SYNTHESIS OF 5,5'-DIALKOXY-2,2'-DIOXAZOLYLSULFIDES

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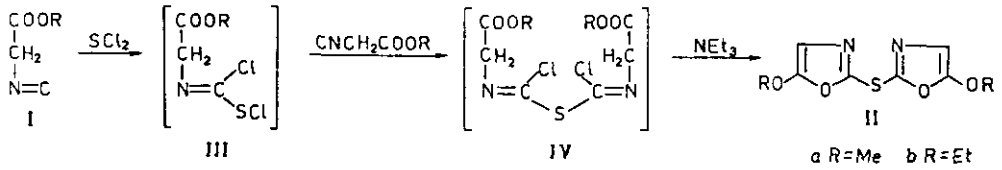
Abstract- Alkyl isocyanoacetates I reacted with sulfur dichloride to give the intermediate sulfides IV which on treatment with triethylamine afforded the hitherto unknown dioxazolylsulfides II.

In a previous paper[1] we reported a novel synthesis of the oxazole ring, starting from alkyl isocyanoacetates and arylsulfenyl chlorides.
Continuing our studies on the reactivity of alkyl isocyanoacetates toward compounds having S-Cl groups, we prepared 5,5'-dialkoxy-2,2'-dioxazolylsulfides II starting from alkyl isocyanoacetates I and sulfur dichloride[2] as described in Scheme I.

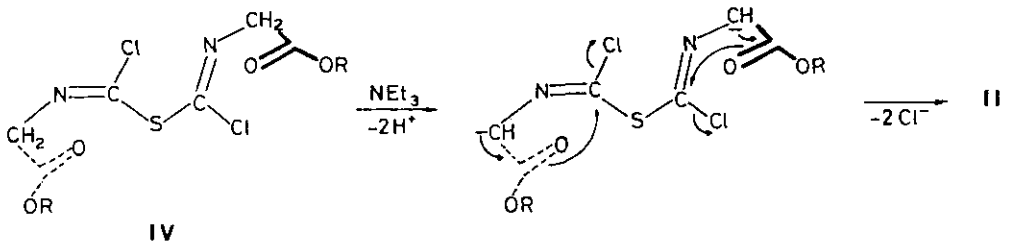
Scheme I



Concerning the synthesis some remarks can be made: it is reasonable to assume that the first attack of sulfur dichloride takes place on the carbenoid carbon of isonitriles I to give S-chloroisothiocarbamoyl chlorides III and then another molecule of alkyl isocyanoacetate will give the key intermediates IV.
A possible pathway for the ring-closure reaction is reported in Scheme II. Even though intermediates IV could not be isolated due to their instability, space filling models suggest a molecular arrangement with one methylene group syn with respect to the sulfur atom whereas the other one lies in the anti position. Accordingly an out of plane attack of electron pair of the oxygen on the sp^2 carbon might be assumed. This would prevent the stereochemistry of IV from being crucial in the for-

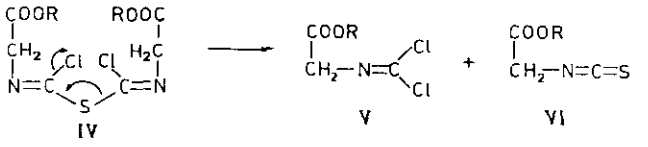
mation of the final product.

Scheme II



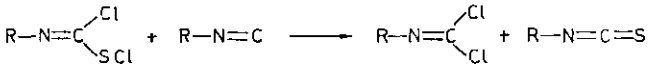
IV

Isolation of sulfides II confirmed the presence of IV in the reaction medium. Sulfides II were obtained in high yields by performing the reaction at -70 °C; when higher temperatures were employed the yields drastically decreased because of the decomposition of the unstable intermediates IV into the isocyanide dichlorides V and the isothiocyanates VI[3]:



IV V VI

Previously Zumach and Kühle[4] stated that reaction between S-chloroisothiocarbamoyl chlorides and isonitriles affords isocyanide dichlorides and isothiocyanates:



but no hypothesis on the reaction mechanism was advanced.

Since the reaction between SCl_2 and isonitriles in molar *ratio* 1:2 can be regarded as the reaction between equimolecular amounts of S-chloroisothiocarbamoyl chlorides and isonitriles, the results of this study account for the presence of the key intermediate R-N=CClSClC=N-R in the reaction described by Zumach and Kühle.

The structure of dioxazolyl sulfides II was assigned on the basis of their ^{1}H-nmr and mass spectra. In the ^{1}H-nmr spectra of II a singlet signal at about 6.5 δ was detected, due to the two equivalent protons at the 4-position. In the mass spectra of II, besides the molecular ions $[M(IIa)]^+$ m/z 228 and $[M(IIb)]^+$ m/z 256, the fragment ions $[Oxazole+S+OR]^+$ m/z 130 (R=Me) or m/z 144 (R=Et) and $[Oxazole+S]^+$

m/z 99 were detected and this agrees with the assigned structure.

REFERENCES AND NOTES

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1. R. Bossio, S. Marcaccini, and R. Pepino, *Heterocycles*, in press.

2. A solution of SCl_2 in CH_2Cl_2 was added to a solution of $CNCH_2COOR$ in CH_2Cl_2 (molar *ratio* SCl_2: $CNCH_2COOR$ = 1:2) maintaining the temperature at -70 °C. The resulting solution was allowed to react for 15 min and then the calculated amount of NEt_3 was added at such a rate that the temperature did not rise above -65 °C. The resulting mixture was stirred, without removing the cooling bath, until the temperature rose to 10 °C and then evaporated to dryness. The residue was stirred with Et_2O and then filtered. Evaporation of the filtrate left II in 87-92% yields.
IIa: mp 60-61 °C from EtOH/water; ^{1}H-nmr (DMSO-d_6): 6.44(s,2H,H-4), 3.87(s,6H, CH_3); ms (70 eV): $[M]^+$ m/z 228, $[Oxazole+S+OCH_3]^+$ m/z 130, $[Oxazole+S]^+$ m/z 99.
IIb: mp 62-63 °C from *EtOH/water*; ^{1}*H-nmr (DMSO-*d_6*)*: 6.52(s,2H,H-4), 4.26-4.06(q, 4H,CH_2), 1.42-1.26(t,6H,CH_3); ms (70 eV): $[M]^+$ m/z 256, $[Oxazole+S+OEt]^+$ m/z 144, $[Oxazole+S]^+$ m/z 99.

3. The presence of V and VI was revealed by means of gc/ms. Furthermore the presence of VI was confirmed by the strong ir absorption at 2065 cm^{-1} due to the -N=C=S group.

4. G. Zumach and E. Kühle, *Angew.Chem.*, 1970, 82, 63; *Angew.Chem.Int.Ed.*, 1970, 9, 54.

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