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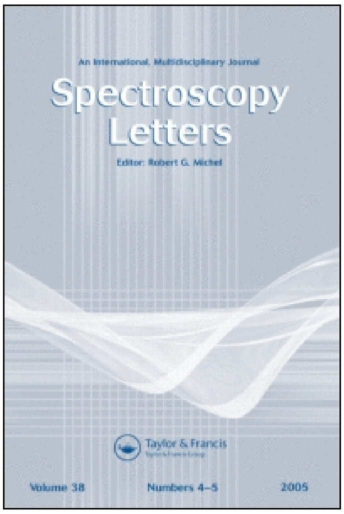

Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

Mass Spectral Fragmentation Patterns of Some Substituted 10,Ll-Dihydro-*5H*-Dibenzo[A,D] Cycloheptene-5-One and 9,10-Dihydro-*4H*-Benzo [4,5]Cyclohepta[1,2-B]Thiophene-4-One

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To cite this Article Karminski-zamola, Grace , Mikotić-Mihun, Zvonimira , Lirvić, Miaden , Cepanec, Ivica and Ranilović, Jasmina(1999) 'Mass Spectral Fragmentation Patterns of Some Substituted 10,Ll-Dihydro-*5H*-Dibenzo[A,D] Cycloheptene-5-One and 9,10-Dihydro-*4H*-Benzo [4,5]Cyclohepta[1,2-B]Thiophene-4-One', Spectroscopy Letters, 32: 4, 601 — 613

To link to this Article: DOI: 10.1080/00387019909350009
URL: http://dx.doi.org/10.1080/00387019909350009

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SPECTROSCOPY LETTERS, 32(4), 601–613 (1999)

MASS SPECTRAL FRAGMENTATION PATTERNS OF SOME SUBSTITUTED 10,11-DIHYDRO-*5H*-DIBENZO[a,d] CYCLOHEPTENE-5-ONE AND 9,10-DIHYDRO-*4H*-BENZO [4,5]CYCLOHEPTA[1,2-b]THIOPHENE-4-ONE

Key words: Mass spectra, substituted 10,11-dihydro-5*H*-dibenzo [a,d]cycloheptene-5-one and 9,10-dihydro-4*H*-benzo[4,5]cyclohepta[1,2-*b*]thiophene-4-one

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ABSTRACT

Electron impact mass spectra of some substituted 10,11-dihydro-5*H*-dibenzo[a,d]cyclohepten-5-one and 9,10-dihydro-4*H*-benzo[4,5] cyclohepta[1,2-*b*] thiophene-4-one have been recorded and the identity of various ions in the mass spectra established. Substituted dibenzosuberones (**2-6**) exhibit one main

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fragmentation route, which include the elimination of the tropolone molecule from the dibenzosuberone fragment cation. Their monothiophene analogues(**7-11**) exhibit characteristic CO elimination from the molecular ion and formation of corresponding naphtho[1,2-*b*]thiophene radical cation which after elimination of CS or HCS from the thiophene nuclei give rise to the benzotrophyne radical cation.

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INTRODUCTION

There is no literature evidence on the EI mass spectral fragmentation pathway of substituted dibenzosuberones; (10,11-dihydro-5*H*-dibenzo[a,d] cycloheptene-5-one) and their monothiophene analogues. Our interest in the synthesis and mass spectral fragmentation pathways of some thiophene compounds[1-3], and in the synthesis of substituted dibenzosuberones[4] and their monothiophene analogues. We were therefore prompted to investigate the mass spectra of the mentioned compounds.

Many dibenzosuberone derivatives and their monothiophene analogues exhibit different biological activities. For example, the effective psychotherapeutic drug, ami- triptyline, has been synthesized earlier [5,6]. The 3-bromo derivative of dibenzosuberone was the intermediate in the synthesis of pharmacologically active derivatives of cyproheptadine which showed antihistaminic and antiserotonin properties[7]. Other derivatives of dibenzosuberone show antidepressant properties[8-11]. Monothiophene analogues of dibenzosuberone show very wide biological activities also, from anti-inflamatory, antipyretic and analgesic activity[12] to antihistaminic[13] and antidepressive properties [14].

In this work, we first examined the fragmentation pathway of unsubstituted dibenzosuberone; 10,11-dihydro-5*H*-dibenzo[a,d]cycloheptene-5-one **1**, prepared earlier[15], and its mono thiophene analogue; 9,10-dihydro-4*H*-benzo[4,5-*b*]cyclohepta-[1,2-*b*]thiophene-4-one **7**, prepared by the described method[16]. We used these substances as the model compounds in the fragmentation study. All other compounds studied, carry one or two substituents in their structures and are as follows: 3-dimethyl-aminopropylamide of 3-dibenzosuberone dicarboxylic acid **2**, 3,7-dibromo-dibenzo-suberone **3**, 3,7-dicyanodibenzosuberone **4**, dihydrodichloride salt of 3,7-dimethylamino propyldiamide of 3,7-dibenzosuberone dicarboxylic acid **5**, and dihydrodichloride salt of 3,7-diamidino-dibenzosuberone **6**, 2-bromo-9,10-dihydro *4H*-benzo[4,5]cyclohepta[1,2-*b*]thiophene-4-one **8**, 2-bromo-9,10-dehydro-*4H*-benzo[4,5]cyclohepta[1,2-*b*]thiophen-4-one **9**, 2,9-dibromo-9,10-dehydro-*4H*-benzo[4,5]-cyclohepta[1,2-*b*]thiophene-4-one **10** and 2,3-dibromo-9,10-dihydro-*4H*-benzo[4,5]-cyclohepta[1,2-*b*]thiophene-4-one **11**. All compounds were prepared in our laboratories (synthetic results are in the process of being published).

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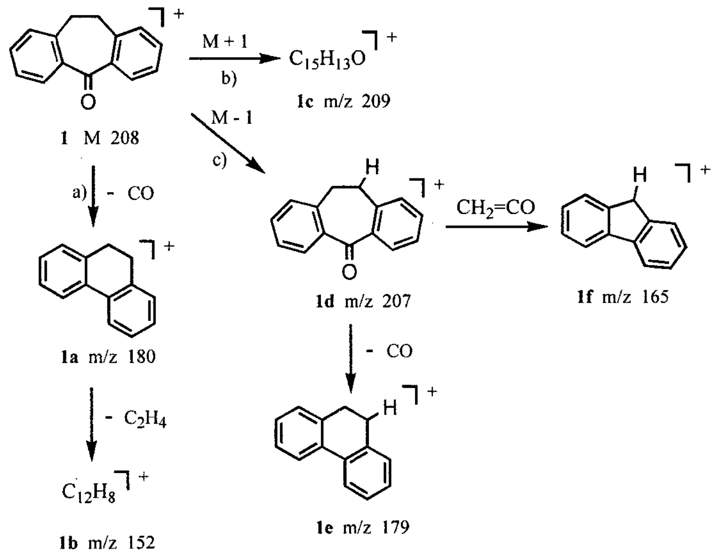
EXPERIMENTAL

Electron impact (EI) mass spectra were recorded using a Varian Saturn 4D GC/MS instrument operated at 70 eV ionizing energy. Samples were introduced using the Septum Equipped Programmable Injector with ion trap temperature of 230°C.

RESULTS AND DISCUSSION

Plausible fragmentation pathways, which are consistent with the spectral data, together with structures which are suggested for fragment ions, are shown in *Schemes 1,2,3* and *4*.

Significant peaks in the EI mass spectra of the compounds examined are reported in Tables 1,2,3,4 and 5. The fragmentation pathway proposed for compound **1** is shown in *Scheme 1*. After the formation of the molecular ion, which is the base peak in the mass spectrum, fragment ion **1a** $C_{14}H_{12}^{+\cdot}$ at m/z 180 is formed (pathway a) by the elimination of a CO molecule. Further fragmentation involves the elimination of one molecule of C_2H_4 and the formation of **1b**, a radical cation $C_{12}H_8^{+\cdot}$ at m/z 152.



Scheme 1

TABLE 1.Characteristic peaks for the compound **1**

	Fragment ions m/z (%)						
No	**M$^+$**	**a**	**b**	**c**	**d**	**e**	**f**
1	208 (100)	180 (67)	152 (16)	209 (15)	207 (25)	179 (93)	165 (72)

Pathway b involves the addition of one hydrogen, and **1c** $(M+1)^+$ ion, pressumably due to self-CI processes within the ion trap, m/z 209 appears with moderate intensity. On the other hand, the fragmentation pathway c involves the elimination of one hydrogen radical from the molecular ion, and **1d** ion $(M-1)^+$ at m/z 207 is also formed with moderate intensity.**Id** fragments further in two different ways. The **1e** ion $C_{14}H_{11}^+$ at m/z 179 appears with high intensity (93%) by the elimination of CO from **1d** while ion **1f** $C_{13}H_9^+$ at m/z 165 (78%) is formed from **1d** by elimination of ketene CH_2=C=O.

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Compounds **2, 3, 4, 5, 6** *(Scheme 2)* fragment via different pathways depending on the substituents introduced. 3-Substituted dibenzosuberone **2**, as well as the di-hydrochloride of 3,7-disubstituted suberone **5** exhibit similar fragmentation pathways. Compound **2** in pathway a loses CH_2= N-CH_3 from the molecular ion, and form **2a** radical cation $C_{19}H_{19}NO_2^{+\cdot}$ at m/z 293 with high intensity. Fragment cations **2b, 3b** and **5b**, $C_{15}H_{11}O^+$ at m/z 207 are formed (as the base peak in **2b**) via two different fragmentation pathways. **2b** was formed by elimination of $CONH(CH_2)_2CH_3$ radical from **2a,** while **3b** and **5b** were formed via **3e** $C_{15}H_{11}BrO^+$ at m/z 287, and **5e** $C_{22}H_{24}O_2N_2^+$ at m/z 336 by elimintion of another substituent R'.

The **3e** and **5e** fragment cations themselves(fragmentation pathway b) were formed by elimination of a Br radical from **3** and of a dimethylaminopropylamide radical from **5**, and subsequent addition of a hydrogen radical. **2c** and **5c** fragment cations $C_8H_6O^+$ at m/z 117 are formed by elimination of one tropolone molecule from **2b** and **5b**. The same fragment ion **4c** $C_9H_5NO^+$ m/z 143 was formed by elimination of C_8H_5 molecule directly from **4**, while the **4a** and **4b** fragment ions are not observed in the mass spectra. Fragment ion **4c** loses one molecule of CO, and **4d** fragment ion $C_8H_5N^+$ at m/z 115 is formed, a reaction which is not followed by **2c** and **5c**. Compound **3** itself also exhibits one specific fragmentation pathway c which includes the elimination of a CO molecule from **3e** and formation of **3f** radical cation $C_{14}H_{11}Br^{+\cdot}$ at m/z 259, while the **3g** radical cation at $C_{14}H_{10}^{+\cdot}$ m/z 178 was formed as a base peak from **3f** by elimination of one molecule of HBr. Fragment cation **3h** $C_7H_5^+$ at m/z 89, was formed after elimination of a C_7H_6 molecule from **3g**.

The dicyano compound **4** also exhibits a fragmentation pathway d, which involves the elimination of a cyanobenziyne molecule from the molecular ion **4**, and the formation of the **4i** $C_{10}H_7NO^{+\cdot}$ ion at m/z 157 moderate intensity. The ion **4j** $C_9H_7N^{+\cdot}$ m/z 129, was formed from **4i** by the elimination of a CO molecule.

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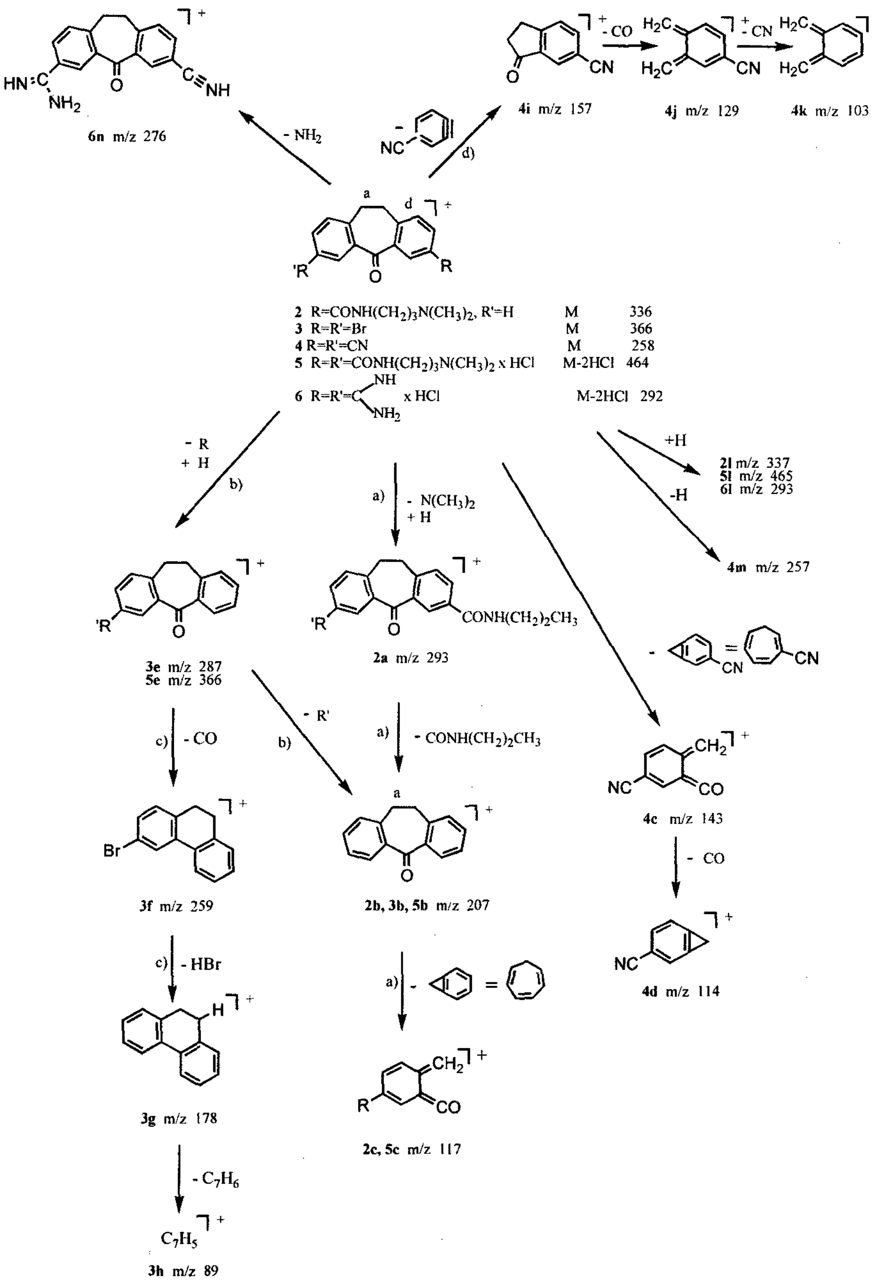

Scheme 2

TABLE 2. Characteristic peaks for the compounds **2-6**

Fragment ions m/z (%)

No	M+	M+-2HCl	a	b	c	d	e	f	g	h	i	j	k	l M+1	m M-1	n
2	-	-	293 (56)	207 (100)	117 (10)	-	-	-	-	-	-	-	-	337 (19)	-	-
3	366 (98)	-	-	207 (18)	-	-	287 (55)	259 (12)	178 (100)	89 (57)	-	-	-	-	-	-
4	258 (10)	-	-		143 (42)	115 (22)	-	-	-		157 (18)	129 (35)	103 (92)	-	257 (100)	-
5	-	464 (53)	-	207 (53)	117 (38)	-	-	366 (100)	-	-	-	-	-	465 (18)	-	
6	-	292 (10)	-	-	-	-	-	-	-	-	-	-		293 (100)	-	276 (27)

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The most intense fragment ion **4k**, $C_8H_7^+$ at m/z 103 is formed from **4j** by the elimination of a CN radical. Compound **2** forms $(M+1)^+$ cation **2l** $C_{21}H_{25}N_2O_2^+$ at m/z 337 while compounds **5** and **6** form (M-2HCl+1) cations **5l** $C_{27}H_{37}N_4O_3^+$ m/z 465 with moderate intensity and **6l** $C_{17}H_{17}N_4O^+$ m/z 293. Dicyano compound **4** gives rise to (M-1) cation **4m** $C_{17}H_9N_2O^+$ at m/z 257 as the base peak. Diamidino compound **6** is very stable under the experimental conditions. Except for **6m** (M-2HCl+1) cation, only one characteristic fragment ion **6n**, $C_{17}H_{14}N_4O^+$ at m/z 276 gives rise by the elimination of the NH_2 radical from one amidino group.

9,10-dihydro-4*H*-benzo[4,5]cyclohepta[1,2-*b*]thiophene-4-one **7** as well as 2-bromo-9,10-dihydro-4*H*-benzo[4,5]cyclohepta[1,2-*b*]thiophene-4-one **8** and 2-bromo-9,10-dehydro-4*H*-benzo-[4,5]cyclohepta[1,2-*b*]thiophene-4-one **9** exhibit generally the same fragmentation pathway with some exceptions.

Compound **7** immediately loses one molecule of CO and forms fragment radical cation **7a** $C_{12}H_{10}S^{+\cdot}$ at m/z 186 which after loss of one molecule of HCS forms **7c** $C_{11}H_9^{+\cdot}$ at m/z 141. **7d** radical cation $C_9H_7^{+\cdot}$ m/z 115 was formed after loss of one acetylene molecule from **7c** and **7e**. $C_7H_5^{+\cdot}$ m/z 89 was formed from **7d**

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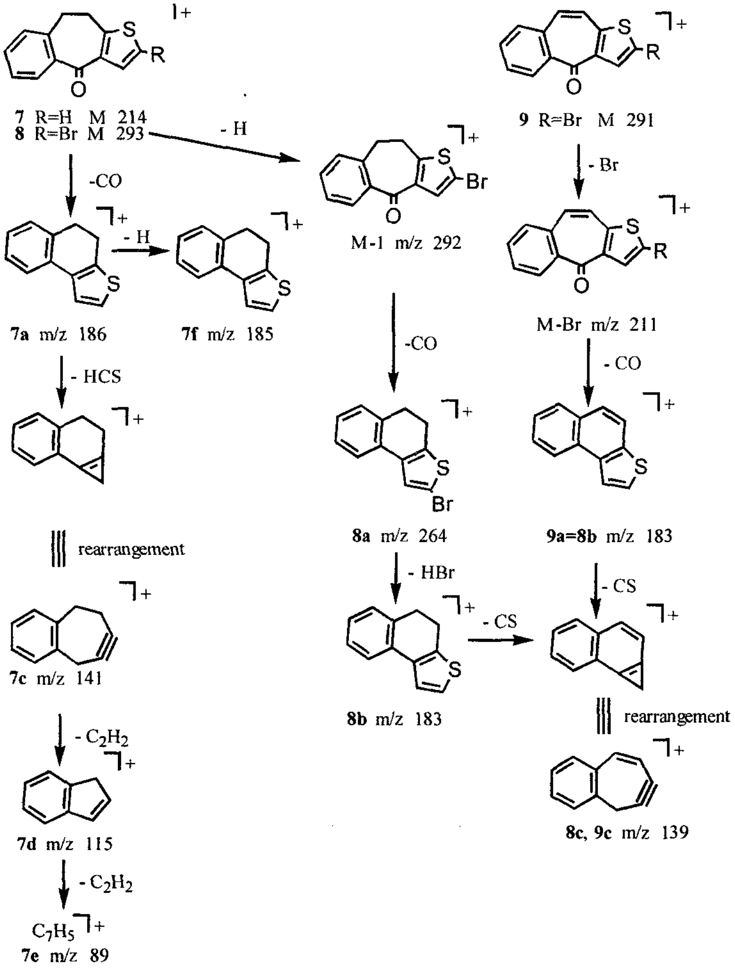

Scheme 3

TABLE 3.Characteristic peaks for the compound **7-9**

Fragment ions m/z (%)

No	M^+	M-1	M-Br+H	a	b	c	d	e	f
7	214	-	-	186	-	141	115	89	185
	(58)			(10)	-	(12)	(13)	(17)	(35)
8	-	292	-	264	183	139	-	-	-
		(17)		(29)	(14)	(35)			
9	291	-	212	184	-	139	-	-	-
	(16)		(16)	(100)		(33)			

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after the loss of one acetylene molecule. **7f** $C_{12}H_9S^{+\cdot}$ was formed from **7a** by elimination of one Compound **7** which immediately loses one molecule of CO and forms a fragment radical cation **7a** $C_{12}H_{10}S^{+\cdot}$ at m/z 186. This in turn, after loss of one molecule of HCS, forms **7c** as $C_{11}H_9^{+\cdot}$ at m/z 141. **7d** radical cation $C_9H_7^{+\cdot}$ m/z 115 was formed after the loss of one acetylene molecule from **7c** and **7e** $C_7H_5^{+\cdot}$ m/z 89 was formed from **7d** after the loss of one acetylene molecule. **7f** $C_{12}H_9S^{+\cdot}$ was formed from **7a** by elimination of one hydrogen radical.

Compound **8** first loses one hydrogen atom and forms $(M-1)^+$ fragment cation $C_{13}H_8OBrS^+$ at m/z 292 and this fragment cation then exhibits the loss of a CO molecule and the formation of **8a** fragment cation $C_{12}H_8BrS^+$ at m/z 264 of the same dihydronaphtho[2,1-*b*]thiophene type as **7a**. After the loss of HBr from **8a**, naphtho[2,1-*b*]thiophene fragment cation **8b** $C_{12}H_7S^+$ at m/z 183 was formed. Compound **9** first loses the Br radical and forms $(M-Br)^+$ fragment cation $C_{13}H_7OS^+$ m/z 211 which then loses a CO molecule and also forms **9a=8b** naphtho-[2,1-*b*]thiophene type fragment cation. **8c** and **9c** $C_{11}H_7^+$ at m/z 139 are further formed by the loss of a CS radical from **8b** respectively **9a**.

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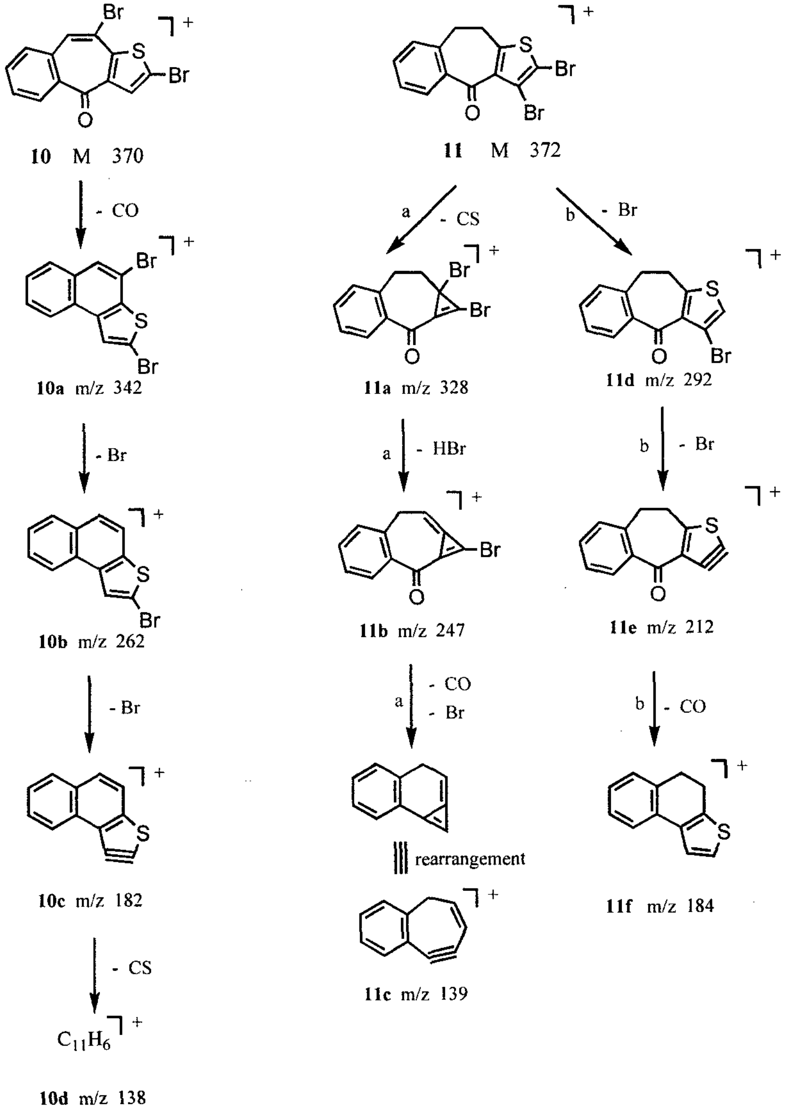

Scheme 4

TABLE 4.Characteristic peaks for compound **10**

	Fragment ions m/z (%)				
No	**M⁺**	**a**	**b**	**c**	**d**
10	370 (48)	342 (25)	262 (16)	182 (64)	138 (43)

TABLE 5.Characteristic peaks for the compound **11**

	Fragment ions m/z (%)						
No	**M⁺**	**a**	**b**	**c**	**d**	**e**	**f**
11	372 (40)	328 (100)	247 (13)	139 (19)	292 (9)	212 (19)	184 (27)

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2,9-Dibromo substituted compound **10** (*Scheme 4*) exhibit the same fragmentation pathway as the monosubstituted compound **9**, namely after the elimination of the CO molecule from the molecular radical cation, the formation of 2,8-dibromo-naphtho-[2,1-b]thiophene radical cation **10a** $C_{12}H_5Br_2S^{+\cdot}$ at m/z 342, with moderate intensity, occurred.

Following the elimination of the bromo radical from **10a** and formation of **10b** fragment cation $C_{12}H_5BrS^+$ at m/z 262 also, with moderate intensity and after the elimination of another bromo radical and subsequent hydrogen transfer. The **10c** fragment cation $C_{12}H_6S^{+\cdot}$ at m/z 182 is formed with a high intensity signal. **10d** $C_{11}H_6^+$ at m/z 138 is formed with moderate intensity, by elimination of CS from fragment cation **10c**. 2,3-Dibromo-substituted compound **11** exhibits some specific pathway of fragmentation in comparison with compound **10**. There are two pathways of fragmentation; a) fragment cation **11a** $C_{12}H_8Br_2O^+$ at m/z 328 as the base peak, is formed by elimination of a CS radical from the molecular radical ion. Then follows the elimination of HBr from **11a** and the formation of fragment cation **11b** $C_{12}H_7BrO^+$ at m/z 247 in the moderate intensity. **11c** $C_{11}H_7^{+\cdot}$ at m/z 139 is formed by elimination of a CO molecule and bromo radical from **11b**. Fragmentation pathway b exhibits first the elimination of a bromo radical from the molecular radical cation and the formation of **11d** cation $C_{13}H_8BrO^+$ at m/z 292 with moderate intensity. **11e** $C_{13}H_8O^{+\cdot}$ at m/z 212 (also with moderate intensity), is formed by the elimination of another bromo radical. Finally **11f** $C_{12}H_8S$ at m/z 184 was formed by the elimination of one CO molecule from **11e** .

ACKNOWLEDGEMENT

The authors wish to express their gratitude to the Ministry of Science of the Republic of Croatia (Scientific project no. 125005) for the financial support of this research.

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REFERENCES:

1. G. Karminski-Zamola, M. Bajić and N. Blažević, *Org. Mass Spectrom.* **27**, 615 (1992).
2. G. Karminski-Zamola, J. Dogan and M. Bajić, *Rapid Commun. Mass Spectrom.* **7**, 460 (1993).
3. G. Karminski-Zamola, V. Tralić-Kulenović, L. Fišer-Jakić, M. Bajić and D.W. Boykin, *Rapid Commun. Mass Spectrom.* **9**, 1345 (1995).
4. Z. Mikotić-Mihun, J. Dogan, M. Litvić, I. Cepanec and G. Karminski-Zamola, *Synth. Comm.*, **28**, 2191, (1998)
5. Hoffsommer R. D., Taub D. and Wendler N.L.J. *Org. Chem.* **27**, 4243, (1962).
6. Hoffsommer R. D., Taub D. and Wendler N.L.J. *Org. Chem.* **28**, 1751, (1963).
7. Engelhardt E.L., Zell C.H., Saari W.S., Christy M.S. and Colton C.D. *J. Med. Chem.* **8**, 829, (1965).
8. Engelhardt E.L. (Merck and Co. Inc.), **U.S. 3,9228.305,** Appl. 1961 C.A. (1976), **84**, 105297q.
9. Engelhardt E.L. (Merck and Co. Inc.), **U.S. 3,978.121,** Appl. 1961 C.A. **6,** 89477g (1977).

10. Kybuz H. and Spiegelberg H. (Hoffman:la Roche Co.) **Swiss 564,506** Appl. 1968, C.A. **84**, 195295n (1976).
11. Jucker E. and Ebnoether A. (Sandoz Ltd) **Belg. 633,261** Appl. 1963. C.A. **61**, 10662 (1964).
12. P. Bolhinger, P. Cooper, H.U. Gubler, A. Leutwiler, T. Payne, *Helv. Chim. Acta,* **73**, (1990), 1197.
13. Z. Polivka, J. Metys, M. Protiva, **Czech**. **CS 260, 087** Appl. 1987., C.A. (1990), **112**, 55927u
14. A. Jimenez, S. Vega, *J. Heterocycl. Chem.* **23**, (1986), 1503.
15. W. Treibs, H.J. Klinkhammer *Chem. Ber.* **84** (1951) 671.
16. J.M. Bastian, A. Ebnöther, E. Jucker, E. Rissi and A.P. Stoll, *Helv. Chim Acta* **49** (1965) 214

Date Received: March 30, 1999
Date Accepted: April 30, 1999

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