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Reaction of 3-Methyl-2-cyclopenten-1-one *N,N*-Dimethylhydrazone with α,β-Unsaturated Carbonyl Compounds. A Novel Synthesis of Bicyclic Compounds

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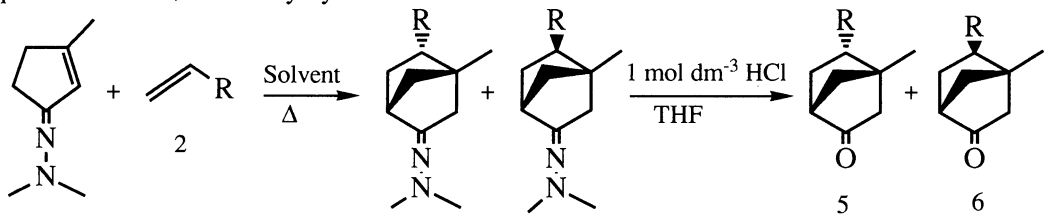
3-Methyl-2-cyclopenten-1-one *N,N*-dimethylhydrazone reacted with methyl vinyl ketone or acrylic acid derivatives to give a new bicyclic bifunctional compound in good yield in a polar aprotic solvent such as dimethylformamide.

Carbonyl compound *N,N*-dialkylhydrazones have been shown to be a useful intermediate in organic synthesis.[1] Previously, we also have reported some reactions using aldehyde or ketone *N,N*-dimethylhydrazones such as the selective α-alkylation of α,β-unsaturated carbonyl compound to α-alkyl-β,γ-unsaturated carbonyl ones.[2] In this letter, we wish to report the new cyclization reactions of 3-methyl-2-cyclopenten-1-one *N,N*-dimethylhydrazone with substituted alkenes as shown in Scheme 1.



1 2 3 4 5 6

a:R=-$COCH_3$
b:R=-CN
c:R=-$COOCH_3$

Scheme 1.

The typical reaction procedure was as follows. To the hexamethylphosphoramide (HMPA) solution (10 ml) of **1** (0.418 g, 3.02 mmol, mixture of *syn* and *anti* isomers), methyl vinyl ketone (5.0 ml) was added and the reaction mixture was stirred at 55°C for 30 h. After concentration of the mixture, tetrahydrofuran (THF, 15 ml) and 1 mol dm^{-3}-hydrochloric acid (15 ml) was added to the residue in order to hydrolyze the hydrazone produced, and the solution was stirred at room temperature overnight. After usual work-up, the mixture of **5a**[3] (*endo*-5-acetyl-4-methylbicyclo[2.2.1]heptan-2-one, colorless oil) and **6a**[4] (*exo*-5-acetyl-4-methylbicyclo[2.2.1]heptan-2-one, mp 54-55°C) were obtained in 66% yield (ca. 1:1 mixture). These compounds were separated by silica-gel column chromatography (hexane: ethyl acetate=1:1) and recrystallization.

The representative results are listed in Table 1. Methyl vinyl ketone, methyl acrylate, and acrylonitrile smoothly reacted with **1** to give the corresponding bicyclic compounds.[5] Acrylic acid, vinyl acetate, and ethyl vinyl ether, however, did not give the desired products. Bicyclic dimethylhydrazones **3a** and **4a** could not be separated at this stage, but after hydrolysis, **5a** and **6a** were separated by column chromatography. The structures of **5a** and **6a** were fully analyzed by ^1H-^1H and ^1H-^{13}C two-dimensional NMR measurements

Table 1. Reaction of **1** and **2**[a)]

Run	2	Solvent	Time	Temp/°C	Yield of 5 and 6/%[b)]
1	**2a**	HMPA	30 h	55	66
2	**2a**	DMF	30 h	55	60
3	**2a**	Dioxane	30 h	55	35
4	**2a**	THF	30 h	55	33
5	**2a**	THF	7 d	55	55
6	**2a**	Hexane	30 h	55	30
7	**2a**	Hexane	7 d	55	40
8	**2a**	Benzene	30 h	55	24
9	**2b**	DMF	14 h	50	90
10	**2b**	DMF	27 d	25	63
11	**2b**	THF	7 d	55	57
12	**2b**	Hexane	7 d	55	47
13	**2c**	DMF	4 d	55	58
14	**2c**	THF	7 d	55	51
15	**2c**	Hexane	7 d	55	34

a) As for **1**, **2**, **5**, and **6**, see Scheme 1. b) Isolated total yields of **5** and **6**, and remains were starting materials. Yields were not optimized.

besides usual NMR, IR, and mass spectroscopic methods. These reactions were dramatically affected by solvents used. Polar aprotic solvents such as HMPA and dimethylformamide (DMF) gave good results. Hexane and benzene were not suitable for this reaction. As for the reaction temperature, best results were obtained at about 50-55°C.

Besides **1**, the hydrazones of 3-penten-2-one and 2-cyclopentenone also reacted with **2a** to give the corresponding mono- and bicyclic compounds, although the yields were rather low compared with those of **1**.

When 3-methyl-2-cyclopenten-1-one itself was treated instead of **1** with **2**, no bicyclo compound was obtained even in HMPA or DMF. This shows that the dimethylhydrazone derivative has a characteristic reactivity to **2**, although the reaction mechanism is not clear at present.

The easy procedure and mild conditions may make this new reaction useful for preparing some bicyclic bifunctional compounds. Other applications of this reaction are currently being explored in our laboratory.

References

1) E. J. Corey and D. Enders, *Chem. Ber.*, **111**, 1337, 1362 (1978); E. J. Corey and D. L. Boger, *Tetrahedron Lett.*, **1978**, 4597; and the references cited therein.

2) M. Yamashita, K. Matsumiya, K. Nakano, and R. Suemitsu, *Chem. Lett.*, **1988**, 1215; K. Matsumiya, K.Nakano, R. Suemitsu, and M. Yamashita, *ibid.*, **1988**, 1837; M. Yamashita, K. Matsumiya, H. Morimoto, and R. Suemitsu, *Bull. Chem. Soc. Jpn.*, **62**, 1668 (1989); and the references cited therein.

3) Colorless liquid; ^{1}H NMR ($CDCl_3$) δ: 1.44(3H, s), 1.66(1H, d, *J*=10.4 Hz), 1.76(1H, dd, *J*=3.7 and 11.0 Hz), 1.80(1H, d, *J*=18.9 Hz), 1.90(1H, ddd, *J*=2.4, 5.5, and 12.8 Hz), 2.11(1H, ddd, *J*=4.9, 11.0, and 12.8 Hz), 2.20(3H, s), 2.25(1H, dd, *J*=4.3 and 18.3 Hz), 2.60(1H, d, *J*=4.9 Hz), and 2.93(1H, ddd, *J*=1.8, 5.5, and 11.6 Hz); IR (neat): 2960, 1745, 1700, 1455, 1410, 1370, 1210, 1175, and 1015 cm^{-1}.

4) Mp 54-55 °C; ^{1}H NMR($CDCl_3$) δ: 1.28(3H, s), 1.42(1H, d, *J*=10.4 Hz), 1.67(1H, ddd, *J*=2.4, 8.5, and 13.4 Hz), 1.92-2.05(3H, m), 2.20-2.28(1H, m), 2.25(3H, s), 2.61(1H, d, *J*=4.9 Hz), and 2.74(1H, dd, *J*=5.5 and 7.9 Hz); IR (KBr): 2940, 1760, 1700, 1466, 1405, 1360, 1280, 1170, 1085, and 1000 cm^{-1}.

5) These compounds gave satisfactory analytical and spectral results.

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