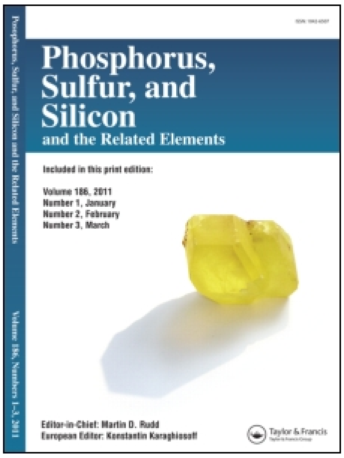

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F. A. Gad[a]; A. A. Fahmy[a]; A. F. El-Farargy[a]; A. B. El-gazzar[a]
[a] National Research Center, Cairo, Egypt

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REACTIONS OF DIBENZO[a,d]CYCLOHEPTEN-5-ONE WITH ETHYL PHOSPHITES AND OTHER SELECTED REAGENTS

F. A. GAD, A. A. FAHMY, A. F. El-FARARGY* and A. B. El-GAZZAR
National Research Center, Dokki, Cairo, Egypt

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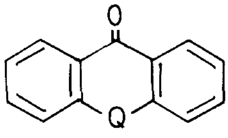
Trans, 10,11-dibromide $\mathbf{I_c}$ reacted with di- and triethyl phosphites to yield 5-hydroxy, 5-phosphonate **II**, while 5-oximes $\mathbf{III_{a-d}}$ gave 5-hydroxylamino-5-phosphonates $\mathbf{IV_{a-d}}$. $\mathbf{I_c}$ reacted with Na_2S to give 10,11-sulphide V that reacted with hydrogen peroxide to yield the sulphone **VI** and with ethyl cyanoacetate gave **VII**.

Key words: Trans-10,11-dibromo-10,11-dihydrodibenzo[a,d]-cyclohepten-5-hydroxy; 5-phosphonate II; 10,11-dihydro-; 10-bromo-; 10,11-dibromo-10,11 dihydrodibenzo-; or dibenzo[a,d]-cyclohepten-5-hydroxylamino,5-phosphonate IV a–d, dibenzo[a,d]-cyclohepten-5-one 10,11-episulphide V; its sulphone VI; 2,8-dioxo, dibenzo[3,4;6,7] cyclohepta[1,2-b] thiophene, 3,3a, dihydro-3-carbonitrile VII.

INTRODUCTION

Dibenzo[a,d]cyclohepten-5-one derivatives are very useful substances as antidepressants,[1–4] antihistaminics,[5] anticonvulsants,[6] antibacterial[7] and other pharmalogical properties.[8] Therefore, we have now endeavoured the synthesis of some new dibenzo[a,d]cyclohepten-5-one derivatives for biological evaluation.**



I

Q = a , CH:CH
b , $CH_2 \cdot CH_2$
c , CHBrCHBr

RESULTS AND DISCUSSIONS

Compound $\mathbf{I_c}$ reacted with di- and triethyl phosphites without using a solvent at 90°C to give the diethylphosphonate adduct **II**, while $\mathbf{I_{a,b}}$ did not react at the same conditions.

The dibenzo[a,d]cyclohepten-5-oximes[9] $\mathbf{III_{a-d}}$ reacted with di- and triethyl phosphites under the same conditions to yield the diethyl phosphonate derivatives $\mathbf{IV_{a-d}}$.

The mechanism of the reaction involves the addition of the phosphite radical to the double bond followed by the hydrogen abstraction from the phosphite ester.[10]

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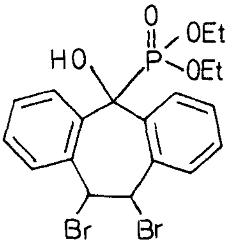
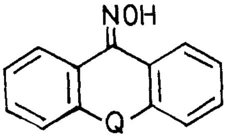
*Faculty of Science, Zagazig.

**The biological evaluation will be published elsewhere.

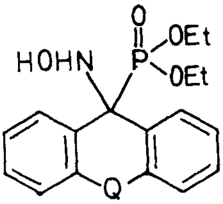


II



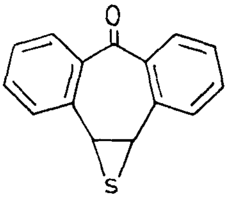
III

Q = a , $CH_2{\cdot}CH_2$
b , $CBr{:}CH$
c , $CHBr{\cdot}CHBr$
d , $CH{:}CH$

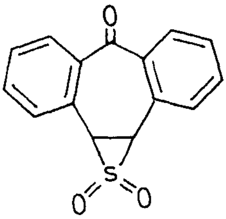


IV

Q as in III



V



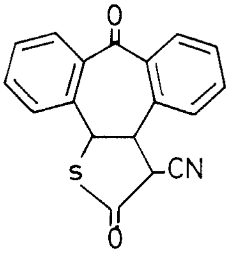
VI

TABLE I

Physical constants and analytical data of the new compounds

Comp.	M.P. °C	Solvent of Crys.	Yield %	Formula Mol.wt.	Analysis Calc./Found C	H	N	P	S
II	68-70	Pet.ether*	90	$C_{19}H_{21}Br_2O_4P$	45.262	4.199	---	6.148	---
				504.15	44.948	3.897	---	5.839	---
IV_a	240-2	Pet.ether*	68	$C_{19}H_{24}NO_4P$	63.149	6.694	3.874	8.578	---
				361.35	62.678	6.234	4.132	7.989	---
IV_b	124-6	Pet.ether*	65	$C_{19}H_{21}BrNO_4P$	52.071	4.831	3.194	7.074	---
				438.23	51.597	4.539	3.487	6.832	---
IV_c	110-12	Pet.ether*	50	$C_{19}H_{22}Br_2NO_4P$	43.954	4.270	2.696	5.971	---
				519.15	43.816	3.967	3.091	5.368	---
IV_d	118-20	Pet.ether*	55	$C_{19}H_{22}NO_4P$	63.451	6.169	3.896	8.627	---
				359.33	62.876	5.983	4.1201	7.893	---
V	48-50	Ethanol**	50	$C_{15}H_{10}OS$	75.601	4.230	---	---	13.454
				238.29	75.234	4.193	---	---	13.297
VI	288-90	Ethanol**	85	$C_{15}H_{10}O_3S$	66.651	3.729	---	---	11.861
				270.29	66.213	3.538	---	---	10.987
VII	171-3	Methanol***	87	$C_{18}H_{11}NO_2S$	70.802	3.632	4.585	---	10.500
				305.33	70.397	3.279	4.841	---	10.239

* Pet.ether 40-60 or 60-80.
** Ethanol absolute.
*** Methanol absolute.



VII

Compound I_c reacted with Na_2S in ethanol to give 10,11-sulphide **V**. Its IR spectrum showed bands at 1640 and 1100 cm^{-1} corresponding to (νC=O) and (νC—S—C).

Its ^1H NMR showed signals at δ5.3 (2H, methine) and the aromatic protons in the region between δ7–8.2 ppm. Compound **V** was oxidized with hydrogen peroxide in glacial acetic acid to yield the sulphone **VI**.

Compound **V** reacted with ethylcyanoacetate to give **VII**, this result is in good agreement with the previous investigators[11] having oxygen instead of sulphur in the molecule. Table I summarizes the physical properties of the prepared compounds.

EXPERIMENTAL

All melting points were uncorrected. The IR spectra (run in KBr and expressed in cm^{-1}) were recorded with a Beckmann 4220 Infrared Model and the ^1H NMR spectra were measured (in $CDCl_3$ or DMSO-d_6 and expressed in the δ-scale) at 60 MHz or 90 MHz on a Varian instrument using TMS as an internal standard. Diethyl and triethyl phosphite was prepared according to an established procedure[12] and twice distilled before use.

Action of diethyl and triethyl phosphite:
General methods. Di- or triethylphosphite (0.05 mol) was added to the ketone or oximes (0.005 mol). The mixture was heated at 90°C for 20 hrs. After removal of the volatile materials in vacuo the residual substance was collected and recrystallized from the proper solvent to give the phosphonate adduct. The IR spectra of **II** showed bands of 3400, 1250, 1025 cm^{-1} (OH, P=O, P—OC_2H_5); its ^1H NMR showed aromatic protons (8H) in the region at δ7.4–8.2, methine protons at δ5.6 (2H, singlet), δ1.4 (6H, $2CH_3$), δ8.2 (1H, OH) and a multiplet signal at δ3.8 (4H, $2OCH_2$); the mass spectrum confirmed its molecular weight 504, m/z (unstable), 207 (48.1%), 206 (61.1%), 179 (96.4%), 152 (16.5%). The ^{31}P NMR shifts (Ref. H_3PO_4) recorded was $\delta = +11.85$. The IR spectrum of $\mathbf{IV}_c$ showed bands at 3400, 3140, 1250, 1025 cm^{-1} (NH, OH, P=O, P—OC_2H_5), its ^1H NMR showed aromatic protons (8H) in the region of δ7.0–7.8, methine protons at δ4.2 (2H), δ1.2 (6H, $2CH_3$), δ11.4 (1H, OH) and a multiplet signal at δ3.8 ppm (4H, $2OCH_2$).

The mass spectrum of $\mathbf{IV}_c$ revealed its molecular weight 519, m/z (unstable), 221 (100%) 117 (14%), 95 (10.6%), 88 (13.2%), 63 (18.9%).

Action of sodium sulfide. Trans,-10,11-dibromide $\mathbf{I}_c$ (0.01 mol) in 20 ml abs. ethanol was added to an alcoholic solution of Na_2S (0.01 mol); after 20 hrs reflux the mixture was poured into a 25% NaCl solution (100 ml) filtered and the precipitate recrystallized from ethanol.

Action of hydrogen peroxide. A mixture of compound **V** (0.01 mol) in glacial acetic acid (50 ml) and excess of hydrogen peroxide (10 ml; 35 vol.) was left overnight, filtered and crystallized from ethanol. The IR spectrum of **VI** showed absorption bands at 1620 (νC=O), 1580 (aromatic bands) and at 1270–1340 (νSO_2).

Action of ethyl cyanoacetate. Ethyl cyanoacetate (0.01 mol) was added to a solution of (0.5 g) of sodium in 50 ml of absolute ethanol, followed by (0.01 mol) of the sulphide V, and the solution was refluxed for 2 hr. The deep red solution, on chilling or evaporation, deposited a thick precipitate of sodium salt, which was collected washed with ether-ethanol, and treated with 10% HCl. The crystals were collected, washed (H_2O), dried (1.2 g yield), triturated and recrystallized from methanol.

The IR spectrum of VII showed absorption bands at 2180, 1640, 1685 and 1100 cm^{-1} corresponding to (νCN), (νC=O), (νC—O) and (νC—S—C) and its ^1H NMR showed signals in the region at δ7.4–7.8 (8H, aromatic protons), 8.2–8.4 (2H, methine) and at δ7.0 singlet for (1H).

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