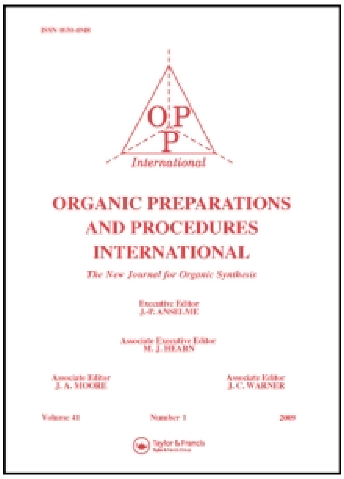

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SELECTIVE TRANSESTERIFICATION OF METHYL AND ETHYL β-KETOESTERS

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Kraus and H. Kim, *Synth. Comm.*, **23**, 55 (1993). d) G. Pattenden and S. Reynolds, *Tetrahedron Lett.*, **32**, 259 (1991). e) J. Cossy and C. Leblanc, *Tetrahedron Lett.*, **30**, 4531 (1989).

11. E. Rosas Alonso, K. Abbaspour Tehrani, M. Boelens, D. Knight, V. Yu and N. De Kimpe, *Tetrahedron Lett.*, **42**, 3921 (2001).

12. N. De Kimpe, R. Verhé, L. De Buyck and N. Schamp, *Bull. Soc. Chim. Belg.*, **88**, 59 (1979).

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SELECTIVE TRANSESTERIFICATION OF METHYL AND ETHYL β-KETOESTERS

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Transesterification, one of the most effective methods of ester synthesis has wide applications both in academic and industrial research.[1] In general, it is accelerated by protic acids,[1] Lewis acids[1] and basic catalysts.[1] More recently various catalysts have been reported to effect transesterifications.[1,2] β-Ketoesters, a class of versatile intermediates used extensively in the agrochemical, pharmaceutical and dyestuff industries,[2] are useful and important building blocks for the synthesis of complex natural products.[2] Various methods have been reported for their preparation, mostly involving ester derivatives as starting materials.[3,4] Most of the reported methods of transesterification of β-ketoesters are not general and are equilibrium driven reactions that require an excess of one of the reactants to obtain good yields. For example, 4-(dimethylamino)pyridine (DMAP) catalyzed transesterification[5] required a large amount of catalyst whereas other methods[6] are restricted to tertiary butyl esters, thus lack generality. Although distannoxanes[7] leads to good yields of β-ketoesters, the catalysts are difficult to prepare. The synthesis of lignan lactones of significant cytotoxic activity required a variety of alkylbenzoyl acetates in larger amounts. However, there are few reports on the synthesis of the

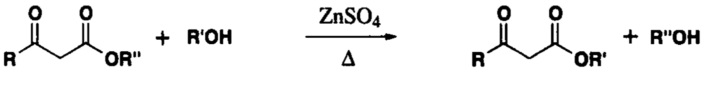
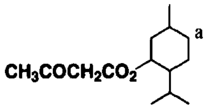
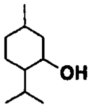
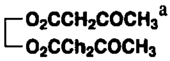
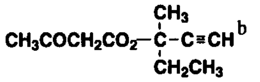
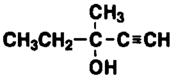
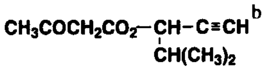
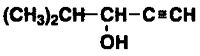
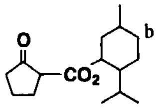
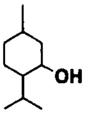
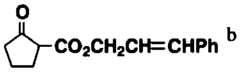
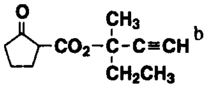
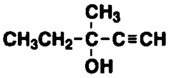
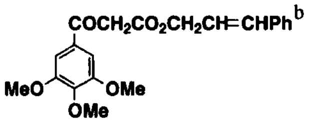
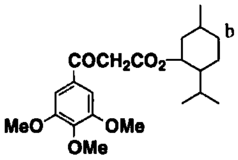
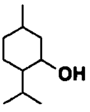
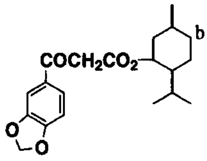
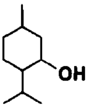


Table. Transesterification of Methyl and Ethyl β-Ketoester

Entry	Product	Reaction Time (h)	Yield	Alcohols
1	$CH_3COCH_2CO_2CH_2Ph$[a]	2.75	89	$PhCH_2OH$
2		5.50	95	
3	$CH_3COCH_2CO_2C(CH_3)_3$[a]	14	78	$(CH_3)_3COH$
4	$CH_3COCH_2CO_2CH_2CH{=}CH{-}Ph$[a]	4.25	97	$PhCH{=}CHCH_2OH$
5	$CH_3COCH_2CO_2(CH_2)_3CH_3$[a]	5.50	91	$CH_3(CH_2)_3OH$
6	 $O_2CCH_2COCH_3$[a] $O_2CCh_2COCH_3$	6	81	$HO{-}(CH_2)_2{-}OH$
7	 $CH_3COCH_2CO_2{-}\overset{CH_3}{\underset{CH_2CH_3}{C}}{-}C{\equiv}CH$[b]	11.25	58	 $CH_3CH_2{-}\overset{CH_3}{\underset{OH}{C}}{-}C{\equiv}CH$
8	 $CH_3COCH_2CO_2{-}\underset{CH(CH_3)_2}{CH}{-}C{\equiv}CH$[b]	8	92	 $(CH_3)_2CH{-}\underset{OH}{CH}{-}C{\equiv}CH$
9	$CH_3COCH_2CO_2Et$[a]	6	87	CH_3CH_2OH
10		1	93	
11		1	81	$PhCH{=}CHCH_2OH$
12		12	46	 $CH_3CH_2{-}\overset{CH_3}{\underset{OH}{C}}{-}C{\equiv}CH$
13		11	95	$PhCH{=}CHCH_2OH$
14		7.50	66	
15	$PhCOCH_2CO_2CH_2CH{=}CHPh$[b]	4.0	72	$PhCH{=}CHCH_2OH$
16		6.0	82	

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a) From methyl β-ketoester; b) From ethyl β-ketoester; c) Products were characterized by spectral analysis and comparison with authentic samples[1,2] β-ketoesters required for the synthesis of lignans. α-Disubstituted β-keto ester enolates underwent 1,3-ester shift under basic conditions.[8] Very few examples are reported on transesterification of β-ketoesters with propargylic alcohols.[1,9] Transesterification of simple esters with stoichiometric amount of iron (III) perchlorate is also reported in the literature.[10] Thus there is a need of general and practical method of transesterification of β-ketoesters involving easily available and inexpensive catalyst. We report here the use of anhydrous zinc sulfate as an inexpensive catalyst for selective transesterification of β-ketoesters

Various β-ketoesters with primary, secondary, tertiary, allylic and benzylic alcohols in the presence of catalytic amount of anhydrous zinc sulfate in toluene at 65 or 80° underwent transesterification in excellent yields (entries 1-16). Even less reactive *t*-butyl alcohol afforded β-ketoesters in moderate to good yields (entries 3, 7, 12), a procedure which is otherwise often problematic in acid catalyzed reactions or which failed completely in transesterifications catalyzed by $TiSi(OEt)_4$. It should be pointed out that transesterification of β-ketoesters with unsaturated alcohols is rather difficult because of facile decarboxylation and rearrangement.[11] However, the present method induced smooth transesterification of β-ketoesters with α,β-unsaturated alcohols (entries 4, 7, 8, 11-13, 16). The superiority of the present procedure is evident in transesterifications leading to the synthesis of β-ketoesters with an aromatic substrates in good yields (entries 13-16). In this context, it should be mentioned that a recent literature report which describes synthesis of alkyl β-ketoesters using sulfated tin oxide (super acid catalyst), failed with aromatic β-ketoesters.[12] We also found that the conversion of methyl β-keto ester to ethyl β-keto ester also proceeded in excellent yield (entry 9). It is noteworthy to mention that the chiral integrity of (-) menthol is maintained under these conditions (entries 10, 14, 15). The important aspect to be noted is that the reaction appears specific only for transesterification of β-ketoesters. Methyl pyruvate and 4-ketopentanoate as well as ethyl chloro- and cyanoacetate could not be transesterified with *n*-butanol after 12 hrs. Similarly methyl 4-phenyl-3-butenoate did not react with benzyl alcohol and phenols such as *p*-phenyl- and *p*-chlorophenol failed to react with ethyl acetoacetate. The effectiveness of this procedure is illustrated by its selectivity towards β-ketoesters whereas the normal esters are found to be unreactive under these reaction conditions.

EXPERIMENTAL SECTION

All chemicals were of analytical grade, and solvents were freshly distilled before use. IR spectra were obtained on Bomem MB 104 FTIR spectrometer and NMR spectra were recorded on a Brucker AC 300F NMR spectrometer (300 MHz).

Typical Procedure.- A mixture of ethyl 3-(3,4-methylenedioxyphenyl)-3-oxopropanoate (5 mmol), (-) menthol (5 mmol) and anhydrous zinc sulfate (1 mmol) in toluene (10 mL) was heated to 80° in a round bottom flask fitted with condenser to remove ethanol. After completion (TLC), the reaction mixture was cooled, filtered and the filtrate was concentrated and chromatographed on silica gel (pet. ether: ethyl acetate = 9:1) to afford of menthyl 3-(3,4-methylenedioxyphenyl)-3-oxopropanoate as a viscous colorless liquid. Yield = 1.42gm. (82%,) IR (neat) : 1605, 1690, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.1 (d, 6H, 2 x CH_3), 1.2 (d, 3H, CH_3), 1.6-2.2 (m, 9H), 3.40-3.61 (m, 1H), [3.85 (s), 5.57 (s), 12.35 (s)] 2H, 6.1 (s, 2H), 6.95 (d, 1H), 7.35 (d, 1H), 7.56 (dd, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ, 5.3 (q, strong), 6.2 (q), 18.4 (t, strong), 21 (d), 22.8 (d), 24.9 (d), 31 (t), 55.7 (d), 61.8 (t), 103.8 (t), 108.1 (d), 108.6 (d), 126.3 (d), 131.7 (s), 148.2 (s), 154.2 (s), 175.3 (s), 191.8 (s).

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REFERENCES

1. (a) T. Fujoita, M. Tanak, Y. Norimine and H. Seumunc, *J. Org. Chem.*, **62,** 3824 (1997); (b) G. Shapiro, M. Marli, *J. Org. Chem.*, **62**, 7076 (1997).

2. S. Benetti, R. Ramagnoli, C. De Risi, G. Spalluto and V. Zamirato, *Chem. Rev.*, **95**, 1065 (1995).

3. P. Kumar and R. K. Pande, *Synlett*, **2**, 251 (2000).

4. (a) B. S. Balaji, M. Sasidharan, R. Kumar and B. Chanda, *Chem. Commun.*,707 **(1996)**; (b) B. C. Ranu, P. Datta and A. Sarkar, *J. Org. Chem.*, **63**, 6027 (1998); (c) B. M. Reddy, V. R. Reddy and B. Manohar, *Synth. Commun.*, **29**, 1235 (1999); (d) B. S. Balaji and B. M. Chanda *Tetrahedron Lett.*, **54**, 13227 (1998); (e) P. Krasik, *Tetrahedron Lett.*, **39**, 4223 (1998). (f) S. Fukuzawa and Y. Hongo, *Tetrahedron Lett.*, **39**, 3521 (1998).

5. D. F. Taber, Jr. J. C. Amedio and Y. K. Patle, *J. Org. Chem.*, **50** 3618 (1985).

6. J. S. Witzeman and W. D. Nottingham, *J. Org. Chem.*, **56,** 1713 (1991).

7. J. Otera, N. Danoh and H. Nozaki, *J. Org. Chem.*, **56,** 5301 (1991).

8. A. Habi and D. Gravel, *Tetrahedron Lett.*, **35,** 4315 (1994)

9. C. Mottet, O. Hamelin, G. Garavel, J. Depres and A. E. Green *J. Org. Chem.*, **64,** 1380 (1999).

10. B. Kumar, H. Kumar and A. Parmar, *Indian J. Chem. B.*, **32,** 292 (1993).

11. (a) M. F. Carrol, *J. Am. Chem. Soc.*, **62,** 704 (1940); (b) W. Kimel and A. C. Cope *J. Am. Chem. Soc.*, **65**, 1992 (1943)

12. S. P. Chavan, P. K. Zubaidha, S. W. Dantale, A Keshavaraja, A. V. Ramaswami, and T. Ravindranathan, *Tetrahedron Lett.*, **37**, 233 (1996).