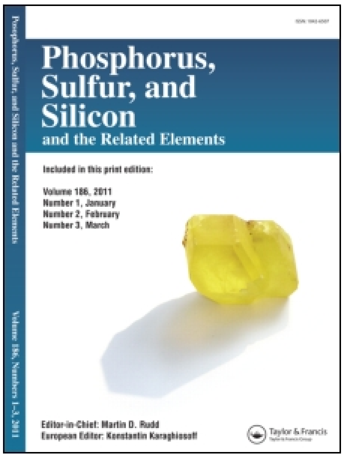

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THERMAL AND PHOTOCHEMICAL REACTIONS BETWEEN α, α'-DIBROMOKETONES AND FIVE-MEMBERED HETEROCYCLES IN THE PRESENCE OF IRON NONACARBONYL

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THERMAL AND PHOTOCHEMICAL REACTIONS BETWEEN α,α'-DIBROMOKETONES AND FIVE-MEMBERED HETEROCYCLES IN THE PRESENCE OF IRON NONACARBONYL

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[3 + 4] Cycloaddition reactions of 2-oxyallilic cations to furan[1] to form seven-membered oxobicyclic compounds have been known for some time. The purpose of this paper has been to try to extend the reaction to five-membered heterocycles with more aromatic character than furan. An analogy has been found between the behavior of thiophene, selenophene and tellurophene in these reactions and in oxetane-forming reactions. The higher the aromaticity of the heterocycle, the more difficult it is to achieve the formation of the seven-membered ring. Contrary to what is observed in oxetane-forming reactions, where it is not possible to isolate a stable tellurium compound, the tellurabicyclic compound was isolated and identified by spectroscopic methods in the present investigation.

INTRODUCTION

It is common to find in the literature numerous examples of cycloaddition reactions where each of the two reactants has an even number of carbon atoms involved at the reaction site. Thus, [2 + 2] and [2 + 4] cycloaddition reactions have been extensively studied throughout the years[2,3] and also, to some extent, the transition-metal catalyzed [4 + 4] cycloaddition reactions.[4] However, cycloaddition reactions where one of the two addends has an odd number of carbon atoms involved at the reaction site, especially those that form large rings, are less common. An example of this type of reaction to form small ring compounds may be cyclopropane formation achieved by means of reactions between olefins and a species that can provide the third carbon atom of the ring. The latter may be obtained by generation of a carbene by any of the usual methods: thermal or photochemical, using metallic complexes or through an ylid.[5] These methods, however, cannot be generalized to the formation of five- or seven-membered rings, [2 + 3] and [3 + 4] cycloaddition reactions, respectively.[5–9]

[3 + 4] cycloaddition reactions between 2-oxyallylic cations, which provide the three-carbon-atom moiety, to a five-membered heterocycle such as furan have been reported in the literature.[1]

It has been the purpose of the present investigation to generalize this reaction to five-membered heterocycles other than furan.

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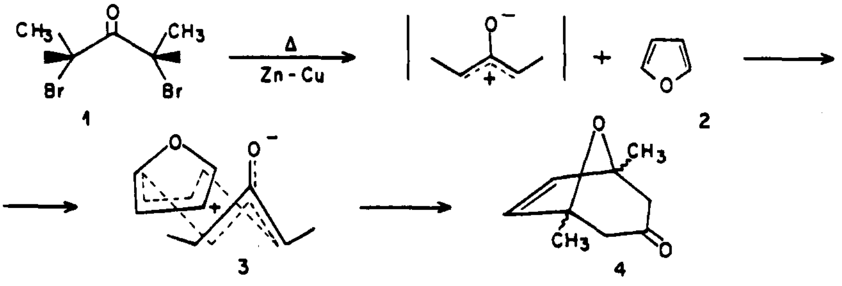
The heterocyclic systems chosen to test the reaction were thiophene, 2,5-dimethylthiophene, selenophene and tellurophene, and the generation of the 2-oxyallylic cation was accomplished by the use of α,α'-dibromoketones in the presence of iron nonacarbonyl.

RESULTS AND DISCUSSION

The stereospecific generation and subsequent reaction of 2-oxyallylic cations with furan which was accomplished by Hoffman *et al.*,[1] afforded bicyclic structures that exemplify [3 + 4] cycloaddition reactions (Scheme 1).



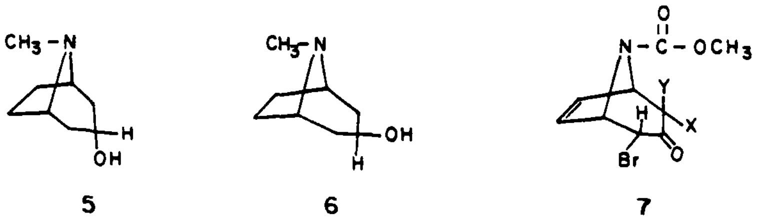
SCHEME 1 [3 + 4] Cycloaddition reaction between furan and the 2,4-dibromoacetone oxyallilic cation.

More recently, Hayakawa *et al.*[11] were capable of synthesizing tropine and pseudotropine (Structures **5** and **6**) by a synthetic route that starts with a reaction between tetrabromoacetone and *N*-carbomethoxypyrrole in the presence of iron nonacarbonyl.

The [3 + 4] cyclocoupling between $\alpha,\alpha,\alpha',\alpha'$,-tetrabromoacetone and *N*-carbomethoxypyrrole leads to *N*-carbomethoxy-2,4-dibromo-8-azabicyclo (3.2.1) oct-6-ene-3-ones which, as far as the carbon skeleton is concerned, are nitrogen analogues of compound **2**.

However, attempts in this laboratory to trap oxyallylic cations with thiophene to yield [3 + 4] cycloaddition products were unsuccessful; instead a substitution product such as **11**[9] was isolated.

These results suggest that furan reacts readily with oxyallylic cations to give a cycloaddition product whereas pyrrole needs an electron-attracting group bonded to



SCHEME 2 [3 + 4] Cycloaddition products derived from pyrrole derivatives.

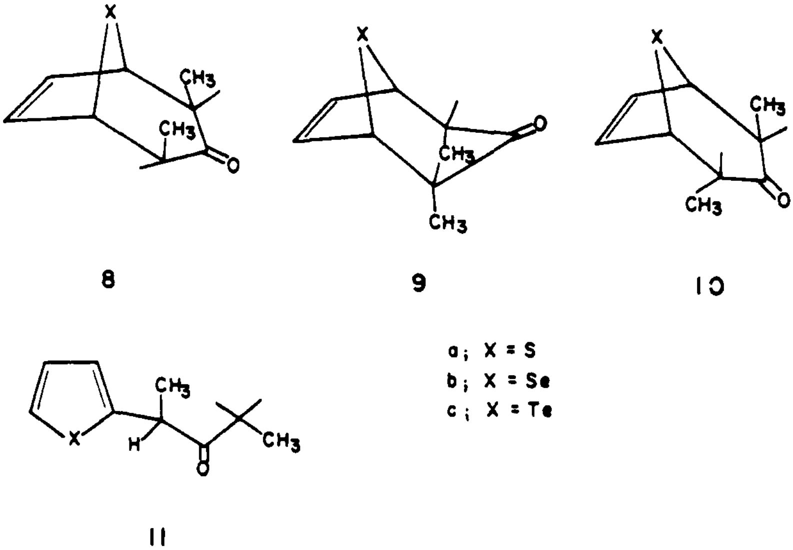
the nitrogen atom, and thiophene does not react at all. This behavior of the common five-membered heterocycles resembles that observed in [2 + 4] cycloaddition (Diels-Alder) and in oxetane-forming reactions.[12] In other words, it may be said that as the aromaticity of the heterocycle increases, its capacity to undergo this type of cycloaddition reaction decreases.

In view of the favorable results obtained with 2,5-dimethylthiophene as a substrate for electronically excited ketones,[13] and taking into account that selenophene and tellurophene are less aromatic than thiophene, all these compounds were considered of interest to be tested in [3 + 4] cycloaddition reactions. In fact, when selenophene and tellurophene were made to react thermally with 2,4-dibromopentanone in the presence of iron nonacarbonyl, a mixture of isomeric products was obtained. After completion of the reaction, it was found that the mixture of products consisted of isomeric [3 + 4] adducts analogous to those obtained from furan and α,α'-dibromoketones; a fourth compound, an electrophilic substitution product, may have originated from the opening of the adducts. These substances were identified by spectroscopic methods, as selenium derivates **8b**, **9b**, **10b**, and **11b** and the tellurium derivatives **8c**, **9c**, **10c**, and **11c**.

On the other hand, when 2,5-dimethylthiophene was used as substrate for the oxiallylic cation derived from 2,4-dibromo-3-pentanone, only compounds **8a** and **9a** were isolated.

Other bromoketones such as 2,3-dibromo-2-methylbutanone, 1,3-dibromo butanone, and 1,3-dibromo-1,3-diphenylacetone were also tested with the above-mentioned heterocycles but no identifiable compounds were isolated.

The structure elucidation of the compounds obtained from these reactions was achieved by careful analysis of their NMR and mass spectra. The NMR spectra of the selenium and tellurium adducts are not first order and, therefore, it was necessary to measure them in $CDCl_3$ in the presence of Eu(fod). The spectra were



SCHEME 3 Products obtained from the reactions studied.

measured at different concentrations of the shift reagent until a constant value for the chemical shift was obtained. The assignments were made by extrapolation to infinite dilution of Eu(fod). It was not possible to separate the [3 + 4] adducts by chromatographic methods and, as a consequence, the NMR spectral study had to be performed on the mixture of isomers. The assignment of resonances was carried out by analogy with the furan derivatives:[1] by the construction of models and by careful inspection of the chemical shifts expected for the different resonances. The α-substitution product could be separate from the [3 + 4] adducts by column chromatography.

The NMR data for the [3 + 4] adducts are illustrated in tables I, II and III; table IV illustrates the NMR data for the open-chain substitution products.

In the symetrical *cis-exo* and *cis-endo* adducts of **8a**, **8b**, **8c**, **9a**, **9b** and **9c**, the NMR spectra consists of 4 resonances, one singlet located between 6.16 and 7.50 ppm which corresponds to the vinylic protons at positions 6 and 7; one resonance at about 4.00 ppm corresponding to the bridgehead protons at positions 1 and 5; the latter may be a singlet or a doublet according to the dihedral angle between these protons and those in the carbon atoms adjacent to the carbonyl function. When methyl groups instead of protons are present at the bridgehead carbon atoms, they appear as one singlet at around 2.15–2.35 ppm; the methyl groups adjacent to the carbonyl function appear as doublets at about 0.93 ppm when they are exo and at about 1.40 ppm when they are *endo*, and finally, the two protons vicinal to these methyl groups (position 2 and 4) appear as a quartet in the region between 2.40 and 3.75 ppm.

TABLE I

NMR data on the tellurophene [3 + 4] adducts

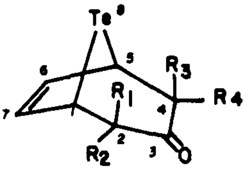
	Protons	Chemical Shift, ppm	Integral and Multiplicity	Coupling Constants Hz
8 $R_2 = R_4 = CH_3$ $R_1 = R_3 = H$	CH_3	0.95	6, *d*	$J_{CH_3,2} = 7.62$
	H_2, H_4	2.51	2, *q*, *q*	$J_{CH_3,4} = 7.62$
	H_1, H_5	4.18	2, *d*	
	H_6, H_7	7.43	2, *s*	$J_{2,4\text{-}1,5} = 5.10$
9 $R_1 = R_3 = CH_3$ $R_2 = R_4 = H$	CH_3	1.40	6, *d*	$J_{CH_3,2} = 7.72$
	H_2, H_4	2.41	2, *q*	
	H_1, H_5	3.86	2, *s* (broad)	$J_{CH_3,4} = 7.72$
	H_6, H_7	7.20	2, *s* (broad)	
10 $R_1 = R_4 = CH_3$ $R_2 = R_3 = H$	CH_3 at C_2	1.38	3, *d*	$J_{CH_3,2} = 7.58$
	CH_3 at C_4	0.98	3, *d*	
	H_2	2.52	1, *q*	$J_{CH_3,4} = 7.55$
	H_4	2.48	1, *q*, *q*	
	H_5	3.76	1, *s* (broad)	
	H_1	4.12	1, *d*	$J_{1,2} = 5.1$
	H_6	7.37	2, *q*	
	H_7	7.10	*AB* system	$J_{6,7} = 2.4$

TABLE II

NMR data on the selenophene [3 + 4] adducts

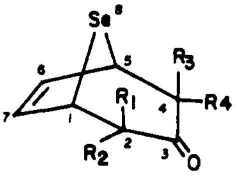
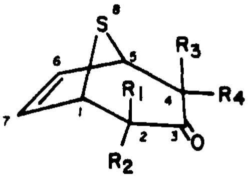
	Protons	Chemical Shift, ppm	Integral and Multiplicity	Coupling Constants Hz
	$2\text{-}CH_3$	0.93	6, *d*	$J_{2\text{-}CH_3,2} = 7.4$
8	$4\text{-}CH_3$			$J_{4\text{-}CH_3,4} = 7.4$
$R_2 = R_4 = CH_3$	H_2, H_4	2.43	2, *q*, *q*	
$R_1 = R_3 = H$	H_1, H_5	4.13	2, *d*	$J_{2,1} = 1.8$
	H_6, H_7	6.42	2, *s*	$J_{4,5} = 1.8$
	$2\text{-}CH_3$	1.44	6, *d*	$J_{2\text{-}CH_3,2} = 7.5$
9	$4\text{-}CH_3$			$J_{4\text{-}CH_3,4} = 7.5$
$R_1 = R_3 = CH_3$	H_2, H_4	2.77	2, *q*	
$R_2 = R_4 = H$	H_1, H_5	3.71	2, *s*	$J_{2,1} = 0.5$
	H_6, H_7	6.16	2, *s*	$J_{4,5} = 0.5$
	$2\text{-}CH_3$	1.41	3, *d*	$J_{4\text{-}CH_3,4} = 7.5$
10	$4\text{-}CH_3$	1.05	3, *d*	$J_{2\text{-}CH_3,2} = 7.6$
$R_1 = R_4 = CH_3$	H_2	2.48	1, *q*	
$R_2 = R_3 = H$	H_4	2.40	1, *q*	$J_{2,1} = 1.6$
	H_1	3.80	1, *s*	$J_{4,5} = 1.6$
	H_5	4.05	1, *d*	$J_{6,7} = 2.2$
	H_6	6.36	2, *q*	
	H_7	6.17		

TABLE III

NMR data on the 2,5-dimethylthiophene [3 + 4] adducts

	Protons	Chemical Shift, ppm	Integral and Multiplicity	Coupling Constants Hz
	$2\text{-}CH_3$	0.96	6, *d*	$J_{2\text{-}CH_3,2} = 7.2$
8	$4\text{-}CH_3$	0.96		
$R_2 = R_4 = CH_3$	H_2, H_4	3.73	2, *q*	
$R_1 = R_3 = H$	$1\text{-}CH_3$	2.16	6, *s*	$J_{4\text{-}CH_3,4} = 7.2$
	$5\text{-}CH_3$	2.16		
	H_6, H_7	6.51	2, *s*	
	$2\text{-}CH_3$	1.30	6, *d*	$J_{2\text{-}CH_3,2} = 7.2$
9	$4\text{-}CH_3$	1.30		
	H_2, H_4	2.81	2, *q*	$J_{4\text{-}CH_3,4} = 7.2$
$R_1 = R_3 = CH_3$	$1\text{-}CH_3$	2.33	6, *s*	
$R_2 = R_4 = H$	$5\text{-}CH_3$			
	H_6, H_7	6.36	2, *s*	

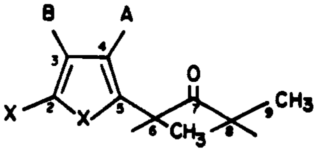
Compounds **10b** and **10c**, which have an axis of symmetry, give an NMR spectrum consisting of 8 resonances whose chemical shifts are very similar to the corresponding resonances in the plane symetrical adducts; the multiplicities of the protons and the methyl groups adjacent to the carbonyl function are the same as in the plane symetrical adducts but the protons at the bridgehead appear as doublets due to their interaction with their vicinal vinylic protons and the latter appear one as an *AB* system due to their coupling with each other and with their vicinal bridgehead protons.

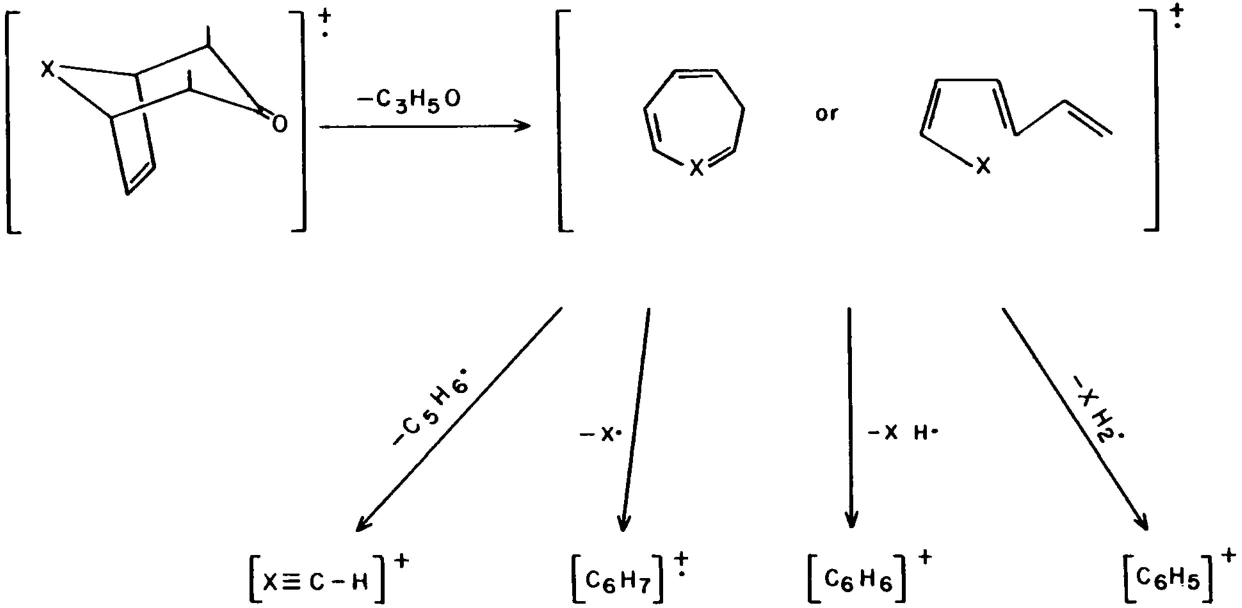
The substituted compound **11** exhibits an NMR spectrum which consists of a typical *ABX* system for the three ring protons, two methyl group resonances at 2.06 and 1.83 ppm, a triplet and a doublet; the latter as expected corresponds to the methyl group bonded to the carbon atom between the carbonyl function and the heterocycle and furthermore it is coupled to its vicinal proton; this and the remaining two protons appear as two quartets as expected.

The mass spectra of the [3 + 4] adducts in addition to the molecular ion exhibit a very important peak at $M^+—C_3H_5O$ which fragments in various ways by loss of C_5H_6, X, XH_2 and XH (X = Heteroatom). Owing to the fact that these compounds slowly decompose, no reliable elemental analyses were obtained. Therefore, the molecular formulae of the compounds were calculated from exact mass measurements.[14] The general mass fragmentation pattern for these compounds is shown in Scheme 4. The mass fragmentation patterns of compounds **11b** and **11c** are illustrated in Scheme 5. In addition to the molecular ion, the following are also important fragments: $M^+—C_3H_5O$, $M^+—C_4H_7O$, $M^+—C_8H_{12}O$ ($Se^+{\equiv}CH$, m/e 93, 100%), $M^+—SeH$ (m/e 135, 58.5%); the latter splits further into C_6 fragments (Scheme 5).

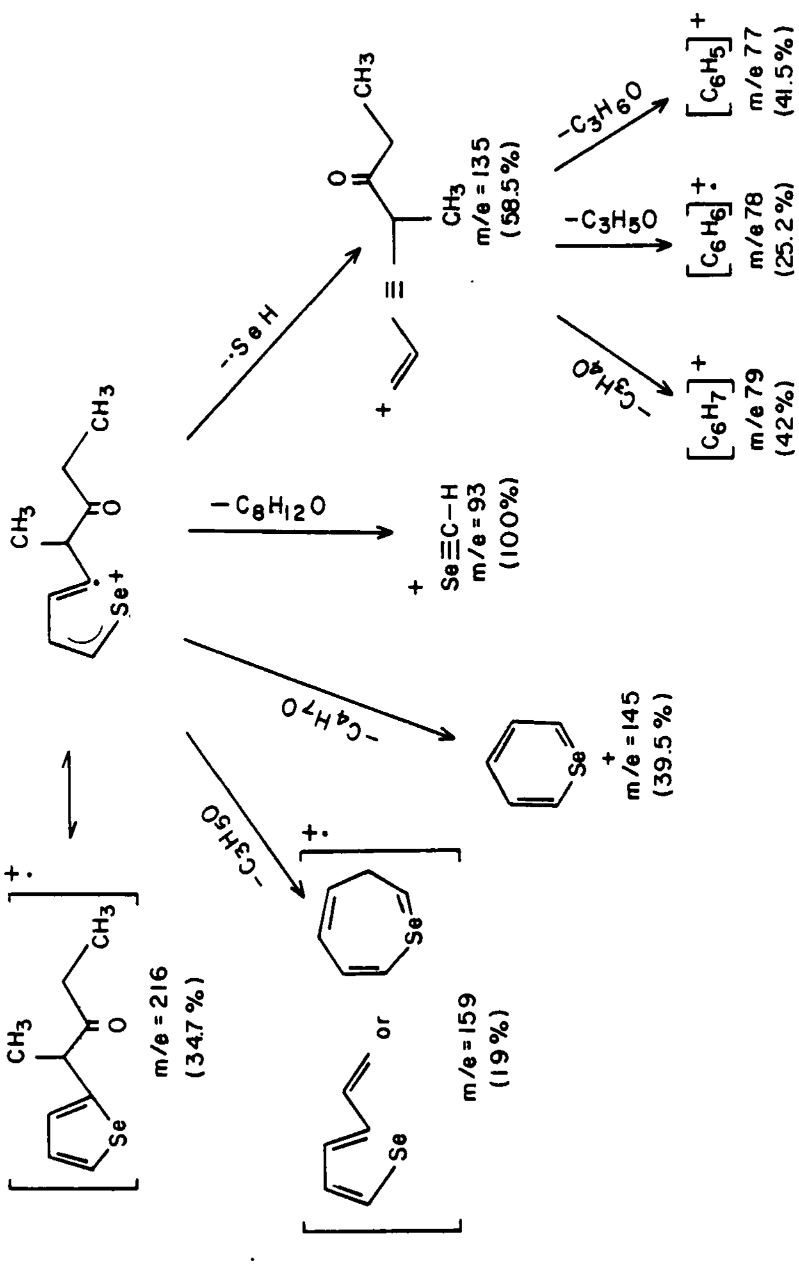
TABLE IV

NMR data on the α-substitution products

	Protons	Chemical Shift, ppm	Integral and Multiplicity	Coupling Constants Hz
	9-CH_3	1.83	3, *t*	$J_{9\text{-}CH_3,8} = 7.20$
11b	6-CH_3	2.06	3, *d*	
x = Se	8-H	3.42	2, *q*	$J_{6\text{-}CH_3,6} = 6.75$
	6-H	3.57	1, *q*	$J_{2,4} = 1.20$
	4-H (A)	6.93	1, *d*	$J_{2,3} = 5.45$
	3-H (B)	7.08	1, *q*	$J_{3,4} = 3.90$
	2-H (C)	7.80	1, *d*	
	9-CH_3	1.62	3, *t*	$J_{9\text{-}CH_3,8} = 7.30$
11c	6-CH_3	1.92	3, *d*	
x = Te	8-H	2.61	2, *q*	$J_{6\text{-}CH_3,6} = 6.80$
	6-H	3.62	1, *q*	$J_{2,4} = 2.20$
	4-H	7.67	1, *d*	$J_{2,3} = 5.89$
	3-H	7.80	1, *q*	$J_{3,4} = 4.11$
	2-H	8.91	1, *d*	



SCHEME 4 Mass fragmentation patterns for the [3 + 4] cycloaddition products.



SCHEME 5 Mass fragmentation patterns for the open chain compounds.

EXPERIMENTAL

NMR spectra were measured in a Varian 390 spectrometer. The mass spectra were determined with a Du'Pont model 21492B spectrometer coupled to a Hewlett Packard 2100 computer system and a gas chromatography instrument Varian 2700 with a flame ionization detector. For the gas chromatographic analyses, an SC-30, 3% over chromosorb-q column 4m long and 0.25 cm in diameter was used with helium as the carrier gas flowing at 70 ml/min. Exact mass measurements for the determination of elemental composition were performed in a MS-25 spectrometer.[14] Elemental analyses were carried out by Mikroanalytisches Labor Pascher, Bonn, Germany.

2,5-Dimethylthiophene (Aldrich), was distilled before use. Selenophene was prepared according to the method of Gronowitz and Freid with modifications as described previously.[15,16] Tellurophene was prepared according to the method of Fringuelli and Taticchi[16] without modifications. 2,4-Dibromopentane-3-one was prepared by acid catalized bromination of pentanone-3 according to the procedure of Rhappe, Hoffman and Clemens.[17]

Iron Nonacarbonyl $Fe_2(CO)_9$. 50 ml of iron pentacarboxyl ($Fe(CO)_5$) was dissolved in 150 ml of acetic acid and poured into a preparative photochemical reactor consisting of a pyrex reaction vessel fitted with a double-walled quartz jacket refrigerated with circulating cold methanol (Colora Thermostat KT 80K). Inside the quartz jacket a Hanovia 450 W medium-pressure mercury lamp was placed and nitrogen was bubbled through the reaction vessel before and during irradiation. The reaction mixture was irradiated at $-20°C$ during 8 hours. At the end of the irradiation a precipitate was filtered and washed with 100 ml of ethyl ether; afterwards, the solid was dried under vacuum for two hours. 60 g of glossy golden crystals was obtained; 70% yield.

Thermal Reactions. A mixture of dry benzene 10 ml, the heterocycle under investigation 0.05 mole, 2,4-dibromopentane-3-one, 2.44 g (0.01 mole), and iron nonacarbonyl, 4.58 g (0.12 mole) was prepared and poured into a 100 ml pyrex ampul. The latter was sealed and placed in an oil bath at 40°C for 6 days. At the end of this time, the dibromoketone had been consumed as confirmed by gas chromatography. The mixture was then filtered under vacuum and the resulting red oil concentrated by evaporation under vacuum of the volatile impurities. The residue was gas-chromatographed and the products isolated by preparative gas chromatography; these were studied by means of the usual spectroscopic methods, especially NMR and mass spectrometry.

Photochemical Reactions. The reaction mixture was prepared using the same molar composition as that employed in the thermal reactions. It was placed in a spiral-shaped pyrex tube 5 mm in diameter which was fitted with a doubled-walled quartz jacket cooled at 20°C (Colora Thermostat KT 80K) and containing a Hanovia 450 W medium-pressure mercury lamp. Nitrogen was bubbled through the reaction mixture before and during irradiation. At the end of 30 hours the irradiation was stopped and the above isolation procedure followed.

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