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1-FORMYLCYCLOHEPTATRIENE. SYNTHESIS BY VILSMEIER REACTION AS NOVEL DIRECT SUBSTITUTION OF CYCLOHEPTATRIENE AND ITS SEVERAL REACTIONS

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1-Formylcycloheptatriene was obtained by Vilsmeier reaction as novel direct substitution of cycloheptatriene accompanying bitropyl. Reduction, Grignard reaction and condensation reaction of the formyl compound were investigated.

In certain of its reactions with electrophilic reagents cycloheptatriene does not undergo simple substitution but rather hydride abstraction to give the tropylium ion.[1] Recently, Friedel-Crafts type benzoylation of cycloheptatriene has also been investigated, and deoxybenzoin, derived by rearrangement of 7-benzoylcycloheptatriene, and/or 1-benzoylcycloheptatriene were obtained depending on the reaction conditions by addition-elimination reaction.[2] Although formylation of cycloheptatriene iron-carbonyl complex by means of Vilsmeier reagent afforded 1-formyl derivative,[3] 1-formylcycloheptatriene itself, which may be potentially important intermediate for the synthesis of novel aromatic compounds, has not been known.

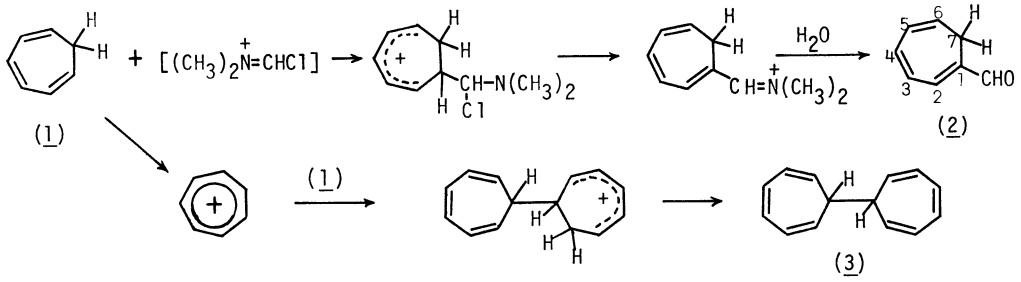
In this paper, we wish to report the synthesis of 1-formylcycloheptatriene by Vilsmeier reaction as novel direct substitution of cycloheptatriene and its several reactions.

The reaction of cycloheptatriene (1) with a small excess of phosphoryl chloride in dimethylformamide at 65°C for 5 hr followed by decomposition with cold water afforded two products, 1-formylcycloheptatriene (2; pale yellow oil, bp 60-65°C/5 mmHg), (2,4-DNP; reddish orange needles, mp 220-222°C)[4] and bitropyl (3)[5] in 18-30% and 1.2-1.5%, respectively, accompanied with a mixture of unidentified hydrocarbons and dark polymeric material. Bitropyl was isolated by chromatographic separation of distillation residue of 2. The reaction of 1 with the Vilsmeier reagent at 90°C gave only resinous product, and the reaction in N-methylformanilide instead of DMF also afforded the compound (2) in 12% yield.

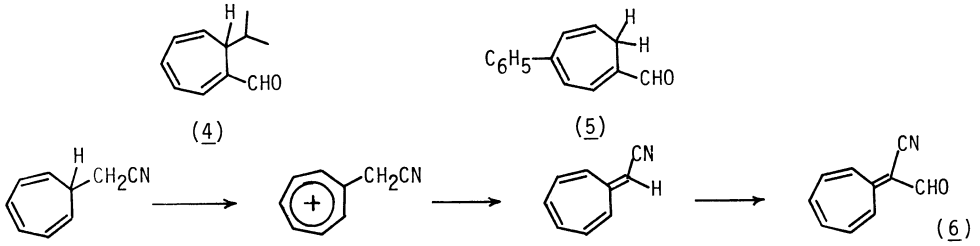
We could not isolate phenylacetaldehyde or its oxidation product, phenylacetic acid, which correspond to deoxybenzoin in the benzoylation, in spite of intensive effort for the isolation.

The difference of the product distributions may depend on the difference of the reaction mechanisms. It is reported that in the benzoylation an adduct of 1 and benzoyl chloride formed as intermediate, which was converted to two products by dehydrochlorination.[2] However, in the present reaction, the reaction must smoothly proceed by electrophilic substitution to give the most stable product.[6]

The formation of bitropyl can be explained by the reaction of 1 with tropylium ion which may be formed by the reaction of 1 with phosphoryl chloride. Incidentally, bitropyl was obtained by the reaction of tropylium tetrafluoroborate with 1 in DMF in about 1% yield.



The formylations of substituted cycloheptatriene were also studied and the corresponding 1-formyl derivatives were obtained although the yields are low, namely 1-formyl-7-isopropyl- (4, 4%) and 1-formyl-4-phenylcycloheptatriene (5, 40%). However, the formylation of 1- and 3-methoxycycloheptatrienes resulted in the decomposition even at low temperature. Interestingly, the formylation of 7-cyanomethylcycloheptatriene afforded 8-cyano-8-formylheptafulvene (6, 16%),[7] which must be formed by the formylation of the initially formed 8-cyanoheptafulvene.



Reduction of 2 with $LiAlH_4$ yielded 1-hydroxymethyl compound (7; quant., colorless oil), which can be converted to acetate (8; colorless oil) and chloromethyl derivative (9; colorless oil), by the reaction with acetic anhydride and thionyl chloride, respectively. The compound (8) underwent further formylation to give a mixture of 1-hydroxymethyl- (10; 1.5%) and 1-acetoxymethyl-6-formylcycloheptatriene (11; 1%), 7 (33%), 8 (19%) and 9 (3%). Oxidation of 10 with MnO_2 afforded 1,6-diformylcycloheptatriene (12; 80%, pale yellow plates, mp 127-128°C), which was identical with authentic sample.[8]

Reaction of 2 with methyl- and phenylmagnesium bromide afforded the corresponding alcohols with methyl (13; 83%, colorless oil) and phenyl (14; quant., colorless oil) groups, respectively. Oxidation of the alcohols with CrO_3-pyridine yielded 1-acetyl- (15, 40%) and 1-benzoylcyclohepta-

triene (16; 56%), respectively.[2)]

It is observed that H-7a and H-7b signals in NMR of the alcohols (13 and 14) appeared each other as double doublet by introduction of asymmetric carbon at the side chain forming racemic compounds.

The condensation of 2 and 15 in the presence of potassium hydroxide yielded a product (17; 10%, yellow sticks, mp 52-53°C), which underwent a hydride abstraction with triphenylmethyl tetrafluoroborate to give a cation (18; 77%, black violet solid, mp darken from around 220°C). UV spectrum of 18 in CH_3CN shows a maximum at 620 nm, and this indicates the compound is a fully conjugated enol-form of monocation.[9)]

The reaction of 2 with acetophenone and its 3-hydroxy and 3,4,5-trimethoxy derivatives also afforded the corresponding products (19; 58%, mp 57-58°C), (20; 89%, mp 130-132°C) and (21; 50%, mp 89-90°C), respectively, and the investigation for derivation of these compounds to colchicine and its analogues are now undertaken.[10)]

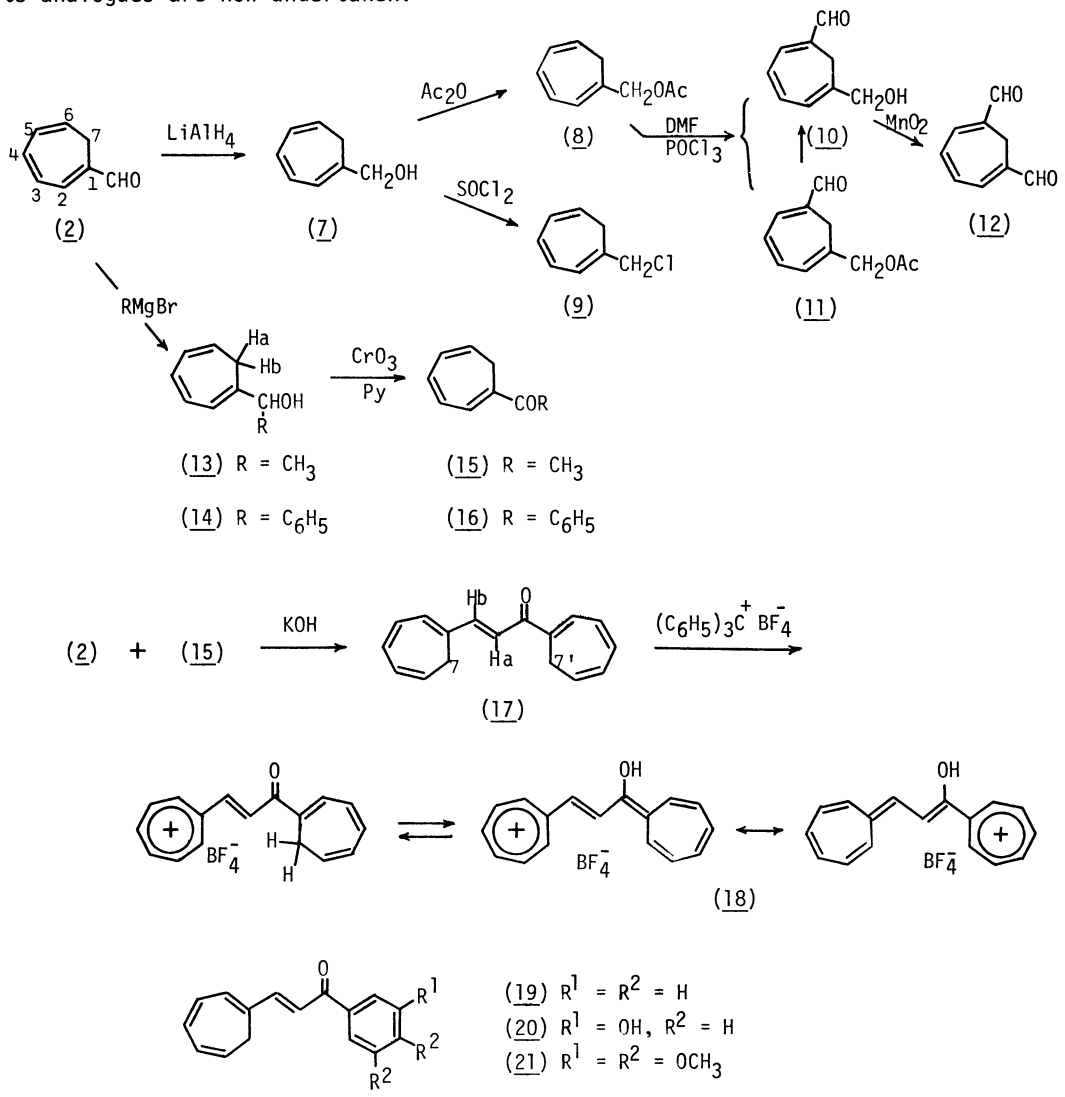


Table 1. Data of ^{1}H-NMR

Compounds	^{1}H-NMR δ ppm (J in Hz)*
2	2.65 (d, J=7, H-7,7), 5.51 (d,t, J=10, 7, H-6), 6.20 (d,d, J=10, 4, H-5), 6.8 (m, H-2,3,4), 9.47 (s, CHO)
5	2.74 (d, J=7, H-7,7), 5.69 (d,t, J=10, 7, H-6), 6.43 (d, J=10, H-5), 6.9 (d, J=6.5, H-2), 7.0 (d, J=6.5, H-3), 7.2~7.5 (m, 5H), 9.50 (s, CHO)
7	2.24 (d, J=7, H-7,7), 4.01 (bs, CH_2O), 4.19 (bs, OH), 5.21 (d,t, J=10, 7, H-6), 6.0 (m, H-2,5), 6.37 (m, H-3,4)
8	2.03 (s, CH_3), 2.32 (d, J=7, H-7,7), 4.60 (s, CH_2O), 5.32 (d,t, J=10, 7, H-6), 6.10 (m, H-2,5), 6.49 (m, H-3,4)
9	2.20 (d, J=7, H-7,7), 4.08 (bs, CH_2Cl), 5.36 (d,t, J=10, 7, H-6), 6.10 (m, H-2,5), 6.45 (m, H-3,4)
10	2.53 (s, H-7,7), 3.56 (bs, OH), 4.11 (s, CH_2O), 6.28 (m, H-5), 6.50~6.93 (m, H-2,3,4), 9.41 (s, CHO)
11	2.03 (s, CH_3), 2.63 (s, H-7,7), 4.57 (s, CH_2O), 6.20 (m, H-5), 6.78 (m, H-2,3,4), 9.46 (s, CHO)
13	1.20 (d, J=6.5, CH_3), 2.06 (d,d, J=13, 7.5, H-7a), 2.47 (d,d, J=13, 7.5, H-7b), 2.98 (bs, OH), 4.22 (q, J=6.5, CHOH), 5.19 (d,t, J=9, 7.5, H-6), 6.0 (m, H-2,5), 6.35 (m, H-3,4)
14	2.12 (d,d, J=13, 7, H-7a), 2.37 (d,d, J=13, 7, H-7b), 2.63 (bs, OH), 4.97 (d,t, J=9.5, 7, H-6), 5.16 (s, CHOH), 5.93 (d,d,d, J=9.5, 4, 2, H-5), 6.15 (m, H-2), 6.45 (m, H-3,4), 7.2 (m, 5H)
15	2.27 (s, CH_3), 2.56 (d, J=7, H-7,7), 5.43 (d,t, J=9.5, 7, H-6), 6.11 (d,d,d, J=9.5, 5, 1, H-5), 6.4~6.8 (m, H-3,4), 6.89 (d, J=6, H-2)
17	2.63 (d, J=7, H-7,7), 2.71 (d, J=7, H-7',7'), 5.3~5.7 (m, 2H), 6.0~6.4 (m, 2H), 6.4~7.1 (m, 6H), 6.95 (d, J=15.5, Ha), 7.23 (d, J=15.5, Hb)

* The NMR was measured with Hitachi R-22 (90 MHz) spectrometer in CCl_4 except 7, 14 and 17 in $CDCl_3$

References and notes

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1) Cf. K. H. Harmon, "Carbonium Ions," ed. by G. A. Olah and P. von R. Schleyer, Vol. IV, Wiley-Interscience, New York (1973), Chapter 29, p. 1579.

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10) The compounds (19-21) have the same carbon skeleton as that of colchicine cleaved between A and C rings.

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