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PRELIMINARY NOTE

A Facile Synthesis of α-Trifluorodiazo Compounds

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SUMMARY

A variety of α-trifluorodiazo compounds which can be used as building blocks for the construction of organic molecules bearing a trifluoromethyl group have been prepared in high yields simply by refluxing trifluoromethylketone 2,4,6-triisopropylbenzenesulphonylhydrazones with a methanolic solution of KOH For characterization, their triphenylphosphazine derivatives were prepared

Trifluoromethyl substitution imparts interesting properties to important organic materials such as bioactive compounds and ferroelectric liquid crystals [1, 2] An attractive method for introducing a CF_3 group into organic molecules is to use appropriate CF_3 containing intermediates as synthetic building blocks [2], but the development of this methodology has been hampered by either the abnormal reactivity* or the limited availability of trifluoromethylated building blocks Therefore, the search for new versatile building blocks from easily accessible fluorinated procursors has been of considerable significance for solving the inherent synthetic problem

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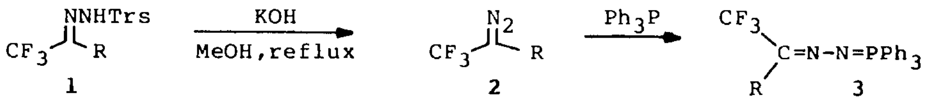
* For example, various α-trifluorocarbanions of otherwise synthetic importance, enolates in particular, are marred by their proclivity towards defluorination [3]

We have recently initiated a study to explore the chemical behavior of trifluoromethylketone arenesulphonylhydrazones under the Bamford-Stevens reaction conditions [4] with the aim of producing α-trifluorodiazo compounds[*] which could be potentially used as trifluoromethyl containing building blocks through their possible transformatioms via carbenoid intermediates[**]. Thus, the decomposition of trifluoromethylketone 2,4,6-triisopropylbenzenesulphonylhydrazone (trisylhydrazones) was studied and, to our satisfaction, the enhanced leaving ability of the trisyl group [7] and the stabilizing effect of the electron withdrawing trifluoromethyl group towards a diazo group [8] facilitated the production of α-trifluorodiazo compounds and did not incur concomitant decomposition of the diazo compounds thus formed[+].



Scheme 1

As shown in Scheme 1, when the trisylhydrazones **1** were treated with 2 equivalents of KOH in methanol[++] under reflux, they rapidly decomposed within a few minutes to give the desired diazo compounds **2** in almost quantitative yield (assayed by ^{19}F NMR). The products obtained from alkaline work-up were essentially free from impurities as indicated by spectroscopic

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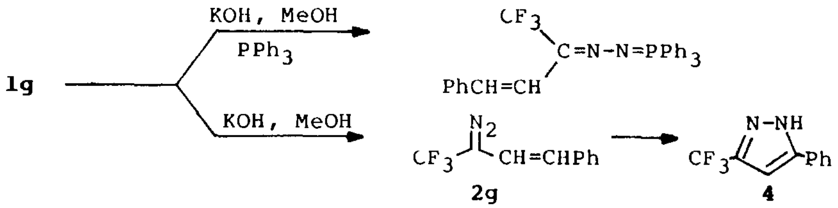
[*] Only very few α-trifluorodiazo compounds are known and their preparations resulted in low yields and impure products [5].

[**] There has been a report that α-trifluorodiazo compounds could react normally via carbene intermediate [6].

[+] Diazo compounds have been postulated as intermediates in the Bamford-Stevens reaction of aliphatic or alicyclic ketone hydrazones, but the only isolable products were usually compounds derived from their decompositions [4].

[++] Although the Bamford-Stevens reaction can be performed under various conditions (see ref. 4), we have found the present condition to be the most suitable and convenient.



TABLE

Trifluorodiazo compounds prepared from trisylhydrazones

Hydrazones[a] 1	Reaction[b] time (min)	Products[d] 2	Phosphazines[f] Yield[g], %	Phosphazines[f] m p, °C
R=		R=		
CH_3 **1a**	15[c]	CH_3 **2a**	73	135-136[h]
$CH_3(CH_2)_3$ **1b**	10	$CH_3(CH_2)_3$ **2b**	81	41-42
$CH_3(CH_2)_5$ **1c**	10	$CH_3(CH_2)_5$ **2c**	70	46-48
$PhCH_2$ **1d**	10	$PhCH_2$ **2d**	78	94-95
Ph **1e**	5	Ph **2e**	76	152-154
c-C_6H_{11} **1f**	10	c-C_6H_{11} **2f**	80	163-164
PhCH=CH **1g**	5	PhCH=CH[e] **2g**	82	160-161

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[a] Prepared by condensation of trifluoromethylketones [11] with an equal molar amount of trisylhydrazide in methanol containing a few drops of conc hydrochloric acid Yield, 75-93%

[b] Trisylhydrazone (2mmol) and KOH(ca 4mmol) in methanol (5ml) heated at refluxing temperature for a given time

[c] Reaction performed in a sealed tube at 60°C

[d] All products except **2g** which was unstable under the reaction condition have been fully characterized spectroscopically (IR, ^{19}F NMR, ^{1}H NMR and MS) and the elemental composition of their phosphazine derivatives was determined by combustion analysis

[e] Spontaneously cyclized to form **4**, m p 126-127°C

[f] For the preparation of phosphazines, see text

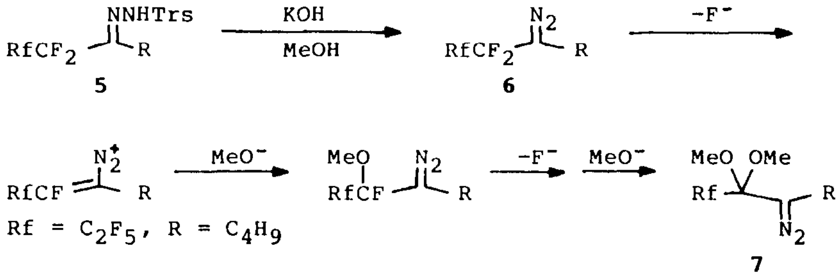
[g] Yields based on trisylhydrazones

[h] Lit [5a], 127-128 5°C

examination (^{1}H NMR, ^{19}F NMR and IR) and could be readily trapped by triphenylphosphine to afford the corresponding phosphazines [9] in high yield The results are summarized in the Table

All diazo compounds listed in the Table generally have reasonable thermal stability with the doubly stabilized one, **2e** , being the most stable Thus further purification for most of the diazo compounds, if necessary, is possible by short-path distillation under slightly reduced pressure using an aspirator Like most other α,β-unsaturated diazo compounds [10], compound **2g** lost its red color to form a pyrazole derivative **4** concomitant with the decomposition of the corresponding trisylhydrazone, however , it could be trapped *in situ* by Ph_3P to afford the corresponding phosphazine

Interestingly, when our method was extended to the preparation of a polyfluorodiazo compound **6** from heptafluoropropyl butyl ketone trisylhydrazone **5**, an α-defluorinated diazo compound **7** was obtained exclusively This unanticipated result revealed a general feature of compounds such as **6**, *i e* , the propensity towards defluorination, which can be rationalized by the process depicted in the following equation



In summary, we have developed a convenient preparative method for a variety of α-trifluorodiazo compounds In view of many transformations of synthetic importance that can be carried out with diazo compounds, inter alia, those catalyzed by transition metals [12], the ready access to these α-trifluorodiazo compounds may open a promising area for the synthesis of trifluoromethylated organic molecules Work along this line is in progress

In a typical experiment, a mixture of trifluoroacetophenone trisylhydrazone (2 mmol) and KOH (*ca* 4 mmol) in methanol (5 ml) was heated under reflux for 5 min Water (10 ml) was added and then three extractions with ether were carried out The extract was washed several times with saturated $NaHCO_3$ solution and dried over Na_2SO_4 Removal of the solvent in a rotary evaporator gave a fairly pure orange product **2e**, IR(neat) 2090 (C=N=N), 1140 (CF_3) cm^{-1}, ^{19}F NMR (CCl_4, δ TFA) -16 6 (downfield, s), ^{1}H NMR (CCl_4, δ) 6 97-7 40 (m), MS, m/z (relative intensity) 186 (18), 159 (100), 139 (22), 77 (11), 69 (20) For the preparation of phosphazine, a slight excess of Ph_3P was directly added to the ether extract After the orange color had faded completely (*ca* 30 min), the solvent was evaporated and the residue was recrystallized from petroleum ether to give colorless crystals in 76% yield, m p 152-154°C $C_{26}H_{20}F_3N_2P$ calcd C 69 62, H 4 46, N 6 25%, found C 69 46, H 4 41, N 6 24%

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