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The Facile Synthesis of Unsymmetrical Ketones Using Acetone Dimethylhydrazone

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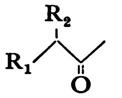
Synopsis. Unsymmetrical ketones were prepared by successive alkylation of acetone dimethylhydrazone. Application of this reaction to the synthesis of dihydrojasmone is described.

Ketones are one of the most important groups of compounds in the field of organic synthesis and many synthetic methods for their preparation have been reported. In this paper, we wish to report a facile and one stage synthetic method to synthesize unsymmetrical ketones using acetone dimethylhydrazone.[1)] The outline of this method is shown in Scheme 1. After addition of butyllithium to a solution of acetone dimethylhydrazone[2)] in THF at −5 °C under argon, 1-iodopentane was added and the mixture was stirred for 10 h at room temperature. After cooling the mixture to −5 °C again, butyllithium was again added followed by benzyl bromide. After stirring for 10 h, 2 mol dm^{-3} hydrochloric acid was added to hydrolyze the mixture and the organic material was extracted with ethyl acetate. Usual work up afforded pure 1-phenyl-3-nonanone in 94% yield. Other results are listed in Table 1.

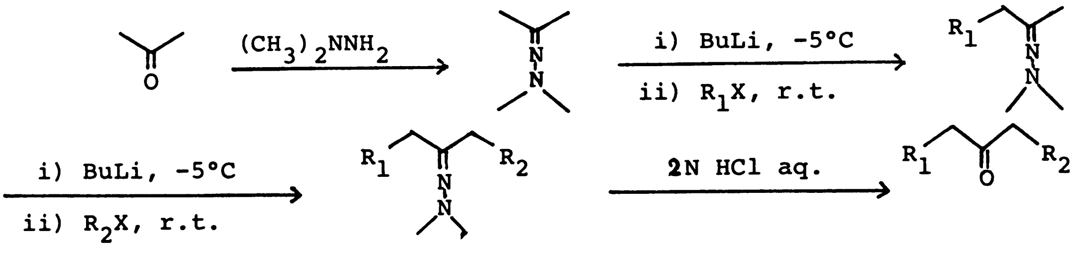
The high yields of the products, the facility of the reaction procedure, and the mildness of the reaction conditions may make it possible to utilize this method for the syntheses of unsymmetrical ketones. The formation of the corresponding isomeric ketones (**1**) was negligible.[3)]


(**1**)

Using this method, synthesis of dihydrojasmone was carried out (Scheme 2). After successive alkylations and hydrolysis, 1-undecen-5-one (**2**) was obtained in 87% yield from acetone dimethylhydrazone. Oxidation of the terminal double bond to 2,5-undecanedione (95% yield) and the succeeding cyclization afforded the desired dihydrojasmone in 61% yield.

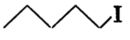
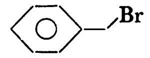
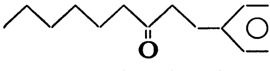
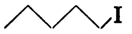
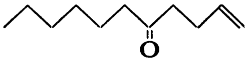
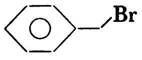
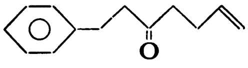
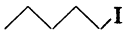
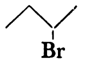
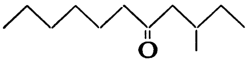
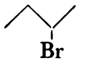
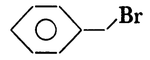
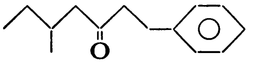
Experimental

The IR spectra were recorded on a Hitachi 260-10 Infrared Spectrophotometer, the NMR spectra were measured on a Hitachi R-600 FT-NMR Spectrometer, and the mass spectra were measured on a Hitachi RM-50 GC–MS. All the experiments were carried out under an atmosphere of argon. The tetrahydrofuran (THF) was dried by distillation from

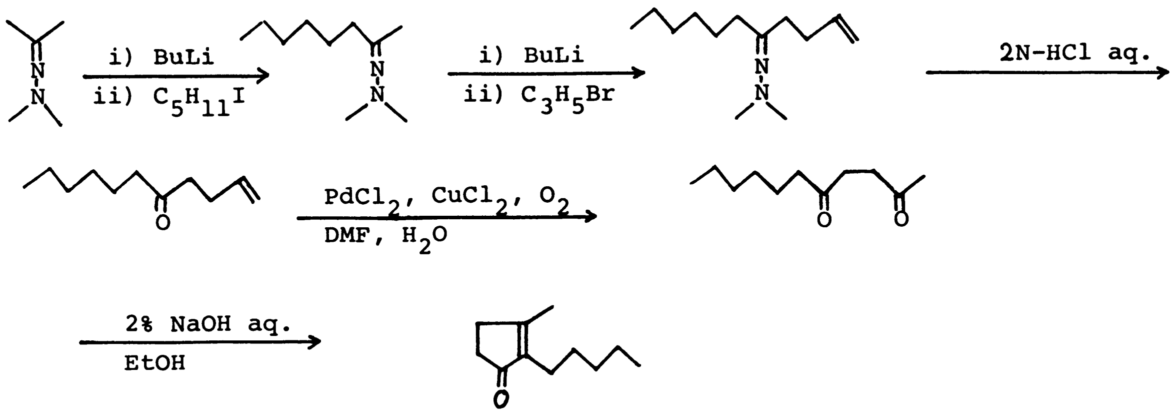


Scheme 1.

TABLE 1. SYNTHESIS OF UNSYMMETRICAL KETONES FROM ACETONE DIMETHYLHYDRAZONE

Run	R_1X	R_2X	Product	Yield/%[a)]
1	CH_3I			85
2				94
3				87
4				73
5				55
6				66

a) Isolated yield.



Scheme 2.

lithium aluminum hydride. The iodomethane, 1-iodopentane, benzyl bromide, allyl bromide, and 2-bromobutane were all commercial products and were distilled before use. Acetone dimethylhydrazone was prepared in 71% yield by refluxing acetone and dimethylhydrazine in benzene in the presence of catalytic amount of trifluoroacetic acid.

Representative Synthesis of 1-Phenyl-3-nonanone. Butyllithium (2.6 mmol) was added *via* a syringe at −5 °C to a solution of acetone dimethylhydrazone (2.4 mmol) in THF under argon. After 1 h, 1-iodopentane (2.4 mmol) was added and the mixture was stirred for 10 h at room temperature. After cooling the mixture to −5 °C again, butyllithium (2.6 mmol) and then benzyl bromide (2.6 mmol) were added, and the reaction mixture was stirred for 10 h at room temperature. Two mol dm^{-3} hydrochloric acid (10 ml) was added for hydrolysis and the organic material was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The preparative TLC of the crude residue (silica gel, hexane–ethyl acetate 10:1) afforded pure 1-phenyl-3-nonanone (0.492g 94% yield).

Acetone Dimethylhydrazone. Bp 95 °C/760 Torr (1 Torr=133.322 Pa); NMR ($CDCl_3$) (δ): 1.93 (3H, s, $C-CH_3$), 1.97 (3H, s, $C-CH_3$), 2.04 (6H, s, $N(CH_3)_2$); IR (cm^{-1}): 1660, 1170, 1090; MS *m/z* (%): 100 (M^+, 8), 44 (90), 42 (83), 28 (100).

1-Undecen-5-one. NMR ($CDCl_3$) (δ): 0.88 (3H, t, $-CH_3$), 1.27—1.70 (10H, m, $-CH_2-\times 5$), 2.44 (4H, t, $-CH_2COCH_2-$), 4.86—6.18 (3H, m, $-CH=CH_2$); IR (cm^{-1}): 1710, 1640, 1130, 1080, 1000, 910; MS *m/z* (%): 168 (M^+, 18), 113 (56), 98 (68), 85 (100), 66 (79).

5-Methyl-1-phenyl-3-heptanone. NMR ($CDCl_3$) (δ): 0.83 (3H, d, $-CHCH_3$), 0.90 (3H, t, $-CH_2CH_3$), 1.15—1.38 (2H, m, $-CH_2CH_3$), 1.66—2.05 (1H, m), 2.20—2.38 (2H, m, $-CHCH_2CO-$), 2.78 (2H, t, $-CH_2Ph$), 2.83 (2H, t, $-COCH_2-CH_2-$), 7.24 (5H, s, $-C_6H_5$); IR (cm^{-1}): 1710, 1600, 1140, 1060, 1030; MS *m/z*: 204 (M^+).

The other compounds listed in Table 1 were identified by comparison of their IR, NMR, and mass spectra with those of authentic samples.

Synthesis of Dihydrojasmone from 1-Undecen-5-one. To a mixture of palladium chloride (60.5 mg, 0.34 mmol) and copper(II) chloride (173 mg, 1.0 mmol) in aqueous *N,N*-dimethylformamide (1.6 ml), 1-undecen-5-one (**2**) (0.191 g, 1.13 mmol) was gradually added under oxygen atmosphere. The mixture was stirred at room temperature for 40 h, poured into 5 mol dm^{-3} hydrochloric acid (15 ml), and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Preparative TLC of the residual liquid gave 2,5-undecanedione 0.20 g (95% yield). The diketone (0.126 g, 0.68 mmol) was added to ethanol (3 ml) and 0.5 mol dm^{-3} aqueous sodium hydroxide (3 ml), and the mixture was refluxed for 7 h. The mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The preparative TLC of the residual liquid gave dihydrojasmone (0.070 g) in 61% yield. This compound was identified by comparison of IR, NMR, and mass spectra with those of a authentic sample.

References

1) Alkylation of acetone dimethylhydrazone with trideuteromethyl iodide and methyl iodide has been reported; M. E. Jung and T. J. Shaw, *Tetrahedron Lett.*, **1979**, 4149.

2) R. H. Wiley, S. C. Slaymaker, and H. Kraus, *J. Org. Chem.*, **22**, 204 (1957).

3) E. J. Corey and D. Enders, *Tetrahedron Lett.*, **1976**, 3, 11; *Chem. Ber.*, **111**, 1337, 1362 (1978); E. J. Corey, D. Enders, and M. G. Bock, *Tetrahedron Lett.*, **1976**, 7; D. Enders and P. Wenster, *ibid.*, **1978**, 2853; E. J. Corey and D. L. Boger, *ibid.*, **1978**, 4597.