

EFFECT OF RING SIZE ON PHOTOREACTIVITY OF MEDIUM AND LARGE RING ESTERS.¹

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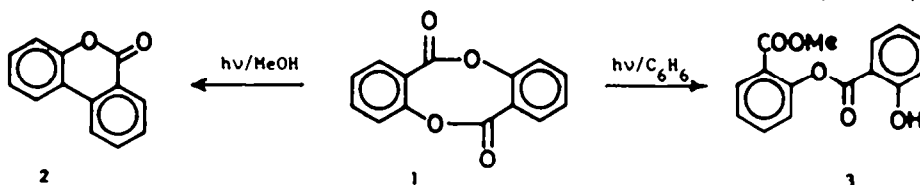
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Abstract - Photochemical studies on 7,8,12,14,16 and 20 membered cyclic esters have been carried out in benzene and methanol. Decarboxylation and solvolysis ascribable to β - and α -scission respectively are observed in case of seven and eight membered cyclic esters. Larger rings do not undergo these photoreactions thus demonstrating effect of ring size on photoreactivity.

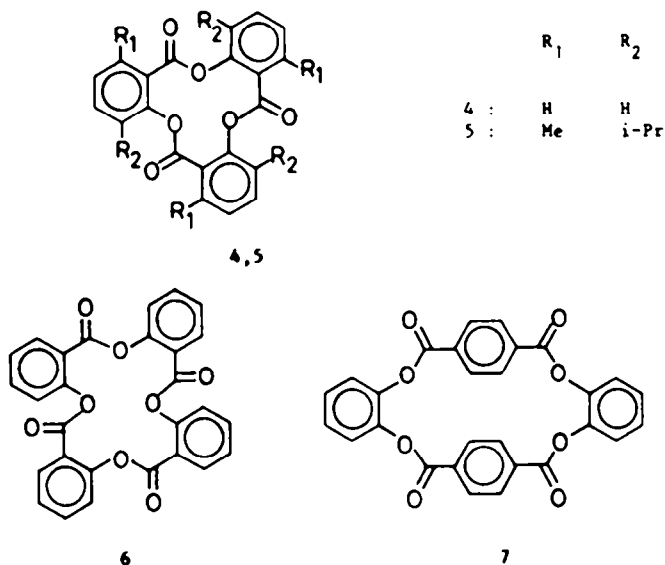
In recent years it is being recognized that lack of conformational mobility might limit the photoreactions available to certain classes of compounds. Such limitations may be "good" if they prevent unwanted reactions or "bad" if they prevent a desired reaction.² Since conformational flexibility and ring size are linked, as a first step, it seemed pertinent to examine the excited state behaviour of cyclic esters with differences in size of the ring, particularly to gain information about the orientational requirements for the occurrence of photodecarboxylation.

Esters and ketones on photoirradiation in solution undergo α - and/or β -cleavage of $-\text{CO}-\text{O}-\overset{\text{O}}{\underset{\text{O}}{\text{C}}}-$ group giving structurally different products. The rupture of bond between ester carbonyl and the oxygen (α -cleavage) for phenyl benzoate system under photoinduced conditions in a solvent like benzene, cyclohexane can lead to a "photo-Fries rearrangement"^{3,4} or to products of solvolysis in solvents like methanol. The β -cleavage reactions involve a homolytic scission of the bond adjacent to the one cleaved in α cleavage and involving the oxygen. This reaction initiated from studies of Finnegan and co-workers^{5,6} over the years has been recognized as a preparatively useful reaction. Photochemically induced solvolytic opening and photoextrusion of carbon dioxide therefore seemed a good ground for probing photobehaviour of cyclic esters of varying ring size and analyzing preparative aspects of the reaction. The results of such a study carried out with 7,8,12,14,16 and 20 membered rings are reported in this paper. Synthesis of these compounds is reported in a separate communication.⁷

Previous studies from our laboratory⁸ have shown that eight membered compound viz. 6H,12H-dibenzo[b,f][1,5]dioxocin-6,12-dione (disalicylide) (1) on photoirradiation in methanol and benzene gave methyl salicyloylsalicylate (2) and 3,4-benzocoumarin (3) respectively. The

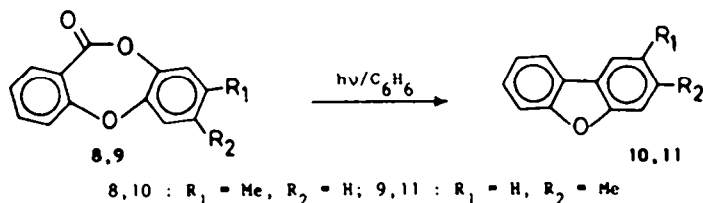


products are ascribed to α and β scission respectively. In order to find out scope of this reaction we subjected some model large ring compounds to photoirradiations. Photoirradiation of twelve-membered model compounds such as 6H,12H,18H-tribenzo[b,f,j][1,5,9]trioxacyclododecin-6,12,18-trione (trisalicylide) (4) and 1,7,13-trimethyl-4,10,16-tris(1-methylethyl)-6H,12H,18H-tribenzo[b,f,j][1,5,9]trioxacyclododecin-6,12,18-trione (tri-*o*-thymotide, TOT) (5) in methanol and benzene for 20 hours did not afford the expected photoproducts and resulted in recovery of the starting materials. Similarly model sixteen-membered cyclic ester tetrasalicylide, that is 6H,12H,18H,24H-tetrabenzo[b,f,j,n][1,5,9,13]tetraoxocyclohexadecin-6,12,18,24-tetrone (6) and a twenty-membered cyclic ester, 7,10:19,22-dietheno-6H,11H,18H,23H-dibenzo[b,1]-[1,4,11,14]tetraoxacycloeicosine-6,11,18,23-tetrone (7) failed to undergo any phototransformation and starting materials were recovered even after prolonged irradiation.



The photoextrusion of CO₂ from 7-membered depsidones, i.e. 11H-dibenzo[b,e][1,4]dioxepin-11-ones was considered interesting due to the presence of an additional chromophore in the form of diphenyl ether linkage. Further, the products of β -scission are expected to be dibenzofurans which form a nucleus of many natural compounds. The validity of this approach was communicated in a preliminary report.⁹

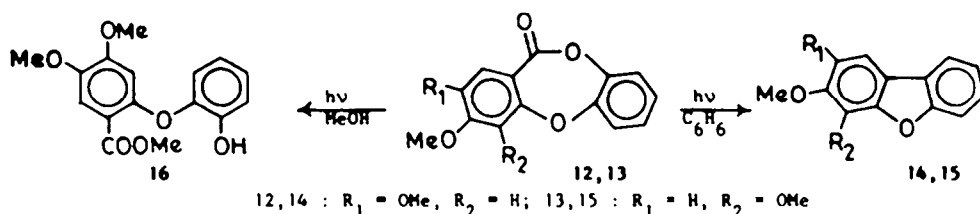
To study the generality and effect of substituents on the reaction pathway, two methyl substituted depsidones, viz. 7-methyl-11H-dibenzo[b,e][1,4]dioxepin-11-one (8) and 8-methyl-11H-dibenzo[b,e][1,4]dioxepin-11-one (10) were irradiated in benzene to afford 3-methyldibenzofuran (9) and 2-methyldibenzofuran (11) respectively in 56% chemical yields in each case.



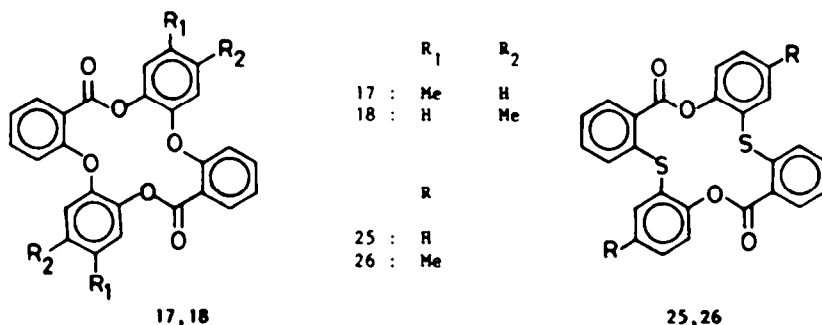
Photoreaction on 2,3-dimethoxy-11H-dibenzo[b,e][1,4]dioxepin-11-one (12) in benzene led to the formation of 2,3-dimethoxydibenzofuran (14) in 60% chemical yields whereas when the same compound was irradiated in methanol it yielded methyl 2-(2-hydroxyphenoxy)-4,5-dimethoxybenzoate (16) in 62% chemical yield.

Expectedly, irradiation of 3,4-dimethoxy-11H-dibenzo[b,e][1,4]dioxepin-11-one (13) in

benzene furnished 3,4-dimethoxydibenzofuran (15). It was observed in all the cases that along with dibenzofurans which were the major photoproducts, traces of other compounds were also formed. These compounds, however, could not be identified.

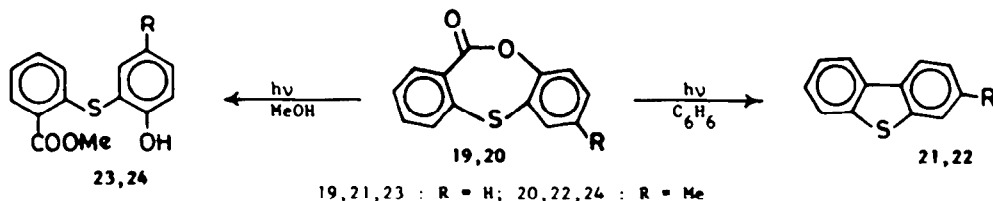


In contrast to these results, the corresponding 14-membered cyclic esters, 11H,22H-tetrabenzo[b,e,i,1][1,4,8,11]tetraoxacyclotetradecin-11,22-diones (17,18) were found to be inactive towards photoirradiation.



The replacement of ether oxygen of these systems by sulfur did not affect the nature of products. When the seven membered thiadepsidones, viz. 11H-dibenzo[b,e][1,4]oxathiepin-11-ones (19,20) were irradiated in benzene the corresponding dibenzothiophenes (21,22) were obtained in 38 and 64% yields respectively. Use of acetonitrile or cyclohexane did not alter the outcome but the products were obtained in lower yields.

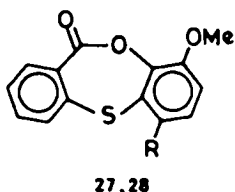
However, photoirradiation of the same compounds in methanol yielded the corresponding esters, viz. methyl 2-(2-hydroxyphenylthio)benzoates (23,24) in 64 and 63% yields respectively.



In this case also the corresponding 14-membered ring esters, viz. 11H,22H-tetrabenzo[b,e,i,1][1,8,4,11]dioxadithiacyclotetradecin-11,22-diones (25,26) were recovered unchanged on prolonged irradiation in benzene, acetonitrile and methanol.

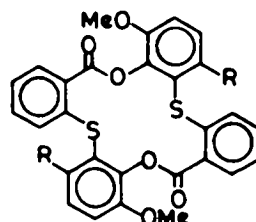
Interestingly, the substrates 27 and 28 prepared to study the effect of functional groups on photodecarboxylation were found to undergo photoextrusion at the functional group viz. CHO or COOH along with the decarboxylation leading to the dibenzothiophene moiety. The corresponding 14-membered systems 29 and 30 were resistant to photoextrusion at both the sites showing the effect of ring size on photoinactivity.¹⁰

Photodecarboxylation is an unsensitized reaction of esters occurring via triplet excited state.¹¹ Since the larger ring systems (4-7, 17, 18, 25, 26) were recovered unchanged under unsensitized conditions, the effect of sensitizers such as benzophenone, acetophenone and 9,10-dicyanoanthracene was probed in number of experiments. In all these cases the compounds were recovered unchanged demonstrating the effect of ring size on photoextrusion.



27,28

R
27,29 : CHO
28,30 : COOH



29,30

EXPERIMENTAL

The melting points were determined in open capillaries and were uncorrected. IR spectra were recorded on Hilger and Watts infra-cord model H-900 and Beckman Spectrophotometer model IR-4250. PMR spectra were scanned in CDCl_3 on Varian EM-360L - 60 MHz and Varian XL-100 MHz Spectrometers. UV spectra were recorded in spectral grade methanol on Bausch and Lomb Spectronic 2000 model. USHIO-UM-452 high pressure mercury vapour lamps were used for all the photoirradiation experiments. Experimental yields of all photochemical reactions denote chemical yields.

Synthesis of compounds 4¹², 5¹³, and 6¹⁴ was carried out according to the procedure reported in literature. The preparation of compounds 7-9, 12, 13, 17-20, 25 and 26 has been reported already in the previous communication.⁷

Photoirradiation of 7-methyl-11H-dibenzo[b,e][1,4]dioxepin-11-one (8).— The depsidone (8) (0.450 g, 2 mmol) was dissolved in spectral grade benzene (2000 ml) and was irradiated for 4 hours under nitrogen atmosphere. The temperature was maintained below 50°C. No fluorescence or phosphorescence was observed at any stage of the reaction. The irradiated solution was concentrated under vacuum using a rotary flash evaporator and the residue was loaded on silica-gel column. Elution with petroleum-ether (60-80°) furnished a colourless compound identified as 3-methyldibenzofuran (10), m.p. 65° (lit¹⁵ m.p. 65°). Yield : 0.203 g (56%).

Further elutions afforded only the starting material in minute amounts. Two minor constituents detected on tlc (CHCl_3) of the irradiated solution, could not be isolated.

Photoirradiation of 8-methyl-11H-dibenzo[b,e][1,4]dioxepin-11-one (9).— Compound 9 (0.405 g, 1.8 mmol) was dissolved in spectral grade benzene (2000 ml) and irradiated for 4 hours under nitrogen atmosphere. After a similar work-up of the reaction and column chromatography as described above afforded a colourless compound characterised as 2-methyldibenzofuran (11), m.p. 44° (lit¹⁶ m.p. 45°). Yield : 0.182 g (56%).

Photoirradiation of 2,3-dimethoxy-11H-dibenzo[b,e][1,4]dioxepin-11-one (12).— A 4 mmol (1.08 g) solution of compound 12 in benzene (2000 ml) was irradiated for 4 hours under nitrogen atmosphere. A work-up of the reaction as described earlier and column chromatography using petroleum-ether (60-80°)-benzene (85:15) system furnished 2,3-dimethoxydibenzofuran (14), m.p. 114°. Yield : 0.542 g (60%). (Found : C, 74.17%; H, 5.55%). $\text{C}_{14}\text{H}_{12}\text{O}_3$ requires : C, 73.67%; H, 5.30%; λ_{max} (MeOH) : 298, 310 nm. IR (KBr) : 2940, 2920 cm^{-1} . PMR (CDCl_3) : δ 4.00 (s, 3H, $-\text{OCH}_3$), 4.04 (s, 3H, $-\text{OCH}_3$), 6.93-7.66 (m, 6H, aromatic).

Irradiation of the depsidone (12) (0.544 g, 2 mmol) using methanol under identical conditions furnished a semisolid which was chromatographed over silica-gel. The petroleum-ether (60-80°)-benzene (50:50) fraction eluted the starting material in trace amounts. Elution with benzene-chloroform (60:40) system furnished methyl 2-(2-hydroxyphenoxy)-4,5-dimethoxybenzoate (16), m.p. 97°. Yield : 0.365 g (62%). λ_{max} : 258, 302 nm. IR (KBr) : 3350, 2990, 2920, 2840, 1660 cm^{-1} . PMR (CDCl_3) : δ 3.87 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.98 (s, 3H, COOCH_3), 6.72 (s, 1H, H at C-3), 6.78-7.29 (m, 4H, aromatic), 7.40 (s, 1H, H at C-6), 7.70 (s, 1H, OH). This compound was found to be identical in all respects with an authentic specimen prepared by esterification (MeOH, H_2SO_4) of the corresponding acid.⁷

Photoirradiation of 3,4-dimethoxy-11H-dibenzo[b,e][1,4]dioxepin-11-one (13). Irradiation of the depsidone (13) (1.08 g, 4 mmol) in benzene and work-up of the reaction mixture in a manner similar to that described for compound 12 yielded 3,4-dimethoxydibenzofuran (15), m.p. 60°. Yield : 0.546 g (60%). (Found : C, 73.89%; H, 5.13%; $\text{C}_{14}\text{H}_{12}\text{O}_3$ requires : C, 73.67%; H, 5.30%). λ_{max} : 256, 286 nm. IR (KBr) : 2940, 2840 cm^{-1} .

Photoirradiation of 11H-dibenzo[b,e][1,4]oxathiepin-11-one (19).— The thiadepsidone (19) (0.66 g, 2.9 mmol) in benzene (1000 ml) was irradiated under inert atmosphere of nitrogen. The reaction was monitored on tlc. At the end of 4 hours the irradiation was stopped and the photolysate

was concentrated on a rotary flash evaporator. The solid obtained was subjected to column chromatography on silica gel. Elution with petroleum-ether (60-80°)-benzene (60:40) furnished a colourless compound. It was crystallised from benzene as colourless needles and identified as dibenzothiophene (21), m.p. 99° (lit¹⁷ m.p. 99°). Yield : 0.204 g (38%).

Irradiation of the same thiadepsidone (0.6 g, 2.6 mmol) in methanol (1000 ml) under similar conditions followed by work-up similar to that described for compound 12 afforded methyl 2-(2-hydroxyphenylthio)benzoate (23) as a colourless compound. m.p. 69°. Yield : 0.438 g (64%). IR (KBr) : 3420, 1700 cm⁻¹. This compound was found to be identical with an authentic sample prepared by esterification of the corresponding acid⁷ using methanol and sulphuric acid.

Photoirradiation of 7-methyl-11H-dibenzo[b,e][1,4]oxathiepin-11-one (20).- A 1.65 mmol (0.4 g) solution of the cyclic ester (20) in benzene (1000 ml) was irradiated for 4 hours under nitrogen atmosphere. After a work-up similar to that described for compound 19, a product characterised as 3-methyldibenzothiophene(22), m.p. 79° (lit¹⁸ m.p. 78-9) was isolated. Yield : 0.203 g (62%).

Similar irradiation of the ester (20) (0.5 g, 2.1 mmol) in methanol for 4 hours under inert atmosphere of nitrogen followed by work-up similar to that mentioned for compound 12 and column chromatography yielded methyl 2-(2-hydroxy-5-methylphenylthio)benzoate (24) as a colourless compound. m.p. 75°. Yield : 0.355 g (63%). IR (KBr) : 3400, 2940, 1710 cm⁻¹. PMR (CDCl₃): δ 2.27 (s, 3H, CH₃), 3.94 (s, 3H, COOCH₃), 6.66-7.33 (m, 7H, aromatic), 7.9 (s, 1H, OH, D₂O exchangeable). This compound was found to be identical in all respects with an authentic sample prepared by esterification (MeOR, H₂SO₄) of the corresponding acid.⁷

General procedure for photoirradiation of cyclic esters (4-7, 17, 18, 25 and 26). A solution of 1 mmol of the cyclic ester in 250 ml spectral grade benzene or methanol or acetonitrile was irradiated under nitrogen atmosphere for 20 hours. Concentration of the photolysate using a flash rotary evaporator resulted in recovery of the starting compounds.

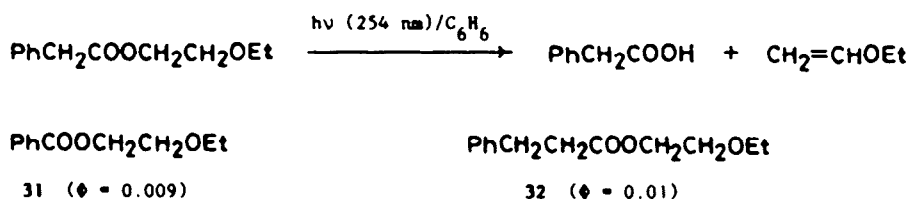
Similar experiments carried out with sensitizers such as acetophenone, benzophenone or 9,10-dicyanoanthracene also failed to furnish any photoproducts.

DISCUSSION

The photoextrusion of CO₂ observed in seven membered cyclic esters in presence of diphenyl ether or diphenyl sulphide linkage has preparative significance and is being explored in this laboratory for synthetic objectives including synthesis of natural products.

The results from larger ring compounds are in contrast to the photoreactivity of cyclic systems such as cyclic benzylic diesters and tetraesters which undergo β-scission and do not retain any ester group on photolysis^{19,20}. An extra methylene group is known²¹ to have an effect on photoreactivity as can be exemplified (eqn. 1) by the Norrish type II fragmentation having the efficiency φ = 0.10 which is 10-fold higher than that for both the conjugated benzoate (31) as well as the propanoate (32).

eqn. 1-



Similar experimental observations have also been made in photodecarboxylation of simple systems²². However, these have not been rationalised. In the present study all the esters studied were conjugated ones and the reasons for apparent inertness of large membered cyclic esters seem to lie in the mode of excitation and energy transfer. In this context the proposal made by Morrison²³ in the case of Norrish type II cleavage of esters can be applied here. In eight/seven membered systems it is possible that the two functional groups ester-ester (8 membered) and ester-ether/thioether (7 membered) are strongly coupled to form a "super chromophore" in which excitation is "delocalised" over both the moieties whereas in large ring systems the functionalities being not in near vicinity mainly due to the different conformational modes being available to them due to large ring sizes, this phenomenon does not seem to occur leading to photostability. In the case of benzylic esters however the role of methylene group seems

to have a pronounced effect since all the ester groups are photodecarboxylated. This argument can be supported by the fact that eight membered cyclic diester (1) is rendered relatively photo-inactive after photodecarboxylation only at one site.

Though other explanations can be put forward the photostability of the larger cyclic esters is presumably due to conformations of the 12, 14, and 16 membered rings which permit the aromatic rings to interact thereby reducing the energy available for scission reaction.

Further detailed investigations on photolysis of large ring systems to study mechanistic aspects are in progress.

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