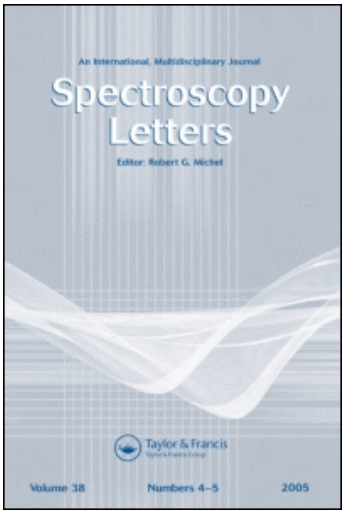


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Mass Spectrometry Study of 7-Chloro-3,4-dihydro-4,5-dioxo-3-substituted Aryl-2-thio-2H, 5H-pyrano [3,4-e]-1,3-Oxazine, their Morpholine and Alcohol Reaction Products

Jasim M. A. Al-rawi[a]; Abdul-Hakim Th. Mahmood[b]
[a] Chemistry Department, College of Science, University of Mosul, Mosul, IRAQ [b] Department of Physiology, Biochemistry and Pharmacology, Veterimary Medicine College, University of Mosul, Mosul, IRAQ

To cite this Article Al-rawi, Jasim M. A. and Mahmood, Abdul-Hakim Th.(1989) 'Mass Spectrometry Study of 7-Chloro-3,4-dihydro-4,5-dioxo-3-substituted Aryl-2-thio-2H, 5H-pyrano [3,4-e]-1,3-Oxazine, their Morpholine and Alcohol Reaction Products', Spectroscopy Letters, 22: 7, 843 — 854
To link to this Article: DOI: 10.1080/00387018908053941
URL: http://dx.doi.org/10.1080/00387018908053941

SPECTROSCOPY LETTERS, 22(7), 843-854 (1989)

MASS SPECTROMETRY STUDY OF 7-CHLORO-3, 4-DIHYDRO-4,5-DIOXO-3-SUBSTITUTED ARYL-2-THIO-2H, 5H-PYRANO [3,4-e] -1,3-OXAZINE, THEIR MORPHOLINE AND ALCOHOL REACTION PRODUCTS

Jasim M. A. Al-Rawi*
Chemistry Department,
College of Science,
University of Mosul,
Mosul, IRAQ

And

Abdul-Hakim Th. Mahmood
Department of Physiology,
Biochemistry and Pharmacology,
Veterinary Medicine College,
University of Mosul,
Mosul, IRAQ.

ABSTRACT

Retro Diels-Alder mechanism is the main fragmentation pattern of the 7-chloro Pyrano oxazine (2),7-morpholino pyrano oxazine (3),5-morpholino carbonyl-4-oxo-3-substituted phenyl-2-thio-1-3-oxazine-6-ylacetomorpholide (4) and ethyl-6-ethoxy carbonyl methyl-4-oxo-3-(substituted phenyl)-2-thio-2H-1,3-oxazine-5-carboxylate (5). Further fragmentation routes were also discussed.

* Author to whom correspondence should be addressed.

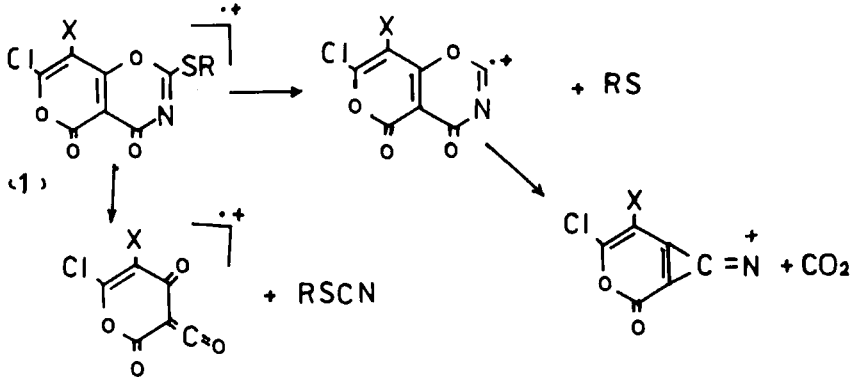
INTRODUCTION

Much effort has been devoted to the synthesis and biochemical properties of 1,3-oxazines[1], i.e. oxazinomycin is an antibiotic[2], while some of the 1,3-oxazines are suggested as antitumer compounds.[3] 7-chloropyrano-1,3-oxazines were obtained from the reaction of malonyl chloride with nitriles[4], thiocyanates[5], isocyanates[6] and isothiocyanates[7]. The structures of the above products were confirmed by chemical degradation, I.R, ^{1}H NMR and some carbone-13 NMR spectroscopy[8]. However, no or very little information is available about the fragmentation pattern of the above prepared compounds.

7-chloro-2-alkyl (or aryl)- mercapto-4,5-dioxo [3,4-e] -1, 3-oxazine(1,x=H) and its 8-bromo-analogue (1,x=Br) showed the loss of SR group, then carbon dioxide molecule[9,10] under electron impact ionization. The carbon dioxide molecule was ejected unexpectedly from the oxazine ring but not from the pyrone ring. Such fragmentation occurs only through rearrangement as a result of interaction between remote functional groups. The mechanism was proved by labelling compound (1) (x = H, R = CH_3) with enriched C-13 at C-2. Furthermore, compound (1) fragmented by Retro Diels-Alder mechanism[11] losing RSCN molecule (scheme 1).

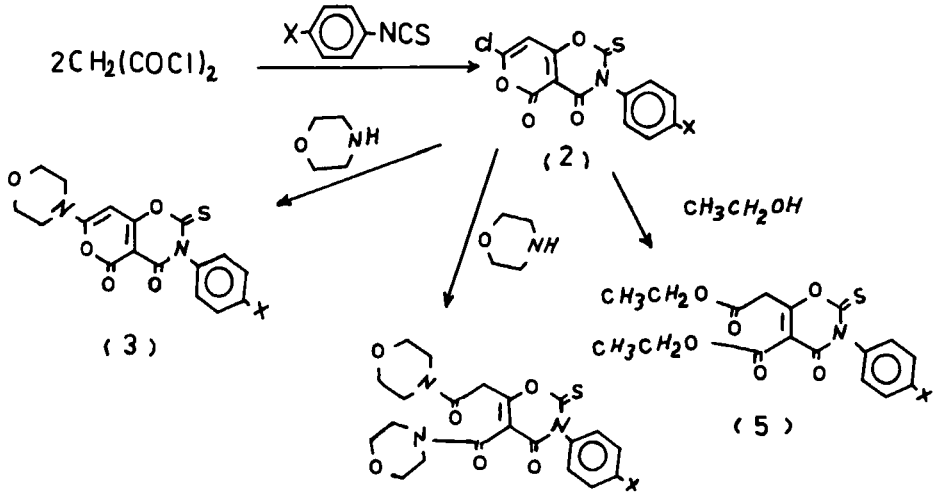
In this paper we are reporting the possible fragmentation pattern of the iso-analogue 7-chloro-3,4-dihydro-4,5-dioxo-3-aryl-2-thio-2H,5H-pyrano [3,4-e] -1,3-oxazine (2).

Furthermore the fragmentation patterns of the reaction products (3) and (4) in addition to the alcohol reaction products (5) (scheme 2) were also discussed.



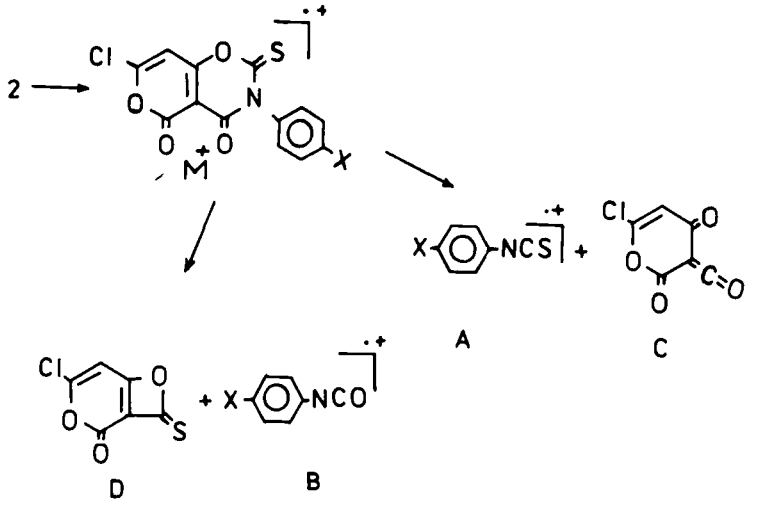
X = H, Br
R = CH_3, CH_2CL, CH_2CH_3, CH_2Ph

Scheme (1)



a,x = H; b, x = F; c, x = CL

Scheme (2)



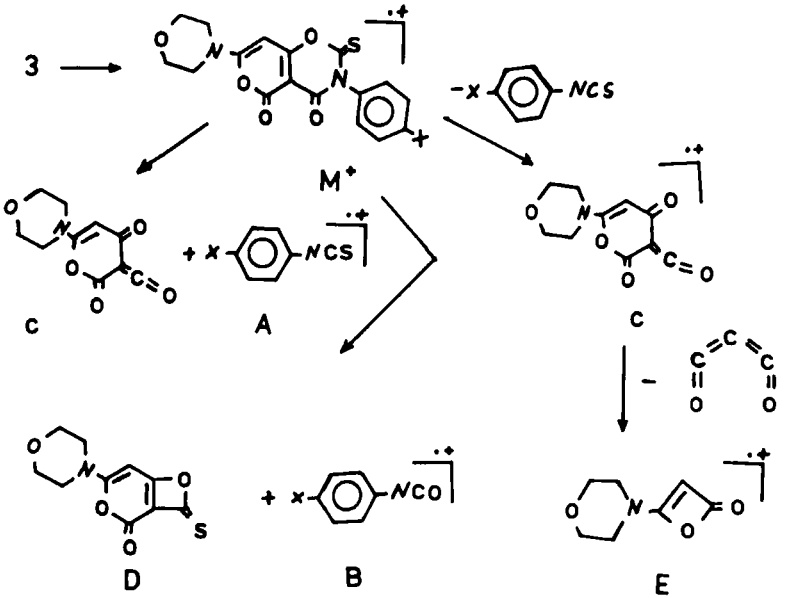
a, x = H; b, x = F; c, x= CL

Scheme (3)

RESULTS AND DISCUSSION

The electron impact (70-ev) mass spectral values of compounds (2 - 5) are summarized in Table (1) and shown in schemes (3 - 6). The structures depicted in all of the fragmentation schemes are based on the chemically reasonable predictions of the observed spectral data.

The 7-chloro pyrano oxazine (2) resulted in a simple fragmentation pattern under electron impact ionization. The most important fragmentation route was the Retro Diels-Alder reaction[11] which involves elimination of the most stable isothiocyanate ion A (Base Peak) (Scheme 3), but the remaining part of the molecule (C) did not show an ion in the mass

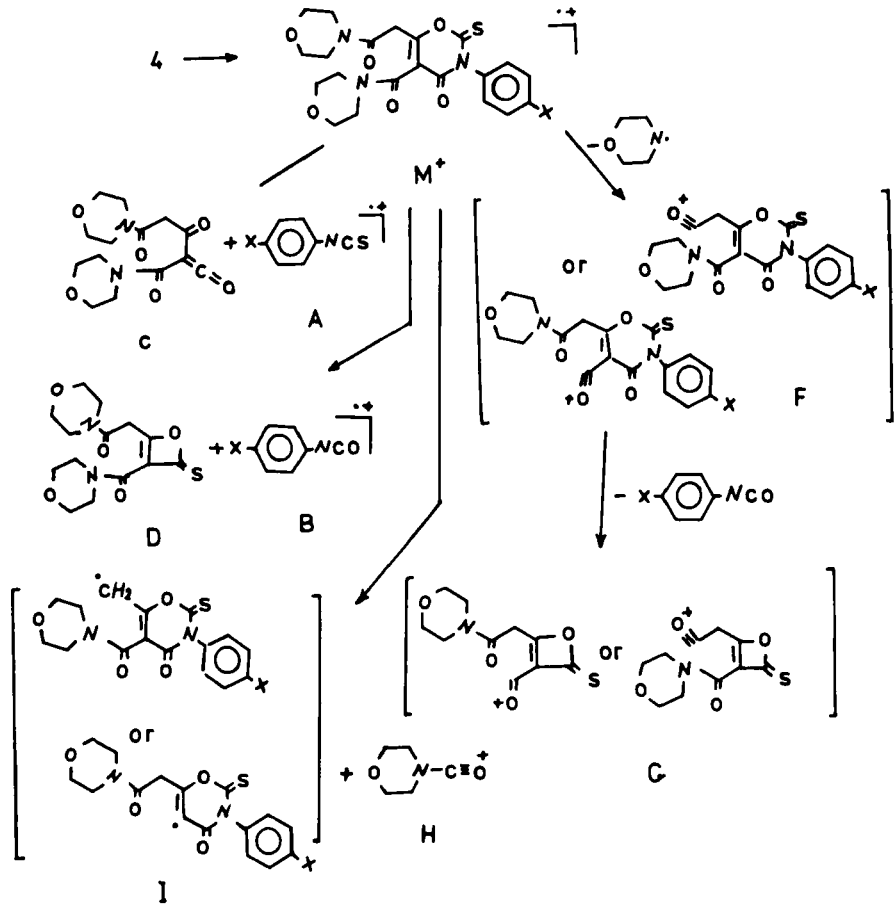


a, x = H; b, x = F; c, x = CL

Scheme (4)

spectrum, possibly due to it's thermal instability. The minor fragmentation route was the loss of isocyanate ion (B), and the remaining part of the molecule (D) did not show a noticable ion in the mass spectrum also due to it's thermal instability.

Replacing the 7-chloro atom of compound (2) by morpholine yielded compound (3) (Scheme 2). The latter is fragmented in a similar manner as compound (2) (Scheme 4). But the ion (C) here is the most stable ion in the spectrum (Base Peak) as shown in Table (1). The stability of the ion (C) could be attributed to



a, x = H; b, x = CL

Scheme (5)

the resonance incorporation of the nitrogen lone pair into the pyrone ring. This ion (C) loses C_3O_2 molecule to afford the fragment (E).

Compound (4) which resulted from the reaction of compound (2) with morpholine in 1:3 molar ratio (Scheme 2) is fragmented

in a similar manner as do compounds (2) and (3), through the loss of isothiocyanate and isocyanate ion (A and B respectively) (Scheme 5). The remaining parts (C) and (D) did not show ions in the spectra of (4), as was the case with compound (2). Furthermore, compound (4) also loses morpholine moiety to give the ion (F) which in turn loses isocyanate fragment y sulting to the ion (G).

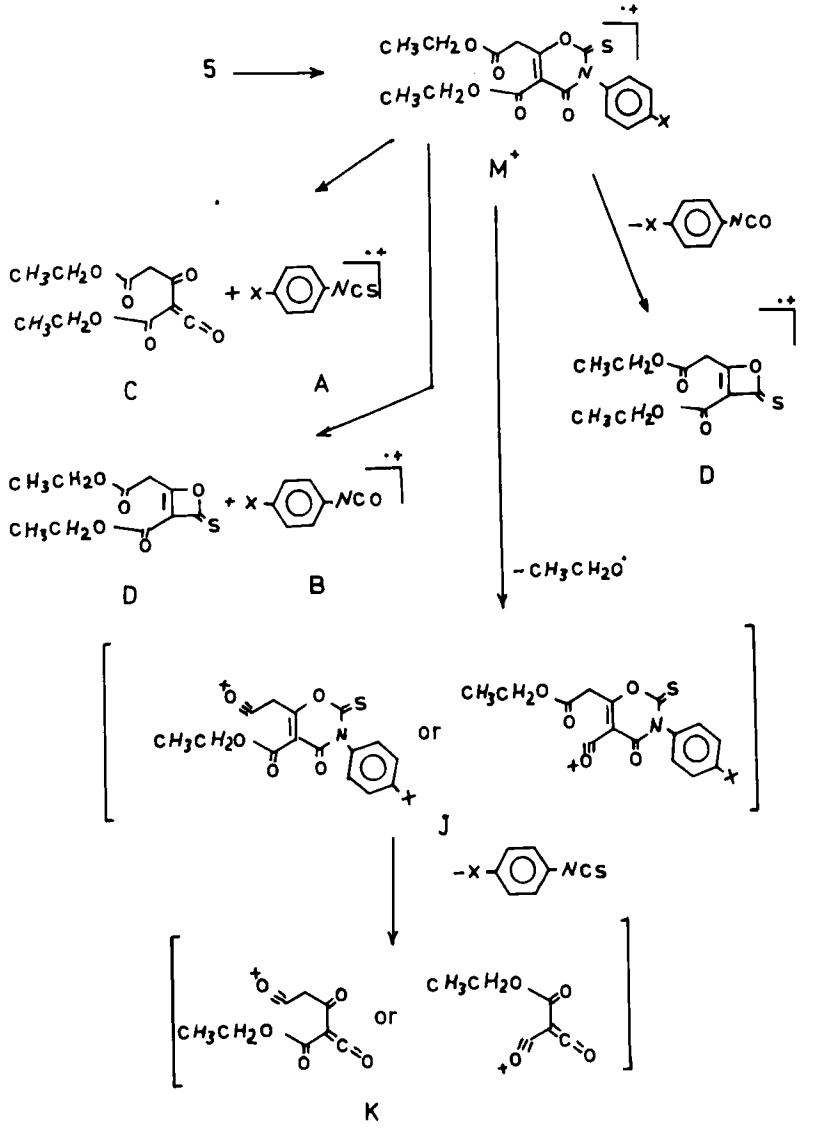
It was worth noting that the molecular ion of (4) generates N-carbonyl morpholine ion (H) by losing the (I), which did not show an ion in the mass spectrum du its relative instability.

The fragmentation pattern of compound (5) (scheme 6) was similar to those of compounds (2 - 4), since it involves the loss of both isothiocyanate and isocyanate ions (A and B respectively). On the other hand, the part (C) did not show an ion, while the part (D) showed an ion with a reasonable intensity in the spectrum.

Moreover, the molecular ion itself loses ethoxy radical to afford the ion (J), which then undergoes Retro Diels-Alder forming the ion (K).

EXPERIMENTAL

Compounds (2) were prepared from the reaction of a mixture of malonyl chloride (40 mmol) and aryl isothiocyanate (20 mmol) with exclusion of moisture. The mixture was slowly heated to 100 ^{o}C, and kept at that temperature until solidi-



a, x = F; b, x = Cl

Scheme (6)

Table 1: Major peaks in the 70-ev mass spectra of compounds 2 - 5.

	M^+ (%)	A (%)	B(%)	C (%)	D (%)	E (%)	F(%)	G (%)	H(%)	J (%)	K(%)
2a	307 (13)	135(100)	119(7)								
2b	325 (11)	153(100)	137(29)								
2c	341 (11)	169(100)	153(22)								
3a	358 (19)	135(45)	119(2)	223(100)		155(16)					
3b	376 (13)	153(60)	137(3)	223(100)		155(21)					
3c*	392 (2)	169(72)	153(17)	223(26)		155(9)					
4a*	445(26)	135(3)	119(7)				359(15)	240(24)	114(45)		
4b*	479 (9)	169(9)	153(34)				393 (5)	240(33)	114(96)		
5a	381 (7)	153(100)	137(52)		244(11)					336(2)	183(10)
5b	397(6)	169(100)	153(17)		244(2)					352(2)	183(11)

*Base peak for 3c, m/z = 57; 4a, m/z = 86,; 4b, m/z = 70.

fication occurred and HCL gas evolusion ceased. The reaction product was kept overnight at room temperature, triturated with cold dry ether and recrystallized from dry toluene-charcoal (2 a and 2b) or from dry CCL_4-charcoal (2c) afforded 7-chloro-3,4-dihydro-4,5-dioxo-3-(substituted phenyl)-2-thio-2H,5H-pyrano [3,4-e] -1,3-oxazines 2(a - c). m.p 200 - 208°C (decomp.), 178°C (decomp.), 174 °C (decomp.) respectively.

Compounds 3(a - c) were prepared from the reaction of 2(a - c) (1 mmol) in dry chloroform (20 ml) with morpholine (2 mmol) in dry chloroform (5 ml) which was added dropwise. The mixture was washed with water, dried with $CaCL_2$, and the chloroform solution evaporated under reduced pressure. The residue was recrystallized from dry Toluene-charcoal (3a and 3b) or dry acetone (3c) to give 3,4-dihydro-7-morpholino-4,5-dioxo-3- (substituted aryl)-2-thio-2H,5H-pyrano [3,4-e] -1,3-oxazines 3 (a - c). m.p. 268°C (decomp.), 192 °C (decomp.), 215 °C (decomp.) respectively.

Compounds 4 (a - c) were prepared as follows:

A solution of morpholine (6 mmol) in dry chloroform (5 ml) was added to a cold stirred solution of compounds 2 (a-c) (2 mmol) in dry chloroform (50 ml). The mixture was refluxed for 1 hr. with exclusion of moisture, cooled, washed with water, dried ($CaCL_2$), and the chloroform solution evaporated under reduced pressure. The oily residue was treated with dry ether and recrystallized from dry toluene to give 5-morpholino carbonyl-4-oxo-3-(substituted aryl)-2-thio-1,3-oxazine-6-ylacetomorpholide (4a, m.p. 183 °C decompose; 4b, m.p. 183 °C decompose; 4c m.p. 196 °C decompose). Synthesis of compounds

5(a,b) was as follows: (10 ml) of absolute ethanol was added to (3 mmol) of compounds 2(b,c). The mixture was refluxed for 15 min., diluted with (30 ml) dry ether, filtered through charcoal, and cooled. The solid that separated was recrystallized from light petroleum (^{o}80 - ^{o}100) 5a (m.p. 116 - 118 ^{o}C) or from dry ether 5b (m.p. 142 - 145 ^{o}C) of ethyl-6-ethoxy carbonyl methyl-4-oxo-3-(substituted phenyl)-2-thio-2H-1,3-oxazine-5-carboxylate 5 (a and b). The structures of the above compounds (1 - 5) were proved from their elemental microanalysis, i.r., ^{1}H and ^{13}C n.m.r. spectra which are reported elsewhere[7].

Mass spectra for compounds (1 - 5) were obtained by Alfred-Bernhardt, Fritz-Pregl, Strabe 24, 5270 Gummbach 1 Elbach, West Germany using SM IB Mass spectrometer with data system SS 100 VARIAN MAT. 70 ev electron energy, 1000 mass resolution, 190 ^{o}C ion source temperature and direct inlet system was used for all samples.

REFERENCES

1. Z. Eckstein and T. Urbanski, Advances in heterocyclic chemistry edited by A. K. Katritzky and A. J. Boulton, Academic Press, Vol. 23, p. 2 - 50, 1978.

2. T. Haneishi, T. Okazak, T. Hata, C. Tamuta, M. Namura, A. Noito, I. Seki and M. Arai, J. Antibiot. 24, 797, 1971.

3. K. Eiter, British Patent 1, 276, 623 CA77, 88515 (1972)

4. S. J. Davis and J. A. Elvidge, J. Chem. Soc., 3553, 1962.

5. a, J. M. A. Al-Rawi and J. A. Elvidge, J. Chem. Soc., Perkin I, 2462, 1976.

b, M. S. Al-Ajely, J. M. A. Al-Rawi and J. A. Elvidge, J. Chem. Soc., Perkin I, 1575, 1982.

6. M. A. Butt, J. A. Elvidge and A. B. Foster, J. Chem. Soc., 3069, 1963.

7. J. M. A. Al-Rawi and A. H. Th. Mahmood, Accepted in J. Parktische Chemie 1988.

8. J. M. A. Al-Rawi and J. A. Elvidge, J. Chem. Soc., Perkin I, 2536, 1977.

9. J. M. A. Al-Rawi, Ph.D. Thesis, University of Surrey, Guildford, England, 1973.

10. J. M. A. Al-Rawi and R. Y. David, accepted in Iraq. J. of Science, 1987.

11. a, V. Nevalainen and P. Vainiotalo, Org. Mass. Spectrom., 21, 543, 1986.

b, J. P. Moritur, T. Mercier and Sarraf, Org. Mass Spectrom., 17, 327, 1982.

c, V. N. Gogle, P. S. Kulkarni, A. S. Modaka and B. D. Tilak, Org. Mass. Spectrom., 16, 515, 1981.

d, F. Turecek and V. Hanus, Org. Mass. Spectrom., 15, 4, 1980.

e, S. M. Ali and M. ILyas, J. Chem. Research(s) 52, 1987.

Date Received: 03/22/89
Date Accepted: 05/03/89