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An Unusual Alkylation with Trifluoroiodomethane Providing a Difluoroiodomethyl Group

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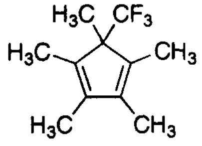
Abstract: Pentamethylcyclopentadienyllithium reacted with trifluoroiodomethane to provide a diene bearing a difluoroiodomethyl group and none of the trifluoromethyl diene. This result was consistent with insertion of difluorocarbene into the C–I bond of an initially formed iodo-diene.

Trifluoroiodomethane is a common reagent for the introduction of a trifluoromethyl group,[1] but even when this appears to be by formal displacement of iodide, there is evidence that this is a radical process.[2]



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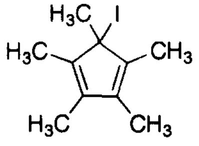

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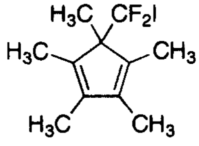

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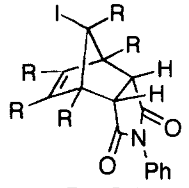
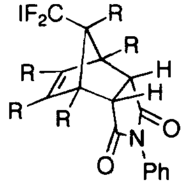
In conjunction with a study of facial selectivity in the Diels-Alder reactions of 5-substituted 1,3-cyclopentadiene derivatives,[3,4] we wished to prepare diene **1**, in which a methyl group would be pitted against a trifluoromethyl group. To the pentamethylcyclopentadienyl anion, generated by the action of *n*-butyllithium in THF at 0 °C, was added CF_3I. The reaction mixture began to darken rapidly; therefore, instead of attempting to isolate the putative diene **1**, an equivalent of a dienophile, *N*-phenylmaleimide, was added. ^1H NMR analysis of the crude reaction mixture revealed signals for only two adducts, in a 2.4 : 1 ratio. These were isolated by flash chromatography. The structure of the major one was not unexpected. It was the adduct **4** derived from 5-iodo-1,3-cyclopentadiene (**2**).[4] The molecular formula ($C_{20}H_{22}F_2INO_2$) of the minor adduct was established by high



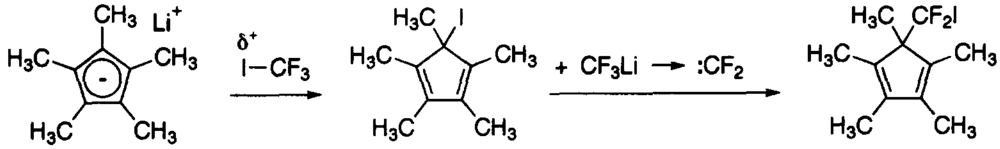
4 R = CH3
6 R = H



5 R = CH3
7 R = H

resolution MS. The ^{1}H NMR spectrum confirmed that this adduct was symmetrical, and the signal for the methyl on the methano bridge was split into a triplet ($^4J_{F,H}$ = 1.5 Hz). Therefore, the minor adduct must have come from diene **3**. The stereochemistry of the minor adduct **5** became clear from nuclear Overhauser effect measurements. Saturation of the two-proton signal at δ 3.10 led to a 5% enhancement of the signal (δ 1.18) for the methyl on the methano bridge, and saturation of the δ 1.18 signal resulted in a 10% increase in the signal at δ 3.10.[5] Thus, **5** was the product of endo-addition to the face of **3** anti to the CF_2I group, an outcome consistent with the facial selectivity being the result of the difference in steric hindrance between CH_3 and CF_2I.

To our knowledge, alkylation with CF_3I by the formal displacement of fluoride is unprecedented, but it does not seem plausible that nucleophilic substitution on CF_3I could lead to diene **3** in a concerted manner. The preponderance of adduct **4** showed that, in contrast with enolate chemistry,[2] the preferred reaction pathway was by capture of the iodine of CF_3I by the 1,2,3,4,5-pentamethylcyclopentadienyl anion, for which the by-product would be trifluoromethyllithium. This in turn should give rise to difluorocarbene. (Trifluoroiodomethane gives difluorocarbene in the presence of alkyllithiums.[6]) There is precedence[7] for the attack by difluorocarbene on the iodide in solution to produce CF_2I^-. Therefore, we can suggest that the CF_2I group arises by insertion of difluorocarbene into the C–I bond of the initially formed iodo-diene:



When the same procedure was used with the unsubstituted cyclopentadienyl anion, CF_3I and then *N*-phenylmaleimide, the result was a complex mixture in which we did not detect adduct **6**, adduct **7**, or any adduct containing a trifluoromethyl group.

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References and Notes

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(5) For **5**: mp 166-167 °C; IR: 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.41 (3H, m), 7.06 (2H, m), 3.10 (2H, s), 1.64 (6H, s), 1.53 (6H, s), 1.18 (3H, t, J = 1.5 Hz); ^{19}F NMR ($CDCl_3$): δ_F –28.7; MS *m/e* (%): 485 (15, M$^+$), 357 (6), 338 (33), 312 (100), 185 (74), 173 (90), 135 (30); HRMS: calcd for $C_{21}H_{22}F_2INO_2$: 485.0664, found: 485.0662.

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