Ethyl 3-Trifluoro-2-diazo-propionate as a Potentially Useful CF_3-containing Building Block: Preparation and $[Rh(OAc)_2]_2$-Catalysed Reaction with Nitriles

Guoqiang Shi and Yuanyao Xu*

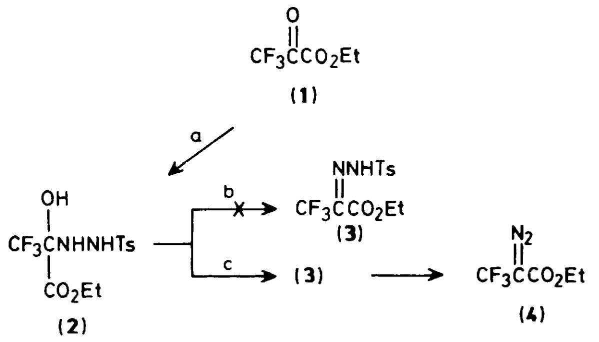
Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai, People's Republic of China

A novel CF_3-containing building block, ethyl 3-trifluoro-2-diazo-propionate, was easily prepared and reacted readily with nitriles in the presence of rhodium acetate to afford CF_3-substituted oxazoles.

Organic molecules bearing a CF_3 group have been drawing considerable attention because of their potential biological activities.[1] An attractive method for the preparation of these compounds is to prepare some versatile intermediates carrying a CF_3 group and utilize them as building blocks. In connection with this, a few methods have been developed, but in some cases their applicability still has much to be desired. For example, various CF_3-attached carbanions which would otherwise be of synthetic importance, enolates in particular, are marred by their proclivity towards defluorination[2] and their modified versions tend to have limited reactivities.[2,3]

In line with our search for new versatile CF_3-containing building blocks, our strategy has been to prepare appropriate α-trifluorodiazo compounds and utilize them as precursors for carbenoid intermediates which would enable us to synthesise a variety of trifluoromethylated molecules if their normal reactivities were ensured. For this purpose, the title compound (**4**) has been chosen, which we expect would be amenable to metal catalysed transformations.[4] Here we report the preparation of this novel diazo compound and initial studies on its rhodium catalysed decomposition.

For the preparation of (**4**), the Bamford–Stevens reaction of ethyl trifluoropyruvate tosylhydrazone (**3**) was contemplated.



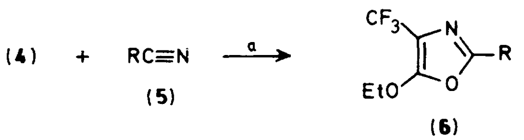
Scheme 1. a, NH_2NHTs, CH_2Cl_2; b, MeOH, HCl (cat.); c, Py, $POCl_3$. Ts = *p*-$MeC_6H_4SO_2$; Py = pyridine.

Ethyl trifluoropyruvate (**1**) can be easily prepared by a recently published Barbier procedure[5] [by careful control of the experimental conditions, (**1**) can be obtained in yields as high as 60%]. However, the formation of its tosylhydrazone (**3**) under usual conditions was deterred by the reluctance of the adduct (**2**) to dehydrate. However, we found that addition of a dehydrating agent such as $POCl_3$/pyridine can not only circumvent this problem but also effect the direct conversion of (**1**) to the desired diazo compound (**4**) in the presence of the organic base pyridine (Scheme 1). Thus, (**1**) (0.1 mol) and tosylhydrazide (0.1 mol) were mixed in CH_2Cl_2 (120 ml) and stirred overnight at room temperature. Pyridine (30 ml) was added and $POCl_3$ (0.1 mol) was added in such a rate that a gentle reflux was maintained. Workup and distillation gave (**4**) as a yellow liquid, 82% yield, b.p. 110 °C.

To demonstrate the synthetic utilities of (**4**), its decomposition in the presence of rhodium acetate and reaction of the carbenoid thus generated, with nitriles (Scheme 2) were examined.[6] As the results show, the carbenoid intermediate has normal reactivity and the presence of the fluorine substituent does not seem to be problematic as has been the case for its enolate counterpart where defluorination occurred.[2b]

As may be seen from Table 1, the reaction is applicable to a wide range of nitriles and the yields are invariably high. Therefore, this reaction can serve as a convenient route to CF_3-substituted oxazole derivatives emerging as a new kind of fluorine-containing herbicide.[7]

It is interesting to note that the reaction of (**5g**) (Table 1, entry 7) has afforded, besides the expected product (**6f**), a pair of isomers (**8**) possibly resulting from an unprecedented

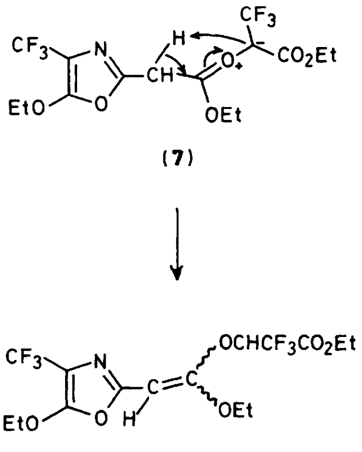


Scheme 2. a, 1 mol% $[Rh(OAc)_2]_2$, $CHCl_3$, reflux.

Table 1. Preparation of CF_3-substituted oxazoles (**6**).

Entry	Nitrile (**5**) R	Reaction[a] time/h	Product (**6**) R	Yield[b]/%	M.p./°C
1	Ph (**5a**)	6	Ph (**6a**)	89	54—56
2	4-ClC_6H_4 (**5b**)	5	4-ClC_6H_4 (**6b**)	92	56—58
3	$PhCH_2$ (**5c**)	6	$PhCH_2$ (**6c**)	86	oil
4	2-C_5H_5N (**5d**)	6	no reaction		
5	MeCH=CH (**5e**)	5	MeCH=CH (**6d**)	88	oil
6	Me (**5f**)	6	Me (**6e**)	80	oil
7	EtO_2CCH_2 (**5g**)	6	EtO_2CCH_2 (**6f**)	30	oil
			(**8**)[c]	65	oil

[a] 1.3 equiv. [for (**5a**—**b**)] or 2 equiv. [for (**5g**)] of (**4**) was used and added within a given period of time. [b] Isolated yield. Satisfactory spectral and microanalytical data were obtained for all new compounds. [c] Obtained as a pair of 1 : 1 geometric isomers.



(**7**)

(**8**)

intermolecular process: attack of an additional CF_3-carbenoid at the carbonyl oxygen of (**6f**) and subsequent abstraction of an acidic α-proton *via* the formation of an oxonium ylide (**7**).

In summary, we have obtained a novel α-trifluoro diazo compound and established its feasibility as a carbenoid precursor possessing normal reactivity. Based on the broad spectrum of chemical transformations of diazo compounds, *inter alia*, those catalysed by transition metals, a variety of other viable processes involving (**4**) should also be possible and, therefore, great potential exists for its further application in the synthesis of trifluoromethylated molecules.

We thank the National Natural Science Foundation of China and Academia Sinica for their financial support.

Received, 30th December 1988; 8/05007D

References

1 (a) R. Filler and Y. Kobayashi 'Biomedicinal Aspects of Fluorine Chemistry,' Kodansha, Tokyo, 1983; (b) J. T. Welch, *Tetrahedron*, 1987, **43**, 3123.

2 For examples, see: (a) F. G. Drakesmith, O. J. Stewart, and P. Tarrant, *J. Org. Chem.*, 1967, **33**, 280; (b) T. Fuchigami and Y. Nakagawa, *ibid.*, 1987, **52**, 5276 and references therein.

3 (a) T. Yokozawa, M. Nakai, and N. Ishikawa, *Tetrahedron Lett.*, 1984, **25**, 3991; (b) *ibid.*, 1984, **25**, 3987; (c) *Chem. Lett.*, 1987, 1971.

4 M. P. Doyle, *Chem. Rev.*, 1986, **86**, 919.

5 C. Francese, M. Tordeux, and C. Wakeselman, *Tetrahedron Lett.*, 1988, **29**, 1029.

6 R. Connel, F. Scavo, P. Helquist, and B. Åkermark, *Tetrahedron Lett.*, 1986, **27**, 5559.

7 (a) K. Burger, D. Huebl, and K. Geith, *Synthesis*, 1988, 194; (b) D. Heubl, M. Ganzer, F. Arndt, and R. Rees, Ger. Offen. DE 3614229 (1988), *Chem. Abstr.*, **109**, 124415c.