

Synthesis of *N*-(Perfluoro-*t*-butyl)pyrazoles from Hexafluoroacetone Azine by Trifluoromethyl Group Migration

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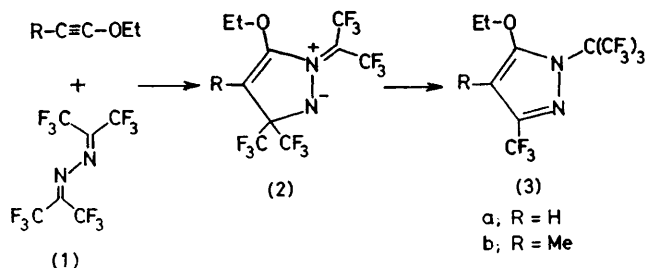
Summary The synthesis of 1-(nonafluoro-*t*-butyl)-3-trifluoromethylpyrazoles (**3**) from hexafluoroacetone azine (**1**) and alkoxyacetylenes is described; the reaction involves an azomethine imide intermediate which rearranges by apparent [1,4] migration of a trifluoromethyl group.

FLUORO-SUBSTITUTED heterocyclic systems are of current pharmaceutical interest;^{1,2} quite often they are biologically more active than their fluorine-free analogues.³ We report here a new method of selective simultaneous introduction of a trifluoromethyl and a perfluoro-*t*-butyl group into a pyrazole system.

Hexafluoroacetone azine^{4,5} reacts with carbon-carbon double bond as well as carbon-carbon triple bond systems to yield 1,5-diazabicyclo[3.3.0]octanes^{6,7} and 1,5-diazabicyclo[3.3.0]octa-2,6-dienes,⁸ respectively. The reaction was shown to proceed *via* a 1,3-dipolar intermediate,

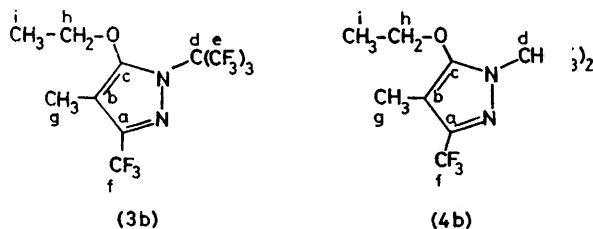
namely an azomethine imide^{7,9,10} which can be isolated in some cases.^{7,8b-11}

We now find that hexafluoroacetone azine (**1**) reacts with ethoxyacetylenes in a similar way to yield (**2**) which, in the



presence of dipolarophiles, can be trapped to give the expected [3+2]cycloadducts.¹² In the absence of trapping reagents, compounds (**2**) on prolonged standing at room temperature [to give (**3a**): 1–2 days] or even at 0 °C [to

give (3b): 4 weeks] rearrange to give 1-(nonafluoro-*t*-butyl)-3-trifluoromethylpyrazoles (3).† To our knowledge this is the first example of a rearrangement involving a trifluoromethyl group migration.



The structural assignment is based on spectroscopic data, (film) (3a): 1588, 1510, and 1475 cm^{-1} ; (3b): 1603 and 1477 cm^{-1} ; ^1H n.m.r. (CDCl_3 ; SiMe_4) δ (3a): 1.46 (3H, t, J 7.2 Hz), 4.25 (2H, q, J 7.2 Hz), 5.94 (1H, s); (3b) (3H, t, J 7.2 Hz), 2.14 (3H, br s), and 4.32 (2H, q, J 7.2 Hz); ^{19}F n.m.r. (CDCl_3 ; $\text{CF}_3\text{CO}_2\text{H}$) \ddagger δ (3a): -13.7 (3F, s) and -14.4 (9F, s); (3b): -14.2 (9F, s) and -14.3 (3F, s). Comparison of the ^{13}C n.m.r. data§ of compounds (3) with those of the 5-ethoxy-3-trifluoromethyl-1-[2,2,2-trifluoromethylethyl]pyrazoles (4) 13 confirms the presence of a pyrazole ring system (see Table), 14

† (3a): yield 52%; b.p. 70–71 °C at 12 Torr. (3b): yield 87%; b.p. 81 °C at 14 Torr. Satisfactory C, H, and N analyses were obtained ($\pm 0.3\%$).

‡ Recorded with a Jeol C60HL instrument operating at 100.645 MHz; trifluoroacetic acid was used as external standard.

§ Recorded with a Jeol FX100 instrument in CDCl_3 with SiMe_4 as internal standard.

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TABLE. ^{13}C Chemical shifts of compounds (3b) and (4b) (δ values in p.p.m. relative to $\text{Me}_4\text{Si} = 0$)

Carbon atom	(3b)	(4b)
a	143.7 (q, J 38 Hz)	143.7 (q, J 37 Hz)
b	100.9	99.3
c	155.7	153.4
d	74.3 (decet, J 31 Hz)	57.9 (septet, J 34 Hz)
e	120.8 (q, J 296 Hz)	121.0 (q, J 284 Hz)
f	121.4 (q, J 270 Hz)	121.4 (q, J 270 Hz)
g	7.3	6.9
h	70.9	71.7
i	14.9	15.2

The overall reaction (1 \rightarrow 2 \rightarrow 3) represents a selective introduction of a trifluoromethyl group into ring position 3 and of a perfluoro-*t*-butyl group into ring position 1 of a pyrazole ring system, starting from the readily accessible hexafluoroacetone azine (1). In contrast, the azomethine imides generated from (1) and ynamines even below room temperature rearrange to give 1,1,6,6-tetrakis(trifluoromethyl)-2,3-diazahexa-1,3,5-trienes quantitatively. 8b,10

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