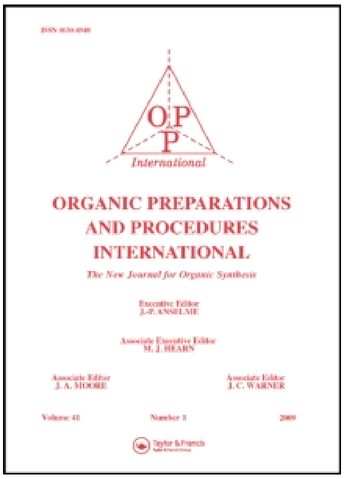


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A SIMPLE ONE-STEP SYNTHESIS OF 5-ACETOXY-6-CHLORO-2-HEXANONE

Naresh K. Sangwan[a]; Kuldip Singh Dhindsa[a]
[a] Department of Chemistry and Biochemistry, Haryana Agricultural University, Hisar, INDIA

To cite this Article Sangwan, Naresh K. and Dhindsa, Kuldip Singh(1989) 'A SIMPLE ONE-STEP SYNTHESIS OF 5-ACETOXY-6-CHLORO-2-HEXANONE', Organic Preparations and Procedures International, 21: 2, 241 — 242
To link to this Article: DOI: 10.1080/00304948909356373
URL: http://dx.doi.org/10.1080/00304948909356373

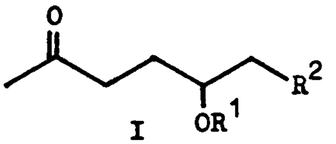
A SIMPLE ONE-STEP SYNTHESIS OF 5-ACETOXY-6-CHLORO-2-HEXANONE

Submitted by
(11/24/87)

Naresh K. Sangwan* and Kuldip Singh Dhindsa

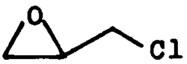
Department of Chemistry and Biochemistry
Haryana Agricultural University
Hisar-125 004, INDIA

The synthesis of 5,6-dihydroxy-2-hexanone (Ia) and its derivatives which serve as models of desoxy sugars,[1] has been studied extensively.[2,3] The general synthetic strategy involved base-catalyzed condensation of ethyl acetoacetate and chloromethyloxirane (II) to give lactone III, which upon treatment with potassium carbonate yielded Ia.[2] As the corresponding 6-chloro derivative Ib could not be prepared by the anticipated ring opening of lactone III with mineral acids, Pojarlieff developed a five-step procedure from ethyl acetoacetate and II and obtained Ib in poor overall yield (*ca*. 3%).[3] Furthermore, because of its strong tendency to undergo internal condensation and polymerization, Ib was directly converted into its stable derivatives such as methyllactolide or acetate Ic.[3] This communication reports a convenient one-step synthetic method for preparation of Ic[4] by treatment of 2,4-pentanedione (IV) with II in aqueous KOH in 40% yield. The compound was fully characterized by analytical and spectral data described in the Experimental Section. The identity of the product was further supported by preparation of its semicarbazone derivative with identical melting point reported in literature[3] and by its spectral and analytical data. Though much remains to be done to establish the mechanism of its transformation, it seems reasonable to assume the intermediacy of 3-acetyl-6-chloro-5-hydroxy-2-hexanone formed by the attack of anion of IV on oxiranyl ring of II, followed by *in-situ* carbon to oxygen acetyl transfer reaction. However, we have not been able

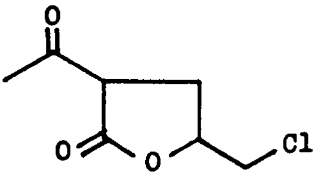


I

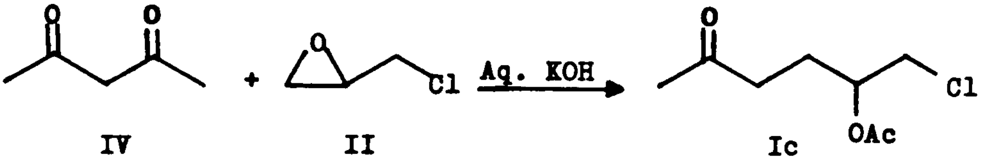
Ia) R^1 = H, R^2 = OH
b) R^1 = H, R^2 = Cl
c) R^1 = Ac, R^2 = Cl



II



III



IV II Ic

to isolate this intermediate.

EXPERIMENTAL SECTION

The purity of the product was checked by TLC over silica gel-G. The proton and carbon-13 NMR spectra were recorded on a Bruker AM 400 instrument at field strengths of 400 and 100 MHz respectively in dueterated chloroform using TMS as an internal standard. Chemical shifts are described in d ppm units.

5-Acetoxy-6-chloro-2-hexanone (Ic).- A solution of 2,4-pentanedione (5.0 g, 0.05 mol) in aqueous KOH (6.7%, 50 ml) was stirred under nitrogen atmosphere[5] with chloromethyloxirane (5.55 g, 0.06 mol) for 48 hrs. The reaction mixture was extracted with ether, the etheral extract was washed with water, dried over sodium sulphate and concentrated. The oily product thus obtained was subjected to distillation under vacuum to give 3.85 g (40%) of pure Ic, bp. 102°/2 mm, lit.[3] 117°/5 mm. ^{1}H NMR: δ 1.88-2.04 (m, 2H, $C_4\underline{H}_2$), 2.09 (s, 3H, $C_5OCOC\underline{H}_3$), 2.16 (s, 3H, $C_1\underline{H}_3$), 2.51 (t, 2H, $C_3\underline{H}_2$, J = 7.3 Hz), 3.57 (dd, 1H, $C_6\underline{H}$, J = 5.5 and 11.7 Hz), 3.64 (dd, 1H, $C_6\underline{H}$, J = 4.6 and 11.7 Hz), 5.03 (m, 1H, $C_5\underline{H}$).

^{13}C NMR: δ 20.89 (C_5-OCO$\underline{C}$), 25.71 (C_1), 29.87 (C_3), 38.97 (C_4), 45.58 (C_6), 72.16 (C_5), 170.43 (C_5-O$\underline{C}$), 207.03 (C_2).

Anal. Calcd for $C_8H_{13}ClO_3$: C, 49.88, H, 6.80. Found: C, 50.10, H, 6.98

Semicarbazone of Ic.- Treatment of Ic with semicarbazide hydrochloride as usual gave instantanously its semicarbazone derivative, mp. 131°, lit.[3] 131°.

^{1}H NMR: δ 1.87 (s, 3H, $C_1\underline{H}_3$), 1.97 (m, 2H, $C_4\underline{H}_2$), 2.09 (s, 3H, $C_5OCOC\underline{H}_3$), 2.30 (t, 2H, $C_3\underline{H}_2$, J = 7.3 Hz), 3.61 (m, 2H, $C_6\underline{H}_2$), 5.14 (m,1H, $C_5\underline{H}$).

^{13}C NMR: δ 15.83 (C_1), 20.94 (C_5-OCO$\underline{C}$), 27.57 (C_3), 34.00 (C_4), 45.39 (C_6), 72.14 (C_5), 148.66 (C_2), 158.22 (NH_2-$\underline{C}$O), 170.40 (C_5-O$\underline{C}$).

Anal. Calcd for $C_9H_{16}ClN_3O_3$: C, 43.29, H, 6.46, N, 16.82

Found: C, 43.42, H, 6.29, N, 17.03

REFERENCES

1. P. A. Levene and A. Walti, J. Biol. Chem., 88, 771 (1930).
2. W. Traube and E. Lehmann, Ber., 34, 1971 (1901); J. Colonge and A. Clerc, Bull. Soc. Chim. Fr., 836 (1955); J. Colonge and A. Girantet, ibid, 1166 (1962).
3. G. Pojarlieff, J. Am. Chem. Soc., 56, 2685 (1934).
4. N. K. Sangwan and S. N. Rastogi, Chem. Ind. (London), 225 (1984); Indian J. Chem., Sect. B, 23, 1284 (1984).
5. Without the nitrogen atmosphere, a complex mixture of intractable products was obtained.

****