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# STUDIES ON CHRYSANTHEMIC ACID—XXI

## PHOTOCHEMICAL ISOMERIZATION OF CHRYSANTHEMIC ACID AND ITS DERIVATIVES

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**Abstract**—Photochemical *cis-trans* isomerization of chrysanthemic acid, its ester and its amide, and of esters of chrysanthemumdicarboxylic acid is described. Sensitized photochemical racemization of *trans*-chrysanthemic acid and ester was accomplished in good yield.

THERE are some reports[1–3] dealing with photochemical *cis-trans* isomerization of cyclopropane derivatives, especially with benzoyl or phenyl substituted cyclopropane derivatives. As to chrysanthemic acid, Sasaki *et al.* briefly reported.[4]

In the course of the studies on the racemization of chrysanthemic acid,[5,6] the authors studied the photochemical isomerization and succeeded in racemizing the optically active *trans*-chrysanthemic acid and ester in good yield.

At first, *cis-trans* isomerization was studied. t-Butyl chrysanthemate was adopted as a representative, because of its easy gaschromatographic separation into the *cis*- and *trans*-isomer.

t-Butyl (±)-*trans*-chrysanthemate in n-hexane was irradiated with a low pressure mercury lamp for 10 hr, but no detectable amount of the *cis*-isomer was found by gaschromatographic analysis. With a high pressure mercury lamp no detectable amount of the *cis*-isomer was found either. However, rapid development of the *cis*-isomer was observed with an addition of sensitizer, acetophenone. Isobutyrophenone was best and benzophenone was not suitable as the sensitizer of the isomerization reaction from a viewpoint of isomerization velocity and recovery of the isomerized esters. The sensitized isomerization reaction gave the same *cis-trans* ration of 36 to 64 in both cases starting either from the *trans*- or from *cis*-isomer, and the reaction was considered to be an equilibrium reaction.

The isomerization reaction was also conducted with chrysanthemic acid and amide. In both cases equilibrium was attained, and the *cis-trans* ratio of the acid was 34 to 66 and that of the amide was 32 to 68 by gaschromatographic analysis.

Now, the isomerization study was directed to chrysanthemum dicarboxylic acid which had another isomeric center of the double bond in addition to the cyclopropane ring. t-Butyl (±)-pyrethrate (I) which was adopted as a representative because of easy gaschromatographic separation of its isomers, was irradiated with a low pressure mercury lamp in n-hexane. Three other peaks than that of I were found on a gaschromatogram and their concentration increased with longer irradiation. Each of

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these three new peaks had the retention time identical with each of the authentic specimen of the three stereo isomers of I,[7] t-butyl 2,2-dimethyl-3-(*cis*-2′-methoxycarbonyl-1′-propenyl)-1,3-*trans*-cyclopropanecarboxylate (II). *t*-butyl 2,2-dimethyl-3-(*trans*-2′-methoxycarbonyl-1′-propenyl)-1,3-*cis*-cyclopropanecarboxylate (III), t-butyl 2,2-dimethyl-3-(*cis*-2′-methoxycarbonyl-1′-propenyl)-1,3-*cis*-cyclopropanecarboxylate (IV). The irradiated sample was separated into four components by column chromatography, which were identified by GLC, IR and NMR spectra.

The isomerization also occurred by the irradiation with a high pressure mercury lamp and was accelerated by addition of isobutyrophenone as sensitizer. In the sensitized experiment, (I) was converted to the isomeric mixture of I, II, III and IV with the ratio of 29:21:28:22, and was unchanged on further irradiation. A similar experiment starting from IV, which had completely different configurations from I with respect to both the cyclopropane ring and to the double bond, gave the same isomeric mixture.

In such a sensitized photochemical *cis-trans* isomerization of cyclopropane derivatives, rupture of the cyclopropane linkage between the carbons bearing substituents had been suggested.[1] As the *cis-trans* isomerization of chrysanthemic acid proceeded in good yield, it may be possible to racemize the optically active centre.

(+)-*trans*-Chrysanthemic acid, $[\alpha]_D^{24}$ −4·26° ($C_6H_6$), was irradiated with a high pressure mercury lamp in benzene at the presence of isobutyrophenone under $N_2$. The original solution had an optical rotation of −0·133° in 1 dm cell and after 6 hr irradiation the solution indicated −0·014°. Treatment of the reaction mixture with $BF_3$ etherate* overnight at room temperature and subsequent distillation and recrystallization afforded racemized dihydrochrysanthemolactone, m.p. 49·5–51°, in 23% yield, and partially racemized *trans*-chrysanthemic acid in 58% yield. The latter gave on recrystallization (±)-*trans*-chrysanthemic acid, m.p. 51–54°, in 38% yield, and semisolid acid retaining 20% of optical activity in 20% yield.

Similar result was obtained with (−)-*trans*-chrysanthemic acid.

t-Butyl (+)-*trans*-chrysanthemate was similarly irradiated, the resulting (±)-*cis*-ester was converted to the *trans* one by treating with *t*-BuOK in *t*-BuOH,[8] and subsequent ester cleavage by heating with *p*-TsOH afforded (±)-*trans*-chrysanthemic acid, m.p. 52–53·5°, in 33% yield and partially racemized *trans*-acid retaining 4·8% of optical activity in 25% yield.

Thus, the racemization of optically active *trans*-chrysanthemic acid was accomplished in about 80% yield including the *cis*-isomer and in about 93% racemization.

## EXPERIMENTAL

NMR spectra were determined on a JEOLCO, JNM-4H-100 spectrometer using TMS (δ 0·00) as internal standard in $CCl_4$, and IR spectra were recorded on a JASCO, IR-S spectrophotometer. Optical rotations were determined with a JASCO, DIP-S automatic polarimeter. Irradiations were carried out with a Riko-sha UVL-300P high pressure mercury lamp (400 W, pyrex water jacket) and a Riko-sha, UVL-300 Q low pressure mercury lamp (10 W). GLC analyses were carried out with a Shimadzu GC-3AH using He as a carrier gas.

* This treatment converts only the *cis*-acid to dihydrochrysanthemolactone without affecting the *trans*-acid, and gives an easy convenient method for the separation of the *trans*-acid.

Guaranteed grade $C_6H_6$ was used without purification. *n*-Hexane was used after washing with concd. $H_2SO_4$ and water, drying over $MgSO_4$ and final distillation with 20 cm Vigreaux column.

All m.ps were uncorrected.

*Sensitized photochemical isomerization of* t-*butyl* (±)-*chrysanthemate.* The *trans*-ester (4·0 g) and isobutyrophenone (0·4 g) in $C_6H_6$ (220 ml) were irradiated with a high pressure mercury lamp at 25–27° under $N_2$ bubbling for 3 hr. The *cis-trans* ratio reached 36 to 64 and further 1 hr. irradiation did not alter the ratio.

The *cis*-ester gave finally the same *cis-trans* ratio under a similar condition. The *cis-trans* ratio was analyzed by GLC, 10% SE-30, Chromosorb G-NAW, 2 m × 3 mm, 115°, 1·0 kg/cm².

*Sensitized photochemical isomerization of* (±)-*chrysanthemic acid.* The *trans*-acid (3·0 g) and isobutyrophenone (0·3 g) in $C_6H_6$ (220 ml) were irradiated with a high pressure mercury lamp at 25–27° under $N_2$ bubbling for 3 hr. The mixture was concentrated. The concentrate was diluted with $C_6H_6$ (20 ml) and after addition $BF_3$ etherate (0·3 ml) kept overnight at room temp. The mixture was washed with water and dried over $MgSO_4$. Thus the *cis*-acid present was converted to dihydrochrysanthemolactone and analysed with GLC, 10% PEGSeb, Chromosorb G-NAW, 2 m × 3 mm, 150°, 1·2 kg/cm² the *cis-trans* ratio was 34 to 66. The *cis*-acid gave finally the same ratio by an analogous treatment.

*Sensitized photochemical isomerization of* (±)-*chrysanthemamide.* The *trans*-amide (2·0 g), m.p. 125·5–126·5°, and isobutyrophenone (0·2 g) in $C_6H_6$ (220 ml) were irradiated similarly for 2 hr. Then an additional 0·2 g of isobutyrophenone was added and irradiation was continued for another 1 5 hr. The *cis-trans* ratio was 30 to 70 after 2 hr and reached 32 to 68 after 3 hr. An additional 0·5 hr irradiation failed to alter the ratio. The *cis*-amide, m.p. 93–94°, gave finally the same ratio by an analogous treatment. The *cis-trans* ratio was determined by direct comparison of the gaschromatogram with that of the standard composition because of incomplete separation of the *cis* and *trans*-isomer. GLC condition: 10% PEGSeb, Chromosorb G-NAW, 2 m × 3 mm, 180°, 1·0 kg/cm².

*Photochemical isomerization of* t-*butyl* (±)-*pyrethrate* I. *By a low pressure mercury lamp.* (I) (2·5 g) was dissolved in n-hexane (100 ml) and irradiated with a low pressure mercury lamp at 25–30°. The mixture was analysed by GLC. The peak of I was decreased but three new peaks increased their intensities with a lapse of time. After 29 hr n-hexane was removed *in vacuo*. The residue (2·4 g) was separated into each component by column chromatography (silica gel; 150 g, $CCl_4$ · n-hexane· ether = 18·1:1). IV, I, II and III were eluted in this order. IV and I were obtained in pure state by GLC analysis. However, as II and III were not pure, they were again treated by column chromatography. The four components were identified with the authentic geometrical isomers of t-butyl pyrethrate by IR, NMR and GLC analyses. (I) · $\nu_{max}$(film) 1721, 1643, 1227, 1150, 835, 765, 739 $cm^{-1}$; δ 1·24 (3H, s), 1·27 (3H, s), 1·44 (9H, s), 1·91 (3H, d, J = 1 c/s), 1·57 (1H, d, J = 5·1 c/s), 2·02 (1H, d–d, J = 5·1, 10 c/s), 3·64 (3H, s), 6·38 (1H, d, J = 10 c/s). (II): $\nu_{max}$(film) 1723, 1643, 1155, 1120, 835, 780, 735 $cm^{-1}$; δ 1·16 (3H, s), 1·25 (3H, s), 1·36 (1H, d?), 1·43 (9H, s), 1·86 (3H, s), 2·72 (1H, d–d, J = 5·9 c/s), 3·70 (3H, s), 5·56 (1H, d, J = 9 c/s). (III): $\nu_{max}$(film) 1717, 1705, 1637, 1144, 1120, 830, 792, 745 $cm^{-1}$; δ 1·26 (3H, s), 1·30 (3H, s), 1·45 (9H, s), 1·7–1·9 (2H, m), 1·88 (3H, d, J = 1 c/s), 3·68 (3H, s), 6·97 (1H, d, J = 8 c/s). (IV): $\nu_{max}$ (film) 1716, 1635, 1220, 1142, 1080, 1022, 830, 790, 781, 735 $cm^{-1}$; δ 1·25 (3H, s), 1·26 (3H, s), 1·43 (9H, s), 1·64 (1H, d, J = 8·5 c/s), 1·92 (3H, d, J = 1·5 c/s), 2·78 (1H, d–d, J = 8·5, 10 c/s), 3·66 (3H, s), 6·32 (1H, d, J = 10 c/s). Retention time of GLC (10% SE-30, Chromosorb G-NAW, 2 m × 3 mm, 170°, 1·0 kg/cm²): (I); 13·0, (II); 10·2, (III); 11·7. (IV); 9 0 min.

*By a high pressure mercury lamp without sensitizer.* A solution of I (1·65 g) in n-hexane (200 ml) was irradiated with a high pressure mercury lamp at 25–27° under $N_2$ bubbling. After 9 hr irradiation the ratio of the four isomers, I, II, III and IV was 46:11:26:17, and only a little amount of unknown byproducts were found by GLC analyses. Further irradiation was not undertaken.

*By a high pressure mercury lamp with sensitizer.* A solution of (I) (1·0 g) and isobutyrophenone (0·10 g) in $C_6H_6$ (220 ml) was similarly irradiated. The isomer ratio became almost constant after 40 min and after 2·5 hr the ratio of I, II, III and IV was 29:21:28:22 on the bases of GLC analyses.

*Sensitized photochemical isomerization of* t-*butyl* (±)-2,2-*dimethyl*-3-(cis-2'-*methoxycarbonyl*-1'-*propenyl*)-1,3-cis-*cyclopropanecarboxylate* (IV). A solution of IV (0·64 g) and isobutyrophenone (0·063 g) in $C_6H_6$ (200 ml) was irradiated as described above. The ratio of the isomers became almost constant after 40 min. After 2·5 hr the ratio of I, II, III and IV was 29:21:28:22.

*Sensitized photochemical isomerization of* (+)-trans-*chrysanthemic acid.* The acid, $[\alpha]_D^{24}$ + 14·1° (EtOH), $[\alpha]_D^{24}$ −4·26° ($C_6H_6$), (8·4 g) and isobutyrophenone (0·42 g) were dissolved in $C_6H_6$ (270 ml) and irradiated with a high pressure mercury lamp at 25–27° under $N_2$ bubbling for 3 hr. Additional isobutyrophenone (0·42 g) was added and irradiation was continued for 3 hr under the same conditions. Sampling of the reaction

mixture were taken and optical rotations determined. Irradiation time (hr); Optical rotation in 1 dm cell (minus degree), 0;0·133, 0·5;0·106, 1·0; 0·079, 2·0; 0·058, 3·0; 0·047, 4·0; 0·024, 5·0; 0·017, 6·0; 0·014. Total sampling loss of chrysanthemic acid was 0·66 g. After 6 hr $C_6H_6$ was removed *in vacuo*. The residue dissolved in $C_6H_6$ (20 ml) was kept standing overnight at room temp with an addition of $BF_3$ etherate (1 ml). The mixture diluted with ether was washed with water, dried over $MgSO_4$ and concentrated. It was distilled, b.p. 100–112° 4 mm, 6·9 g. The distillate diluted with ether was extracted with 5% $Na_2CO_3$. The aqueous extract was acidified with HCl and extracted with ether. The ether soln. was dried over $MgSO_4$ and concentrated to give an acidic material (4·6 g), which was recrystallized from light petroleum to give (±)-*trans*-chrysanthemic acid (3·0 g), m.p. 51–54°, and partially racemized semisolid *trans*-chrysanthemic acid (1·55 g), $[\alpha]_D^{24}$ +2·81° (EtOH), of which IR spectrum was identical with that of (±)-*trans*-chrysanthemic acid.

On the other hand, above neutral ether soln was concentrated to give a neutral material (2·3 g). On recrystallization from light petroleum it gave (±)-dihydrochrysanthemolactone (1·42 g), m.p. and m.m.p. 49·5–51°, and semisolid material (0·83 g). The semisolid material was purified by column chromatography (silica gel, $CCl_4$) to give (±)-dihydrochrysanthemolactone (0·39 g), m.p. 49–51°, $[\alpha]_D^{24}$ 0·00° (EtOH), of which IR spectrum in nujol was completely identical with that of the authentic one.

*Sensitized photochemical isomerization of* t-*butyl* (+)-trans-*chrysanthemate*. The ester (3·9 g), $[\alpha]_D^{20}$ −2·63° (EtOH), and isobutyrophenone (0·30 g) dissolved in $C_6H_6$ (220 ml) were irradiated with a high pressure mercury lamp at 25–27° under $N_2$ bubbling for 6 hr. $C_6H_6$ was removed *in vacuo*. The residue was dissolved in t-butanol (30 ml) containing potassium (1·0 g) and heated under reflux for 8·5 hr.[8] After cooling the mixture was diluted with water and extracted with ether. The ether extract was washed with water, dried over $MgSO_4$ and concentrated. The concentrate was distilled, b.p. 113–4° (14 mm Hg), $[\alpha]_D^{20}$ −0·26° (EtOH). 2·7 g. The distillate was heated under reflux for 2·5 hr in toluene with a small amount of *p*-TsOH. After cooling it was dissolved in ether and extracted with 5% $Na_2CO_3$. The aqueous extract acidified with HCl was extracted with ether. The ether extract gave 1·72 g of *trans*-chrysanthemic acid which on recrystallization from light petroleum afforded (±)-*trans*-chrysanthemic acid (0·98 g), m.p. 52–53·5°, and semisolid partially racemized *trans*-chrysanthemic acid (0·74 g), $[\alpha]_D^{25}$ +0·68° (EtOH), of which IR spectrum was identical with that of (±)-*trans*-chrysanthemic acid.

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