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Synthesis of 1-Aminocyclopropane-1-carboxylic Acid Functional Derivatives

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The synthesis of certain functional derivatives of 1-aminocyclopropane-1-carboxylic acid, a potential plant growth regulator (particularly its methacryloyl- and isocyanate-containing derivatives) has been carried out.

1-Aminocyclopropane-1-carboxylic acid (ACC), the precursor compound in the biosynthetic pathway of phytormonal ethylene in plants, is considered to be a potential plant growth regulator distinguished from its ecologically harmless variants.[1–5] An investigation of facile synthetic methods of ACC and its various derivatives is therefore of considerable interest.

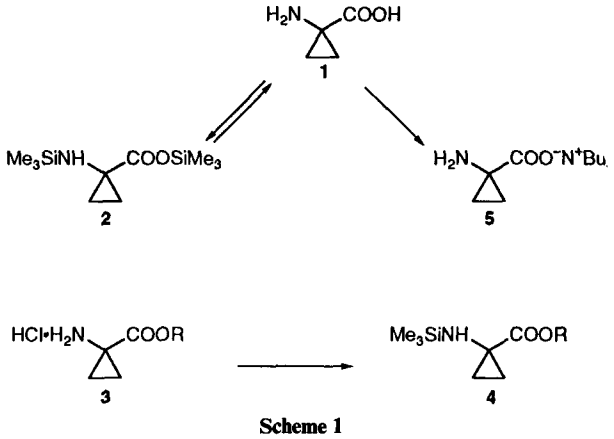
A series of low molecular weight ACC derivatives possessing biological activity has been already described.[1,6,7] In the present paper the synthesis of certain functional derivatives of ACC which can be further involved in various transformations, particularly the preparation of polymeric systems, has been investigated.

We describe here the synthesis of *N*-methacryloyl derivatives of ACC and its methyl ester, together with an unconfirmed synthesis of an ACC isocyanate derivative. These compounds are suitable for the creation of immobilized polymeric systems by substitution of the functional groups of polymer carriers. The ACC synthesis was conducted either *via* preparation of *N*-phthaloylmethionine or the preparation of 1,1′-cyclopropanedicarboxylic acid according to methods described by us earlier.[9,†]

† **1**, m.p. 248 °C (decomp.). Found: C 47.52; H 6.88; N 13.62. Calc. for $C_4H_7NO_2$:C 47.52; H 6.90; N 13.86%. TLC: R_f 0.083, methanol–chloroform (3:7); 0.25 butanol–acetic acid–water (60:10:30). TLC was performed on Silufol plates with iodine steam as developing agent. IR spectrophotometry was carried out on a Specord UV–VIS and mass spectrometry on an FM–8200 instrument.

The prepared ACC **1** was isolated as the *N,O*-di(trimethylsilyl) derivative **2** by treatment of the amino acid with excess trimethylsilyldiethylamine at 120 °C and simultaneous evaporation of diethylamine.‡

The *N*-trimethylsilyl derivative of ACC methyl ester **4** and the tetrabutylammonium salt of the acid **5**, which are soluble in many organic solvents, were used in further transformation stages (Scheme 1).



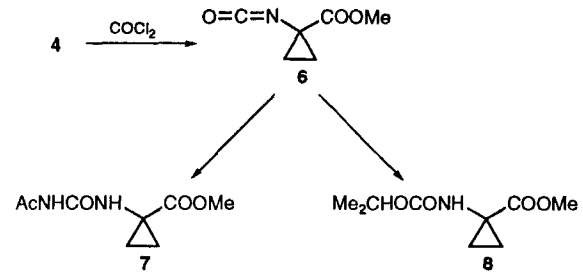
Scheme 1

N-Trimethylsilyl derivative **4** was obtained from methyl ester hydrochloride **3**[10] by treatment with trimethylsilyldiethylamine.‡ The esterification process was performed in excess alcohol and in the presence of thionyl chloride. This method of ACC ester synthesis included hydrogen chloride infusion through an alcohol suspension of the amino acid and further treatment of the reaction mixture with ethyl orthoformate, and has been proved to be very convenient.

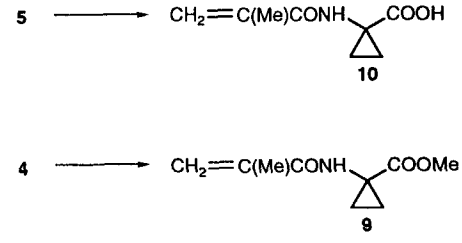
The trimethylsilyl derivative of ACC ester prepared was further involved in the synthesis of the methyl ester of 1-isocyanatocyclopropane-1-carboxylic acid **6**. It was reported earlier that esters of 1-isocyanatocyclopropane-1-carboxylic acid can be prepared in low yield by using the ethyl ester of isocyanatoacetic acid as an intermediate compound.[8] The last ethyl ester was prepared by treatment of the glycine hydrochloride ethyl ester with phosgene.

In the present work the methyl ester of 1-isocyanatocyclopropane-1-carboxylic acid **6** was synthesized by treatment of the methyl ester of the *N*-trimethylsilyl derivative of ACC **4** with phosgene in the presence of triethylamine as hydrogen chloride acceptor. Our method showed a considerable increase in the final product yield.§ To confirm the structure of **6**, 1-(*N*-acetylcarbamoylamino)cyclopropane-1-carboxylic acid methyl ester **7** and (isopropoxycarbonylamino)cyclopropane 1-carboxylic acid methyl ester **8** were synthesised by treatment with excess acetamide and isopropyl alcohol, respectively (Scheme 2).§

The need for ACC derivatives with the ability to be directly involved in radical polymerisation reactions led us to the synthesis of *N*-methacryloyl ACC derivatives. In this case the preparation of 1-(*N*-methacryloylamino)cyclopropane-1-carboxylic acid **10** and 1-(*N*-methacryloylamino)cyclopropane-1-carboxylic acid methyl ester **9** was undertaken by reaction of methacrylic acid chloroanhydride with **4** (in ether and in the presence of triethylamine) and with the tetrabutylammonium salt of the acid **5** (in dimethylformamide), respectively (Scheme 3).¶ The last amide in particular was an oily product prepared by treatment of ACC with a 10% solution of tetrabutylammonium hydroxide.



Scheme 2



Scheme 3

Thus, the synthesis of new derivatives of the plant growth regulator 1-aminocyclopropane-1-carboxylic acid has been investigated. Some of the above compounds are appropriate for the preparation of polymeric derivatives.

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‡ **2**, yield 92%, b.p. 53–55 °C/1 mm Hg. Found: C 48.73; H 9.62; N 5.83; Si 23.06. Calc. for $C_{10}H_{23}NO_2Si_2$: C 48.98; H 9.39; N 5.71; Si 22.86%.

4, yield 88%, b.p. 52 °C/1 mm Hg. Found: C 51.08; H 9.27; N 7.38; Si 14.75. Calc. for $C_8H_{17}NO_2Si$: C 51.34; H9.09; N 7.49; Si 14.97%.

§ **6**: **4** was treated with phosgene in dry ether cooled at −40 °C in the presence of triethylamine, yield 6.6 g (93.5%), b.p. 46 °C/1 mm Hg. Found: C 50.87; H 4.96; N 9.72. Calc. for $C_6H_7NO_3$: C 51.06; H 4.96; N 9.92%. IR (v/cm^{-1}): 2260 (N=C=O); 1735 (C=O); 1048; 866 (cyclopropane).

7, yield 75.4%, m.p. 174–176 °C. Found: C 48.91; H 6.52; N 13.85. Calc. for $C_8H_{12}N_2O_4$: C 47.99; H 6.00; N 13.99%. *m/z*: M$^+$ 200.

8, yield 81.4%, m.p. 46 °C. Found: C 53.99; H 7.56; N 6.85. Calc. for $C_9H_{15}NO_4$: C 53.73; H 7.46; N 6.96%. *m/z*: M$^+$ 201.

¶ **9**: To a solution of ACC tetrabutylammonium salt **5** (10.3g, 0.03 mol) in dimethylformamide (100 ml), was added the chloroanhydride of methacrylic acid (3.8 ml, 0.045 mol) dropwise with continuous stirring. The reaction mixture was filtered, the filtrate was dried *in vacuo* and the residue was treated with 25 ml of a 20% $KHSO_4$ solution. The treated residue was extracted with ethyl acetate and the extract was dried over potassium sulfate after which the solvent was evaporated. The final product was further purified by recrystallisation from ethanol–benzene (1:1), yield 2.4 g (46.7%, m.p. 156 °C). Found: C 56.36; H 6.64; N 8.06. Calc. for $C_8H_{11}NO_3$: C 56.80; H 6.51; N 8.28%. TLC: R_f 0.55 (methanol–chloroform, 1:9). IR (v/cm^{-1}): 1540, 3420 (NH).

10: To a solution of *N*-trimethylsilyl-1-aminocyclopropane-1-carboxylic acid methyl ester **4** (5.61 g, 0.03 mol) in dry ether (20 ml) was added triethylamine (4.5 ml, 0.035 mol) and then, with continuous stirring, methacrylic acid chloroanhydride (3 ml, 0.035 mol) in dry ether (10 ml) were additionally added. After 2 h the precipitated triethylamine hydrochloride was filtered, the ether was evaporated and the residue was distilled *in vacuo*, yield 3.8 g (70.1%, b.p. 52 °C/10 mm Hg). Found: C 58.73; H 7.08; N 7.81. Calc. for $C_9H_{13}NO_3$: C 59.01; H 7.10; N 7.65%. TLC: R_f 0.73 (methanol–chloroform, 1:9).