

Polish Patent Office

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Process for the preparation of dichloropropane derivatives

This invention relates to a method for producing derivatives of 1,1-dichloropropane which are important intermediates in the synthesis of a wide variety of chemicals used in pharmaceuticals, pesticides, and other synthetic materials. Known methods for manufacturing derivatives of dichloropropane derivatives rely on the reaction between olefins and chloroform, led to the dried potassium alkoxides of tertiary alcohols such as tertiary butoxide, or the reaction between olefins and esters or salts of trichloroacetic acid to sodium and potassium alkoxides. The response time transiently formed highly unstable dichlorocarbene, which attaches to an olefin to form a derivative dichloropropane. (Organic Reactions Vol.XIII N.Y. 1963).

These methods work because of metallic sodium or potassium alkoxides without receiving alcohol and the need for large excess olefins pose a significant fire hazard and are uneconomical. Additional difficulties arise from the need for strictly anhydrous substrates and protection against moisture, the reaction mixture the air. All these difficulties have been eliminated in the method according to the invention. According to the invention derivatives of 1,1-dichlorocyclopropane presented by the general formula 1, where R^1 , R^2 , R^3 and R^4 are hydrogen atoms, alkyl groups, saturated or unsaturated, aryl groups, alkoxy groups, thioalkoxy and hydrocarbon radicals containing functional groups such as ether, ester or nitrile or R^1 together with R^2 or R^1 together with R^3 isocyclic means of the ring or heterocycle, is obtained by connecting dichlorocarbene to olefins in the reaction between compounds of the general formula 2, wherein R^1 , R^2 , R^3 and R^4 are switched fundamentals are important and chloroform, carried ion to the alkali metal hydroxides and quaternary ammonium compounds, serving as catalysts.

The catalysts used are quaternary ammonium to build a $R^I R^{II} R^{III} R^{IV} N + Y^-$, where R^I , R^{II} , R^{III} , R^{IV} equal, or different, represent alkyl substituents such as methyl, ethyl, propyl, aralkyl, as benzyl or form part of a saturated heterocyclic ring nitrogen, such as piperidine or pyrrolidone, and Y is Cl, Br, OH or SO_3H^- . Alkali metal hydroxides can be used in powdered form, either directly or as a suspension in inert organic solvents, but the best is to use a form of concentrated aqueous solutions. The reaction is carried out at 0-60 °C (boiling point of chloroform) depending on the type of unsaturated compound, a catalyst and as they apply an alkali metal hydroxide. Depending on the type of unsaturated compound and its structure, fixed proportions apply between the unsaturated compound and chloroform.

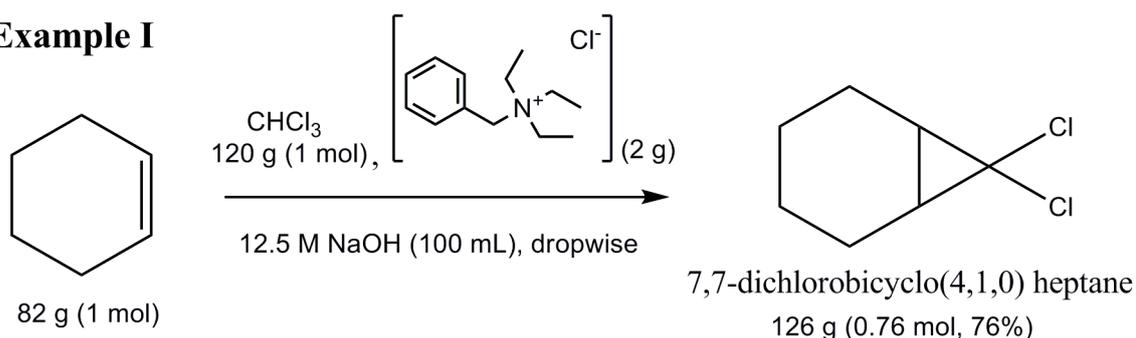
The resulting 1,1-dichlorocyclopropane derivatives differ significantly in physical properties from start materials (unsaturated compound and chloroform). They are isolated and purified by known methods - usually by distillation under normal or reduced pressure or crystallization. Used in excess starting materials - olefin or chloroform - are recovered almost completely unchanged. Synthesis of dichlorocyclopropanes of formula 1 according to the invention eliminates the the need for anhydrous conditions, dangerous & difficult reagents and allows a high

yield. The following examples explain the essence of the invention without limiting its scope.

Example I. Preparation of 7,7-dichlorobicyclo(4,1,0) heptane (R^1 and $R^2 = -(CH_2)_4-$, $R^3=R^4=H$).

To a mixture of 82 g (1 mol) of cyclohexene, 120 g (1 mol) of chloroform and 2 g of triethylbenzylammonium chloride, 100 mL of 50% $NaOH_{(aq)}$ is slowly added over 3 h. The solution is stirred and temperature kept between 20-40 °C. The mixture is then diluted with water, the organic product separated into DCM, washed and distilled under reduced pressure. 126 g of 7,7-dichlorobicyclo(4,1,0) heptane is obtained with BP 71-73 °C / 8 mmHg. Yield of 76%.

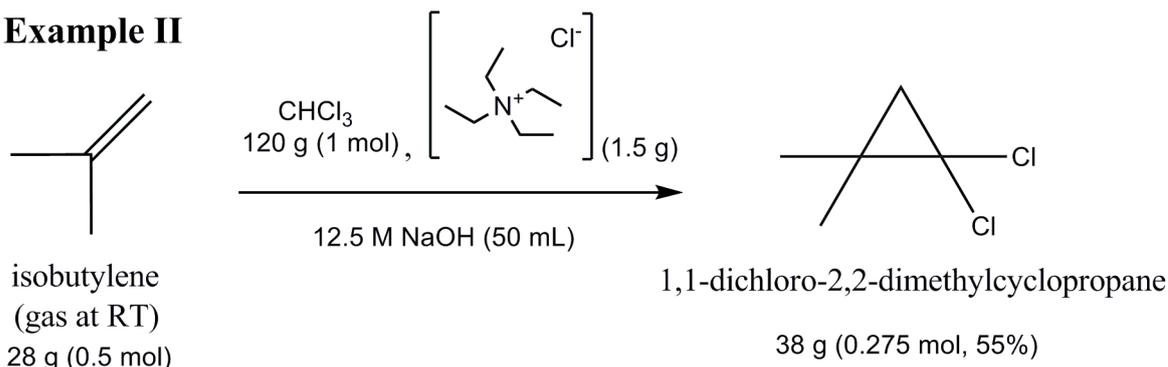
Example I



Example II. Preparation of 1,1-dichloro-2,2-dimethylcyclopropane ($R^1=R^3=CH_3$, $R^2=R^4=H$).

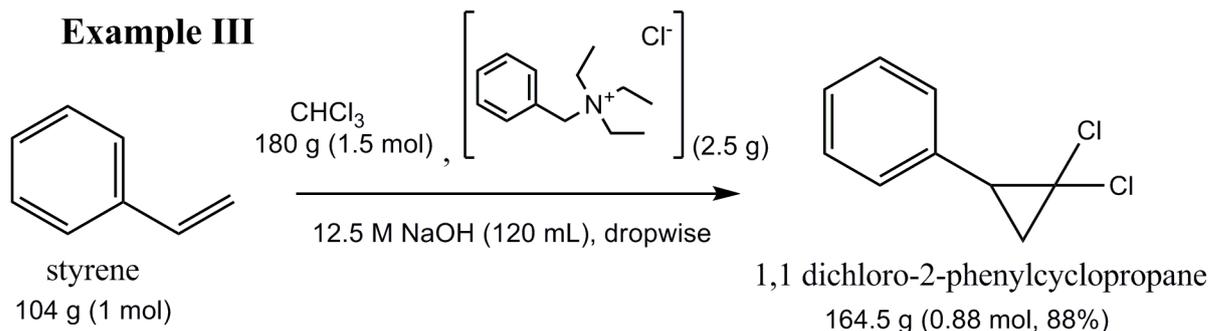
Into a thick-walled glass cylinder is placed a solution of 28 g (0.5 mol) of isobutylene at 120 g (1 mole) of chloroform, 1.5 g of tetraethylammonium chloride and 50 mL of 50% $NaOH_{(aq)}$. The bottle is tightly closed and shaken for 4 h. Mixture then diluted with water and worked up as in Example I. Yield: 38 g of 1,1-dichloro-2,2-dimethylcyclopropane, BP of 118-119 °C. Yield 55%.

Example II



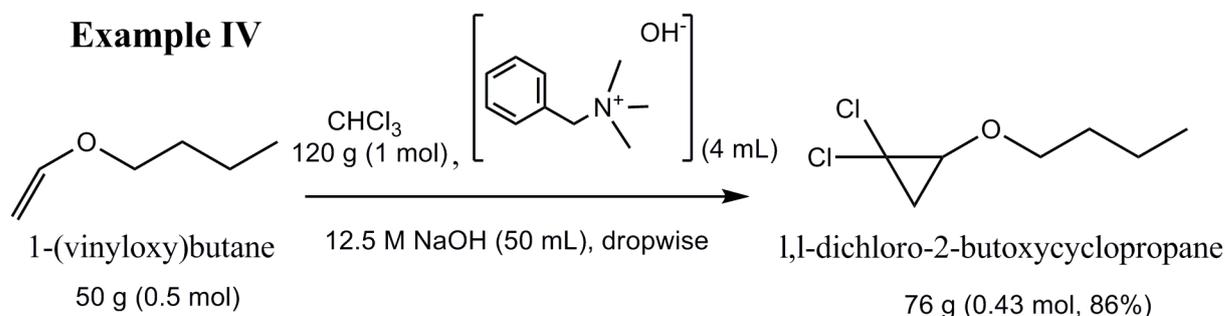
Example III. Preparation of 1,1-dichloro-2-phenylcyclopropane ($R^1=C_6H_5$, $R^2=R^3=R^4=H$).

Proceeding analogously to the method described in Example I with 104 g (1 mol) of styrene, 180 g (1.5 mol) chloroform, 120 mL 50% $NaOH_{(aq)}$ and 2.5 g of triethylbenzylammonium chloride obtained by 1,1-dichloro-2-phenylcyclopropane. BP 124 °C/20 mmHg. Yield 164.5 g, or 88%.



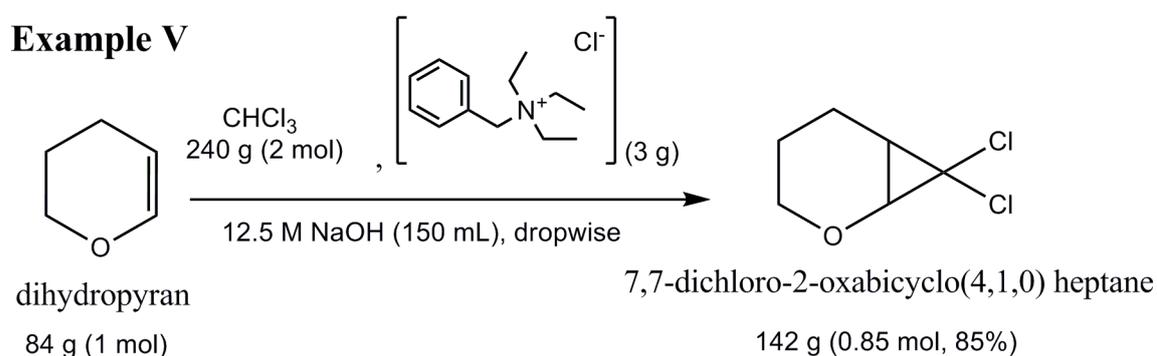
Example IV. Preparation of 1,1-dichloro-2-butoxycyclopropane ($\text{R}^1\text{OC}_4\text{H}_9$, $\text{R}^2=\text{R}^3=\text{R}^4=\text{H}$).

To a vigorously stirred solution of 50 g (0.5 mol) 1-(vinyl)oxybutane in 120 g (1 mol) of chloroform, containing 4 mL of Triton B was added dropwise 50 mL of 50% $\text{NaOH}_{(\text{aq})}$ maintaining the temperature at 30-35 °C over 3 h. Workup as for example I gave 1,1-dichloro-2-butoxy-cyclopropane with BP 82.5 °C at 20 mmHg. Yield 76 g or 83%.



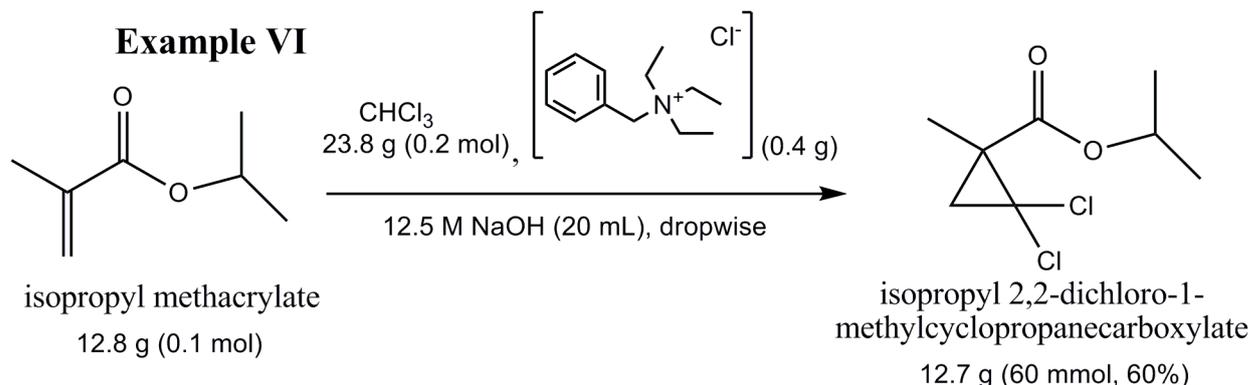
Example V. Preparation of 7,7-dichloro-2-oxabicyclo(4,1,0) heptane (R^1 and $\text{R}^2=(\text{CH}_2)_3\text{O}^-$, $\text{R}^3=\text{R}^4=\text{H}$).

Proceeding analogously to the method described in Example I: 84 g (1 mol) dihydropyran, 240 g (2 mol) of chloroform, 3 g of triethylbenzylammonium chloride and 150 mL of 50% $\text{NaOH}_{(\text{aq})}$ was obtained 7,7-dichloro-2-oxabicyclo(4,1,0) heptane with BP 76 °C / 9 mmHg. Yield 142 g, 85%.

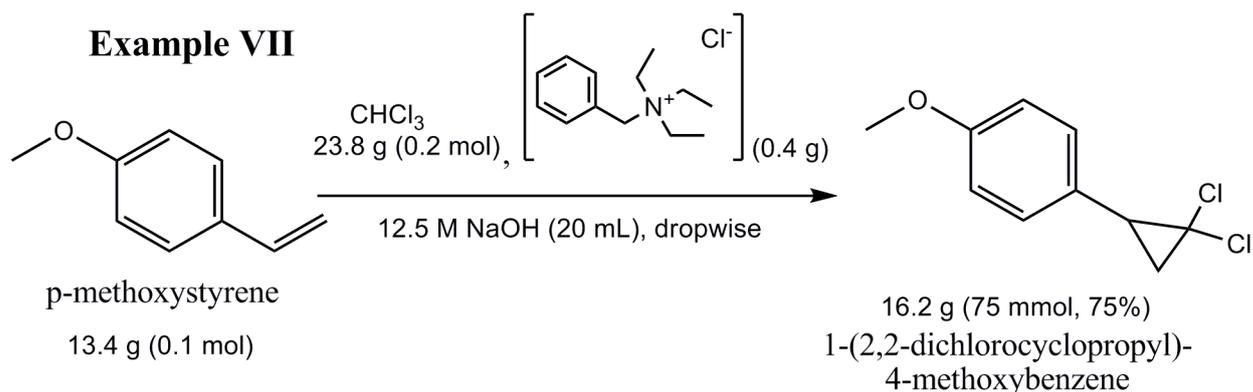


Example VI. Preparation of isopropyl 2,2-dichloro-1-methylcyclopropanecarboxylate. To 12.8 g (0.1 mol) of isopropyl methacrylate, 23.8 g (0.2 mol) chloroform and 0.4 g of triethylbenzylammonium chloride, 20 mL of 50% $\text{NaOH}_{(\text{aq})}$ is added dropwise while stirring keeping the temperature below 30 °C. The reaction mixture is poured into water, extracted with 30 mL of DCM, washed, dried and distilled to give an

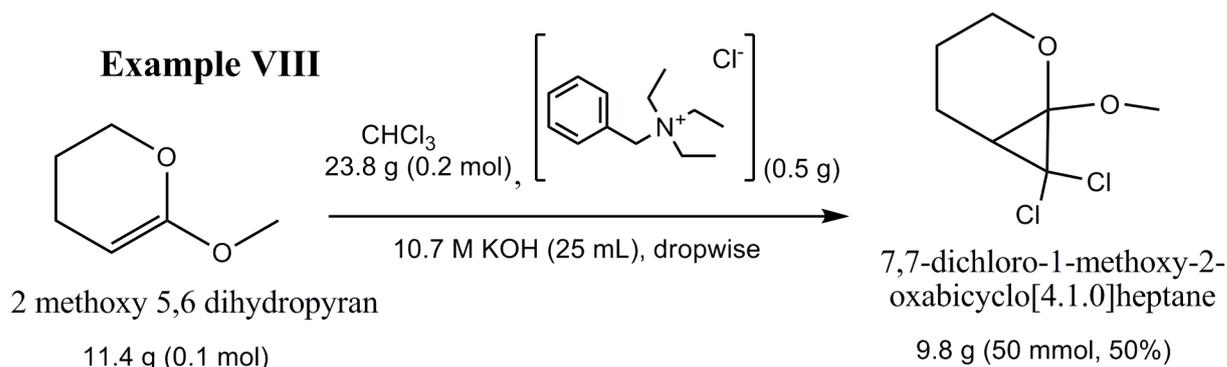
isopropyl ester of tert-butyl 2,2-dichloro-1-methylcyclopropanecarboxylate with BP 80 °C at 11 mmHg. Yield 12.7 g, 60%.



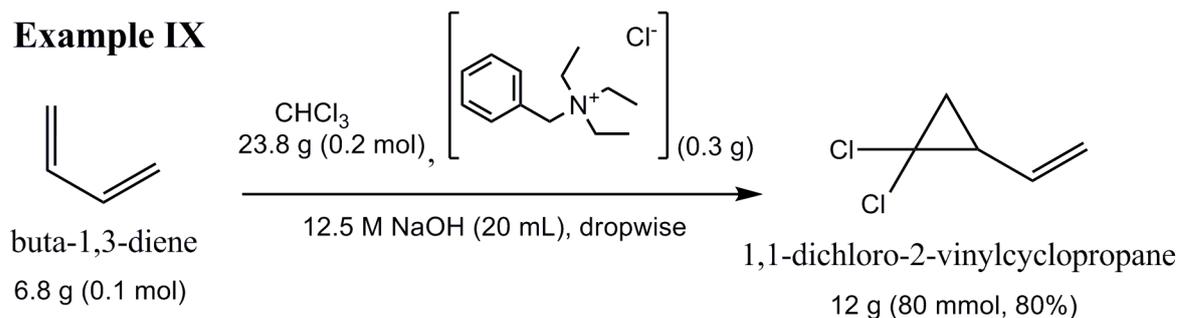
Example VII. Preparation of 1-(2,2-dichlorocyclopropyl)-4-methoxybenzene. 13.4 g (0.1 mol) of *p*-methoxystyrene, 23.8 g (0.2 mol) of chloroform, 0.4 g of tetraethylammonium chloride are mixed and 20 mL of 50% NaOH_(aq) is added dropwise, keeping the temperature below 35 °C. The reaction mixture is poured into water, extracted with DCM and evaporated, yielding 16.2 g, 1-(2,2-dichlorocyclopropyl)-4-methoxybenzene, BP of 150 °C at 14 mmHg, which represents 75% of theoretical.



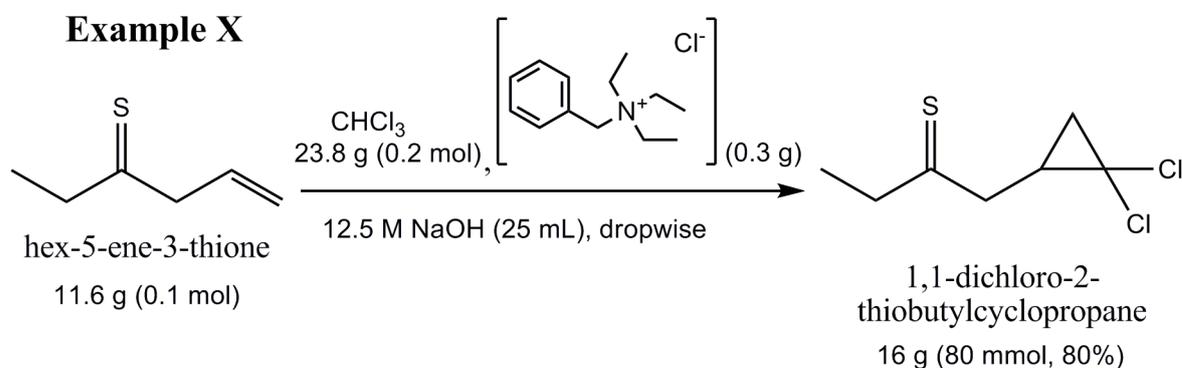
Example VIII. Preparation of 7,7-dichloro-1-methoxy-2-oxabicyclo(4.1.0)heptane. Mixed is 11.4 g (0.1 mol) of 2-methoxy-5,6-dihydropyran, 23.8 g (0.2 mol) of chloroform, 0.5 g of triethylbenzylammonium chloride and 25 mL of 60% KOH_(aq) so that the temperature does not exceed 35 °C. The mixture is stirred at this temperature for 3 h, then diluted with water, extracted with 30 mL of DCM. After washing with water the organic phase is evaporated and the residue distilled under reduced pressure, collecting 7,7-dichloro-1-methoxy-2-oxabicyclo(4.1.0)heptane. BP 110 °C at 20 mmHg. Yield 9.8 g, or 50%.



Example IX. Preparation of 1,1-dichloro-2-vinylcyclopropane. To a mixture of 6.8 g (0.1 mol) 2-methyl-1,3-butadiene, 23.8 g (0.2 mol) of chloroform and 0.3 g triethylbenzylammonium chloride is added dropwise 20 mL of 50% NaOH_(aq) keeping the temperature below 20 °C with stirring. After the reaction mixture was diluted with water, extracted with DCM, washed and rotavapped the 1,1-dichloro-2-vinylcyclopropane with BP of 44 °C at 15 mmHg. Yield: 12 g, 80% of theoretical.

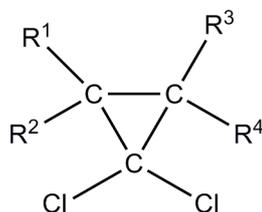


Example X. Preparation of 1,1-dichloro-2-thiobutylcyclopropane. Mixed are 11.6 g (0.1 mol) hex-5-ene-3-thione, 0.3 g of triethylbenzylammonium chloride, 23.8 mL (0.2 mol) of chloroform and added dropwise with vigorous stirring in 25 mL of 50% NaOH_(aq). The reaction temperature is kept below 40 °C, mixed for 3 h, then quenched with water. It is extracted twice into chloroform, washed with water and dried with anhydrous magnesium sulfate. Evaporation of solvent gave 16 g of 1,1-dichloro-2-thiobutylcyclopropane of BP of 70 °C, at 11 mmHg. (80% yield).

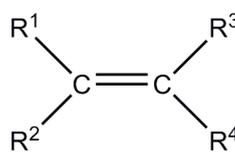


Reservations

First Process for the preparation of derivatives of 1,1-dichlorocyclopropane of the general formula 1 when R¹, R², R³ and R⁴ are hydrogen atoms, alkyl groups saturated or unsaturated, aryl groups, alkoxy groups, thioalkoxy group and hydrocarbon radicals containing functional groups such as ether, ester, or nitrile or R¹ together with the R² or R³ means of the ring or heterocyclic isocyclic road connecting dichlorocarbene to olefins, characterized in that the unsaturated compounds Formula 2, where R¹, R², R³, R⁴ are as defined above importance reacted with chloroform and alkali metal hydroxides with quaternary ammonium compounds as catalyst. **Second** All rights reserved; 1 when the alkali metal hydroxides are used as concentrated aqueous solutions. **Third** All rights reserved; When 1 and 2 are characterized by using quaternary ammonium chloride compound as catalyst in an amount not exceeding 0.1 mol per 1 mol of chloroform.



Formula 1.



Formula 2.

END OF PATENT TRANSLATION

Translated by Matthew Leonard, PhD Chemistry student on 03-Mar-2012.