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PRELIMINARY NOTE

Synthesis and Some Reactions of Mono(bistrifluoromethylamino-oxy)benzenes; Formation and Rearrangement (Meisenheimer) of Phenylbis(trifluoromethyl)amine Oxide

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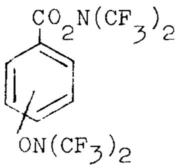
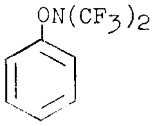
Except for derivatives (I) produced by attack of bistrifluoromethyl nitroxide (II) on (bistrifluoromethylamino-oxy)-carbonylbenzene [1], mono(bistrifluoromethylamino-oxy)arenes of the hydrocarbon class are conspicuously absent from the host of $(CF_3)_2NO$-substituted organic compounds reported in the literature. After failing to prepare the parent compound III via treatment of benzene with the nitroxide (II) [2,3], attention was turned to development of methods of synthesis for bistrifluoromethylamino-oxybenzenes based on the hydroxylamine IV or its sodium salt (V) as reagents.



(I) p- and m- or o-isomers

$(CF_3)_2NO\cdot$

(II)



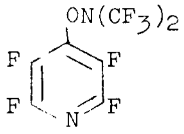
(III)

$(CF_3)_2NOH$

(IV)

$(CF_3)_2NO^- Na^+$

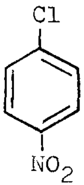
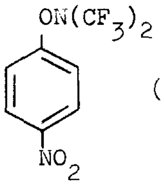
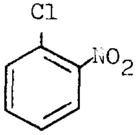
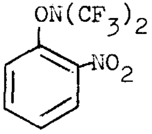
(V)

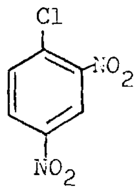
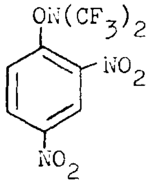
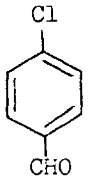
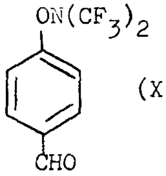


(VI)

TABLE

Synthesis of mono(bistrifluoromethylamino-oxy)benzenes from chlorobenzenes and $(CF_3)_2NO^-Na^+$

Substrate (g, mmole)	$(CF_3)_2NO^-Na^+$ (g, mmole)	Conditions [solvent (cm^3)]	Product (% yield)
 (0.78, 4.95)	(3.82, 20.0)	2h, 100 °C [DMF (35)]	 (VII) (70)
 (2.63, 16.7)	(10.51, 55.0)	16h, 21 °C [DMF (30)]	 (VIII) (83)

 (2.84, 14.0)	(3.82, 20.0)	2h, 21 °C [Et_2O (30)]	 (IX) (100)
 (2.08, 15.0)	(5.18, 27.1)	3h, 80 °C [DMF (25)]	 (X) (16)[a]

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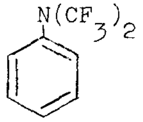
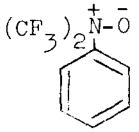
[a] The carbonyl compound _p_-$ClC_6H_4CO_2N(CF_3)_2$ (14%) was also obtained, presumably _via_ oxidation of $(CF_3)_2NO^-Na^+$ to $(CF_3)_2NO\cdot$ (_cf_. ref. 6) followed by radical attack on the aldehydic substrate [1].

In the fluorocarbon field, the salt V has been shown to effect nucleophilic substitution in pentafluoropyridine [4] to give the mono(bistrifluoromethylamino-oxy) derivative (VI); the salt was prepared in situ from NN-bistrifluoromethylhydroxylamine (IV) and powdered sodium hydroxide in THF in the presence of a molecular sieve to remove water, and the yield of (VI) was 28%. This (presumed) bimolecular S_NAr reaction has now been successfully extended to activated monochlorobenzenes, as shown in the Table; the sodium salt was prepared by treating the parent hydroxylamine with sodium hydride in the solvent subsequently employed in the halogen-displacement reaction [5].

Reaction of $(CF_3)_2NO^-Na^+$ with the iodonium bromide $Ph_2I^+Br^-$ in DMF at room temperature (12 h) provided the parent compound $PhON(CF_3)_2$ (III) in 34% yield, presumably via. an S_N1 mechanism. An alternative route to III, discovered during researches in another area [7], involves thermal decomposition of the azo-compound $PhN{=}NCPh_3$ in the presence of an excess of the nitroxide $(CF_3)_2NO\bullet$. A second alternative, based on the hydroxylamine $(CF_3)_2NOH$, was sought in the form of a trapping reaction involving benzyne generated from anthranilic acid and isoamyl nitrite; surprisingly, with boiling acetone-methylene chloride (1:3 v/v) as solvent and a 3 h reaction period, this gave only the known [8] compound bistrifluoromethylaminobenzene (XI) in 15% yield (after g.l.c. separation); with a shorter reaction period (1 h) in diethyl ether-carbon tetrachloride (1:4 v/v) the yield of XI fell to 1% and the novel amine oxide XII was isolated in 18% yield. The mechanism of this intriguing reaction is under investigation.

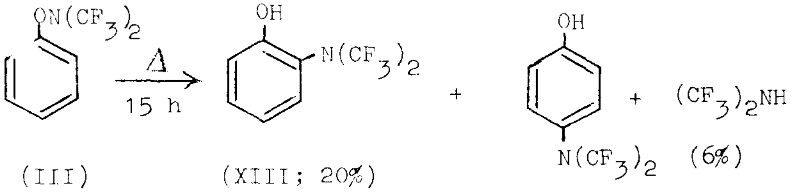


(XI)

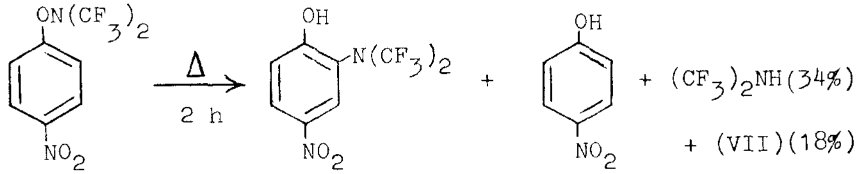


(XII)

Pyrolysis (105-110 °C) of the $(CF_3)_2NO$- substituted benzenes III and VII-X in Pyrex yields the amine $(CF_3)_2NH$, $(CF_3)_2N$-substituted phenols and tars, e.g.,

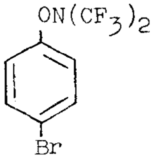


(III) (XIII; 20%) (XIV; ca. 25%)

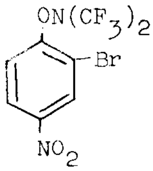


(VII) (XV; 13%) (34%)

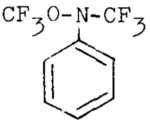
Electrophilic bromination of III (80 °C, 10 h) and VII (58 °C, 24 h; iron filings present) gave the monobromides **XVI** (56%) and **XVII**(36%), respectively.



(XVI)



(XVII)



(XVIII)

Phenylbis(trifluoromethyl)amine oxide (XII) (m.p. 41-42 °C) undergoes a Meisenheimer rearrangement [9] at 100 °C, giving its trifluoromethoxy-isomer (XVIII).

The structures of compounds III and VII—**XVIII were** established spectroscopically [i.r., n.m.r. (^{1}H and ^{19}F) and mass], and all these products except XVIII (which was not analysed) possessed correct elemental compositions.

1 R.E. Banks, D.R. Choudhury and R.N. Haszeldine, J.C.S. Perkin Trans. I, (1973) 80.

2 The literature contains conflicting reports on the susceptibility of benzene towards attack by $(CF_3)_2NO\cdot$ (II). Thus, while American investigators [W.D. Blackley and R.R. Reinhard, J. Amer. Chem. Soc., 87 (1965) 802] maintain that the nitroxide (II) is 'not affected chemically' by benzene, Russian workers, having noted evidence of a reaction during e.s.r. experiments [I.V. Miroshnichenko, G.M. Larin, S.P. Makarov and A.F. Videiko, Zhur. Strukt. Khim., 6 (1965) 776], claimed the slow (2-3 days at room temperature) formation of $(CF_3)_2NOH$ and material believed to be 1,2,4-tris(bistrifluoromethylamino-oxy)benzene [S.P. Makarov, A.F. Videiko, T.V. Nikolaeva and M.A. Englin, Zhur. obshchei Khim., 37 (1967) 1975]; except for a reasonable elemental analysis (C,H,F and N) and a molecular weight value (method not given), evidence for the identity of this tri-substituted benzene appears restricted to formation in unspecified yield of a derivative produced *via* hydrolysis (hot KOH aq.) and stated to be 1,2,4-trihydroxybenzene on the basis of a melting point (145 °C) which does not compare well with a literature value (141 °C [J. Böeseken, Rec. Trav. Chim., 34 (1915) 272]. The latter Russian paper also contains a claim (based on elemental analysis) that the nitroxide (I) attacks fluorobenzene at room temperature to yield a bis(bistrifluoromethylamino-oxy) derivative of unknown orientation.

3 In our hands (R.E. Banks, D.L. Connell, R.N. Haszeldine and G. Shaw) the nitroxide (I) attacks benzene at 21 °C to yield $(CF_3)_2NOH$, $(CF_3)_2NON(CF_3)_2$ and a complex, multi-component, salmon pink, unidentified oil [containing carbonyl compounds (i.r. analysis)] that does not yield 1,2,4-trihydroxybenzene when heated with 10% aqueous KOH.

4 R.E. Banks, R.N. Haszeldine and D.L. Hyde, Chem. Comm., (1967) 413.

5 This method of preparation of $(CF_3)_2NO^-Na^+$ was pioneered by R.E. Banks and R.A. Hughes.

6 Formation of bistrifluoromethyl nitroxide *via* treatment of *NN*-bistrifluoromethylhydroxylamine with hot sodium fluoride

has been noted previously [R.E. Banks, R.N. Haszeldine and M.J. Stevenson, J. Chem. Soc. (C), (1966) 901].

7 B.L Booth, R.N. Haszeldine and E.D. Kosinsky, unpublished work. The reaction was carried out in benzene and, not unexpectedly, gave III in poor yield.

8 F.S. Fawcett and W.A. Sheppard, J. Amer. Chem. Soc., 87 (1965) 4341.

9 J. Meisenheimer, Ber., 52 (1919) 1667; J. Meisenheimer, H. Greeske, and A. Willmersdorf, Ber., 55 (1922) 513. See T.S. Stevens and W.E. Watts, 'Selected Molecular Rearrangements', Van Nostrand-Reinhold, London, 1973, p. 98.