



Cite this: *Org. Biomol. Chem.*, 2015, **13**, 5625

Received 27th March 2015,
Accepted 15th April 2015

DOI: 10.1039/c5ob00610d

www.rsc.org/obc

Simultaneous introduction of trifluoromethyl and λ^6 -pentafluorosulfanyl substituents using $\text{F}_5\text{S}-\text{C}\equiv\text{C}-\text{CF}_3$ as a dienophile[†]

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$\text{F}_5\text{S}-\text{C}\equiv\text{C}-\text{CF}_3$ can be easily prepared in high yields in two steps from 3,3,3-trifluoropropyne. It is a powerful, versatile dienophile in Diels–Alder reactions. Reactions at room temperature provide the corresponding products in up to quantitative yields allowing the introduction of the pentafluorosulfanyl group and trifluoromethyl group at the 1,2 position.

Since the discovery of the Diels–Alder reaction (DA) in 1928,¹ its value in organic chemistry as a perfect synthetic protocol towards the formation of six-membered rings has been continuously growing.² The use of this methodology has also been applied in modern medicinal, agrochemical and materials science.² It is well known that introducing fluorinated groups into organic molecules remarkably alters their physical, chemical and biological properties.³ As the CF_3 group is one of the most important substituents there are several reviews concerning its introduction including radical, nucleophilic and electrophilic reactions.⁴ The incorporation of the trifluoromethyl group *via* DA reactions produces new six-membered hetero- and carbocyclic compounds.⁵ In this matter, CF_3 -substituted alkynes are used instead of the corresponding dienes.

So far there exist no comparable protocols for the introduction of the pentafluorosulfanyl group, which possesses unique features, including high stability (chemical and thermal) and lipophilicity of SF_5 -substituted molecules.⁶ Because it is regarded as a larger version of the CF_3 group, the SF_5 group is very often referred to as a “super CF_3 ” group. In comparison with trifluoromethyl, the chemistry of SF_5 is still largely unexplored probably because of the limited availability of SF_5 -containing reagents.⁶ Therefore, new methods to introduce this group into organic molecules are challenging and highly required.

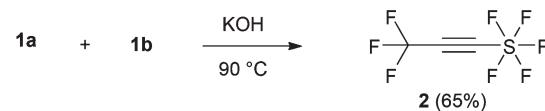
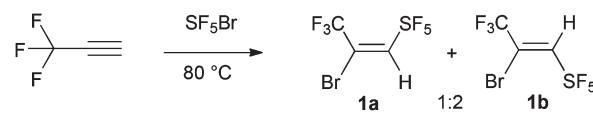
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† Electronic supplementary information (ESI) available: The experimental details and copy of ^1H , ^{13}C and ^{19}F NMR spectra. CCDC 1020179 and 1020180. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5ob00610d

Despite the significance of organofluorine chemistry, there are no reports of using a reagent that can introduce these two particularly interesting groups simultaneously. Thus, a suitable protocol that will give rise to substituted organic molecules with unique physical, biological and chemical properties is undoubtedly very important. We envisioned that 3,3,3-trifluoromethyl-1-pentafluorosulfanyl-1-propyne,⁷ $\text{F}_5\text{S}-\text{C}\equiv\text{C}-\text{CF}_3$ (2) would be the ideal reagent for this purpose (Scheme 1).

The synthesis of the dienophile (2) follows the literature protocol and involved the addition of SF_5Br to terminal CF_3 -alkyne (1) to form the alkenes **1a–b** as a mixture of *E/Z* isomers (1 : 2) (Scheme 1) in 80% yield.⁸ Carrying out the reaction in dry DCM or *n*-hexane at $-40\text{ }^\circ\text{C}$ and $-10\text{ }^\circ\text{C}$ in the presence of catalytic BET_3 as described by Dolbier *et al.*⁹ for other systems gave lower yields (47–50%, 1 : 1 ratio of *E/Z* isomers). A mixture of **1a–b** was subsequently treated with KOH resulting in the target alkyne (2) in 65% yield.⁷

Diphenylbenzoisofuran (3a) was chosen as a model substrate for the DA reaction. The progress of the reaction in dry DCM at room temperature was controlled by ^{19}F NMR spectroscopy. Within 1 h we observed 100% conversion of 2 towards the target product **4a** (Scheme 2). Lowering the reaction temperature to $-60\text{ }^\circ\text{C}$ results in a 50% conversion after



Scheme 1 Synthesis of the alkyne 2.



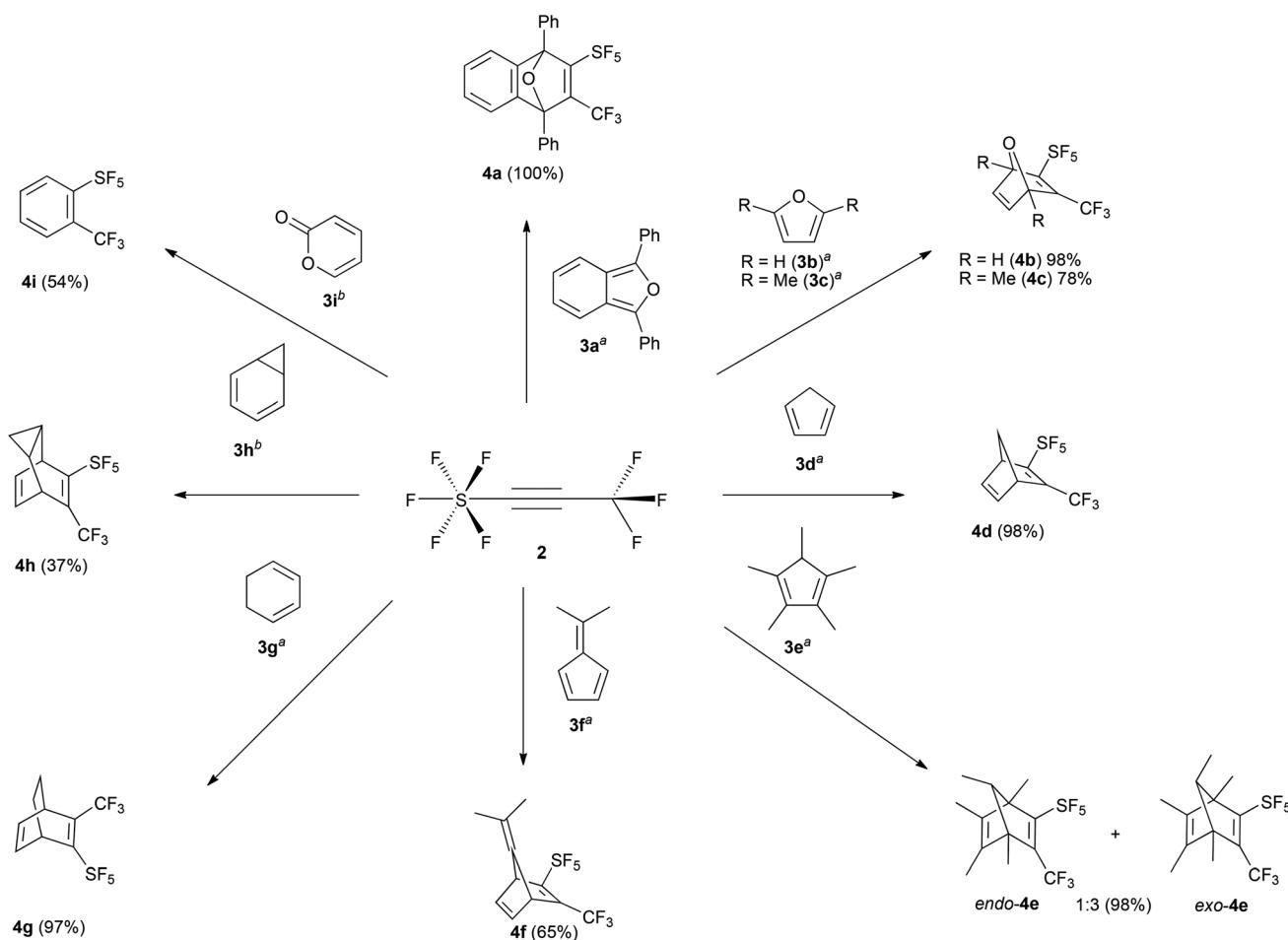
1 h. Screening of the reaction conditions, by using different solvents, revealed that this cycloaddition was not affected by the polarity of solvents. For instance, performing such a process in DCM and *n*-pentane gave comparable isolated yields within the same reaction time. Based on the ^{19}F NMR spectroscopic analysis no side-reactions occurred even when performing this process at elevated temperatures. The crude mixture was purified by flash column chromatography using DCM/*n*-pentane (1:2 v/v) as the eluent giving **4a** in almost quantitative yield. Compound **4a** was easily identified by ^{19}F NMR spectroscopy. The resonance of the trifluoromethyl group splits into a quintet ($^5J_{\text{FF(eq)}} = 12$ Hz) due to coupling with the four *cis* fluorine nuclei of the SF₅ group. As expected we observed a characteristic inversion of the axial and equatorial chemical shifts of the SF₅ group.¹⁰ With the reaction conditions established, **2** was then treated with selected dienes (Scheme 2), such as furan (**3b**), 2,5-dimethylfuran (**3c**), cyclopentadiene (**3d**), pentamethylcyclopentadiene (**3e**), 6,6-dimethylfulvane (**3f**), cyclohexa-1,3-diene (**3g**), and cyclohepta-1,3,5-triene, which is in equilibrium with **3h**. Apart from **4f**

and **4h** conversions and yields are excellent although due to steric hindrance longer reaction times can be required.

The ^1H NMR spectrum of **4d** exhibits a doublet at δ 2.09 ($^2J_{\text{HH}} = 7$ Hz) and a doublet of quintets at 2.37 ($^2J_{\text{HH}} = 7$ Hz, $^5J_{\text{HF(eq)}} = 1$ Hz) (see the ESI†) for the chemically inequivalent protons of the *-CH₂* group. The regiochemistry of the *endo* and *exo*-**4e** was determined by ^1H NMR spectroscopy. The bridged C–H proton shows characteristic splittings: for *exo*-**4e** the resonance is split into a quartet with a coupling constant of $^3J_{\text{HH}} = 6$ Hz; whereas for *endo*-**4e** we observed a quartet of quintets ($^3J_{\text{HH}} = 6$ Hz, $^5J_{\text{HF(eq)}} = 1$ Hz) due to additional coupling to the four equatorial fluorine nuclei of the SF₅ group.

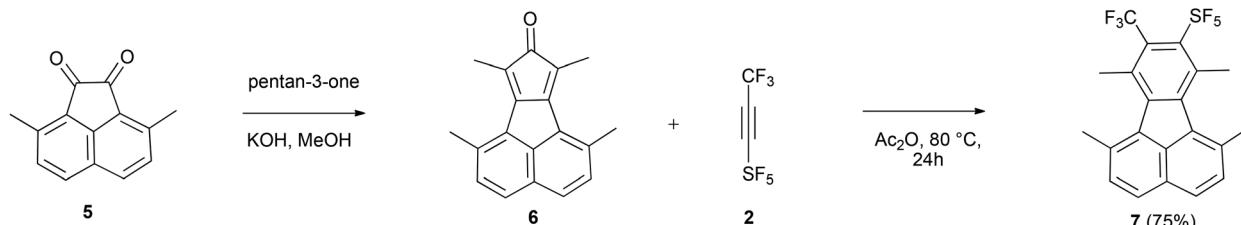
The ratio of *endo*/*exo*-**4e** depends on the reaction temperature; at ambient temperature the isomers are formed in a 1:3 ratio whereas at -40 °C a 1:1 ratio is obtained. Thus we can conclude that *endo*-**4e** is kinetically favored due to less steric hindrance in the transition state.

Cyclopentadienones and 2*H*-pyran-2-ones (**3i**) are ideal precursors for the synthesis of substituted aromatic compounds by Diels–Alder reaction with an alkyne in one step. The latter reacted with **2** in toluene at 110 °C affording a benzene ring



Scheme 2 Diels–Alder reaction of **2** with selected dienes. Reaction conditions: (a) **2** (1 mmol), **3a**–**g** (1.2 mmol), DCM (or *n*-pentane) 5 mL, RT, 3 h; (b) **2** (1 mmol), **3h**–**i** (1.2 mmol), PhMe 5 mL, 110 °C, 24 h.





Scheme 3 Synthesis of fluoranthene 7.

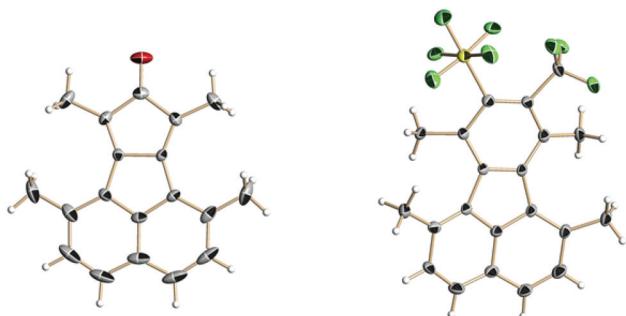


Fig. 1 Single-crystal X-ray structures (thermal ellipsoids at 50% probability) of cyclopentadienone 6 (left) and fluoranthene 7 (right).

with only CF_3 and SF_5 substituents **4i** in 54% isolated yield (Scheme 2). The former has been used by us and others in reactions to construct fluoranthene derivatives with adjacent substituents as precursors of substituted corannulenes.¹¹ The acenaphthaquinone derivative (**5**) reacts with pentan-3-one in the presence of KOH yielding the cyclopentadienone derivative (**6**) (see Scheme 3). Compound **6** is usually not isolated and treated directly with a dienophile, for example **2** in Ac_2O at 80 °C for 24 h furnishing the target fluoranthene **7** in 75% yield containing both SF_5 and CF_3 groups in the *ortho* position (Scheme 3). The structures of compounds **6** and **7** were elucidated by single-crystal X-ray diffraction (Fig. 1).[‡] Compound **6** forms perfect planar molecules with columnar stacks along the crystallographic *c* axis with the shortest intermolecular C–C distance of 3.28 Å. The cyclopentadienone **6** is not stable in the solution and undergoes rapid dimerization (see the ¹H NMR spectrum in the ESI[†]). Compound **7** showed a characteristic *C_s*-fold¹² configuration of the methyl groups.

In conclusion, we have reported a protocol for the synthesis of compounds with SF_5 and CF_3 in the 1,2-position *via* Diels–Alder reaction by employing a corresponding alkyne. The reaction occurs at room temperature or below within a few hours and in the absence of any side-reactions. Further studies using SF_5 substituted alkynes as synthones for a variety of novel organic compounds with interesting new physical, biological and chemical properties are currently underway in our group.

Acknowledgements

Support from the Deutsche Forschungsgemeinschaft GRK 1582 “Fluorine as a Key Element” is gratefully acknowledged.

Notes and references

[‡] Crystal data for **6**: $\text{C}_{19}\text{H}_{16}\text{O}$, $M = 260.32$, orthorhombic, $a = 11.088(2)$ Å, $b = 18.565(4)$ Å, $c = 13.258(3)$ Å, $V = 3591(2)$ Å³, $T = 138(2)$ K, space group $C222_1$, $Z = 8$, $\mu(\text{Mo K}\alpha) = 0.077$ mm^{−1}, 15 171 reflections measured, 4184 independent reflections ($R_{\text{int}} = 0.0231$), The final R_1 value was 0.0476 ($I > 2\sigma(I)$). The final $wR(F^2)$ value was 0.1150 ($I > 2\sigma(I)$). The final R_1 value was 0.0565 (all data). The final $wR(F^2)$ value was 0.1215 (all data). The goodness of fit on F^2 was 1.119.

Crystal data for **7**: $\text{C}_{21}\text{H}_{16}\text{F}_8\text{S}$, $M = 452.40$, monoclinic, $a = 16.519(6)$ Å, $b = 12.951(5)$ Å, $c = 17.522(6)$ Å, $\beta = 106.652(7)$ °, $V = 2729.2(10)$ Å³, $T = 133(2)$ K, space group $C2/c$, $Z = 8$, $\mu(\text{Mo K}\alpha) = 0.266$ mm^{−1}, 28 650 reflections measured, 5477 independent reflections ($R_{\text{int}} = 0.0241$), The final R_1 value was 0.0468 ($I > 2\sigma(I)$). The final $wR(F^2)$ value was 0.1230 ($I > 2\sigma(I)$). The final R_1 value was 0.0636 (all data). The final $wR(F^2)$ value was 0.1411 (all data). The goodness of fit on F^2 was 1.099.

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