A NOVEL REACTION OF 3-ETHOXYCARBONYL-2-METHYLTHIO-THIAZOLO[2,3-a]ISOQUINOLINIUM SULFATE WITH ACTIVE METHYL COMPOUNDS.

Kazumichi Mizuyama, Yoko Matsuo, Yoshinori Tominaga, Yoshiro Matsuda, and Goro Kobayashi*

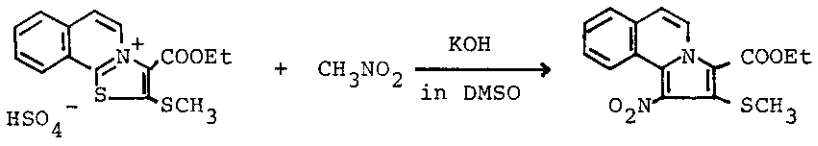
Faculty of Pharmaceutical Sciences, Nagasaki University, 1-14 Bunkyo-machi, Nagasaki, Japan.

The reaction of 3-ethoxycarbonyl-2-methylthio-thiazolo[2,3-a]isoquinolinium sulfate with active methyl compounds(nitromethane, acetophenone)in the presence of base produced ethyl 2-methylthio-1-nitropyrrolo[2,1-a]isoquinoline-3-carboxylate(II) and ethyl 2-methylthiopyrrolo[2,1-a]isoquinoline-3-carboxylate(III).

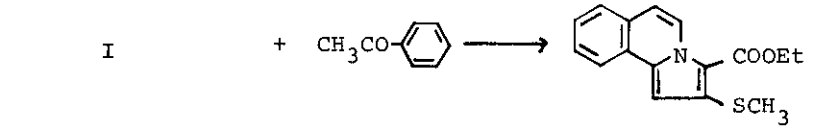
It has been reported about the syntheses of anhydro 3-substituted thiazolo[2,3-a]isoquinolinium hydroxide derivatives[1] and the reaction of methiodide of mesoionic 3-p-nitrophenyl-thiazoloisoquinolinium-2-thion with aliphatic amines to give mesoionic imidazoloisoquinolinium thiones[2]. Grashey[3] reported that the reaction of 3,4-dihydro-2-methylthio-1,3,4-triazolo-[5,1-a]isoquinolinium iodide with active methylene compounds

(malononitrile, methyl cyanoacetate) gave the mesoionic compounds, which were obtained by the substitution of methylthio group with active methylene compound. There has not been examined about the reaction of 3-ethoxycarbonyl-2-methylthiothiazolo[2,3-a]isoquinolinium sulfate(I)[4] with various nucleophiles.

In this paper, it is reported that 3-ethoxycarbonyl-2-methylthiothiazolo[2,3-a]isoquinolinium sulfate(I) reacts with active methyl compound(nitromethane, acetophenone) to give benzoindolizine derivatives(II, III).



I II



III

Chart I

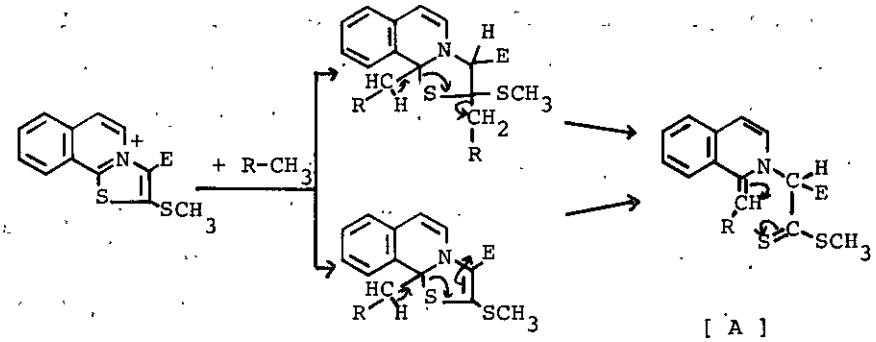
The reaction of 3-ethoxycarbonyl-2-methylthiothiazolo[2,3-a]-isoquinolinium sulfate(I) (0.83 g, 0.002 mole) and nitromethane(0.24 g, 0.004 mole) in the presence of powdered

potassium hydroxide(0.23 g, 0.008 mole) in DMSO(30 ml) gave yellow leaflets of mp 115-116° in 36 % yield. The nmr spectrum(δ in $CDCl_3$) displayed one sharp signal due to methyl proton at 2.49(3H, s, SCH_3) and one triplet signal due to methyl proton of ethyl group at 1.40-1.58(3H, t, CH_3). IR(KBr): 1690(ester carbonyl), 1505 and 1340 cm^{-1}(NO_2). UV λ_{max}^{EtOH} nm(logε): 220(4.42), 257(4.45), 279(4.55), 340(3.89), 390(3.58). From these spectral data and elemental analysis, this compound was assigned to be ethyl 2-methylthio-1-nitro-pyrrolo[2,1-a]isoquinoline-3-carboxylate(II).

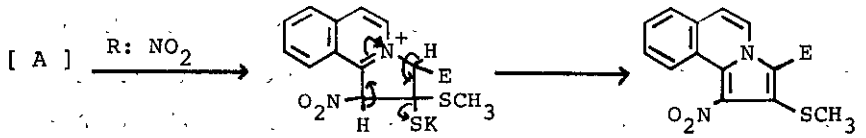
In a similar method, the reaction of I with acetophenone gave a red oil. This oil was chromatographed on aluminum oxide with benzene to give white needles of mp 120-121° in 18 % yield. The nmr spectrum(δ in $CDCl_3$) of this compound displayed two sharp signals due to ring proton of 1-position at 6.78 and due to methyl proton of methylthio group at 2.53. IR(KBr): 1670 cm^{-1}(ester carbonyl). UV λ_{max}^{EtOH} nm(logε): 220(3.86), 288(4.41), 318(3.91), 330(3.86), 351(3.71),369(3.79). From these spectral data and elemental analysis, this compound was assigned to be ethyl 2-methylthiopyrrolo-[2,1-a]isoquinoline-3-carboxylate(III).

A possible reaction mechanism is outlined in Chart II.

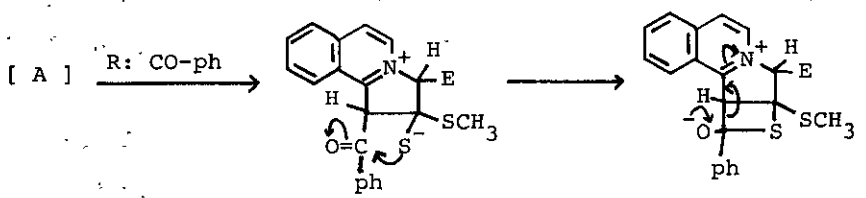
In conclusion, it is of interest to investigate the reaction of 3-ethoxycarbonyl-2-methylthiothiazolo[2,3-a]isoquinolinium sulfate with other active methylene compounds, and this reaction may be able to be applied to the synthesis of benzoindolizine derivatives.

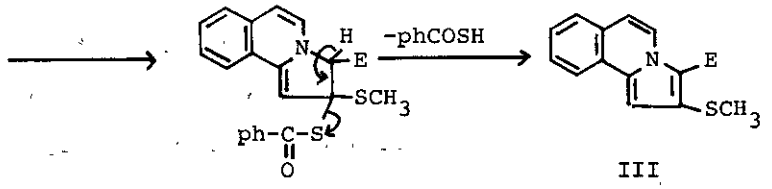


[A]



II





III

E: COOEt

Chart II

REFERENCES

1) a) F.Kröhnke and H.H.Steuernagel, Chem.Ber., 1964, 97, 1118. b) M.Ohta, H.Kato, and T.Kaneko, Bull.Chem.Soc.Japan, 1967, 40, 579. c) M.Ohta and H.Kato, in "Nonbenzenoid Aromatics", ed. J.P.Snyder, Academic Press, New York,1969, p.117-248. d) T.Shiba and H.Kato, Bull.Chem.Soc.Japan, 1970, 43, 3941. e) W.D.Ollis and C.A.Ramsden, Chem.Comm., 1971, 1222, 1223. f) P.B.Talukar, S.K.Sengupta, and A.K. Datta, Indian J.Chem., 1971, 9, 1417.

2) P.B.Talukar, S.K.Sengupta, and A.K.Datta, J.C.S.Chem. Comm., 1972, 696.

3) R.Grashey and M.Baumann, Tetrahedron Letters, 1969, 2177.

4) Compound I was synthesized by the similar method to the following literature. 1) a), Angew.Chem., 1961,73, 26.

5) All new compounds reported herein gave satisfactory elemental analysis and spectral data.

Received, 30th April, 1975