2 (%)	*o* :	*m* :	*p*
p-C_6H_4Me[7]	0	hν(20)	H	18[7]		--	
p-C_6H_4Me[7]	0	hν(20)	OCH_3	100[7]	55	3	42
p-C_6H_4Me	0	hν(48)	OCH_3	19	55	3	42
d[7]	0	Δ(36-48)	OCH_3	60[7]	56	7	37
p-C_6H_4Me	0	Δ(48)	OCH_3	4	66	3	31
p-C_6H_4Me	0.5	Δ(48)	OCH_3	6	60	3	37
p-C_6H_4Me	0.5	hν(48)	OCH_3	13	71	2	27
CH_3	1	Δ[a] (96)	H	13[b]		--	
CH_3	3	Δ[a] (96)	H	6[c]		--	
CH_3	0.5	Δ(48)	OCH_3	8	74	0	26
CH_3	0.5	hν(48)	OCH_3	48	61	4	35
2,4,6-$Me_3C_6H_2$	0.5	Δ(48)	OCH_3	17	13	3	84
2,4,6-$Me_3C_6H_2$	2	Δ(48)	OCH_3	17	25	5	70
2,4,6-$Me_3C_6H_2$	5	Δ(48)	OCH_3	14	34	1	65
2,4,6-$Me_3C_6H_2$	0.5	hν(48)	OCH_3	28	38	10	52
2,4,6-$Me_3C_6H_2$	2	hν(48)	OCH_3	12	58	10	32
2,4,6-$Me_3C_6H_2$	5	hν(48)	OCH_3	21	33	1	66

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[a] Sealed tube, 120°C. [b] Aniline (8.5%), phthalic acid (6.7%) and methyl phenyl sulfone (22%) were also formed. [c] Aniline (17%), phthalic acid (8%), and methyl phenyl sulphone (31%) also formed. [d] *N*-Chlorosulfonylphthalimide was used as the source of phthalimido radicals generated thermally.

1-Phthalimido-2,4,6-triphenylpyridinium tetrafluoroborate (**5**), mp 285-286°C (from the pyrylium and *N*-aminophthalimide and boiling methanol), was thermolyzed in mesitylene and hexafluoroisopropanol at 180°C to give *N*-mesitylphthalimide (**6**), mp 178-179°C (42.8%). Thermolysis of **5** in degassed mesitylene-trifluoroacetic acid (3:1 v/v) at 180°C for 60 h gave **6** (9.5%), together with 2,4-diphenyl-6-(*o*-phthalimidophenyl)pyridine (**7**), mp 216-217°C (8.5%) and 2,4-diphenyl-6-(*p*-phthalimidophenyl)pyridine (**8**), mp 220-222°C (traces). In all cases, 2,4,6-triphenylpyridine (**9**) was also isolated. The structures of **7** and **8** were consistent with their spectral and analytical data and that of **7** was confirmed by

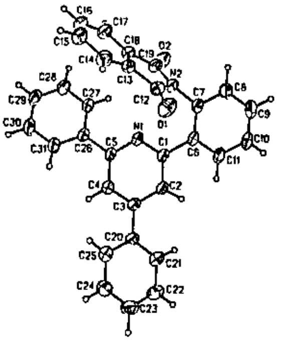
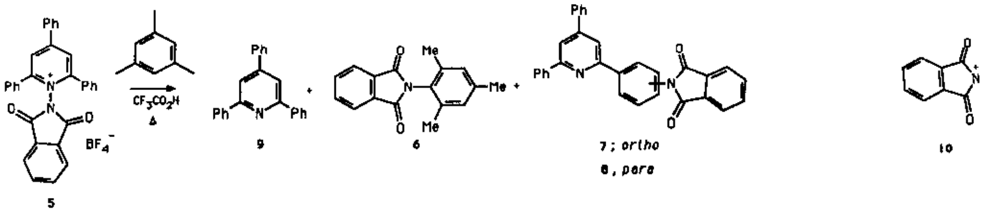


Fig. 1 ORTEP diagram of **7**

a single crystal X-ray analysis (Fig.1).[10]



Photolysis (2537Å) of **5** in mesitylene containing CF_3CO_2H (degassed)(N_2 atmosphere) at room temperature proceeded very cleanly to give **6** (62.6%), together with **7** (10%) and **8** (0.2%). On the other hand, similar photolysis in benzene/CF_3CO_2H did not give any **2** (X=H), only **7** (25.7%) and **8** (12.6%) being obtained in addition to **9** (60.6%). When, however, **5** was photolyzed in a large volume of benzene containing small amounts of equal parts of CF_3CO_2H and $(CF_3)_2CHOH$, **2** (X=H) was obtained in 32% yield, together with **7** (but no **8**). Finally, photolysis of **5** in anisole containing $CF_3CO_2H/(CF_3)_2CHOH$ (1:1 v/v) gave **2** (X=OCH_3)(mainly <u>o</u>- and <u>p</u>-) (71.6%).

Thermolysis of 1-(<u>N</u>-acetyl-<u>N</u>-aryl)aminopyridinium salts gives <u>N</u>-acyl-<u>N</u>-arylnitreniums,[4] and photolysis of 1-amino-2-methyl-4,6-diphenylpyridiniums in the presence of TFA also produces nitrenium ions.[2e] It is likely, therefore, that the thermolysis and photolysis of **5** also lead to the diacylnitrenium (**10**). Depending on the solvent and reaction conditions this can diffuse away from the pyridine and be trapped by the arene or the 2-phenyl group in **9** (the fact that <u>para</u>-isomer **8** is formed suggests an intermolecular process in these cases). If the solvating power of the medium is insufficient the nitrenium is trapped internally before it can diffuse away (C_6H_6/CF_3CO_2H in the absence of

$(CF_3)_2CHOH$). When **8** is not observed then intramolecular trapping of the phthalimido group by the 2-phenyl cannot be ruled out. Competing inter- and intramolecular reactions are also a possibility.

These results, though preliminary, show that such reactions have promise as convenient methods of generating acylnitrenium ions under mild conditions. Studies are under way to eliminate byproduct (**7** & **8**) formation, to improve the yields of direct amination products, and to determine the mechanism of the reaction.

ACKNOWLEDGEMENTS

We thank the National Science Foundation for partial support (to R. A. A.) of this work.

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10. **Crystallographic data for 7:** $C_{31}H_{20}N_2O_2$, triclinic crystal, space group $P\bar{1}$ (#2) with a = 7.9921(26), b = 11.6779(34), c = 12.9772(34)Å, α = 96.842(22)°, β = 105.199(23)°, γ = 99.509(24)°, V = 1135.7(6)Å^3, d_{calc} = 1.32g/cm^3. Data obtained on a Nicolet R3mV diffractometer with graphite-monochromated MoK radiation. Of 4339 reflections collected, 4027 were unique (R_{int}= 0.023). The least squares refinement was based on 3096 observed reflections ($I > 3\sigma(I)$), ω-2θ scan mode for 2$\theta \leq 50$. The structure was solved by direct methods, R_f= 0.0371, R_w= 0.0488.

Received, 2nd September, 1988