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An improved pathway to 6,6-disubstituted fulvenes

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Abstract—Pentafulvenes with alkyl and/or aryl substituents at the exocyclic position are formed rapidly in high yields through reaction of crystalline sodium cyclopentadienide directly with the appropriate ketones.

Fulvenes are an interesting class of cyclic cross-conjugated molecules that display a wide range of reactions with both nucleophiles, electrophiles and various cycloaddition partners.[1–3] Pentafulvenes also serve as activated dienes in Diels–Alder reactions and as synthetic precursors to several biologically occurring compounds.[4–6] Further, they are interesting compounds for theoretical and spectroscopic reasons relating to the charge distribution and π-electron delocalisation in cross-conjugated molecules.[7,8]

Often, pentafulvenes are prepared by condensation of cyclopentadiene with ketones or aldehydes under Thiele's conditions using an alkali metal base in an alcohol, providing the product in modest to good yields.[9–17] The scope and limitation of this method depends on the reactivity of the particular carbonyl compound and on the stability of the fulvene formed. Whereas the cyclopentadienide part in most transition metal complexes is strongly bound and not easily substituted,[18] cyclopentadienyl copper tributylphosphine and nickelocene are less stable and more reactive, and represent alternatives to alkali metal cyclopentadienides.[19] Oda and co-workers worked out a high yield procedure to 6,6-disubstituted pentafulvenes using *N*,*N*-dialkylamides, instead of ketones, with organolithium compounds and cyclopentadiene.[20]

Another alternative route towards a range of structurally diverse fulvenes was found by Stone and Little.[21] They showed that pyrrolidine promotes fulvene formation between cyclopentadiene and carbonyl compounds such as ketones, aldehydes with acidic α-hydrogens, and sterically encumbered aldehydes. Even though the yields when following this pathway are high (45–98%), the reaction times vary greatly (12 min–48 h), and the use of this route with bulky ketones, for example, diaryl ketones, was not reported.

We now report an improved route to fulvenes in which a ketone is reacted with crystalline sodium or potassium cyclopentadienide. Following the recent procedure of Roesky and co-workers,[22] the metal cyclopentadienides were prepared as white crystals in one-pot, directly through reaction of the alkali metals with neat dicyclopentadiene. No solvents are needed and no coloured impurities are observed. This pathway provides alkali metal cyclopentadienide in higher yields than achieved under Thiele's conditions, and it complements the route of Little in which the carbonyl compound is activated.

A set of 12 different 6,6-disubstituted fulvenes (Table 1) was prepared, and all except one were made through condensation of sodium cyclopentadienide with the appropriate ketone (Scheme 1). For the synthesis of **10** we used 2-chloroethyl chloroformate, as employed by Hong et al. (Scheme 2),[16] instead of the corresponding carbonyl compound, ethylene carbonate. Although the sodium salt is a potent source of cyclopentadienide, its addition to ethylene carbonate did not yield the desired product.

When compared to previously reported results, the use of crystalline sodium cyclopentadienide in all cases gives 6,6-disubstituted fulvenes in good to excellent yields (50–95%) after short reaction times (~30 min). The yield for fulvene formation is increased by up to 60%, and the

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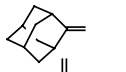
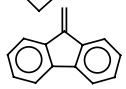
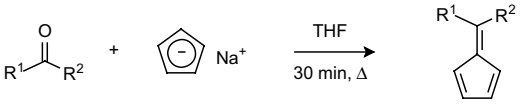
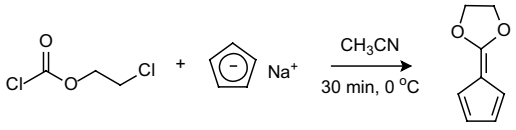
Table 1. Formation of 6,6-disubstituted fulvenes

Fulvene		Yield [%]	
R^1	R^2	Reported All procedures	This work[a] Na^+Cp^-
1, Phenyl	Phenyl	45[b], 54[c], 85[d]	74
2, *p*-Chlorophenyl	*p*-Chlorophenyl	35[b]	82
3, *p*-Methoxyphenyl	*p*-Methoxyphenyl	10[b]	65
4, *p*-Nitrophenyl	*p*-Nitrophenyl	16[e]	50
5, Methyl	Phenyl	45[f], 95[d]	65
6, Methyl	*p*-Fluorophenyl	63[f]	82
7, Methyl	Methyl	96[g], 46[h]	95
8, Ethyl	Ethyl	95[i]	95
9, *tert*-Butyl	*tert*-Butyl	—	Trace
R^1/R^2			
10, –O–CH_2–CH_2–O–		82–85[j]	84
11, 		22[c], 81[k]	60
12, 		26[l]	33

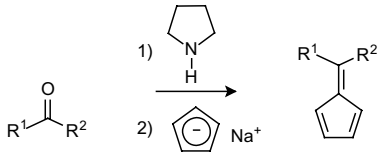
[a] The yields given are based on the isolated compounds prepared according to the descriptions found under general synthetic procedures.
[b] Value from Ref. 18.
[c] Value from Ref. 13.
[d] Value from Ref. 23.
[e] Value from Ref. 15.
[f] Value from Ref. 16.
[g] Value from Ref. 24.
[h] Value from Ref. 17.
[i] Value from Ref. 25.
[j] Value from Ref. 20.
[k] Value from Ref. 21.
[l] Value from Ref. 26.



Scheme 1.



Scheme 2.



Scheme 3.

time required is reduced considerably. Diphenylketones with electron donor groups in *para*-position can be used, in addition to those with electron acceptor groups. The procedure further saves one synthetic operation as the cyclopentadienide salt is prepared directly from dicyclopentadiene. The improvement in reaction time also favours the modified procedure towards fulvenes, which are already available in high yields. For example, the method of Oda and co-workers was reported to need 5 h.[20]

The reaction with sodium cyclopentadienide is most efficient when carried out in THF for 30 min at 60 °C. The progress of the reaction correlates with a colour change of the solution; from light purple in the beginning to intense brown when completed. This colour change was observed in the formation of all fulvenes except **10** for which the colour turned light yellow. Longer reaction times (6 h) lead to dark solutions and lower yields, probably due to intermolecular cycloadditions or decomposition of the pentafulvenes. Surprisingly, potassium cyclopentadienide, which should be more potent than the sodium salt, gave yields for **1**, **2**, **5**, **6**, **10** and **11** that were lower by 20–30% than those found when the sodium salt was used, and **3**, **4**, **7** and **9** could not be formed with the potassium salt regardless of reaction time.

High yields of the fulvenes are also obtained when the bulk of the ketone increases. Fulvene **11** was produced in a slightly lower yield than reported by Olah and co-workers (Table 1), but after shorter reaction time (30 min vs 3 h). 6,6-Di-*tert*-butyl-fulvene **9**, which has not been reported previously in the literature, can prob-

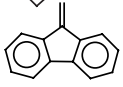
ably be formed in very low yields as a yellow compound. Its formation, which required a longer time (3–6 h) than for the other fulvenes, was therefore only verified through NMR and GCMS of the crude mixture.[27] The use of potassium cyclopentadienide instead of the sodium salt did not improve the result, but it is likely that further modifications of the reaction conditions could lead to a process that gives **9** in reasonable yields.

Under the conditions of Scheme 1 the reaction between sodium cyclopentadienide and the aldehydes, pentanal, butanal and benzaldehyde, did not work. Benzaldehyde was reduced instead. Moreover, we initially expected that the potent sodium cyclopentadienide would add to esters and amides forming fulvenes with hetero-substituents at the 6-position. However, reactions of sodium and potassium cyclopentadienide with ethylbenzoate and the amides *N*,*N*-dimethylacetamide, 3-methyl-2-oxazolidine, 1-methyl-2-pyridone and 1,3-dimethyl-2-imidazolidinone led to complex mixtures that could not be separated.

Since the procedure of Little worked through activation of the ketone and the present procedure functions through activation of the cyclopentadienide, a combination of the two methods could possibly give higher yields (Scheme 3). We tested those fulvenes that were formed in yields below 80% when using sodium cyclopentadienide. The combined reaction was carried out both with reflux in THF for 30 min and at room temperature for 1 h. However, the results were irregular because improved yields were obtained for **1**, **2** and **5**, whereas drastic cuts resulted for the others (Table 2). The yield of **3** could be increased to 50%, but only when run overnight at room temperature with a three-fold excess of sodium cyclopentadienide. On this occasion, the pyrrolidine was added to the ketone 1 h before the cyclopentadienide.

In summary, reaction of alkyl and/or aryl substituted ketones with crystalline sodium cyclopentadienide, prepared according to the recently published procedure of Roesky, generally leads to 6,6-disubstituted fulvenes in higher yields than previously reported and after shorter reaction times.

Table 2. Formation of 6,6-disubstituted fulvenes through the combined route of Scheme 3[a]

Fulvene		rt, 1 h	Reflux, 30 min
R^1	R^2	Na^+	Na^+
1, Phenyl	Phenyl	60	85
2, *p*-Chlorophenyl	*p*-Chlorophenyl	90	67
3, *p*-Methoxyphenyl	*p*-Methoxyphenyl	6	11
4, *p*-Nitrophenyl	*p*-Nitrophenyl	4	10
5, Methyl	Phenyl	31	71
8, Ethyl	Ethyl	92	—
9, *tert*-Butyl	*tert*-Butyl	—	Trace
R^1/R^2			
11, 		36	25
12, 		10	18

[a] General conditions: Pyrrolidine (18.7 mmol, freshly distilled) was added to a solution of ketone (12.5 mmol) in THF (25 mL), the mixture was stirred under nitrogen for 3 min followed by the addition of sodium cyclopentadienide (25 mmol). The procedure for purification described in general synthetic procedures was followed.

General synthetic procedures: Sodium cyclopentadienide was synthesised using the procedure described recently by Roesky and co-workers.[22] This procedure gives white crystals that can be stored at 0 °C under argon for several days. In a typical reaction, sodium cyclopentadienide (11 mmol) was added to tetrahydrofuran (10 mL, distilled from sodium) under nitrogen. A solution of the appropriate ketone (11 mmol) in THF was added dropwise, while stirring. The mixture was then refluxed for 30 min. After extraction with ether, the organic phase was washed with 5% hydrochloric acid, dried with sodium sulfate and concentrated. The fulvene was separated by column chromatography on silica using pentane as eluent.

4,4′-Dinitrobenzophenone, needed for synthesis of 6,6-bis(4-nitrophenyl)fulvene, was prepared through nitration of diphenylmethane followed by oxidation using tetramethylammonium fluoride and *N*,*N*-dimethylacetamide under a positive pressure of oxygen.[28,29] The synthesis of 2-cyclopentadienyliden-1,3-dioxolane **10** was carried out at 0 °C for 30 min.

All compounds were identified by NMR, UV/Vis and GCMS, and agree with reported literature data.

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