Pergamon

Tetrahedron Letters 40 (1999) 2127–2128

TETRAHEDRON LETTERS

β -Oxopropyl Formate As a Formylating Agent of Sterols

Ahmed Kabouche , Zahia Kabouche*

Laboratoire de synthèse organique et organométallique, URC, I. Chimie, Université de Constantine, route de Aïn El Bey, 25000 Constantine (Algérie).

Received 22 September 1998; accepted 14 January 1999

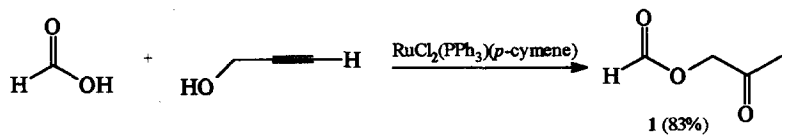
Key words: propargylic alcohol ; β–oxopropyl formate ; sterols ; 1,5-diazabicyclo[4.3.0]non-5-ene.

Abstract: *Propargylic alcohol reacts with formic acid in the presence of mononuclear catalysts of ruthenium to selectively afford β-oxopropyl formate which has been shown as an exellent mild formylating agent of sterols when the reaction is catalyzed by 1,5-diazabicyclo[4.3.0]non-5-ene (DBN).*

Two initial reports [1,2] described the synthesis of β-oxopropyl esters by the catalytic addition of carboxylic acids, involving α-amino acids to propargylic alcohol and its 1,1-dimethylderivatives. Complexes of type $RuCl_2(PR_3)$(arene) which were shown to be efficient catalyst precursors for the regioselective synthesis of enol esters [1-6], also catalyze the synthesis of β-oxopropyl esters in milder conditions, via a transesterification, however, it seems that the synthesis of β–oxopropyl formate has not been addressed. We now report that β–oxopropyl formate obtained by the catalytic addition of formic acid to propargylic alcohol is an excellent formylating agent of sterols in the presence of a catalytic amount of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN).

1- Catalytic synthesis of β–oxopropyl formate

Until now, the synthesis of β–oxopropyl formate has not been described; we have prepared it according to the published method for the synthesis of β–oxopropyl esters. Thus, the reaction of 10 mmol of propargylic alcohol and 10 mmol of formic acid in toluene at 60 °C for 6 h in the presence of 1mol % of complex $RuCl_2(PPh_3)$(*p*-cymene) gave β–oxopropyl formate in 83% yield [7].

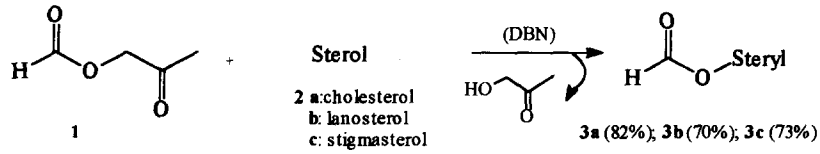


1 (83%)

2- β–oxopropyl formate as a formylating agent

The good reactivity of enol formates towards amines and alcohols, under mild conditions [5,6], prompted us to study the behaviour of β–oxopropyl formate as an acylation reagent for the formation of C-N and C-O bonds. We report here that β–oxopropyl formate is an excellent formylating agent of primary amines and alcohols, under very mild conditions, while the formylation of secondary amines and alcohols requires the use of KCN [5,6] as catalyst. Nevertheless, the formylation of sterols in the presence of catalytic amounts of KCN gave rise to the corresponding formates in only 20-30 % yields, even at 70 °C. We tried several classical catalysts of acylation reactions but no significant formate was observed. Fortunately, the use of 1,5-diazabicyclo[4.3.0]non-5-ene allows the unprecedented access to the steryl formates **3** in good yields, with elimination of a hydroxyketone as the only by-product easy to remove.

0040-4039/99/$ - see front matter
PII: S0040-4039(99)00155-0



Thus, when 10 mmol of the sterol, 10 mmol of β–oxopropyl formate and 1 mmol of DBN were heated at 50-70 °C, for 3 hours in 10 ml of THF, the steryl formates **3** were isolated in 70-82% yields [8].

These results show that β–oxopropyl formate, prepared in one step from formic acid and propargylic alcohol under ruthenium catalysis, is an excellent formylating agent of sterols, in the presence of a catalytic amount of DBN.

Acknowledgment

The authors are very grateful to Professor P.H. Dixneuf and Doctor C. Bruneau (Université de Rennes I, France) and Professor A.Gaudemer (Université de Paris-sud, France) for their encouragement, grant of material and valuable advice.

References

1. D. Devanne, C. Ruppin, P.H. Dixneuf, *J. Org. Chem.*, **1988**, *53*, 925-926.
2. C. Bruneau, M. Neveux, Z. Kabouche, C. Ruppin, P.H. Dixneuf, *Synlett*, **1991**, *11*, 755-763.
3. C. Bruneau, Z. Kabouche, M. Neveux, B. Seiller, P.H. Dixneuf, *Inorg. Chim. Acta*, **1994**, *222*, 154-163.
4. C. Ruppin, S. Lécolier, P.H. Dixneuf, *Tetrahedron Lett.*, **1988**, *29*, 5365-5368.
5. Z. Kabouche, C. Bruneau, P.H. Dixneuf, *Tetrahedron Lett.*, **1991**, *32*, 5359-5362.
6. M. Neveux, C. Bruneau, P.H. Dixneuf, *J. Chem. Soc., Perkin Trans I*, **1991**, 1197-1199.
7. *β–oxopropyl formate (1).* 83%, colourless liquid ; **IR** 1728 (CO) cm^{-1}. **^{1}H NMR** δ ($CDCl_3$, 300.133 MHz): 8.12 (s, 1 H, HCO); 4.72 (s, 2 H, CH_2); 2.15 (s, 3 H, CH_3). **MS** (*m/z*) 102 (M^+).
8. *Cholesteryl formate (3a).* 82%, white crystals m.p. 139-142 °C. **IR** 1727 (CO) ; 2936 (CH) cm^{-1}. **^{1}H NMR** δ ($CDCl_3$, 300.133 MHz): 7.99 (s, 1 H, CHO); 5.36 (d, 1 H, $^3J_{HH}$ = 3.9 Hz, CH-6); 4.70 (m, 1 H, CH-3); 2.33 (d, 2 H, $^3J_{HH}$ = 7.7 Hz); 1.98 (m, 2 H); 1.87 (m, 4 H); 1.59÷1.03 (m, 20 H). 1.00 (s, 3 H, Me-19); 0.89 (d, 3 H, $^3J_{HH}$ = 6.4 Hz, Me-21); 0.84 (d, 6 H, $^3J_{HH}$ = 6.4 Hz, Me-26 and Me-27); 0.65 (s, 3 H, Me-18). **MS** (*m/z*) 386 ($M\text{-}CO^+$).
   Lanosteryl formate (3b). 70%, white crystals m.p. 128-131 °C. **IR** 1729 (CO); 2930 (CH) cm^{-1}. **^{1}H NMR** δ ($CDCl_3$, 300.133 MHz): 8.04 (s, 1 H, CHO); 5.02 (t, 1 H, J = 6.9 Hz, CH-24); 4.54 (m, 1 H, CH-3); 1.95 (m, 4 H); 1.90÷0.93 (m, 19 H); 1.6 (s, 3 H, Me-29); 1.53 (s, 3 H, Me-27); 1.18 (s, 3 H, Me-19); 0.92 (d, 3 H, $^3J_{HH}$ = 4.9 Hz, Me-21); 0.83 (s, 3 H, Me-29); 0.80 (s, 3 H, Me-30); 0.73 (s, 3 H, Me-28); 0.62 (s, 3 H, Me-18). **MS** (*m/z*) 454 (M^+).
   Stigmasteryl formate (3c). 72%, white crystals m.p. 166-169 °C. **IR** 1710 (CO); 2920 (CH) cm^{-1}. **^{1}H NMR** δ ($CDCl_3$, 300.133 MHz): 8.02 (s, 1 H, CHO); 5.28 (d, 1 H, J = 4.7 Hz, CH-6); 5.08 (dd, 1 H, J = 15.1 and 8.5 Hz, CH-23); 4.94 (dd, 1 H, J = 15.1 and 8.5 Hz, CH-22); 4.72 (m, 1 H, CH-3); 2.42 ÷ 0.85 (m, 25 H); 1.00 (d, 6 H, $^3J_{HH}$ = 6.2 Hz, Me-26 and Me-27); 0.83 (d, 3 H, $^3J_{HH}$ = 6.4 Hz, Me-21); 0.82 (s, 3 H, Me-19); 0.79 (t, 3 H, $^3J_{HH}$ = 7.3 Hz, Me-29); 0.69 (s, 3 H, Me-18). **MS** (*m/z*) 412 ($M\text{-}CO^+$).