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CESIUM FLUORIDE-PROMOTED REACTION OF ALDEHYDES WITH S-(2-BENZIMIDAZOLYL)ALKANETHIOATES
A NEW METHOD FOR THE PREPARATION OF ENOL ESTERS

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Aldehydes are converted to the corresponding enol esters in good yields by treatment with S-(2-benzimidazolyl)alkanethioates in the presence of cesium fluoride.

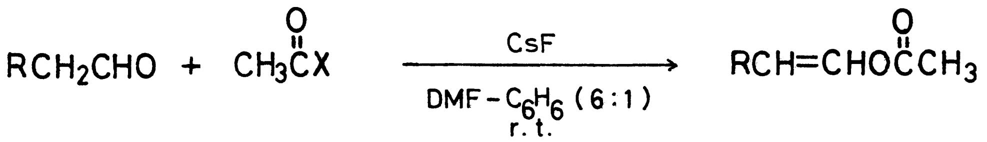
In previous papers,[1),2)] it was shown that cesium fluoride activates protic organic compounds to increase their nucleophilicity, and at the same time works as an excellent acid captor. For example, the condensation reaction of carboxylic acids with alcohols using 2-fluoropyridinium salt proceeded smoothly under mild conditions to afford the corresponding carboxylic acid derivatives in good yields.[2)] During our continuous experiment on the exploration of new synthetic reactions using cesium fluoride, it was observed that the reaction of an aldehyde was promoted to result in the formation of the self-condensation product.[3)] It was presumed that the enol, equilibrating with the aldehyde, is activated by the strong hydrogen bond between the acidic proton and the fluoride ion. This assumption prompted us to investigate the reaction of aldehydes with an appropriate electrophile such as acylating reagents in the presence of cesium fluoride. Now, we wish to report the efficient method for the preparation of enol esters by the reaction of aldehydes with S-(2-benzimidazolyl)alkanethioates.[4)]

Several acylating reagents were screened at first, and it was found that the use of S-[1-(3,6,9-trioxadecyl)-2-benzimidazolyl]ethanethioate gave the best result as shown in the Table I. Apparently, the yield does not exactly parallel the activity of the acylating reagent. This result indicates that the coordination of carbonyl oxygen and appropriately located hetero atom to cesium ion helps the generation of an active intermediate and the transfer of the acyl group to aldehyde oxygen proceeds quite rapidly.

Examinations of reaction conditions revealed a solvent effect. Addition of a small amount of benzene to the dimethylformamide (DMF) solution raised the yield of the enol ester as shown in the Table II.

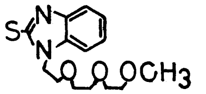
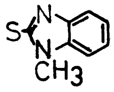
Based on the observations, a variety of aldehydes (**1**) were treated with 1.5 equivalents of various S-[1-(3,6,9-trioxadecyl)benzimidazol-2-yl]alkanethioates (**2**) in the presence of excess cesium fluoride at room temperature employing DMF-benzene mixture (6:1) as a solvent, and enol esters (**3**) were obtained in good yields as depicted in the Scheme III and the Table III.

Scheme I



$$RCH_2CHO + CH_3\overset{O}{\overset{\|}{C}}X \xrightarrow[\text{DMF-}C_6H_6\ (6:1)\ \text{r.t.}]{CsF} RCH{=}CHO\overset{O}{\overset{\|}{C}}CH_3$$

Table I The effect of the acylating reagents.

R	X	Time (h)	Yield(%)
n-$C_{10}H_{21}$	$OCOCH_3$	24	25 (43)a)
	Cl	24	trace
n-C_7H_{15}		2	25b)
	$SC_6H_4NO_2$-p	24	20
		5	80
		9	68

a) Catalytic amount of 4-(N,N-dimethylamino)pyridine was used.
b) Considerable amount of unidentified by-product was formed.

Scheme II

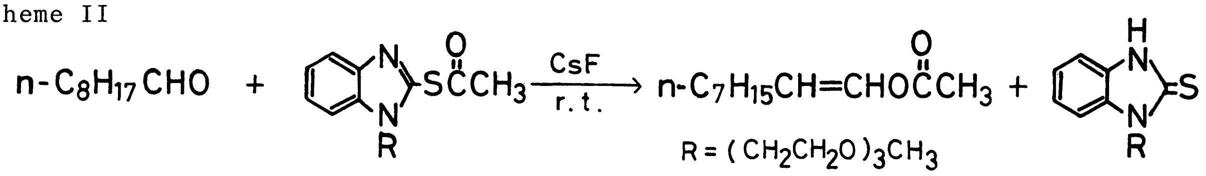


Table II The effect of the solvents.

Solvent	Time	Yield(%)
DMF	overnight	55
DMF-C_6H_6 (1:3)	5 d	56
DMF-C_6H_6 (6:1)	5 h	80

Since a slightly excess of acylating reagent is sufficient to complete the reaction by the present procedure, enol esters may be synthesized without wasting the starting materials. The examination of the stereochemistry of the enol esters showed that (Z)-olefins are major products in the cases of α-monosubstituted aldehydes. As 1:1 mixtures of stereoisomers resulted by the conventional methods,5),6) the present procedure is expected to be a synthetically useful method for the preparation of (Z)-olefins.

Although aldehydes are rather easily converted to enol esters, the reaction of ketones such as 1-phenyl-1-propanone, 1-indanone, 1-benzyloxy-2-propanone and 1-phenyl-2-pentanone with S-(2-benzimidazolyl)ethanthioate is quite slow under the present reaction conditions. Based on the reactivity difference we could introduce an acyl group selectively at the aldehyde oxygen of the steroidal keto-aldehyde (Table III, No 11). However, the reaction of 1,2-diphenyl-1-ethanone with

Scheme III

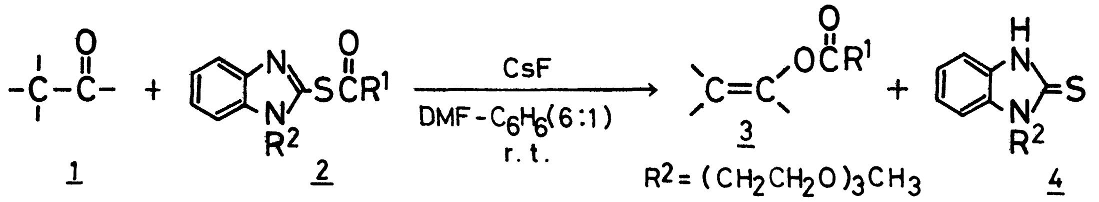
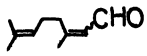
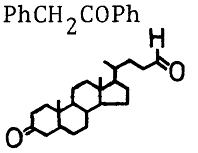
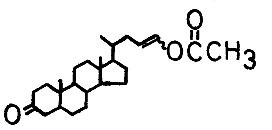


Table III The formation of enol esters.

No	Carbonyl	R^1	Time	Yield(%)[a]	E/Z[b]
1	n-C_8H_{17}CHO	CH_3	5 h	80[c]	29/71
2	n-$C_{11}H_{23}$CHO	CH_3	4 h	76[c]	33/67
3	Ph(CH_3)CHCHO	CH_3	3 h	86[d]	e)
4		CH_3	overnight	73[f]	—
5	n-Pr(CH_3)CHCHO	n-C_5H_{11}	2 d	97[g]	h)
6	$PhCH_2CH_2CHO$	n-C_5H_{11}	overnight	90[g]	25/75
7	$PhCH_2CH_2CHO$	$CH(CH_3)_2$	overnight	73[g]	28/72
8	$PhCH_2CH_2CHO$	$CH_2CH_2CO_2CH_3$	overnight	63[g]	32/68
9	$PhCH_2CH_2CHO$	Ph	1 d	72[g]	29/71
10	$PhCH_2COPh$	CH_3	50 min	92[i]	0/100
11	 j)	CH_3	overnight	73[k]	37/63
12	Ph(CH_3)CHCHO	CH_2OCH_2Ph	overnight	75[g]	86/14

a) All the products gave satisfactory NMR and IR spectra.
b) The ratio was determined by NMR spectra or GLC analysis.
c) P. Z. Bedoukian, J. Am. Chem. Soc., 79, 889 (1957).
d) R. F. Heck, Organometal. Chem. Syn., 1, 455 (1972).
e) The product is a mixture of stereoisomers (72:28).
f) The product is a mixture of isomers.
g) Satisfactory elemental analyses were obtained for these compounds.
h) The product is a mixture of stereoisomers (69:31).
i) D. S. Noyce and A. M. Myers, J. Org. Chem., 35, 2460 (1970).
j) The compound was prepared from 5β-cholane-3α, 24-diol by the method of R. Ratcliffe and R. Rodehorst, J. Org. Chem., 35, 4000 (1970).
k) The product is 

S-(2-benzimidazolyl)ethanethioate exceptionally gave (Z)-1-acetoxy-1,2-diphenylethene stereoselectively in high yield (Table III, No 10). It was also observed that the methoxy carbonyl group did not interfere with the reaction as shown in the case of succinic acid derivative (Table III, No 8).

A typical procedure is described for the synthesis of 3-phenyl-1-propenyl acetate: A suspension of cesium fluoride (360 mg, 2.4 mmol) in DMF (2 ml) was stirred for 1 h at room temperature under argon atomosphere. Benzene (1 ml) was added and stirring was continued for another 30 min. Then, a DMF (2 ml) solution of 3-phenylpropanal (72 mg, 0.54 mmol) and a DMF (2 ml) solution of S-[1-(3,6,9-trioxadecyl)benzimidazol-2-yl]hexanethioate (291 mg, 0.74 mmol) were added. After stirring overnight, the reaction was quenched with water, and organic substances were extracted with ether (3 times). The combined extracts were dried over $MgSO_4$. 3-phenyl-1-propenyl hexanoate (112 mg, 90%) was isolated by column chromatography on silica gel: bp 160°C (bath temperature)/1.5 mmHg; IR (neat) 1750, 1670 cm^{-1}; NMR($CDCl_3$) δ=0.87 (3 H, br. t, J=5 Hz), 1.0-1.9 (6 H, m), 2.1-2.5 (2 H, m), 3.1-3.6 (2 H, m), 4.8-5.7 (1H, m), 6.9-7.2 (1H, m), 7.06 (5 H, s); Found: C, 77.84; H, 8.98%; Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

Several reports appeared for the preparation of enol esters from aldehydes: Classical methods employing acid anhydride and potassium acetate[7)] or p-toluenesulfonic acid[8)] required refluxing reaction temperature. The application of a useful method,[9)] reported for the synthesis of ethenyl alkanoates from acid chlorides and pyridine, was limited to acetaldehyde. Use of a large excess amount of acetic anhydride was necessary in the synthesis of enol esters using 4-(N,N-dimethylamino)pyridine as a promoter.[5)]

Thus, it should be noted that the present procedure utilizing cesium fluoride is of value in organic synthesis based on the following facts: Various aldehydes are converted to enol esters in good yields under mild reaction conditions employing slightly excess amount of acylating reagents, S-[1-(3,6,9-trioxadecyl)-benzimidazol-2-yl]alkanethioates.

References and Notes

1) T. Mukaiyama, N. Morito, and Y. Watanabe, Chem. Lett., 1979, 531.
2) S. Shoda and T. Mukaiyama, Chem. Lett., submitted to publication.
3) Our initial attempt to transfer allyl moiety from 2-hexenyloxy-1-methylbenzimidazole to nonanal led to the formation of condensation product of the aldehyde, 2-heptyl-2-undecenal, in 19% yield instead of alkylated product.
4) S-(2-Benzimidazolyl)alkanethioates were prepared in 69-93% yields from acid chlorides or acids with 2-mercaptobenzimidazoles[10)] according to the method of S. Nakajima, I. Tanaka, T. Seki, and T. Anmo, Yakugaku Zasshi, 78, 1378 (1958); Y. Watanabe, S. Shoda, and T. Mukaiyama, Chem. Lett., 1976, 741.
5) T. J. Cousineau, S. L. Cook, and J. A. Secrist III, Synth. Commun., 9, 157 (1979).
6) H. O. House and V. Kramar, J. Org. Chem., 28, 3362 (1963).
7) P. Z. Bedoukian, J. Am. Chem. Soc., 66, 1325 (1944).
8) N. Wakabayashi, J. Org. Chem., 32, 489 (1967); C. P. Casey and C. R. Cyr, J. Am. Chem. Soc., 95, 2240 (1973).
9) A. M. Sladkov and G. S. Petrov, Zhur. Obshchei. Khim., 24, 450 (1954).
10) 2-Mercaptobenzimidazoles were prepared from corresponding 2-chlorobenzimidazoles according to the method of D. Harrison and J. T. Ralph, J. Chem. Soc., 1965, 3132.

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