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A Method for the Cyclic Enone Synthesis Using Lithium Chloride - Hexamethylphosphoramide System

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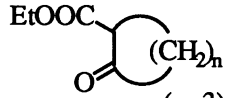
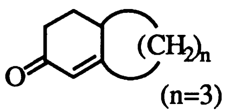
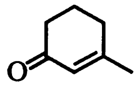
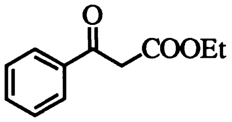
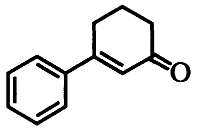
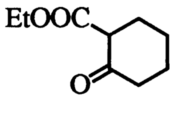
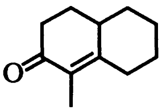
Cyclic enones were obtained from the reactions of β-keto esters with acyclic α,β-unsaturated ketones by using lithium chloride in hexamethylphosphoramide. The products were brought about *via* the Michael addition, decarboxylation, and the aldol condensation.

The Robinson annulations are widely employed in organic synthesis for effecting the six-membered ring formation. The reactions giving cyclic enones were carried out under basic or acidic conditions in almost all the cases.1) In this communication, we report a new practical synthesis of the enones *via* the Robinson annulation accompanied by the decarboxylation under the neutral environment.

In the course of our study on the annulation, we examined the cyclic enone formations using a new system. Several reactions of β-keto esters (10 mmol) with the acyclic α,β-unsaturated ketones (10 mmol) were carried out in hexamethylphosphoramide (HMPA) (5 ml) at 160 °C in the presence of lithium chloride (LiCl) (10 mmol). The reactions gave the cyclic enones in good yields except entry 5 using an aromatic keto ester which has a relatively inactive ketone as shown in Table 1. It should be emphasized that entry 2 showed one-pot synthesis of 4,4a,5,6,7,8-hexahydro-2(3*H*)-naphthalenone ($\Delta^{1,9}$-octalone-2) which is an important compound in organic chemistry.2) The isomer, 3,4,5,6,7,8-hexahydro-2(1*H*)-naphthalenone ($\Delta^{9,10}$-octalone-2), was not detected on the basis of ^{13}C-NMR and GC analyses.3) The procedure is not only practical, but also the overall yield of $\Delta^{1,9}$-octalone-2 based on 3-buten-2-one is the best one reported in the literature.3, 4) These annulated products in the Table were the results of the sequence of the Michael addition, decarboxylation, and the aldol condensation.5)

In conclusion, the process employing LiCl - HMPA is one of the best methods to obtain the cyclic enones on the simple operation and the reasonable yield.3, 4, 6) The system brought about the compounds *via* the Michael addition, decarboxylation, and the aldol condensation in one-pot.

Table 1. Synthesis of Cyclic Enones

Entry	Donor	Acceptor a)	Product	Temp °C	Time h	Yield %
1	 (n=3)	A	 (n=3)	160	2	65
2	(n=4)	A	(n=4)	160	2	77
3	(n=5)	A	(n=5)	160	2	50
4		A		160	2	73
5		A		160	1	21
6		B		160	6	66

a) A: 3-buten-2-one, B: 1-penten-3-one.

References

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2) This compound has been used frequently for studies on the organic chemistry. See, for example: Y. D. Wu, K. N. Houk, J. Florez, and B. M. Trost, *J. Org. Chem.*, **56**, 3656 (1991); H. Ahlbrecht, M. Dietz, C. Schoen, and V. Baumann, *Synthesis*, **1991**, 133; M. J. Gula, D. E. Vitale, J. M. Dostal, J. D. Trometer, and T. A. Spencer, *J. Am. Chem. Soc.*, **110**, 4400 (1988).

3) R. L. Augustine and J. A. Caputo, *Org. Synth.*, Coll. Vol. V, 869 (1973).

4) See, for example: R. S. Olsen, Z. A. Fataftah, and M. W. Rathke, *Synth. Commun.*, **16**, 1133 (1986); J. C. Aumiler and J. A. Whittle, *J. Org. Chem.*, **41**, 2955 (1976).

5) Lithium iodide has been used for Michael reaction and aldol condensation, respectively: R. Antonioletti, F. Bonadies, E. S. Monteagudo, and A. Scettri, *Tetrahedron Lett.*, **32**, 5373 (1991); R. G. Kelleher, M. A. McKervey, and P. Vibuljan, *J. Chem. Soc., Chem. Commun.*, **1980**, 486. Lithum chloride and lithium iodide have been used for decarboxylation: J. McMurry, *Org. React.*, **24**, 187 (1976).

6) See, for example: E. Wada, J. Funakoshi, and S. Kanemasa, *Bull. Chem. Soc. Jpn.*, **65**, 2456 (1992); T. Sato, Y. Wakahara, J. Otera, and H. Nozaki, *Tetrahedron Lett.*, **31**, 1581 (1990); J. Tsuji, *Pure Appl. Chem.*, **58**, 869 (1986); E. J. Corey and D. L. Boger, *Tetrahedron Lett.*, **1978**, 2461.

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