CHEMISTRY LETTERS, pp. 1799 - 1802, 1984.

LEWIS ACID CATALYZED RACEMIZATION OF CHRYSANTHEMOYL CHLORIDE

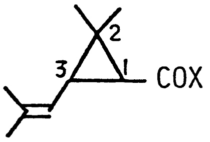
Gohfu SUZUKAMO,* Masami FUKAO, and Tsuneyuki NAGASE
Takatsuki Research Laboratory, Sumitomo Chemical Co. Ltd.,
Takatsuki, Osaka 569

The facile racemization of chrysanthemic acid was achieved by treatment of chrysanthemoyl chloride with a catalytic amount of Lewis acid followed by hydrolysis. The reaction mechanism is also proposed.

Chrysanthemic acid 1a, an acid component of the pyrethroid insecticides, has four stereoisomers originating from the two asymmetric carbons at the C_1 and C_3 positions. Insecticidal activity of the synthetic pyrethroids derived from these optical isomers is shown as follows: (+)-trans $\geq$ (+)-cis $\gg$ (-)-trans$\sim$(-)-cis.$^{1)}$

Optical resolution of synthetic chrysanthemic acid conveniently provides (+)-acid, bioactive enantiomeric component of pyrethroid insecticides,$^{2)}$ and leaves (-)-acid. The racemization of the antipode is not only important for the practical production of the desired (+)-acid, but is also particularly interesting, because it has two asymmetric carbons in the cyclopropane molecule. However, there have been only a few reports on this problem, which involve photo-irradiation$^{3)}$ and multi-step conversions.$^{4)}$

We have recently reported that the C_3 epimerization of ethyl chrysanthemate 1c is brought about by a certain Lewis acid,$^{5)}$ and our further investigation of the reaction led to the discovery of the facile racemization of chrysanthemoyl chloride 1b.



1a, X=OH
1b, X=Cl
1c, X=OEt

Treatment of (-)-chrysanthemoyl chloride 1b with a catalytic amount of Lewis acid gave rise to racemization under mild reaction conditions. Among the Lewis acids examined, boron halides gave excellent results. The isomeric ratio of the product was independent of the configuration of the starting material, and the trans content increased as the reaction temperature was lowered. The results are summarized in Table 1.

Table 1. Racemization of optical isomers of chrysanthemoyl chloride[6)]

Catalyst[a)]	Starting material	Temp °C	Time h	Product/ % (+)cis	(-)cis	(+)trans	(-)trans	Yield %
BCl_3	(-)-trans	-10	0.5	3.7	3.5	46.5	46.3	95.0
BCl_3	(-)-cis	-10	0.5	3.6	3.6	46.5	46.3	94.8
BBr_3	(-)-trans	+10	0.5	4.0	3.9	45.7	46.4	93.9
BF_3	(-)-trans	-78	0.5	1.1	1.0	48.9	49.0	b)
$AlCl_3$	(-)-trans	+70	5.0	4.5	5.5	43.3	46.8	72.9
$FeCl_3$	(-)-trans	+70	5.0	5.1	5.2	43.9	45.8	67.7

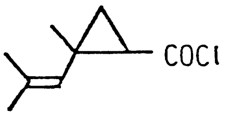
Solvent: Toluene (substrate 40 wt%).

a) The amount of catalyst was 5 mol% of the starting materials.

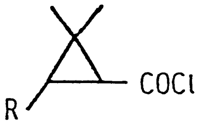
b) Product not isolated.

A typical experimental procedure is as follows (the first run in Table 1): To a 40 wt% toluene solution of (-)-trans-chrysanthemoyl chloride (10 mmol) was added boron trichloride (0.5 mmol) at -10 °C under nitrogen and stirred for 0.5 h. The reaction mixture was poured into 10% NaOH solution and stirred for 0.5 h. The aqueous layer was acidified with 10% HCl and extracted with toluene. Distillation of the crude product gave (±)-cis/trans-chrysanthemic acid in a yield of 95%.

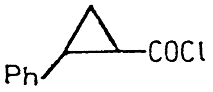
Similarly, 2-substituted derivative 2 was racemized smoothly by the same procedure. On the other hand, cyclopropanecarbonyl chlorides 3, 4, and 5, which are not substituted with 2-methyl-1-propenyl group, failed to undergo racemization. These facts demonsrate that the 2-methyl-1-propenyl group plays a crucial role in the reaction.



2

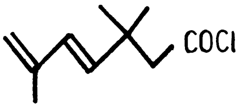


3 R=$(CH_3)_2CHCH_2$-
4 R= H



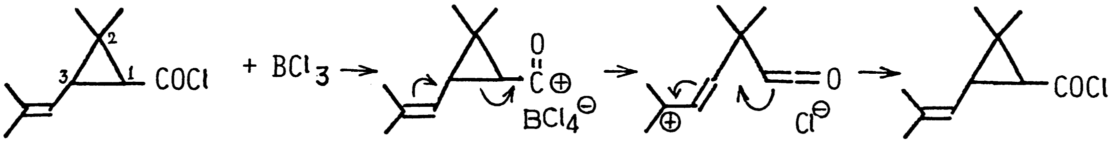
5

At elevated temperatures, C_1-C_3 bond cleavage in 1b occurred to give diene 6.[7,8)]



6

These results suggest that the racemization takes place through C_1-C_3 bond cleaved intermediate 8 as illustrated in Scheme 1. Coordination of Lewis acid (BCl_3) to the carbonyl chloride 1b would afford an acyl cation 7, whose C_1-C_3 bond was cleaved with the participation of 2-methyl-1-propenyl group to give the ring-opened cation 8.[9)] Nucleophilic attack of a chloride ion on 8 followed by ring closure leads to racemized product. The formation of 6 would also be explained as deprotonation of the ring-opened cation 8, followed by the addition of hydrogen chloride to the ketene group.



1b 7 8

Scheme 1.

We thank Prof. M. Matsui and Dr. H. Yoshioka for their valuable advice, and we are also indebted to Dr. Y. Sakito for helpful discussion and assistance.

References

1) M. Matsui and I. Yamamoto, "Naturally Occuring Insecticides," ed by M. Jacobson and D. G. Crosby, Marcel Dekker Inc., New York (1971), p. 3.

2) I. Miyamoto, H. Yoshioka, K. Fujimoto, T. Kadota, and Y. Okuno, Sumitomo Kagaku, Special Issue II, 1 (1973); M. Elliot and N. F. Janes, "Pyrethrum," ed by J. E. Casida, Academic Press, New York and London (1973), p. 74.

3) K. Ueda and M. Matsui, Tetrahedron, 27, 2771 (1971); T. Sasaki, S. Eguchi, and M. Ohno, J. Org. Chem., 33, 676 (1968).

4) M. Matsui, M. Uchiyama, and H. Yoshioka, Agric. Biol. Chem., 27, 558 (1963); K. Ueda and M. Matsui, ibid., 34, 1115 (1970).

5) G. Suzukamo, M. Fukao, and M. Tamura, Tetrahedron Lett., 25,1595 (1984).

6) The isomer ratio was determined by gas chromatography after conversion into (+)-2-octyl ester, see: A. Murano, Agric. Biol. Chem., 36, 2203 (1972). By using a glass capillary column (Silicon DC QF-1, 15 m x 0.25 mm I.D.), a complete separation of the diastereomeric peaks in a short retention time can be obtained.

7) Diene 6 (bp 80 °C/8.3 mmHg) was formed in 7% yield as a by-product of the racemization reaction at 105 °C for 1 h. Diene 6 was analyzed by gas chromatography after conversion into the anilide. 4,4-Dimethyl-2-isopropenyl-2-cyclopentenone (see: T. Sasaki, S. Eguchi, and M. Ohno, Tetrahedron, 25, 2145 (1965).) was also isolated (1% yield), which resulted from diene 6.

8) For the C_1-C_3 bond cleavage in trans-chrysanthemylaldehyde with p-toluenesulfonic acid, see: L. Crombie, P. A. Firth, R. P. Houghton, D. A. Whiting, and D. K. Woods, J. Chem. Soc., Perkin Trans. 1, 1972, 642.

9) Ring opening/ring closure mechanism was proposed for methyl 2-trimethylsilyloxycyclopropanecarboxylates. (H-U. Reissig and I. Bohm, Tetrahedron Lett., 24, 715 (1983).)

(Received July 19, 1984)