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Use of 1-menthyl ester as chiral auxiliary in the synthesis of useful chiral synthons

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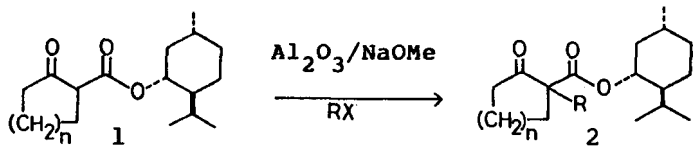
Abstract : A simple method has been developed for the access to useful chiral synthons involving alkylation and Michael addition to l-menthyl esters of cycloalkanone carboxylic acids.

The achievement of an efficient methodology for the synthesis of useful chiral synthons through simple operations constitutes an important goal in organic synthesis. For past few years we have been actively engaged in utilizing surface-mediated reaction for the development of simple and efficient alternative procedures for several important and fundamental synthetic transformations.[1] As a part of this programme we have decided to use l-menthyl 2-oxocycloalokanecarboxylate as a probe for asymmetric alkylation and Michael addition through our recently developed technologies on surface-mediated solid phase reaction.[1e,1b]

The l-menthyl 2-oxocyclopentane-, 2-oxocyclohexane- and 2-oxocycloheptane-carboxylates were prepared by l-menthol exchange of the corresponding methyl carboxylates through a simple procedure.[2] For alkylation,[1e] the menthyl ester **1** (1 mmol) was stirred on the surface of alumina impregnated with sodium methoxide (1 mmol) for 30 min at 0 °C (ice-water bath), after which the alkyl halide (1 mmol) was added also at 0 °c and stirring was continued under nitrogen without further cooling until completion of the reaction, as monitored by TLC or GC. The product was isolated in a pure state by simple filtration chromotography of the solid mass through a short plug of silica gel. The Table 1 shows the results of alkylation of l-menthyl 2-oxocyclopentane-, 2-oxocyclohexane- and 2-oxocycloheptane carboxylates with methyl iodide, allyl bromide and benzyl bromide. The products were obtained in

Table 1. Alkylation of 1-menthyl 2-oxocycloalkanecarboxylates



entry	1-menthyl ester 1	alkyl halide RX	time (h)	yield(%)[a] of 2	ratio of diastereoisomers[b]
1	n=1	CH_3I	6	95	67 : 33
2	n=1	CH_2=$CHCH_2Br$	0.5	92	62 : 38
3	n=1	$PhCH_2Br$	5	96	56 : 44
4	n=2	CH_3I	6	92	95 : 5
5	n=2	CH_2=$CHCH_2Br$	0.5	92	62 : 38
6	n=2	$PhCH_2Br$	5	95	75 : 25
7	n=3	CH_3I	6	94	95 : 5
8	n=3	CH_2=$CHCH_2Br$	0.5	92	60 : 40
9	n=3	$PhCH_2Br$	5	96	75 : 25

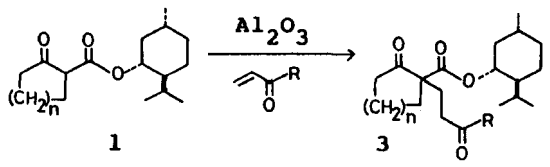
[a]The yield refers to pure isolated product, fully characterized by IR and ^{1}H NMR.
[b]The ratio of diastereoisomers was determined by ^{13}C NMR analysis.

excellent yields. The ratio of diastereoisomers, as determined by ^{13}C NMR analysis, is also very good, in a few cases (entries 4,7) these being excellent.

For Michael addition,[1b] the menthyl ester 1 (1 mmol) was stirred on the surface of activated alumina at 0 °C (ice-water bath) for 10 min after which the Michael acceptor (1 mmol) was added and stirring was continued under nitrogen till completion of the reaction, as monitored by TLC or GC. The Michael adduct was isolated in a pure state by simple filtration of the solid mass through a short plug of silica gel. The results are reported in Table 2. A modest diastereoselectivity is observed in all the additions, the entry 4 being the excellent.

By careful column chromatography it has been possible to isolate one single diastereoisomer in a number of cases, although absolute stereochemistry of each isomer is yet to be determined. In general, it has been observed that better diastereoselectivity is achieved in six- and seven-membered rings than in five-membered one.

Table 2. Michael addition to 1-menthyl 2-oxocycloalkanecarboxylates



1 3

entry	1-menthyl ester 1	R	time (h)	yield(%)[a] of 3	ratio of diastereoisomers[b]
1	n=1	$R=CH_3$	0.5	94	60 : 40
2	n=1	$R=OCH_3$	24	90	65 : 35
3	n=2	$R=CH_3$	0.5	92	60 : 40
4	n=2	$R=OCH_3$	24	88	99 : 01
5	n=3	$R=CH_3$	0.5	90	73 : 27
6	n=3	$R=OCH_3$	24	86	67 : 33

[a]The yield refers to pure isolated product, fully characterized by IR and ^1H NMR.
[b]The ratio of diastereoisomers was determined by ^{13}C NMR analysis.

Thus, the present method provides an easy access to a variety of chiral synthons of high synthetic potential. We are presently investigating the utility of these chiral ester synthons in natural product synthesis.

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References

1. (a) B.C. Ranu and A.R. Das, J. Chem. Soc., Chem. Commun., 1334 (1990). (b) B.C. Ranu, S. Bhar and D.C. Sarkar, Tetrahedron Lett., 32, 2811 (1991). (c) B.C. Ranu and A.R. Das, J. Org. Chem., 56, 4796 (1991). (d) B.C. Ranu, S. Bhar and R. Chakraborti, J. Org. Chem., 57, 7349 (1992). (e) B.C. Ranu and S. Bhar, J. Chem. Soc., Perkin Trans.1, 365 (1992). (f) B.C. Ranu, D.C. Sarkar and R. Chakraborty, Synth. Commun., 22, 1095 (1992). (g) B.C. Ranu and A.R. Das, J. Chem. Soc., Perkin Trans.1., 1881 (1992). (h) B.C. Ranu, M. Saha and S. Bhar, Tetrahedron Lett., 34, 1989 (1993). (i) B.C. Ranu and R. Chakraborty, Tetrahedron, 49, 5333 (1993). (j) B.C. Ranu, R. Chakraborty and M. Saha, Tetrahedron Lett., 34, 4659 (1993). (k) B.C. Ranu, M. Saha and S. Bhar, J. Chem. Soc., Perkin Trans.1., 2197 (1994). (l) B.C. Ranu, A. Sarkar and R. Chakraborty, J. Org. Chem., 59, 4114 (1994). (m) B.C. Ranu, A. Sarkar, M. Saha and R. Chakraborty, Tetrahedron, 50, 6579 (1994). (n) B.C. Ranu, A. Majee and A.R. Das, Synth. Commun, In press. (o) B.C. Ranu and M. Saha, J. Org. Chem., In press.

2. C.P. Decicco and R.N. Buckle, J. Org. Chem., 57, 1005 (1992).