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Simple and Practical Routes to 4,5-Benzocycloheptenone. Ring Enlargement of 3,4-Dihydro-2-ethoxynaphthalene and 2-Alkoxynaphthalenes with Dichlorocarbene

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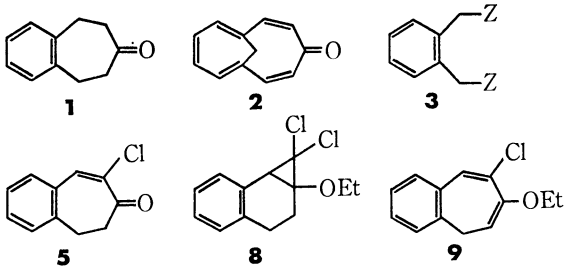
Synopsis. An addition of dichlorocarbene generated by a phase-transfer reaction, to 3,4-dihydro-2-ethoxynaphthalene gave 7,7-dichloro-6-ethoxy-2,3-benzobicyclo[4.1.0]-hept-2-ene, from which 4,5-benzocycloheptenone was derived in preparative yield. 2-Methoxy- and 2-ethoxynaphthalene were converted into 2-chloro-4,5-benzotropone in 33 and 66% yield, respectively, by treatment with large excess of ethyl trichloroacetate and sodium methoxide.

4,5-Benzo-4-cyclohepten-1-one (**1**) is an important compound to obtain 4,9-methano[11]annulenone (**2**),[1] a ten-pi-electron analog of tropone. During investigation of polycondensed novel aromatics containing a methano-eleven-membered ring, we were in need of large amount of **1**.

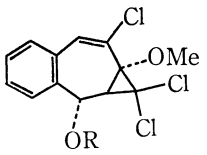
Standard synthetic methods of **1** are intramolecular acylations of diethylbenzene derivatives (**3**, Z= CO_2R,[2] CN,[3] and $CO_2^-M^{+4}$)), derived from *o*-xylene *via* once or twice of elongation of the side chains, under the basic conditions followed by decarboxylation. The other procedure is ring enlargement of *β*-tetralone enamine (**4**) using dichlorocarbene, generated from sodium trichloroacetate, to give 2-chloro-4,5-benzo-2,4-cycloheptadien-1-one (**5**), from which the ketone **1** is derived by catalytic hydrogenation.[5] The latter is relatively simple to handle, but the yield of the crucial compound **5** is not high enough. Parham *et al.* have reported that 2-chloro-4,5-benzo-2,4,6-cycloheptatrien-1-one (**6**) is obtained from 2-methoxynaphthalene by the treatment with ethyl trichloroacetate and sodium methoxide.[6] The benzotropone **6** should be converted into the desired ketone **1**, easily. However, the optimum conditions to obtaine **6** were not established. We wish to describe a simple route to the ketone **5** in a practical yield and a reaction to give **6** more than 65% yield.



1 **2** **3** **5** **8** **9**

In order to use dichlorocarbene generated from inexpensive reagents: chloroform, 50% aqueous sodium hydroxide and a phase-transfer catalyst: and to avoid multiple additions of the carbene to a 1:1 adduct, we chose 2-ethoxy-3,4-dihydronaphthalene (**7**) as the substrate. The addition of dichlorocarbene to the enol ether **7**, which was derived easily from *β*-tetralone, proceeded smoothly to give the adduct (**8**), as colorless oil, which decomposed slowly on silica gel TLC. An attempt of purification of the adduct by distillation *in vacuo* was not successful: elimination of hydrogen chloride proceeded under the conditions to form 1,2-benzo-4-chloro-5-ethoxy-1,3,5-cycloheptatriene (**9**). Compound **9** was obtained cleanly in 86% yield (from **7**), when a solution of the adduct **8** in pyridine was heated under reflux for 90 min under a nitrogen atmosphere. Conversion of the enol ether **9** into the ketone **5** was performed with heating under reflux for 90 min in a mixture of methanol and hydrochloric acid. Catalytic hydrogenation of **5** in the presence of potassium acetate gave 4,5-benzo-4-cyclohepten-1-one **1** in an excellent yield.[5]

It has been reported that a treatment of 2-methoxynaphthalene with 0.75 equiv of the carbene source (ethyl trichloroacetate) and sodium methoxide gives the benzotropone **6** in 13% yield with recover of 73% of the naphthalene.[6] In order to know synthetic utility of the ring enlargement, we changed the ratios of the carbene source and the base to the substrate. When 7 equiv of the carbene source and sodium methoxide were used, **6** was obtained in 33% yield with unexpected by-products (**10**, **11** and **12**; in 6.0, 23.0 and 0.2%, respectively).[7] Replacement of the substrate to 2-ethoxynaphthalene (**13**) gave better results. The yield of **6** was increased to 66%, when **13** was treated with 7 equiv of ethyl trichloroacetate and 8 equiv of sodium methoxide. Catalytic hydrogenation of the tropone **6** gave the ketone **1** in 97% yield.



10 R=Me
11 R=CH_2CHCl_2
12 R=$CH(CHCl_2)_2$

Experimental

Instruments. Melting points were determined on Thomas Hoover MP Apparatus using an uncorrected thermometer. NMR spectra were recorded with a JEOL JNM-PMX-60 spectrometer or a Varian Model A-60 spectrometer using tetramethylsilane as an internal standard. IR spectra were measured with a Hitachi Model 215 grating infrared spectrophotometer.

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*2-Ethoxy-3,4-dihydronaphthalene (**7**).*[8] A solution of β-tetralone (15.2 g, 0.104 mol), ethyl orthoformate (41.6 g, 0.312 mol) and *p*-toluenesulfonic acid (50 mg) in ethanol (60 ml) was heated under reflux for 40 min. Removal of the solvent followed by distillation gave **7** (16.95 g, 93.7%) : bp 84—86 °C/0.2 Torr; NMR (CCl_4) δ=1.34 (3H, t, J=7.0 Hz), 2.21—3.0 (4H, m), 3.89 (2H, q, J=7.0 Hz), 5.63 (1H, s) and 6.72—7.02 (4H, m).

*1,2-Benzo-4-chloro-5-ethoxy-1,3,5-cycloheptatrine (**9**).* To a solution of **7** (16.54 g, 95 mmol) and benzyltrimethylammonium chloride (262 mg) in chloroform (38.7 ml) was added dropwise 50% aqueous sodium hydroxide (38.4 g) at 0 °C under an inert atmosphere (N_2). The mixture was allowed to warm to room temperature and stirred for 14 h. The mixture was diluted with dichloromethane and water, and the organic layer was separated. After dried over magnesium sulfate, evaporation of the solvent to dryness *in vacuo* (0.06 Torr, 4 h) gave **8** (24.03 g) as brown oil: NMR (CCl_4) δ=1.24 (3H, t, J=7.0 Hz), 2.15—2.94 (4H, m), 2.64 (1H, s), 3.74 (1H, q, J=7.0 Hz), 3.77 (1H, q, J=7.0 Hz) and 6.95—7.26 (4H, m). A mixture of **8** (24 g, 93.5 mmol) and dry pyridine (36.5 ml) was heated under reflux for 90 min. Pyridinium hydrochloride was removed by filtration and the filtrate was diluted with water and extracted with three portions of ether (60 ml each). The extract was washed successively with 10% hydrochloric acid, water and brine, and dried over magnesium sulfate. Evaporation of the solvent followed by distillation gave **9** (17.8 g, 86.4%) as pale yellow oil: bp 113 °C/0.05 Torr; IR (neat) 1684 (m), 1630 cm^{-1} (s); NMR (CCl_4) δ=1.20 (3H, t, J=7.0 Hz), 2.85 (2H, d, J=7.4 Hz), 3.60 (2H, q, J=7.0 Hz), 4.88 (1H, t, J=7.4 Hz), 7.08—7.19 (4H, m), 7.23 (1H, s).

*2-Chloro-4,5-benzo-2,4-cycloheptadien-1-one (**5**).* A suspension of **9** (17.6 g, 80.1 mmol) in a mixture of concd hydrochloric acid (0.143 ml), methanol (20 ml) and water (5.7 ml) was heated under reflux for 90 min. White precipitate was formed, after addition of ice (30 g) followed by vigorous stirring. The product was filtered, washed with water, dried over calcium chloride *in vacuo* and recrystallized from hexane (13.66 g, 88.6%). **5**: mp 66.5—67.5 °C (lit,[5] 63—65 °C)

*2-Chloro-4,5-benzo-2,4,6-cycloheptatrien-one (**6**).* To a mixture of dry sodium methoxide (21.6 g, 0.4 mol), 2-ethoxynaphthalene (8.6 g, 0.05 mol) and dry ether (50 ml) was added dropwise with vigorous stirring a solution of ethyl trichloroacetate (62.76 g, 0.35 mol) in ether (50 ml) under a nitrogen atmosphere below 0 °C. The reaction mixture was kept at 0 °C for an additional hour, and then allowed to stand over night at room temperature, whereupon water was added and extracted with ether. The extract was dried over sodium sulfate, concentrated and chromatographed on a dry column of silica gel (240 g, Wako C-200). Elution with hexane gave a mixture of 2-ethoxynaphthalene, ethyl trichloroacetate and less polar products (*ca.* 10 g). 2-Chlorobenzotropone **6** was eluted with hexane–benzene (2 : 1) and benzene, and recrystallized from hexane (6.3 g, 66%). **6**: mp 103—104 °C (lit,[6] 105—106 °C).

*4,5-Benzo-4-cyclohepten-1-one (**1**). Hydrogenation of **5**:* The chloro ketone **5** (25 g, 0.130 mol) and potassium acetate (14 g, 0.143 mol) were suspended in ethanol (150 ml) and hydrogenated at atmospheric pressure over 5% Pd on charcoal (0.9 g). After 20 h the catalyst was filtered, the solvent was removed *in vacuo* and the residue was dissolved in ether. The etherial solution was washed with water, aqueous sodium hydrogencarbonate and brine, and dried over sodium sulfate. Evaporation of the ether to dryness gave white solid (20.2 g, 97%). **1** : mp 41—42 °C (lit,[4] 41—42 °C).

*Hydrogenation of **6**:* A mixture of **6** (3.2 g, 16.6 mmol), potassium acetate (2.1 g, 21.4 mmol) and methanol (50 ml) was hydrogenated over 5% Pd–C (0.1 g) for 96 h. The product **1** was obtained as colorless needles (2.6 g, 98%) from hexane.

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7) Elucidation of the structures and formation mechansims of the by-products will be published soon.

8) Reduction of 2-ethoxynaphthalene with sodium and ethanol (*Org. Synth.*, Coll. Vol. IV, 903) gave **7** less than 75% of purity.