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FACILE SYNTHESES OF 2,4,6-CYCLOHEPTATRIENYL KETONES[1)]

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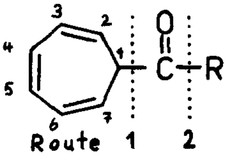
Abstract: The synthesis of the 2,4,6-cycloheptatrienyl ketones 1a-1e by two alternative routes is reported:
Route 1): The adducts 3a-c from the phenyl(trimethylsiloxy)-acetonitriles 2a-c, known as "umpolung" reagents, and tropylium tetrafluoroborate are cleaved by triethylammonium fluoride to form the aromatic cycloheptatrienyl ketones 1a-1c.
Route 2): The phenyl, methyl, and cyclopropyl ketone (1a, 1d, 1e) are prepared by treatment of the acid chloride 7 with the corresponding organomanganese iodides RMnI (8a, 8d, 8e). The Fe-catalyzed coupling reaction of the acid chloride 7 with a Grignard reagent was also used for the preparation of ketone 1b.

For a planned synthesis of 8-substituted heptafulvenes we needed the 2,4,6-cycloheptatrienyl ketones 1a-1e. These structurally interesting and important class of compounds are not easy to synthesize and their preparation is only sporadically reported in the literature. Thus the synthesis of the methyl ketone 1d from the corresponding acid chloride with dimethylcadmium in low yield has been reported[2)]. Reaction of cycloheptatriene carboxylic acid with methyl lithium affords a mixture of ketone and carbinol[3)]. The dicycloheptatrienyl ketone 1f has been obtained involving a 11-step synthesis[4)] and several attempts to prepare the phenyl ketone 1a have failed[5)].



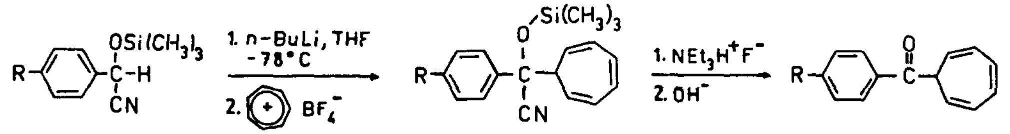
1a R = Phenyl
1b R = p-Methoxyphenyl
1c R = p-Trifluoromethylphenyl
1d R = Methyl
1e R = Cyclopropyl
1f R = Cycloheptatrienyl

We report here the synthesis of the ketones 1a-1e by two alternative routes:

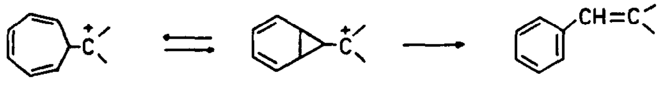
1) reaction of an "umpolung" reagent 2 with tropylium tetrafluoroborate,
2) reaction of the acid chloride 7 with organometallic reagents.

Route 1): The silyl protected cyanohydrins 2 were chosen as an acyl anion equivalent. Treatment of the anions of the easily available phenyl(trimethylsiloxy)-acetonitriles 2a-2c[6)] with tropylium tetrafluoroborate affords the adducts 3 in moderate to good yield[7)] (see Scheme 1). Cleavage of the masking groups is achieved by stirring the acetonitriles 3a-3c with triethylammonium fluoride6) and workup with aqueous sodium hydroxide (yields of the ketones see Scheme 1). The advantage of the silyl protected cyanohydrins is the presence of the preformed C-O unit of the ketone as a silyl ether. Other, often used "umpolung" reagents like 1,3-dithianes produce cationic intermediates during hydrolysis8). In the case of the acetonitriles 3 no such intermediate cycloheptatrienyl methyl cation (4) can be formed during hydrolysis. It is well known that such cations 4 rearrange through the norcaradienyl methyl cation (5) to benzylderivatives 6, similar to a cyclopropylcarbinyl-homoallyl-cation-rearrangement9).

Scheme 1



2a R = H	3a 56%	1a 84%
2b R = OCH$_3$	3b 40%	1b 82%
2c R = CF$_3$	3c 85%	1c 65%



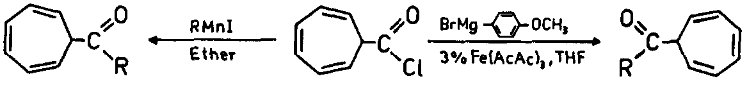
4 5 6

The above described method provides an easy access to aromatic cycloheptatrienyl ketones 1.

Route 2): A more general route for the preparation of the ketones 1 is the reaction of the known cycloheptatriene carbonyl chloride 710) with organomanganese halides in ether at temperatures between -20°C and 0°C. The organomanganese reagents 8a, 8d, 8e are formed by adding lithium compounds to the easily available manganese(II)iodid in ether11). The ketones 1a, 1d, 1e were purified after workup by distillation or chromatography. The NMR and IR data of the prepared compounds are given in Table 1 and 2.

Direct reaction of Grignard reagents with acid chlorides normally affords a mixture of ketone and undesired carbinol. Catalytic amounts of $FeCl_3$ 12) or CuCl 13) are added to improve the yield of the ketone. Recently the coupling reaction of various acid chlorides with Grignard reagents in the presence of catalytic amounts of tris(acetylacetonate)iron(III) to give ketones in good yield has been reported14). We have tried this convenient method for the preparation of a representative ketone; e.g. ketone 1b was isolated after chromatography in 55% yield. This very simple method seems also to be generally applicable for the preparation of the ketones 1.

Scheme 2



1a R = C_6H_5 75% 8a
1d R = CH_3 60% 8d
1e R = c-C_3H_5 50% 8e

7

1b R = p-CH_3O-C_6H_5 55%

Table 1: ^{1}H-NMR and IR data of ketones 1a-1e.

Comp. No.	H^1 t	H^2,H^7 dd	H^3,H^6 m	H^4,H^5 m	others	IR $\nu_{C=O}$(cm^{-1})
1a	3.03	5.19	6.23-6.41	6.63-6.70	7.41-7.57; 7.87-7.98	1685
1b	3.01	5.26	6.21-6.39	6.63-6.70	3.83; 6.81-6.97; 7.81-7.98	1675
1c	2.97	5.10	6.25-6.54	6.62-6.70	7.64-8.06	1698
1d	2.42	5.10	6.15-6.33	6.50-6.58	2.02	1718
1e	2.61	5.28	6.19-6.37	6.57-6.64	0.84-1.11; 1.90-2.18	1700

Table 2: ^{13}C-NMR data of ketones 1a-1e.

Comp.	C^1	C^2,C^7	C^3,C^6	C^4,C^5	C=O	others
1a	43.7	106.8	125.4	129.8	198.5	128.5, 133.0, 136.1
1b	44.1	109.4	125.3	130.1	197.2	55.4, 113.7, 129.1, 131.0, 163.6
1c	43.5	104.2	125.7	129.8	197.4	123.5 q (CF3), 125.4, 128.8, 134.2 q, 138.7
1d	49.1	108.9	126.1	129.9	206.5	28.7
1e	49.5	111.4	126.0	130.2	208.8	11.1, 19.7

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Literature and notes:

1) We thank Prof. G. Boche for informing us about the independent preparation of the ketones 1a, 1d in his laboratory (see accompanying publication).

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