[Chem. Pharm. Bull. 25(1) 179—181 (1977)]

UDC 615.282.011.5 : 541.144.8

Photo-decomposition of Captan and Difolatan

Yoshio Kaneda,[1a] Akira Yamaji,[1b] Masahiro Iwaida,[1a] and Yosuke Ohkura[1c]

National Institute of Hygienic Sciences, Osaka Branch,[1a] Department of Pharmacy, Osaka University Hospital[1b] and Faculty of Pharmaceutical Sciences, Kyushu University 62[1c]

(Received May 13, 1976)

Captan and difolatan, widely used fungicides, decomposed rapidly when irradiated with light of a low pressure mercurry lamp to *cis*-4-cyclohexene-1,2-dicarboximide.

Keywords——captan and difolatan in organic solvents; photo-decomposition rate; product isolation; low pressure mercury lamp; gas chromatography; thin-layer chromatography

Captan[2] and difolatan[3] have been widely used as fungicides for fruits and vegetables. Although it was reported that the fungicides were rapidly decomposed when exposed to sunlight,[4] their decomposition rates and the structures of the decomposition products have remained unknown.

This paper describes the decomposition rates of captan and difolatan dissolved in organic solvents on exposure to light of a low pressure mercury lamp, the isolation of the decomposition products and the characterization of their chemical structures.

Captan and difolatan were insoluble in water, and so they were dissolved in *n*-hexane and in ethanol, which were selected as non-polar and polar solvents, respectively. The solutions were irradiated with light of the mercury lamp and the residual concentrations of the fungicides were determined with the elapse of irradiation by gas chromatographic technics with flame photometric detection established previously for the method of screening the fungicides in vegetables and fruits.[5]

As shown in Fig. 1, the fungicides decomposed more rapidly in ethanol than in *n*-hexane and a linear relationship was observed between logarithm of the residual concentration and the irradiation time for each fungicide.

The decomposition products of difolatan in ethanol was first investigated. Ethanolic solutions of difolatan were irradiated with the light for periods and the resulting solutions, after evaporating the solvent, were separated chromatographically on silica gel thin-layer. As shown in Fig. 2, with the elapse of time of irradiation, a spot located at Rf=0.41 increased while a spot corresponding to difolatan remained undecomposed, located at Rf=0.70, decreased. A minor spot was also observed at the original point on the chromatogram and did not increase with time of irradiation.

The observation indicated that a compound responsible for the spot at Rf=0.41 was the main decomposition product, which was then obtained as colorless needles of mp 138° (I) from the spot, as described in Experimental. I was identified as *cis*-4-cyclohexene-1,2-dicarboximide[6] by the comparison of its physical properties[7] with those of the authentic

1) Location: *a*) *No. 6, Hoenzaka-cho, Higashi-ku, Osaka*; *b*) *1-1-50, Fukushima, Fukushima-ku, Osaka*; *c*) *Maidashi, Higashi-ku, Fukuoka.*
2) N-Trichloromethylthio-4-cyclohexene-1,2-dicarboximide.
3) N-1,1,2,2-Tetrachloroethylthio-4-cyclohexene-1,2-dicarboximide.
4) G. Serra, *Phytiat. Phytopharm.*, 13, 107 (1964).
5) M. Iwaida, A. Yamaji, and Y. Kaneda, *Yakugaku Zasshi*, **94**, 1334 (1974).
6) E.D. Mitchell Jr. and N.E. Tolbert, *Biochemistry*, **7**, 1019 (1968).
7) Infrared, nuclear magnetic resonance and mass spectra.

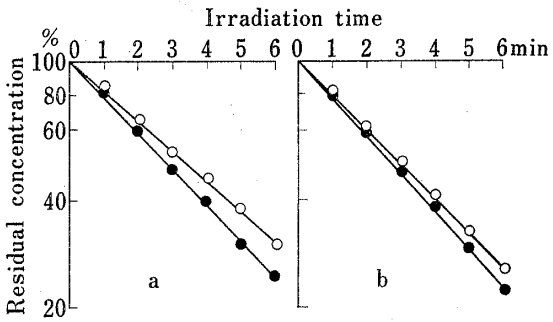

Fig. 1. Photo-decomposition of Captan and Difolatan

a, captan: b, difelatan

○—○: decomposition in *n*-hexane

●—●: decomposition in ethanol

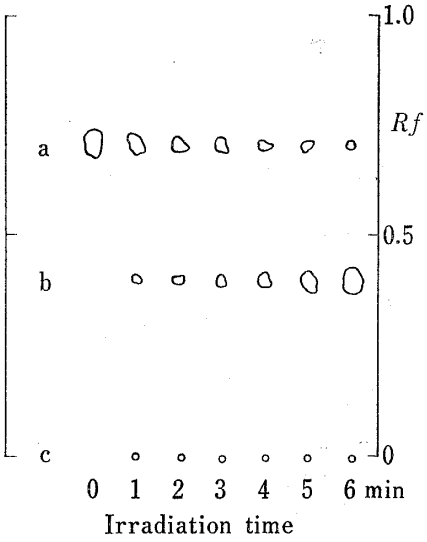

Fig. 2. Thin-Layer Chromatogram of Photo-decomposition Products of Difolatan

a, difolatan; b and c, decomposition products

sample. A substance located at Rf=0.00 on the chromatogram could not be treated successfully.

The investigations on the photo-decomposition products of difolatan in *n*-hexane and of captan in ethanol and in *n*-hexane were carried out in the same way as described above. In all cases, I was obtained as main decomposition product.

It is now clear that, in the photo-decomposition of captan and difolatan, the first step is their decomposition to I. The origin of the imide hydrogen of I and the fates of trichloromethylthio-moiety in captan and 1,1,2,2-tetrachloroethylthio-moiety in difolatan have remained unsolved.

Experimental[8]

Captan and Difolatan——The fungicides[9] were recrystallized from C_6H_6, respectively, and confirmed to be single substances gas[5] and thin-layer chromatographically as described below.

Decomposition Rates of Captan and Difolatan——Captan or difolatan was dissolved in 7.0 ml of EtOH or *n*-C_6H_{14} in the concentration of 0.025%, placed in the reaction tube of the irradiation apparatus and irradiated at 35° with the light after the brightness of the lamp became constant. Aliquots of 3 μl of the solution were taken out of the tube with time of the irradiation and captan or difolatan remained undecomposed was determined by the gas chromatography.[5]

Thin-Layer Chromatography of Photo-decomposed Difolatan in Ethanol——Aliquots of 7.0 ml of 0.025% difolatan solution in EtOH were irradiated with the light at 35° for periods and concentrated to almost dryness *in vacuo*. The residues, on dissolving in a small amount of C_6H_6, respectively, were spotted on silica gel thin-layer[10] and developed with *n*-C_6H_{14}–C_6H_6 (7:3). The spots were visualized by spraying 0.05% $KMnO_4$ solution in $(CH_3)_2CO$ and then heating at 110° for 5 min.

Isolation of I——A solution of captan or difolatan (200 mg) in 800 ml of EtOH or *n*-C_6H_{14} was irradiated with the light as described above for 10 min and concentrated to dryness *in vacuo*. The residue was dissolved

8) The light irradiation was performed on an Eiko HALOS-PIL-60 Photo-chemical Reaction Apparatus (inner irradiation type) equipped with a low pressure mercury lamp. The gas chromatography was carried out in the same manner as previously described[5] by use of a Yanako G-80 Gas Chromatograph equipped with flame photometric detector. Infrared spectra were taken on a Hitachi EPI-G2 or a Nihonbunko 701G Spectrometer in KBr pellets, nuclear magnetic resonance spectra on a JEOL JNM-PS-100 Spectrometer at 100 MHz with tetramethylsilane as an internal standard, and mass spectra on a Nihondenshi JMS-Ol-SG Spectrometer. Melting point was uncorrected.

9) Captan and difolatan, reagent grade, Nishio Kogyo.

10) 0.25 mm layer of Silica gel GF_{254}, activated at 110° for 1 hour.

in a small amount of C_6H_6 and subjected to the preparative separation on silica gel thin-layer[11] with n-C_6H_{14}–$(CH_3)_2CO$ (2: 3) as developing solvent. The major fraction due to I was scraped, extracted with $CHCl_3$–EtOH (1: 1) and centrifuged to remove the silica gel. The supernatant solution was concentrated to dryness *in vacuo* and the residue was recrystallized from n-C_6H_{14}–C_6H_6 (9: 1) to colorless needles(I), mp 138°. Yield approximately 26 mg in each case of the decomposition experiments. No depression of mp was observed on admixture with the authentic sample of *cis*-4-cyclohexene-1,2-dicarboximide.[6] The infrared, nuclear magnetic resonance and mass spectra were entirely identical with those of the authentic sample. Mass Spectrum *m/e*: 151.065 (M^+, Calcd. for $C_8H_9O_2N$ 151.063), 123 (M^+—CO), 108 (M^+—CONH).

11) 0.5 mm layer of Silica gel GF_{254}, activated at 110° for 1 hour.

[Chem. Pharm. Bull. 25(1) 181—184 (1977)]

UDC 547.571'554.04 : 547.412.133.04

A Stereoselective Synthesis of α-Chloro-α-phenylacetamide by the Reaction of optically Active Schiff Base with Dichlorocarbene

Mitsuru Furukawa, Tadashi Okawara, and Yuriko Terawaki

Faculty of Pharmaceutical Sciences, Kumamoto University[1]

(Received May 17, 1976)

Optically active N-benzylidene-*R*(+)- and *S*(−)-α-methylbenzylamines (**1b,c**) were allowed to react with dichlorocarbene to give optically active α-methylbenzylamine-α-chloro-α-phenylacetamides (**3b,c**), and the ratio of diastereomers was R–R: S–R=73: 27 and S–S: R–S=79: 21, respectively.

Keywords——stereoselective synthesis; α-chloro-α-phenylacetamide; optically active Schiff base; dichlorocarbene; ^{1}H–NMR

Fields and Sandri[2] reported that the addition of dichlorocarbene to the carbon-nitrogen double bond of N-benzylideneaniline gave 1,3-diphenyl-1,2-dichloroaziridine, followed by facile conversion to α-chloro-α-phenylacetamide by rearrangement under hydrolysis conditions. Several similar aziridine formations have been also recorded.[3–6] The mechanism of these reactions was proposed by Brooks and co-workers to proceed through the formation of the intermediate carbonium ion.[7]

We tried to apply these reactions to the stereoselective synthesis of α-chloro-α-phenylacetamides (**3**) using the optically active Schiff bases (**1b, c**). The Schiff bases (**1b, c**), N-benzylidene-*R*(+)-α-methylbenzylamine (**1b**) and N-benzylidene-*S*(−)-α-methylbenzylamine (**1c**), were prepared by the reaction of the corresponding optically active amine with benzaldehyde in benzene. Prior to the reactions with **1b** and **1c**, dichlorocarbene, generated *in situ* from sodium methoxide and chloroform, was allowed to react with N-benzylidenebenzylamine (**1a**) in anhydrous n-hexane to give N-benzyl-α-chloro-α-phenylacetamide (**3a**) in a 37% yield. Furthermore, in order to examine the racemization of the optically active Schiff base during the reaction, hydrolysis of **1c** with 6N hydrochloric acid was attempted, but the specific rotation

1) Location: *5–1, Oe-hon-machi, Kumamoto, 862, Japan.*
2) E.K. Fields and J.M. Sandri, *Chemical Industry* (London), **1959**, 1216.
3) J.A. Deyrup and R.B. Greenwald, *Tetrahedron Letters*, **1965**, 321.
4) J.A. Deyrup and R.B. Greenwald, *J. Am. Chem. Soc.*, **87**, 4538 (1965).
5) A.G. Cook and E.K. Fields, *J. Org. Chem.*, **27**, 3686 (1962).
6) M.K. Meilahn, L.L. Augenstein, and J.L. McManaman, *J. Org. Chem.*, **36**, 3627 (1971).
7) R.E. Brooks, J.O. Edwards, G. Levey, and F. Smith, *Tetrahedron*, **22**, 1279 (1966).