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for the Preparation
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Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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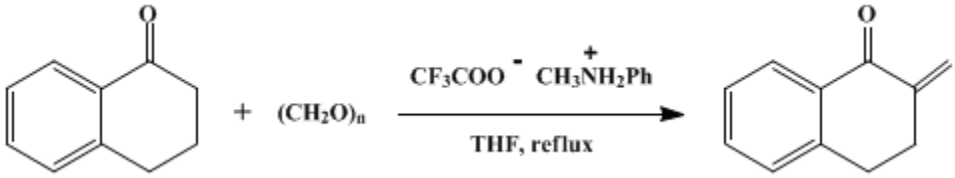
METHYLENE KETONES AND ALDEHYDES BY SIMPLE, DIRECT METHYLENE TRANSFER: 2-METHYLENE-1-OXO-1,2,3,4-TETRAHYDRONAPHTHALENE

[1(2*H*)-Naphthalenone, 3,4-dihydro-2-methylene-]



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1. Procedure

A 250-mL flask equipped with a reflux condenser is charged with 6.75 g (0.225 mol) of paraformaldehyde (Note 1) and 16.57 g (0.075 mol) of *N*-methylanilinium trifluoroacetate (Note 2). A solution of 7.30 g (0.05 mol) of α-tetralone (Note 3) in 50 mL of dry tetrahydrofuran (Note 4) is added at room temperature. The *N*-methylanilinium trifluoroacetate dissolves, and the magnetically stirred mixture is refluxed for 4 hr under a nitrogen atmosphere (Note 5). During this time a red color develops and the paraformaldehyde dissolves after 2 hr. After 4 hr the heating oil bath is removed and the red solution allowed to cool for 10 min. Diethyl ether (100 mL) is gradually added under efficient magnetic stirring, which induces the separation of a red gum. The ethereal solution is decanted from the red gum into a separatory funnel and washed with 50 mL of half-saturated sodium bicarbonate solution. The red gum is triturated with 50 mL of diethyl ether, and the resulting ethereal solution is then used to extract the washing water (Note 6). The combined organic layers are dried over magnesium sulfate. Filtration and concentration of the extract, first on a rotary evaporator then under high vacuum, afford 8.05–8.6 g of a heavy red oil (Note 7). Trituration of this oil with 70 mL of diethyl ether precipitates impurities and causes some polymerization. Filtration through Celite and concentration under high vacuum give 6.8–7.2 g (86–91%) of material that solidifies in a freezer (Note 8). Further purification by column chromatography over silica gel affords analytically pure material (mp 46–46.5°C) but lowers the yield to 70–82%.

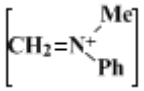
2. Notes

1. Paraformaldehyde is sometimes sold commercially under the label "polyoxymethylene," and commercial polyoxymethylene (Prolabo—France) was used.
2. This crystalline white salt can be obtained by adding dropwise 1 mol of commercial trifluoroacetic acid (Fluka AG) to a stirred solution of 1 mol of commercial *N*-methylaniline (Fluka AG) in 1 L of dry diethyl ether in a nitrogen atmosphere with cooling in an ice bath. After addition the solution is stirred magnetically for 1 hr. The white precipitate that forms is filtered, washed with 100 mL of pentane, and dried overnight in a desiccator under high vacuum. The salt (195 g, 88%) thus obtained had mp 66.5°C.
3. Commercial α-tetralone, 95% pure, was purchased from Fluka AG and used without purification.
4. Tetrahydrofuran was distilled from the ketyl prepared from benzophenone and sodium, but the reaction does not suffer from moisture. Dioxane can also be used, but the iminium salt polymerizes rapidly at the reflux temperature of this solvent (101°C). To avoid polymerization the *N*-methylanilinium trifluoroacetate should be added in portions to the reaction mixture.
5. The reaction can be monitored by TLC. The α-methylene ketones exhibit higher R_f values than starting material when eluted in a diethyl ether-pentane (1 : 1) solvent system.
6. Workup and isolation should be completed in minimum time to avoid polymerization of the product. The heavy red gum thus obtained is soluble in methylene chloride and contains some β-methylene-α-tetralone.

7. A TLC analysis reveals a major component accompanied by two minor, more polar impurities. Because of the relative instability of α-methylene carbonyl compounds, isolation of these substances is associated with dimerization or polymerization. This crude material exhibits satisfactory NMR and IR data and can be used as such for many synthetic purposes.
8. The checkers found that storage of this material at room temperature results in the total conversion to polymer in less than 12 hr. The stability of the product is greatly increased if it is stored at temperatures below −5°C. The spectral properties are as follows: IR (CCl_4) cm^{-1}: 3065, 3030, 1680, 1620, 1604, 918; ^1H NMR (CCl_4) δ: 2.9 (singlet, 4), 5.37 (thin multiplet, 1), 6.17 (thin multiplet, 1), 7.3 (multiplet, 3), 8.07 (multiplet, 1).

3. Discussion

The procedure described herein demonstrates a general synthetic method to form α-methylene ketones by direct methylene transfer. A number of methods have been previously described and reviewed.[2,3] The advantages of direct methylene transfer for the formation of α-methylene ketones are the aprotic, nearly neutral conditions utilized. Although the reaction is not regiospecific, it is highly sensitive to steric hindrance, and transfer occurs at the less hindered site of unsymmetrical ketones. The reaction has been applied to cyclic and acyclic ketones[4] and extended to the synthesis of vinyl ketones[5] and α-methylenealdehydes. It is not applicable to γ- or δ-lactones, or strained cyclic ketones such as norcamphor or cyclobutanone. With cyclohexanone, cyclopentanone,[6] or aldehydes as substrates, preformation of the iminium intermediate



is recommended prior to the addition of the carbonyl compound. This can be achieved by heating the reagents to reflux in tetrahydrofuran for 20 min, followed by the addition of the carbonyl compound at reflux temperature or lower, if necessary. When higher reflux temperatures are required, dioxane can be used as a solvent. Addition in portions of *N*-methylanilinium trifluoroacetate to the reaction mixture minimizes polymerization of the iminium intermediate. In some cases, large-scale experiments may suffer from polymerization; it is recommended that the reaction be quenched before completion.

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

polyoxymethylene

diethyl ether (60-29-7)

sodium bicarbonate (144-55-8)

Cyclohexanone (108-94-1)

nitrogen (7727-37-9)

Benzophenone (119-61-9)

sodium (13966-32-0)

Cyclopentanone (120-92-3)

methylene (2465-56-7)

Pentane (109-66-0)

methylene chloride (75-09-2)

magnesium sulfate (7487-88-9)

dioxane (123-91-1)

N-Methylaniline (100-61-8)

Tetrahydrofuran (109-99-9)

α-Tetralone (529-34-0)

trifluoroacetic acid (76-05-1)

Cyclobutanone (1191-95-3)

Norcamphor (497-38-1)

diethyl ether-pentane

2-Methylene-1-oxo-1,2,3,4-tetrahydronaphthalene,
β-methylene-α-tetralone,
1(2H)-Naphthalenone, 3,4-dihydro-2-methylene- (13203-73-1)

N-methylanilinium trifluoroacetate

paraformaldehyde (30525-89-4)