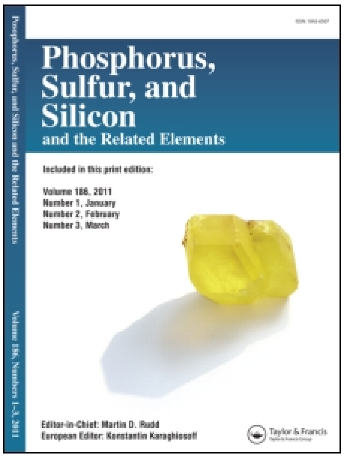

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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N. M. Yousif[a]; A. F. M. Fahmy[b]; M. S. Amine[c]; F. A. Gad[a]; H. H. Syed[a]
[a] National Research Centre, Dekki, Caire, Egypt [b] Faculty of Science, Chemistry Department, Ain Shams University, Cairo, Egypt [c] Faculty of Science, Chemistry Department, Benha University, Benha, Egypt

To cite this Article Yousif, N. M. , Fahmy, A. F. M. , Amine, M. S. , Gad, F. A. and Syed, H. H.(1998) 'REACTIONS WITH α,β-SPIROEPOXY-ALKANONES. PART II. USES OF SPIROOXIRANES FOR THE SYNTHESIS OF CONDENSED HETEROCYCLES WITH POTENTIAL BIOLOGICAL ACTIVITY', Phosphorus, Sulfur, and Silicon and the Related Elements, 133: 1, 13 — 20

To link to this Article: DOI: 10.1080/10426509808032450

URL: http://dx.doi.org/10.1080/10426509808032450

Phosphorus, Sulfur and Silicon, 1998, Vol. 133, pp. 13-20
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REACTIONS WITH α,ß -SPIROEPOXY-ALKANONES. PART II.* USES OF SPIROOXIRANES FOR THE SYNTHESIS OF CONDENSED HETEROCYCLES WITH POTENTIAL BIOLOGICAL ACTIVITY

N. M.YOUSIF[c†], A.F.M. FAHMY[a], M.S. AMINE[b], F.A. GAD[c] and H.H. SYED[c]

[a]*Ain Shams University, Faculty of Science, Chemistry Department, Cairo, Egypt,*
[b]*Benha University, Faculty of Science, Chemistry Department, Benha, Egypt and*
[c]*National Research Centre, Dekki, Caire, Egypt*

(Received 11 September, 1997; In final form 24 November, 1997)

2-Aryl-1-oxaspiro(2,5)octa-4-ones Ia,b reacted with carbon-disulfide, phenylisocyanate, or phosphorus pentasulfide to yield compounds II, III, IV respectively. The bis-spirodioxane V is produced when compound Ib was heated at 150 °c for 1 hr.

Keywords: Oxaspire(2,5) octanes; oxathiospirodecanes; benzoxazines; tetrahydrobonzodithiols

INTRODUCTION

Recently it was reported that exathiolanes and oxazines have antibacterial[2,3], antitumer[4,5]and anticonvulsant[6,7]activities. This lead the authors to use spirooctanones as synthetic auxiliaries to produce some heterocycles having potential biological effects.

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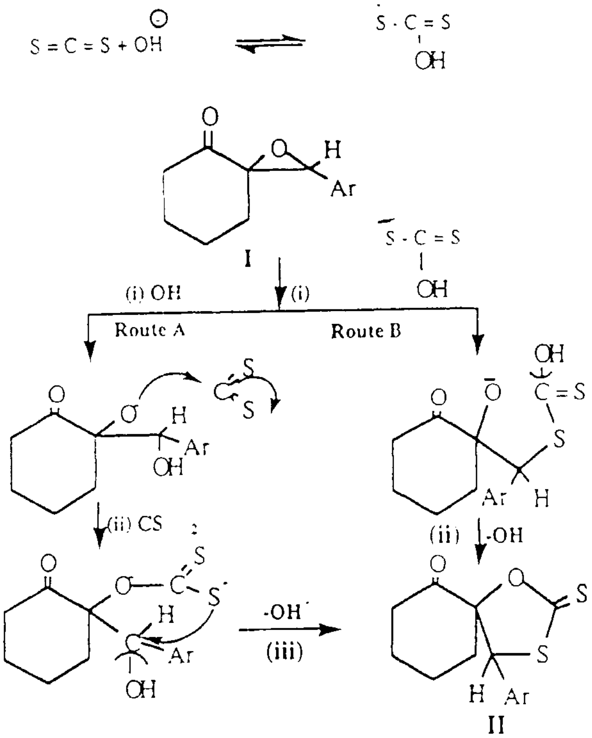
* Part I see ref. 1.

† Corresponding Author.

RESULTS AND DISCUSSION

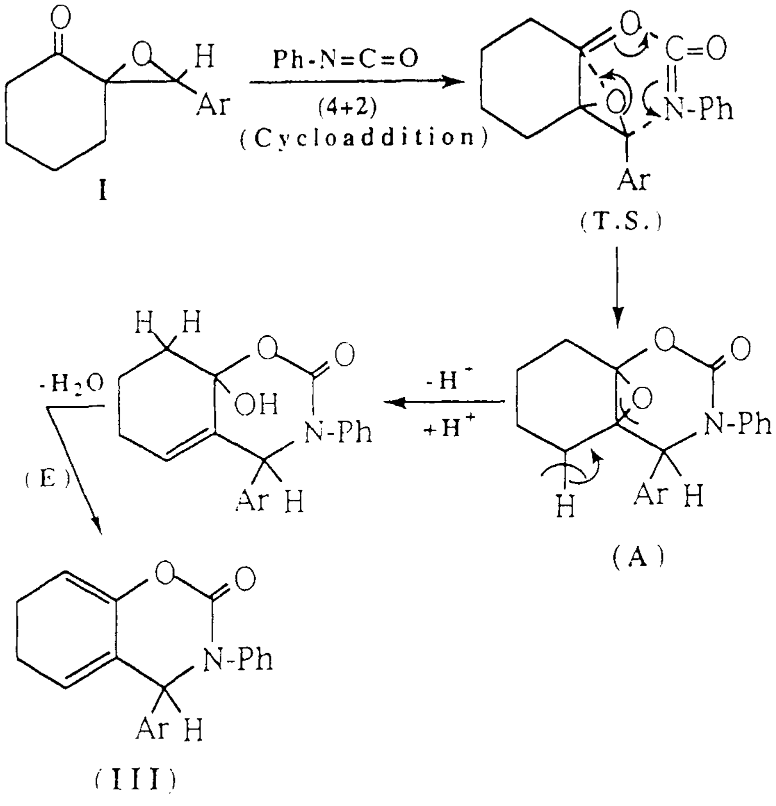
2-Aryl-1-oxaspiro (2,5)octa-4-ones Ia,b react with carbon disulfide in alkaline medium to produce 4-aryl-1-oxa-3-thiospiro (4,5)deca-2-thione-6-ones IIa,b. Infrared spectra of IIa,b show γ C=O at 1695 cm^{-1} and γ C=S at 1315 cm^{-1}. The ^1H NMR spectrum of IIa (DMSO-d_6) showed signals at (1.4–2.2) ppm (8H, m, CH_2),(4.2) ppm (1H, s, CH), and (7.5–8) ppm (5H, m, ar.). The mass spectrum of IIb showed a molecular ion peak M+ at (m/z= 308) which undergoes fragmentation to the followimg ions m/z s 292, 280, 276, 261, 245, 229, 220, 201, 156, 151. The formation of compounds IIa,b may take place via an addition-elimination mechanism (cf. Scheme 1).



a) Ar= C_6H_5 ; b) Ar = C_6H_4-OCH_3 (P-)

SCHEME 1

Compounds Ia,b reacted with phenylisocyanate to yield 6,7-dihydro-3, 4-diaryl-benz-1 ,3-oxazin-2-ones IIIa,b via a novel (4+2) cycloaddition reaction, in which the spirooctanone acts as a 1,4 -dipole to give the intermediate adduct (A), followed by a cycloaddition in which a molecule of water is eliminated to give the final product III (cf. scheme 2).



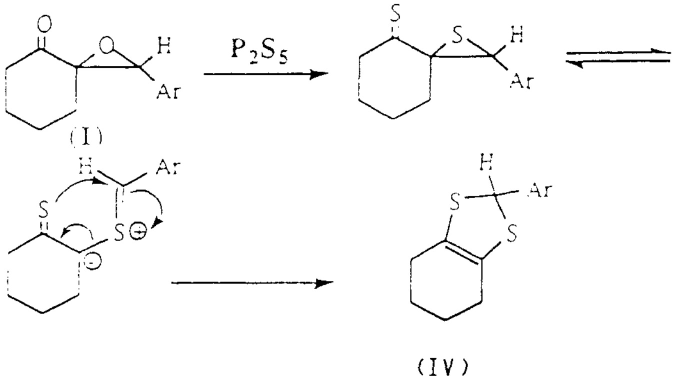
a) $Ar=C_6H_5$; b) $Ar=C_6H_4\text{-}OCH_3$ (P-)

SCHEME 2

The structure of compounds IIIa,b was proved by correct elemental analysis and spectral data. The IR spectrum showed an absorption band at 1686 cm^{-1} (γ C=O). The ^1H NMR spectrum (DMSO-d_6) of IIIb shewed signals at δ (1.2–2.2) ppm (4H, m, CH_2) ; 3.7) ppm (3H, s, OCH_3), (4–4.2) ppm (2H, 2t, CH_2) ; (6.1), ppm (1H, s, CHAr), (6.7–7.5) ppm (9H, m, ar.).

The mass spectrun of IIIa showed a molecular ion peak M^+ at (m/z = 303) which undergoes fragmentation to ions m/z's (212, 184, 114, 106, 105, 93, 91). All these data are in agrement with the assigned structures.

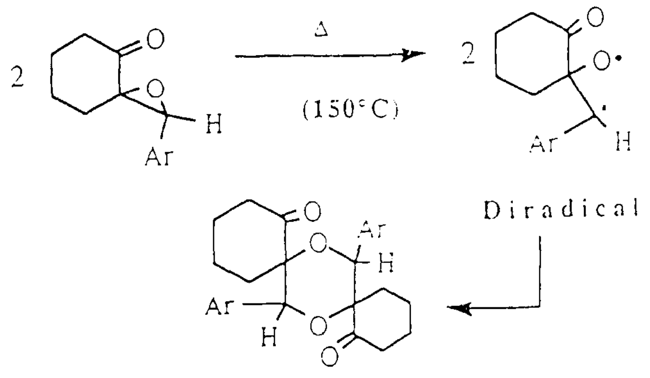
Thiation of 2-aryl-1-oxaspiro (2,5) octa-4-ones Ia,b with phosphorus pentasulfide in the presence of sulfur powder produced 2-aryl-1,2,3 ,4-tetrahydrobenzo (5,6-d)-1,2-dithiols IVa,b. The aaignment of structure IV was based on correct elemental analysis and spectral data. The IR spctra revealed the absence of γ C=O group. The ^1H NMR spectrum ($CDCl_3$) of IVb showed signals at δ (1.5–2.5) ppm (8H , m, $4CH_2$) ; (3.8) ppm (3H, s, OCH_3) ; (4.8–5)ppm (1H, br, CHAr); (6.7–7.5) ppm (4H, 2d, ar.). The M.S, of compound IVa showed a molecular ion M^+ peak at (m/z = 234) which undergoes fragmentation to give leas m/z s (202, 192, 122, 121, 112). A possible reaction mechamism for the described thiation is illustrate is scheme 3.



a; Ar=C_6H_5 , b; Ar=$C_6H_4.OCH_3$ (P-)

SCHEME 3

The bis-spire-dioxane V was obtained when 2-aryl-1-oxaspiro (2,5)octa-4-ones Ib was heated at 150 °c is an oil bath for one hr. The assignment of structure V was based on correct elemental analysis and spectral data. The IR spectrun showed an absorption band at 1707 cm^{-1}attributed to γ C=O. The ^1H NMR spectrum ($CDCl_3$) of V showed signals at δ (1.3–2.5) ppm (16H, m, $8CH_2$); (3.6–4) ppm (8H, s, OCH_3 + CHAr);(6.8–8) ppm (8H, 2d, ar.), and and the M.S. of V gave a M^+ peak at (m/z = 464) supporting its molecular formula. The formation of the bis-spirodioxane V may be take place according to scheme 4.



(V)

$Ar = C_6H_4 \cdot OCH_3$ (P-)

SCHEME 4

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded on a Beckmann IR-18 spctrometer. The mass spectra were recorded on a micromass 7070 f spectrometer operating at 70 ev. using direct inlet. The ^1H NMR spetra were recorded at 180 Mz on a Varian EM 360 spectrometer. TMS was used as internal standard.

The antimicrobial activities of the synthesized compounds were determined in vitro using the hole plate and filter disc method(8). Two different species of Gram-positive bacteria and two strains of Gram-negative bacteria, yeast and fungi were employed. The chloramphenicol was used as reference, The author thanks Dr. A.S. El-Deen, National Centre for Research and Technology, Caire, Egypt, for carring cut the antimicrobial activity.

Starting material

2-Aryl-1-oxaspiro (2,5),octa-4-ones Ia,b was prepared according to our previous work(1).

Reaction of compound I with carbon disulfide

A mixture of compound Ia,b (0.01 mol), carbon disulfide (3 ml),,NaOH (1 g) in 50 ml ethanol was refluxed for 3 hours. The solid formed was collected and recrystallized from the proper solvent to give IIa,b (cf. Table I).

TABLE I Physical and analytical data for the prepared compounds

Compd.	*M.p.°C* *Solvent*	*Mol. Formula* *Mol. Wt.*	*Yield (%)*	*Analysis %*			
				Calc. / Found			
				C	*H*	*N*	*S*
II a	108	$C_{14}H_{14}O_2S_2$	50	60.40	5.07	-	23.03
	B. Pet.	278.4		60.50	5.00		23.40
IIIb	127	$C_{15}H_{16}O_3S_2$	60	58.41	5.23	-	20.79
	E	308.4		58.80	5.30		21.00
IIIa	204	$C_{20}H_{17}NO_2$	55	79.19	5.65	4.62	-
	E	303.3		79.40	5.60	4.80	
IIIb	259	$C_{21}H_{19}NO_3$	60	75.65	5.74	4.20	-
	D	333.4		75.80	5.70	4.40	
IV a	132	$C_{13}H_{14}S_2$	45	66.61	6.02	-	27.36
	M	234.4		66.80	6.00		27.50
IVb	147	$C_{14}H_{16}OS_2$	50	63.59	6.10	-	24.25
	E	264.4		63.80	6.00		24.40
V	241	$C_{28}H_{32}O_6$	30	72.40	6.94		-
		464.5		72.50	7.00		

B = benzene, E = ethanol, D = dioxane. M = methanol. Pet. = petrolum ether.

Reaction of compound I with phenylisocyanate

A mixture of compound Ia,b (0.01 mol), phenylisocyanate (0.01 mol), and triethylamine (0.5 ml) in dry benzene (30 ml) was refluxed for 3 hours. The solid substance that seperated was collected and recrystallized from the proper solvent to give IIIa,b (cf. Table I).

Thiation of compounds I, formation of IVa,b

A mixture of compound Ia,b (0.01 mol), sulfur powder (1 g) and P_2S_5 in dry benzene (50 ml) was refluxed for 2 hours. The solid residue which was a by product was removed. The filtrate was concentrated under reduced pressure and the solids formed are cellected and recrystallized from the proper solvent to give IVa,b (cf. Table I).

Action of heat on compound I

Compounds Ib (0.01 mol) was heated at 150 °c for 1 hour. It sublimed to give colorless crystals of V.

TABLE II Antimicrobial activity for compounds IIa,b; IIIa and IVa

Compound	*Microorganisms*					
	1	*2*	*3*	*4*	*5*	*6*
reference						
chloramphenicol	+++	+++	-	++	+++	+++
IIa	++	+	-	-	+	++
IIb	++	++	-	-	+	++
IIIa	+	+	-	-	+	++
IVa	++	++	+	-	+	++

(1) Bacillus subtilis, (2) Staphylococus aureus, (3) Escherichia coli, (4) Pseudomanas aruginosa, (5) Candida albicans, (6) Aspergillus niger.
+++ = Highly active (inhibition zone > 13 mm).
++ = Active (" " 9–12 mm).
+ = Slightly active (" " 6–9 mm).
- = not sensitive.

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