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NOTE

AN IMPROVED SYNTHESIS OF ETHANAL-1-^{13}C

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Summary The title compound is obtained from sodium acétate-1-^{13}C by a shorter synthesis than the usual one . In the last step, acetyl chloride-1-^{13}C is reduced by tri-butyltin hydride with palladium(0) complexe .

Key words Ethanal, Carbon labelling .

Ethanal has a widespread use in synthesis of labelled compounds . We needed the 1-^{13}C enriched compound for preparation and spectroscopic study of thiazolidines-2-^{13}C , so it seems of interest to improve the yields of its preparation .

Ethanal-1-^{13}C is generally obtained by reaction of sodium acetate-1-^{13}C with an acyl chloride , reduction of the acetyl chloride to the labelled ethanol and oxidation of the alcohol [1] .

Since the Rosenmund process[2] , many reagents have been used to achieve the one-step reduction of acyl chlorides to aldehydes . Included among these were organosilicon hydrides[3] , tri-tert-butoxyaluminium hydride [4], bis

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(triphenylphosphine) cuprous borohydride[5], complex copper cyanotrihydroborate salts[6], sodium borohydride with dimethylformamide[7], pyridine[8] or cadmium chloride[9], anionic iron -[10], chromium - or tungsten -[11] carbonyl complexes and tributyltin hydride with tetrakis (triphenylphosphine) palladium (0)[12].

The low-boiling point of ethanal and its acid- or base-catalyzed fast self-condensation restrict the choice of the reagent. We have obtained pure labelled acetyl chloride in a 80 % yield from commercial sodium acetate-1-^{13}C and benzoyl chloride. Acetyl chloride is best reduced by tributyltin hydride with palladium (0) complex ; the mechanism of this reaction has been the subject of several investigations[13,14]; the crude product is contaminated by toluene used as solvent but is correct for many purposes ; if necessary, it can be purified by distillation.

The synthesis of ethanal-1-^{13}C in this manner has several advantages : it requires no particular apparatus, the process is shortenned and the yields are improved.

Experimental

Acetyl chloride-1-^{13}C - 1.98 g (23.8 mmol.) of commercial sodium acetate-1-^{13}C are placed in a 25 ml round bottom flask ; the salt is vacuum-dried by warming the flask during a few minutes with a little flame and then allowed to cool to room temperature. The vacuum is broken and 10 ml of freshly distilled benzoyl chloride are added to the anhydrous salt. The flask is fitted with a column head equipped with a thermometer, and a water-cooled trap protected from moisture by calcium chloride. The mixture is then warmed until the distillate temperature reaches 80°C. The liquid in the trap is distilled. Yield : 80 % ; bp 51-52°C ; ^{1}H NMR ($CDCl_3$) : 2.66 ppm, d, J_{CCH} = 7.5 Hz.

Ethanal-1-^{13}C - A 50 ml three-necked flask is fitted with a nitrogen inlet , a thermometer , a dropping funnel and a short air condenser connected to a trap cooled to -70°C . A slow nitrogen stream is then admitted . 0.173 g (0.15 mmol.) of (tetrakis) triphenylphosphine palladium and a solution of 1.19 g (15 mmol.) of labelled acetyl chloride in 15 ml of anhydrous toluene are placed in the flask . 4.95 g (17 mmol.) of tributyltin hydride are added over a period of ten minutes . The mixture becomes warm and ethanal is carried in the trap by bubbling nitrogen during one hour ; the trap contains 1.284 g of a solution of ethanal in toluene (ethanal : 45 parts by weight , 63 parts by mole as measured by integration of the NMR signals) . Yield : 82 % ; ^{1}H NMR ($CDCl_3$) : 2.13 ppm , dd , 3H , J_{HCCH} = 3.0 Hz , J_{CCH} = 6.5 Hz ; 9.74 ppm , dq , 1H , J_{CH} = 172.3 Hz .

References

1 . Braun J. and Metzger J. - Bull. Soc. Chim. Fr. 503 (1967) .

2 . Mossetig E. and Mozingo R. - Org. React. 4 : 362 (1948) .

3 . Citron J. - J. Org. Chem. 34 : 1977 (1969) .

4 . Brown H. and Subba Rao B. - J. Am. Chem. Soc. 80 : 5377 (1958) .

5 a . Fleet G. and Harding P. - Tetrahedron Lett. 975 (1979) .

b . Sorrell T. and Pearlman P. - J. Org. Chem. 45 : 3449 (1980) .

6 . Hutchins R. and Markowitz M. - Tetrahedron Lett. 21 : 813 (1980) .

7 . Babler J. and Invergo B. - Tetrahedron Lett. 22: 11 (1981) .

8 . Babler J. - Synth. Commun. 12 : 839 (1982) .

9 . Johnstone R. and Telford R. - J. Chem. Soc. Perkin Trans. 1 27 (1980) .

10 a. Watanabe Y., Mitsudo T., Tanaka M., Yamamoto K., Okajima T. and Takegami Y. - Bull. Chem. Soc. Jpn. 44: 2569 (1971) .

b. Cole T. and Petit R. - Tetrahedron Lett. 781 (1977) .

11 . Kao S., Gaus., Youngdahl K. and Darensbourg M. - Organometallics 3 : 1601 (1984) .

12 . Four P. and Guibe F. - J. Org. Chem. 46 : 4439 (1981) .

13 . Labadie J. and Stille J. - J. Am. Chem. Soc. 105 : 6129 (1983) .

14 a. Lusztyk J., Lusztyk E., Maillard B., Lunazzi L. and Ingold K. - J. Am. Chem. Soc. 105 : 4475 (1983) .

b. Lusztyk J., Lusztyk E., Maillard B. and Ingold K. - J. Am. Chem. Soc. 106 : 2923 (1984) .