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N-TRIFLUOROMETHYL-N-NITROSOBENZENESULFONAMIDE A NEW TRIFLUOROMETHYLATING AGENT.

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N-Trifluoromethyl-N-nitrosobenzenesulfonamide was synthesized. It was demonstrated that it acted as a new trifluoromethylating agent.

Recently much attention has been denoted to trifluoromethyl group because of its physicochemical effects.1) Although there have been many investigations on the trifluoromethylation,2) little is known concerning the reagents for the displacement of hydrogens with trifluoromethyl groups. In most cases, trifluoromethyl iodide has been used as the reagent.2a,b,3) We now wish to report the synthesis of N-trifluoromethyl-N-nitrosobenzenesulfonamide (TNS-B) as a new trifluoromethylating agent

Based on our assumption that the compounds consisting of an eliminable heteroatom between a perfluoroalkyl group and a strong leaving group should act as perfluoroalkylating agents, we have previously synthesized (perfluoroalkyl)aryliodonium trifluoromethanesulfonates and demonstrated that they served as highly reactive electrophilic perfluoroalkylating agents 4) We intended to synthesize a new trifluoromethylating agent starting from trifluoronitrosomethane on the basis of the assumption.

It was reported that trifluoronitrosomethane reacted with hydroxylamine in methanol at low temperature (-75°C) to evolve nitrogen and trifluoromethyl methyl ether at elevated temperature (-55°C).5) We found that the nitrosomethane was allowed to react with hydroxylamine in DMF/THF/ether (4/5/1) at -75°C, followed by the treatment with a base in the coexistence of benzensulfonyl chloride at -75°C to produce TNS-B6) as a stable crystalline solid in a 57% yield.

$$CF_3NO \xrightarrow[-75^\circ C]{NH_2OH} [\ CF_3\text{-}N{=}N\text{-}OH\ ] \xrightarrow[t\text{-}BuOK]{PhSO_2Cl} \underset{\text{TNS-B}}{CF_3N(NO)SO_2Ph}$$

It was found that TNS-B became to be photochemically a good trifluoromethylating agent for aromatic compounds in the presence of biacetyl as a sensitizer. Irradiation of a solution of TNS-B, a substrate (1 eq), and biacetyl (1 eq) in a solvent using a Pyrex-tube under water bath-cooling with 400W high-pressure Hg lump gave the corresponding trifluoromethylated aromatic compounds in reasonable yields (Table 1). The reaction showed the behavior similar to the photochemical

Table 1. Trifluoromethylation with N-trifluoromethyl-N-nitrosobenzenesulfonamide

Run	Substrate[a]	Solv.	Time(h)	Product[b]	Yield(%)
1	Benzene(4 eq)	CH_3CN	5	Benzotrifluoride	24[c]
2	Naphthalene	"	5	CF_3-Naphthalene(α:β)	39[c] (6.3:1)[e]
3	Phenol	"	5	CF_3-Phenol(o:m·p)	51[c] (6:1:3.5)[e]
4	p-t-Butylphenol	"	5	2-CF_3-4-t-Butylphenol	59[c], 50[d]
5	p-Dimethoxybenzene	$(CH_3)_2CO$	5	2-CF_3-1,4-Dimethoxybenzene	54[d]
6	Pyrrole(2 eq)	CH_3OH	5	α-CF_3-Pyrrole	51[c]
7	$\{S\text{-}n\text{-}C_{10}H_{21})_2$	$(CH_3)_2CO$	6	$CF_3S\text{-}n\text{-}C_{10}H_{21}$	55[d]
8	$\{SCH_2COOH)_2$	"	14	CF_3SCH_2COOH	63[d]
9	$\{SCH_2CH_2COOH)_2$	"	3.5	$CF_3SCH_2CH_2COOH$	50[d]
10	$\{SCH_2CH_2\underset{NHCOCF_3}{CH}COOCH_3)_2$	"	7	$CF_3SCH_2CH_2\underset{NHCOCF_3}{CH}COOCH_3$	59[d]
11	$\{SCH_2CH(OAc)CH_2OAc\}_2$	CH_3CN	14	$CF_3SCH_2CH(OAc)CH_2OAc$	64[d]

a) One equivalent amount of a substrate to TNS-B was used except for Run 1 and 6 b) All products exhibited spectral data (^1H- and ^{19}F-NMR, IR, and Mass) in accord with the assigned structures or with the authentic samples c) ^{19}F-NMR yields d) Isolated yields e) Isomer ratios

reaction of trifluoromethyl iodide with aromatic compounds.[3b,c] However the method using TNS-B is favorable because of better yields and shorter reaction time, as well as easiness in handling crystalline TNS-B compared to gaseous trifluoromethyl iodide (bp -22.5°C).

TNS-B was also found to be a good reagent for the conversion of disulfides to trifluoromethylthio compounds under the same reaction conditions (Table 1). This new reaction presented a convenient synthetic approach to biologically active trifluoromethionine[7] from homocystine (Run 10). Thus, the hydrolysis of N-trifluoroacetyltrifluoromethionine methyl ester gave trifluoromethionine in a 75% yield.

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