Quantitative reactions for the chain elongation of aliphatic compounds

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SUMMARY Procedures are described for the reaction of methanesulfonates with potassium cyanide and for the conversion of the resulting nitriles to methyl esters. Both reactions in this method of chain elongation are quantitative and do not lead to alterations of olefinic double bonds.

KEY WORDS synthesis · alcohols · methanesulfonates · mesylates · alkyl cyanides · nitriles · methyl esters · fatty acids · chain elongation · *cis,trans* double bonds

LONG-CHAIN ALKYL METHANESULFONATES (mesylates) are versatile intermediates in lipid synthesis (1–4). The present communication describes the use of these alkylating agents for the elongation (5) of aliphatic chains.

An alkyl methanesulfonate, which can be obtained from a methyl ester via the alcohol (6), is converted to a nitrile by reaction with potassium cyanide. The reaction proceeds in dimethyl sulfoxide (7), without the formation of side products, and is complete after 1 hr. The alkyl cyanide is treated with methanol–HCl and the imino ether formed is hydrolyzed with aqueous, concentrated hydrochloric acid. Thus, a methyl ester having one methylene group more than the starting methyl ester is obtained in quantitative yield. The preparation of methyl *cis*-10-nonadecenoate is described here as an example for the elongation of aliphatic chains.

cis-9-Octadecenyl Cyanide. Powdered potassium cyanide (1.96 g, 0.03 mole) is placed in a 250 ml, three-necked flask fitted with a condenser, inlet and outlet tubes for purified nitrogen, and a stirrer. A solution of 6.94 g (0.02 mole) of *cis*-9-octadecenyl methanesulfonate (1) in 120 ml of dimethyl sulfoxide is added. The mixture is stirred vigorously and heated in a water bath at 80°C for 1 hr. 100 ml of diethyl ether and then 40 ml of air-free water are added slowly to the cold reaction mixture, and after addition of another 100 ml of ether, the phases are separated in a funnel. The aqueous layer is extracted with four portions of ether (40 ml), and the combined ether phases are washed with two 40 ml portions of water and dried over anhydrous sodium sulfate. The solvent is removed in a rotary evaporator and then under high vacuum, yielding 5.46 g (96%) of *cis*-9-octadecenyl cyanide; mp −16 to −15°C, CST with nitromethane (8) 8.5°C.

Methyl cis-10-Nonadecenoate. Thoroughly dried *cis*-9-octadecenyl cyanide (2.77 g, 0.01 mole) is placed in a 250 ml, three-necked flask fitted with a condenser, inlet and outlet tubes for dry nitrogen, magnetic stirrer, dropping funnel, and calcium chloride tubes. A freshly prepared ice-cold solution (50 ml) of hydrogen chloride in anhydrous methanol (30%, w/w) is added dropwise. The reaction mixture is stirred for 2 hr at room temperature. Aqueous concentrated hydrochloric acid (5 ml) is then added carefully and stirring is continued for 2 hr. Air-free water (60 ml) and 150 ml of diethyl ether are added, and the aqueous layer is separated and extracted with four 100 ml portions of ether. The combined ether phases are washed twice with 100 ml of water, 1% potassium carbonate solution (until basic), and water, and are dried over anhydrous sodium sulfate. The solvent is removed on a rotary evaporator, then under high vacuum, yielding 3.00 g (97%) of methyl *cis*-10-nonadecenoate; mp −5 to −4°C, CST with nitromethane 50.5°C.

cis-9-Octadecenyl cyanide and methyl *cis*-10-nonadecenoate were analyzed and characterized also by thin-layer chromatography on Silica Gel G, on adsorbent layers impregnated with silver nitrate, and by gas–liquid chromatography on ethylene glycol succinate. The IR spectra of these preparations showed the bands to be expected for unsaturated long-chain nitriles and esters. The spectra did not exhibit absorptions near 965 cm^{-1} associated with a *trans*-C–H out-of-plane deformation. Chromatographic and spectroscopic analyses indicated that *cis–trans* isomerizations and other alterations of double bonds did not occur in the course of synthesis.

We have applied the procedures described for the preparation of methyl *cis,cis*-10,13-nonadecadienoate and methyl *cis,cis,cis*-10,13,16-nonadecatrienoate from methyl linoleate and methyl linolenate, respectively.

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Abbreviation: CST, critical solution temperature.