Flash vacuum pyrolysis of trifluoromethylated diphenyldiazomethanes. Role of trifluoromethyl group in the arylcarbene rearrangement

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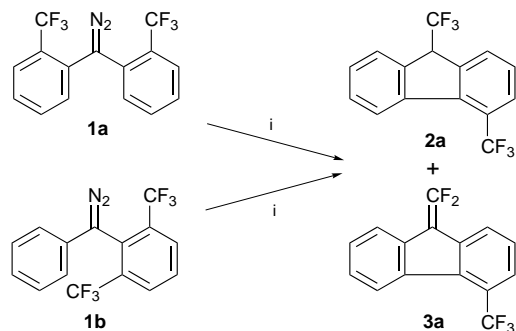
Flash vacuum pyrolysis (350 °C/10⁻⁴ Torr) of the title diazo compounds gives trifluoromethylated fluorenes, indicating that the C–F bonds are completely unreactive toward carbene even in the gas phase at high temperatures.

Fluorinated molecules often display unique reactivity relative to their nonfluorinated analogues and have been the object of considerable interest for many years.[1] This is also true in the field of carbene chemistry.[2,3] The fluoro group is especially interesting in carbene chemistry because it can play key roles either intramolecularly or intermolecularly. On the other hand, C–F bonds are known to be almost the only type of bond unreactive toward carbenic centres. In spite of these unique characteristics, the influence of aryl CF$_3$ groups on the reactivity of arylcarbenes has been poorly characterized.[4] In this regard, we have examined the effect of CF$_3$ groups on the rearrangement of diarylcarbenes in the gas phase. The study not only reveals that CF$_3$ groups show a profound influence on the selectivity of the rearrangement, but also confirms that the C–F bond is completely unreactive toward carbenes, even in the gas phase at high temperature.
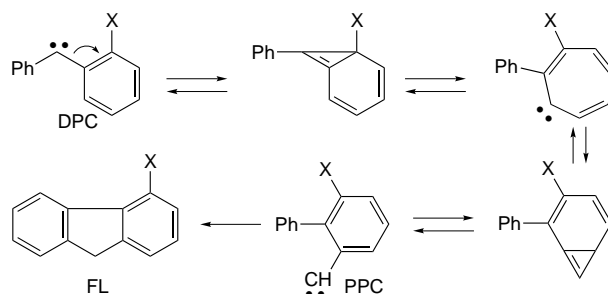
Flash vacuum pyrolysis (FVP)[5] of bis(2-trifluoromethyl-phenyl)diazomethane **1a**† at 350 °C/10⁻⁴ Torr gave two fluorene derivatives **2a** (38%)‡ and **3a** (8%)‡ as volatile products (Scheme 1). Control experiments showed that FVP of **2a** under similar conditions gave **3a**, suggesting that **3a** can be produced by a secondary reaction of **2a** as a result of HF elimination.

It is well-documented that arylcarbenes undergo repeated rearrangement in the gas phase, where a divalent carbon is transmitted through a benzene ring to a position that is accessible for intramolecular reactions. Diphenylcarbene (DPC), for instance, rearranges to produce 2-phenylphenyl-carbene (PPC), where the carbene centre is trapped by the 2-phenyl ring to form fluorene (FL) Scheme 2.
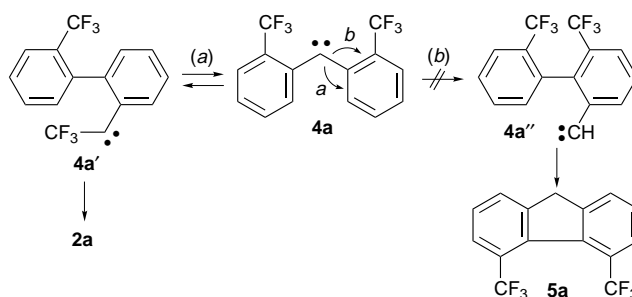
According to the mechanism, carbene **4a** generated from **1a** can undergo ring-expansion in two directions, one [path (*a*)] away from the CF$_3$ group and the other [path (*b*)] toward the substituent (Scheme 3). The former will produce carbene **4a′**, a precursor to **2a**, while the latter should generate **4a″** which should produce **5a**. Exclusive formation of **2a** suggests that the rearrangement of **4a** is highly selective with respect to the
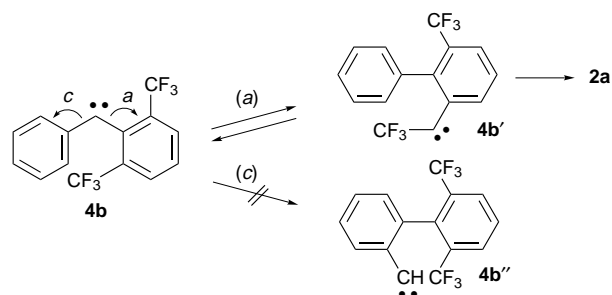
Scheme 2

Scheme 3

substituent. The fact that neither 1,2-F migration nor C–F bond insertion was observed indicates, on the other hand, that the C–F bond is unreactive toward carbenic centres even in the gas phase at this high temperature.

FVP of 2,6-bistrifluoromethylphenyl(phenyl)diazomethane **1b**,† a positional isomer of **1a**, under similar conditions gave essentially the same result, thus affording the same products, **2a** (48%) and **3a** (9%), in similar yields (Scheme 1). The results, although initially puzzling, can also be understood in terms of the carbene rearrangement (Scheme 4). Since the two rings in **4b** bear different substituents, regioselectivities in terms of ring arise in this case [*i.e.* path (*a*) and (*c*)], while there is no selection with respect to the ring substituents [*i.e.* Scheme 3, path (*a*) = path (*b*)]. The ring-expansion toward the substituted ring [path (*a*)] can generate carbene **4b′** responsible for the observed

Scheme 1 *Reagents and conditions*: i, 350 °C/10⁻⁴ Torr

Scheme 4

products, while the another movement [path (c)] should produce carbene **4b″**, which is not responsible for the product. The exclusive formation of **2a** might then indicate that the selectivity with respective to the rings is also very high in this case. It may be, however, that since the CF_3 group has been shown to be unreactive even under these conditions, the carbene **4b″** has no intramolecular reaction channels and hence regenerates **4b** which eventually produces **2a**.
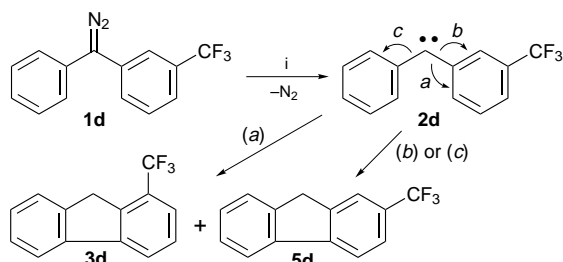
In order to check this possibility, we generated carbenes **4c** where the *ortho* C–H bonds are available for the carbenes from both types of rearrangement, *i.e.* **4c′** and **4c″**. FVP of **1c**† produced **2c**‡ (32%) and **3c**‡ (27%) again as the main products and only a very small amount of **5c**‡ (1%) was detected. The result shows that path (a) rearrangement is favoured over path (c), although not exclusively (Scheme 5).
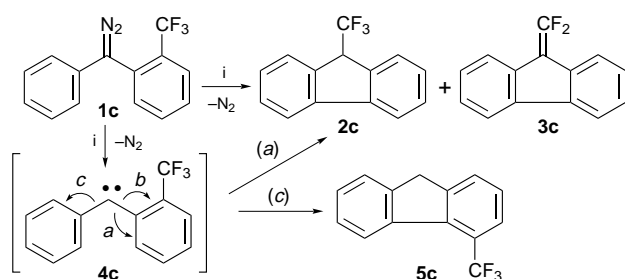
Scheme 5 *Reagents and conditions*: i, 350 °C/10⁻⁴ Torr

Both types of regioselectivity are completely lost when the CF_3 group is introduced at the 3-position of diphenylcarbene. Thus, FVP of **1d**† afforded **2d**‡ (33%) and **5d**‡ (35%) in comparable yields (Scheme 6). Formation of **2d** is explicable in terms of type (a) rearrangement while **5d** might be produced by either type (b) or (c) rearrangement.

The regioselectivities of the rearrangement of diarylcarbenes carrying different substituents on the aryl rings can be interpreted in terms of a simple frontier MO analysis.[6] Thus, the occupied σ-orbital of carbene can interact with the LUMO of the aromatic ring in the ipso-position, while the vacant p orbital can interact with the aromatic HOMO in the *ortho*-position. The two interactions are synergetic. The σ-LUMO interaction is favoured by low-lying LUMOs possessing large coefficients in the *ipso* position and the p-HOMOs interactions is favoured by high-energy HOMOs with large coefficients in the *ortho*-positions. Phenyl(4-pyridyl)carbene, for instance, undergoes exclusive rearrangement involving the pyridine ring, since the pyridine LUMO has a large coefficient at positions 2 and 4. On the other hand, the rearrangement of phenyl(3-pyridyl)carbene does not involve the pyridine ring, since the LUMO coefficient at the 3-position is very small. Essentially the same explanation can be applied to the selectivities observed for the present system. Thus, a CF_3 group will lower the LUMO energy of the benzene ring, and trifluoromethylbenzene has large coefficients at positions 2 and 4. A high preference for the 2-tri-

fluoromethylated phenyl ring will result in carbenes **4a–c**, while the regioselectivity is lost in **4d** where the LUMO coefficient of the aromatic ring in the *ipso*-position is small, and hence the p-HOMO interaction becomes competitive.

Regioselectivities with respect to the ring substituent are not well characterized. In the case of *ortho*-substituted phenylnitrenes, the nitrene nitrogen movement away from the substituent is preferred but is not exclusive and depends on other factors such as the nature of the reaction partner and electronic effects.[7] On the other hand, this issue has been examined extensively only for tolylcarbenes in the carbene rearrangement, where the methyl group is acting as a trap.[7,8] The 'away' selectivity is slightly favoured in this case. However, this again depends on the other factors such as the reaction conditions and precursors.[8]

Finally we wish to emphasize here that the present results reveal that trifluoromethylated diphenylcarbenes can be regarded as synthetically useful intermediates for trifluoromethylated fluorene derivatives which are otherwise not easily obtained. The method is specially advantageous since the CF_3 group is intact during the reaction, and its position in the resulting fluorene is predictable based on the regioselectivities shown above.

Footnotes and References

† All diazomethanes except **1b** employed in this study were prepared by the conventional hydrazonation–oxidation procedure and obtained as unstable red oils. 2,6-Bistrifluoromethylphenyl(phenyl)diazomethane **1b** was prepared by treating the corresponding *N*-nitrosocarbamate with KOBu^t.
‡ *Selected spectral properties* for **2a**: δ_H(CDCl₃) 4.61 (1 H, *J* 9.3 Hz), 7.41–7.56 (3 H, m), 7.74 (1 H, d, *J* 7.3 Hz), 7.79 (1 H, d, *J* 7.9 Hz), 7.93 (1 H, d, *J* 7.6 Hz), 8.12 (1 H, d, *J* 7.9 Hz); *m/z* 302 (M⁺, 77%), 233 (100). For **3a**: δ_H(CDCl₃) 7.41–7.47 (3 H, m), 7.69–7.80 (2 H, m), 7.94 (1 H, d, *J* 7.6 Hz); 8.11–8.13 (1 H, m); *m/z* 282 (M⁺, 100%). For **2c**: δ_H(CDCl₃) 4.59 (1 H, q, *J* 9.2 Hz), 7.30–7.50 (6 H, m), 7.58 (2 H, d, *J* 7.6 Hz), 7.77 (2 H, d, *J* 7.3 Hz); *m/z* 234 (M⁺, 53%), 165 (100). For **3c**: δ_H(CDCl₃) 7.32–7.42 (4 H, m), 7.71–7.80 (4 H, m); *m/z* 214 (M⁺, 100%). For **5c**: δ_H(CDCl₃) 4.11 (2 H, s), 7.41–7.45 (3 H, m), 7.66–7.78 (2 H, m), 7.92 (1 H, d, *J* 7.5 Hz), 8.10–8.12 (1 H, m); *m/z* 234 (M⁺, 60%), 165 (100). For **2d**: δ_H(CDCl₃) 4.09 (2 H, s), 7.34–7.60 (6 H, m), 7.81 (1 H, d, *J* 6.6 Hz), 7.95 (1 H, d, *J* 7.3 Hz); *m/z* 234 (M⁺, 66%), 165 (100). For **3d**: δ_H(CDCl₃) 3.96 (2 H, s), 7.36–7.65 (6 H, m), 7.83 (1 H, d, *J* 7.6 Hz), 8.01 (1 H, s); *m/z* 234 (M⁺, 66%), 165 (100).

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Scheme 6 *Reagents and conditions*: i, 350 °C/10⁻⁴ Torr