

1,4-DIPOLAR ADDITION OF 2,3-DIMETHYLISOQUINOLINIUM-4-DITHIOCARBOXYLATE WITH DIMETHYL ACETYLENEDICARBOXYLATE.

Kazumichi Mizuyama, Yoshinori Tominaga, Yoshiro Matsuda,  
and Goro Kobayashi\*

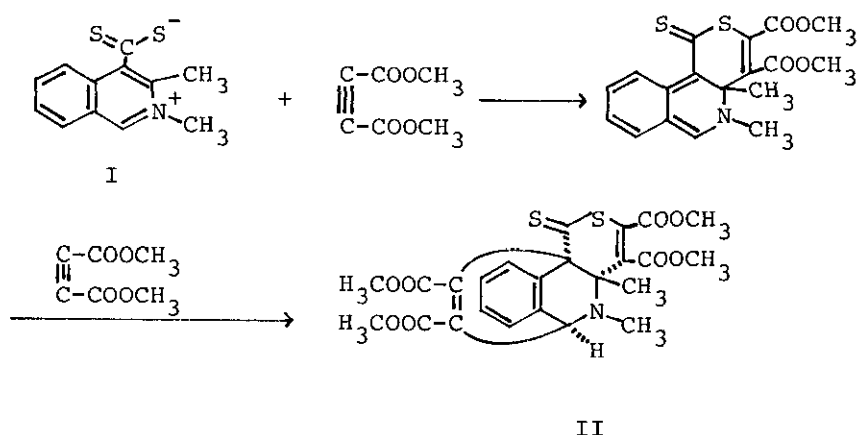
Faculty of Pharmaceutical Sciences, Nagasaki University,  
1-14, Bunkyo-machi, Nagasaki, Japan

Reaction of 2,3-dimethylisoquinolinium-4-dithiocarboxylate with dimethyl acetylenedicarboxylate in dimethylformamide gave 1,4a,6,10b-tetrahydro-3,4,11,12-tetramethoxycarbonyl-4a,5-dimethyl-1-thioxo-6,10b-etheno-thiapyrano-[4,3-c]isoquinoline which might be resulted in both cycloaddition reactions, simultaneous 1,4-dipolar cycloaddition and Diels-Alder reaction.

The purpose of the present work is to investigate the versatility of some functionalized enamino-dithiocarboxylate and the existing knowledge of the chemistry of enamino-dithiocarboxylate. In a continuation of our studies of the enamino-dithiocarboxylate derivatives, the authors have reported the reactions of these compounds with dimethyl acetylenedicarboxylate as a dienophile to give the corre-

sponding Diels-Alder reaction product<sup>1-3</sup>. These reactions are also thought to be 1,4-dipolar addition, reported by Huisgen<sup>4-8</sup>.

In this paper, a typical 1,4-dipolar reaction of dithiocarboxylate derivative with dimethyl acetylenedicarboxylate is reported.



A mixture of 2,3-dimethylisoquinolinium-4-dithiocarboxylate<sup>9</sup> ( I ) and dimethyl acetylenedicarboxylate ( I : DMAD= 1 : 2 ) in dimethylformamide was heated on a boiling water bath for 20-30 min. After cooling at room temperature, the solution was poured into ice-cooled water with vigorously stirring. The precipitates were collected by filtration and recrystallized from acetone to give orange-red needles of mp 189-192 °C in 55% yield. Elemental analysis of this product corresponded to  $C_{24}H_{23}NO_8S_2=517.43$  (Calcd.: C, 55.71; H, 4.48; N, 2.71. Found: C, 55.63; H, 4.53; N, 2.72%). The molecular weight of this product was determined by mass spectroscopy (  $M^+$ : 517 ). The nmr spectrum (  $\delta$  in  $CDCl_3$  ) of this compound

displayed four sharp singlets due to methyl protons at 2.48 (3H,s,CH<sub>3</sub>), 3.16(3H,s,NCH<sub>3</sub>), 3.60(3H,s,OCH<sub>3</sub>), 3.84(9H,s,OCH<sub>3</sub>) and one sharp singlet due to methine proton of 1-position at 6.12 ppm. The methyl protons of 3-position at 2.48 ppm appeared at lower magnetic field under the influence of a methoxycarbonyletheno groups than those protons at saturated carbon in other similar thiapyron system. This result may support a bridged structure of II of the same orientation of the etheno and the methyl groups and this structure is also the least hindrance of all possible diastereomers. The ir spectrum of this compound showed carbonyl bands of the methyl ester groups at 1730 and 1710 cm<sup>-1</sup>. The uv spectrum revealed maxima at 229, 317, and 378 nm<sup>a</sup>. From these spectral data and elemental analysis, this compound was assigned to be 1, 4a,6,10b-tetrahydro-3,4,11,12-tetramethoxycarbonyl-4a,5-dimethyl-1-thioxo-6,10b-ethenothiapyrano[4,3-c]isoquinoline ( II ). The result was explained by the double cycloaddition reaction of dithiocarboxylate and 1- and 4-position of isoquinoline with 2 mole of DMAD. There are also a very few reports in the literature concerning the use of isoquinoline derivatives as dienes in the Diels-Alder reaction<sup>10-15</sup>.

## REFERENCES

- 1 Y.Tominaga, R.Natsuki, Y.Matsuda, and G.Kobayashi, Chem. and Pharm.Bull.(Japan), 1973, 21,2770.
- 2 Y.Tominaga, K.Mizuyama, and G.Kobayashi, Chem. and Pharm.Bull.(Japan), 1974,22,1670.

- 3 G.Kobayashi, Y.Matsuda, Y.Tominaga, and K.Mizuyama, Heterocycles, 1974,2,309.
  - 4 R.Huisgen and K.Herbig, Annalen, 1965,688,98.
  - 5 R.Huisgen, M.Morikawa, K.Herbig, and E.Brunn, Chem.Ber., 1967,100,1094.
  - 6 R.Huisgen, K.Herbig, and M.Morikawa, Chem.Ber., 1967, 100,1107.
  - 7 R.Huisgen, M.Morikawa, D.S.Breslow, and R.Grashey, Chem.Ber., 1967,100,1602.
  - 8 M.Morikawa and R.Huisgen, Chem.Ber., 1967,100,1616.
  - 9 K.Mizuyama, Y.Tominaga, Y.Matsuda, and G.Kobayashi, J.Pharm.Soc.Japan, 1974,94,702.
  - 10 S.F.Dyke, M.Sainsbury, D.W.Brown, and R.D.Clipperton, Tetrahedron, 1970,26,5969.
  - 11 J.Hamer, "1,4-cycloaddition reactions", Academic Press, New York, 1967.
  - 12 J.Saver, Angew.Chem.Interal.Edn., 1966,5,211; 1967,6,16.
  - 13 A.Wasserman, "Diels-Alder Reaction", Elsevier, Amsterdam, 1965.
  - 14 S.B.Needlemann and M.C.Chang, Chem.Rev., 1964,62,405.
  - 15 Y.A.Arbutov, Russ.Chem.Rev., 1964,35,407.
- a Concentration is unknown because of insufficient solubility.

Received, 13th August, 1974