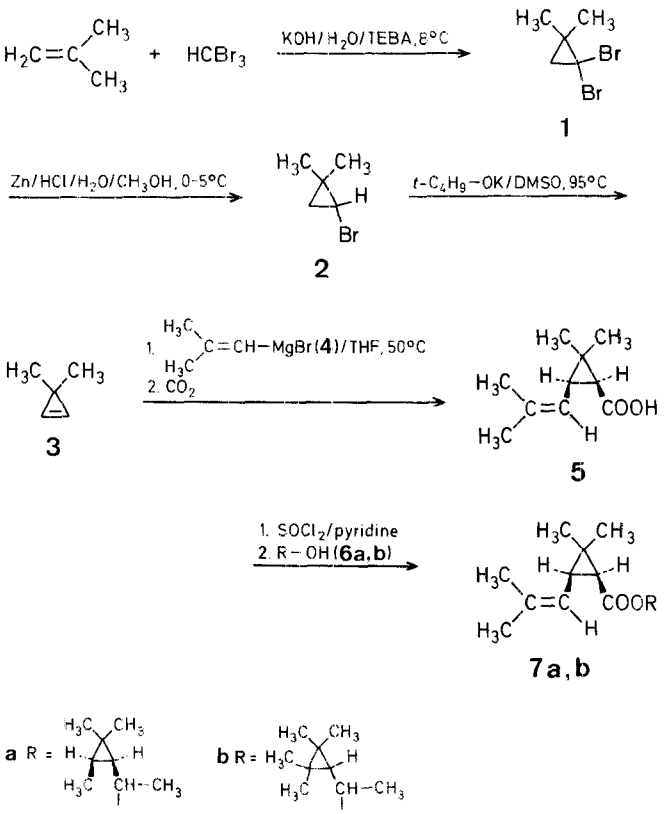

A New Synthesis of *cis*-Chrysanthemic Acid

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Chrysanthemic acid, a cyclopropane ring-containing component of the widely used insecticide pyrethrine, has received much attention in the chemical literature. In our previous study of the behavior of cyclopropene hydrocarbons toward alkyl- and arylmagnesium halides we found that these organometallic reagents add to the cyclopropene double bond under very mild conditions (ether, 0 °C)[1,2]; subsequent carboxylation affords stereospecifically *cis*-alkyl- or *cis*-arylcyclopropanecarboxylic acids, respectively. The increased interest in chrysanthemic acid and data[3] suggesting higher insecticidal activities of derivatives of *cis*-chrysanthemic acid **(5)** in comparison with that of the *trans* form prompted us to explore the possibility of adding 2-methylpropenylmagnesium bromide **(4)** to the double bond of 3,3-dimethylcyclopropene **(3)**.

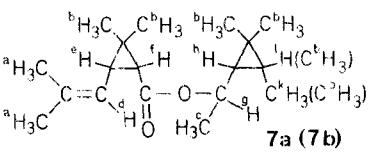
We report here that under somewhat more vigorous conditions (tetrahydrofuran, 50 °C) 2-methylpropenylmagnesium bromide **(4)** adds stereospecifically to 3,3-dimethylcyclopropene **(3)** to give, after carboxylation, *cis*-chrysanthemic acid **(5)** in 70% yield. This reaction might provide a useful method for the synthesis of *cis*-chrysanthemic acid **(5)** if the precursors **3** are readily available. In the three-step preparation of 3,3-dimethylcyclopropene **(3)** described in Ref.[4], isobutene is cyclopropanated with bromoform in the presence of potassium *t*-butoxide, the resultant 1,1-dibromo-2,2-dimethylcyclopropane **(1)** is hydrodebrominated (reduced) by means of tributylstannane, and the 1-bromo-2,2-dimethylcyclopropane **(2)** thus obtained is dehydrobrominated with potassium *t*-butoxide. In order to use, at least in part, cheaper and easier-to-handle reagents, we elaborated a modified synthesis of 3,3-dimethylcyclopropene **(3)** which involves cyclopropanation of isobutene under catalytic phase-transfer conditions and reduction of **1** with zinc dust in hydrochloric acid/methanol.

To our knowledge, the cyclopropanation of isobutene with bromoform under catalytic phase-transfer conditions has hitherto not been reported. The cyclopropanation of other alkenes with bromoform under catalytic phase-transfer conditions proceeds with good yields (70–80%) only when excess bromoform is used[5]. We have found that the phase-transfer catalyzed cyclopropanation of isobutene with bromoform proceeds with high yields when carried out in excess isobutene at 10 °C; the excess of isobutene can be easily removed from the reaction mixture and used in the next run. We optimized the reaction conditions by varying the ratio of reagents, solvent, and catalyst so that we can now obtain 1,1-dibromo-2,2-dimethylcyclopropane **(1)** in 98% yield based on bromoform. Hydrodebromination of **1** with zinc dust activated by hydrochloric acid (0–5 °C, 2 h, methanol) affords 1-bromo-2,2-dimethylcyclopropane **(2)** in high selectivity and 80% yield. To our knowledge, this process is simpler and more effective than other methods[7,8,9] of monoreduction of *gem*-dihalocyclopropanes.

Two esters of *cis*-chrysanthemic acid **(7a, b)** were obtained by reaction of acid **5** with thionyl chloride in the presence of pyridine followed by reaction with the previously described[11] tri- and tetramethylcyclopropylethanols **6a** or **6b**.

Thus, in the present study a new synthesis of *cis*-chrysanthemic acid is described and significant improvements in the preparation of the starting materials have been realized.

The structures of the synthesized products were established by ^{1}H-N.M.R. spectrometry where necessary. This applies in particular to compounds **7a, b**.



7a (7b)

The ^{1}H-N.M.R. spectra were recorded on Varian DA-60 JL (60 MHz) and Tesla BS-497 (100 MHz) spectrometers. The mass spectra were recorded using a MAT-111 instrument and the I.R. spectra on a Specord-75 IR spectrophotometer. G.L.C. analyses of the products were performed on a Pye-104 gas chromatograph using glass columns 1.5

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m × 4 mm (for compounds **1, 2, 7a, b:** SE-30 on Gas Chrom Z, 80–100 mesh; for **3:** β,β'-dioxypropionitrile on Celite C-20, 20–100 mesh; for **5:** 25% polyethylene glycol on Chromosorb Gas Chrom W, 80–100 mesh, treated with 2% orthophosphoric acid).

1,1-Dibromo-2,2-dimethylcyclopropane (1):
Aqueous 50% sodium hydroxide solution (200 ml) is added dropwise during 1 h to a stirred mixture of isobutene (150 g, 2.6 mol), bromoform (126 g, 0.5 mol), ethanol (20 ml), dichloromethane (250 ml), and benzyltriethylammonium chloride (TEBA; 1 g). The temperature during the addition is kept at +8 °C. The resultant mixture is stirred for 5 h. The excess of isobutene is removed and the residue is poured into water (900 ml). The mixture is extracted with dichloromethane (3 × 300 ml), the organic extract washed with 10% hydrochloric acid (100 ml) and water (450 ml), and dried with calcium chloride. The solvent is removed in vacuo and the residual product distilled in vacuo; yield: 121.5 g (98%); b.p. 58–59 °C/20 torr (Ref.[6], b.p. 59–59.2 °C/20 torr).

1-Bromo-2,2-dimethylcyclopropane (2):
A mixture of concentrated hydrochloric acid (30 ml) and methanol (90 ml) is added dropwise to a stirred suspension of zinc dust (200 g, 3.06 g atom) in methanol (450 ml). The mixture is then cooled to 0–5 °C and a solution of 1,1-dibromo-2,2-dimethylcyclopropane (**1**; 85.0 g, 0.37 mol) in methanol (135 ml) is added over a 2 h period with stirring. After the addition is complete, the mixture is filtered, the filtrate diluted with 5 volumes of water, and extracted with pentane (4 × 150 ml). The organic extract is dried with calcium chloride, the solvent distilled off, and the residual product purified by distillation; yield: 44 g (80%); b.p. 107–108 °C/750 torr. [The product thus obtained was identified by its ^{1}H-N.M.R. spectrum[7]].

3,3-Dimethylcyclopropene (3):
This compound is prepared following Ref.[4], Method A; yield: 80%.

***cis*-Chrysanthemic Acid (5):**
3,3-Dimethylcyclopropene (**3**; 4.56 g, 0.067 mol) is distilled into a solution of 2-methylpropenylmagnesium bromide (**4**; 0.0587 mol) in dry tetrahydrofuran (~50 ml) under an argon atmosphere. During the distillation (30 min), the temperature of the mixture is kept at 50–55 °C. Stirring is continued at 60 °C for 1 h and the mixture then poured onto finely crushed Dry Ice (~150 g). The resultant mixture is acidified to pH 6 with 0.5 normal sulfuric acid and extracted with ether (3 × 75 ml). The extract is dried with magnesium sulfate and the solvent removed in vacuo to give **5**; yield: 7.18 g (72%); m.p. 115–116 °C (after recrystallization from pentane); mixture m.p. with an authentic sample[12]: 115–116 °C. [^{1}H-N.M.R. data identical with those reported in Ref.[13]].

***cis*-Chrysanthemic Acid (−)-1-(2,2,*cis*-3-Trimethylcyclopropyl)-ethyl Ester (7a):**

cis-*Chrysanthemic Acid Chloride*[10]: A mixture of *cis*-chrysanthemic acid (**5**; 0.802 g, 4.772 mmol) and thionyl chloride (0.748 g) is heated to boiling under a hood for 60 min. Excess thionyl chloride (b.p. 75.6 °C) is then distilled off; last traces of thionyl chloride are removed in vacuo. The residual acid chloride is distilled in vacuo; yield: 0.622 g (70%); b.p. 87 °C/12 torr.

Ester **7a**: A solution of *cis*-chrysanthemic acid chloride (0.62 g, 3.333 mmol) in anhydrous benzene (2 ml) is added dropwise to a stirred solution of (−)-1-(2,2,*cis*-3-trimethylcyclopropyl)-ethanol[11] (**6a**; 0.38 g, 2.969 mmol) in a mixture of anhydrous benzene (5.5 ml) and anhydrous pyridine (0.45 ml) under an argon atmosphere at room temperature. Stirring is continued for 48 h, the precipitated pyridine hydrochloride filtered off, and the filtrate washed with aqueous 20% sodium hydroxide solution (2 × 10 ml), water (2 × 40 ml), and saturated sodium chloride solution (3 × 40 ml). The solution is dried with magnesium sulfate, benzene is removed in vacuo, and the residual product **7a** distilled in vacuo; yield: 0.51 g (62%); b.p. 123–129 °C/15 torr.

$C_{18}H_{30}O_2$	calc.	C 77.69	H 10.79
(278.4)	found	77.67	10.95

M.S.: *m/e* = 168, 153, 151, 123, 111, 95, 81, 69, 67, 55, 41.

I.R. (KBr): ν = 673, 1030, 3070 (cyclopropane); 1140, 1170 (C—O); 1720 cm^{-1} (C=O).

^{1}H-N.M.R. (C_6H_6/HMDSO$_{int}$): δ = 1.65, 1.77 (d, *J* = 1.5 Hz, 2 ^{a}CH$_3$); 1.44 (d, *J* = 2.7 Hz, ^{c}CH$_3$); 0.78–1.18 (overlapped s, 4 ^{b}CH$_3$; and d, ^{e}CH$_3$); 0.5–0.8 (overlapped, m ^{h}H; and m, ^{g}H); 0.56–1.92 (overlapped m, ^{c}H; and d, ^{f}H); 3.60 ppm (m, ^{d}H).

***cis*-Chrysanthemic Acid 1-(2,2,3,3-Tetramethylcyclopropyl)-ethyl Ester (7b):**
The preparation of this ester is analogous to that of **7a**; yield of **7b**: 53%; b.p. 132–135 °C/15 torr.

$C_{19}H_{32}O_2$	calc.	C 78.08	H 10.96
(292.5)	found	77.96	11.19

M.S.: *m/e* = 168, 153, 123, 107, 95, 91, 81, 69, 67, 55, 41.

I.R. (KBr): ν = 673, 1030, 3070 (cyclopropane); 1140, 1170 (C—O); 1720 cm^{-1} (C=O).

^{1}H-N.M.R. (C_6H_6/HMDSO$_{int}$): δ = 0.51 (d, *J* = 10 Hz, ^{h}H); 0.86–1.18 (overlapped s, 6 ^{b}CH$_3$); 1.4–1.6 (overlapped m, ^{c}H; and d, ^{f}H); 1.44 (d, *J* = 2.7 Hz, ^{e}CH$_3$); 1.66, 1.76 (d, *J* = 1.5 Hz, 2 ^{a}CH$_3$); 3.5 (m, ^{d}H); 5.4 ppm (m, ^{g}H).

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