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An Efficient Approach to γ-Alkylidene γ-Butyrolactones : Application to the Syntheses of Pyridazinones and Diazocinones

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Abstract : The efficient phototransformation of a variety of spirodiones **3** to γ-alkylidene γ-butyrolactones **4** and their application to the syntheses of biologically useful pyridazinones **14** and diazocinones **15** are described. © 1998 Elsevier Science Ltd. All rights reserved.

γ-Alkylidene γ-butyrolactones are an important class of compounds and interest in their chemistry continues unabated because of their usefulness as synthons and/or as biologically active agents.[1] They are synthetic equivalents of 1,4-diketones and versatile intermediates for the synthesis of many heterocyclic and carbocyclic compounds.[2] Besides they are known to possess carcinogenic, antitumour activity and other biological properties as well.

While a variety of synthetic methodologies for γ-alkylidene γ-butyrolactones involving palladium and mercury mediated cyclization have appeared in recent times,[3] the literature describing novel one-pot methodology based on consecutive process is rather scarce. Recently in our preliminary communication we have reported the efficient phototransformation of model spiro[4.n]-2,5-diones related to antitumour antibiotic Fredericamycin A.[4] Further, we have studied this phototransformation in detail and extended the scope of this reaction for a variety of other spirodiones as well. The synthetic utility of butyrolactones for the construction of biologically useful pyridazinones and diazocinones was also explored.

The synthesis of various spirodiones was accomplished as per recently published methodology involving coupling of 1,2-disilyloxycyclobutene **2** with ethylene glycol ketals of corresponding ketones, in the presence of an excess of $BF_3.Et_2O$ at -78°C (Scheme-1).[5] The structures of various spirodiones prepared were confirmed on the basis of chemical, analytical and spectral evidence and also by comparison with literature data.[5-7] Irradiation of the 2,2-disubstituted cyclopentane-1,3-dione (**3a-c**) at 300 *nm* Rayonet (*ca.* 0.1mol dm^{-3} in dry benzene) was examined and conversion to γ-butyrolactones **4a** (92%), **4b** (95%) with *Z* to *E* ratio 3 : 2 and **4c** (96%) with *Z* to *E* ratio 3 : 2 was observed. Similarly, other spirodiones e.g. **3d-f** under identical concentration and irradiation conditions furnished > 90% isolated yields of **4d-f** after 2-4 h of photolysis.

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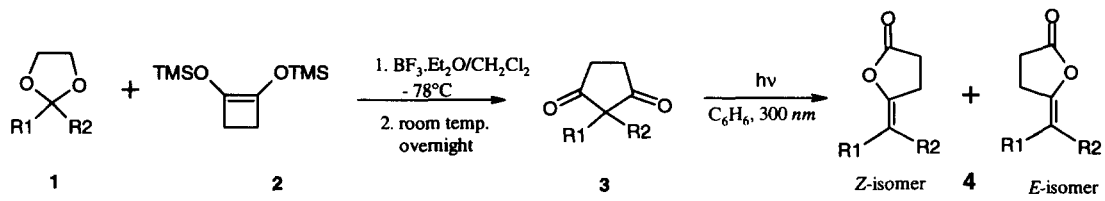
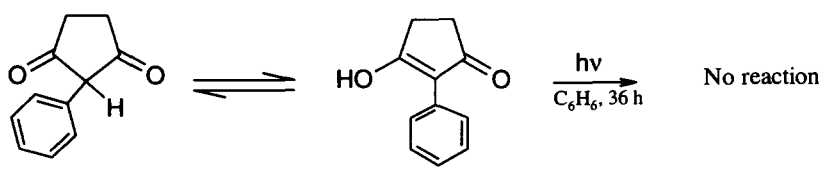


1 2 3 4

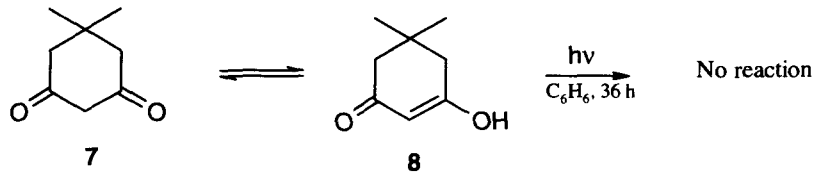
a : $R^1 = CH_3$, R2 = CH_3
b : R1 = CH_3, R2 = C_2H_5
c : R1 = Ph, R2 = CH_3
d : —$(CH_2)_5$—
e : —$(CH_2)_6$—
f : —$(CH_2)_{12}$—

Scheme -1

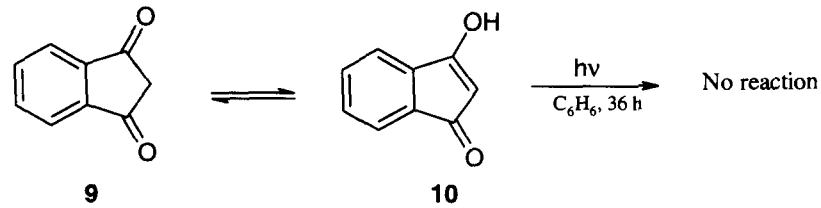
The structures of *E* and *Z* butyrolactones were established based on chemical, analytical and spectral evidence.[8] Interestingly, the two *Z* and *E* isomers of **4c** could be separated by column chromatography and both the structures could be easily assigned from ^{1}H-NMR. In the *E*-isomer of **4c** in which methyl is *syn* to oxygen (enol oxygen), a deshielding to δ 2.1 was observed, but phenyl which is *anti* to oxygen went upfield to δ 7.15-7.5 (m). However, in the *Z*-isomer, the methyl is *anti* to oxygen (enol oxygen) and was upfielded to δ 2.0 whereas phenyl which is *syn* to oxygen was deshielded slightly to δ 7.2-7.67 (m) as compared to *E*-isomer. Similar interpretation can be seen in the literature as well.[9] However, the two isomers in the case of **4b** could not be separated and the approximate ratio of *Z* and *E* (3 : 2) butyrolactones was determined on the basis of integration from ^{13}C-NMR spectrum, in which all carbons appeared as doublets. Thus the phototransformation of spirodiones was found to be quite a general and efficient process. However no photochemical rearrangement of 2-phenyl-cyclopentane-1,3-dione **5** could be observed. This could perhaps be attributed to the monosubstituted nature of 1,3-cyclic dione **5** which prefers to stay in its tautomeric enone form **6** leading to no photoreaction.[10]



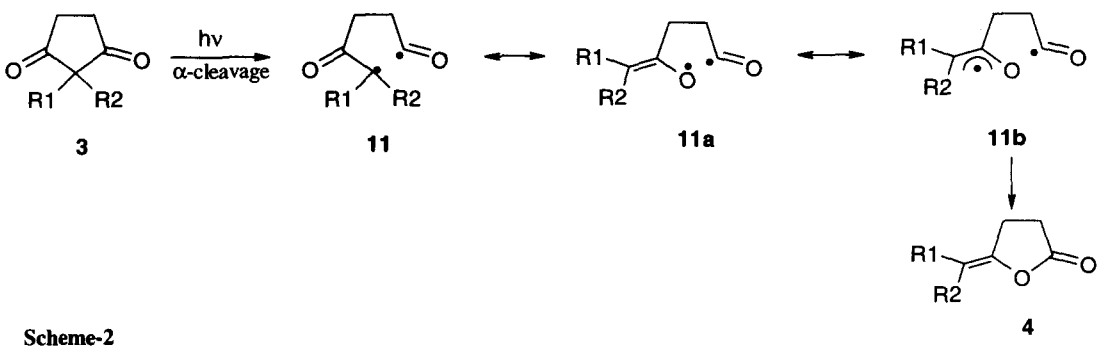
5 6



Similarly, the unsubstituted 1,3-cyclic diones **7** & **9** preferred to stay in photoequilibrium enol forms **8** & **10** and did not lead to any rearranged product upon irradiation in benzene.



The mechanism of phototransformation could be visualized as initial efficient α-cleavage[11] and subsequent bond reorganization to the biradicals **11, 11a, 11b** from starting materials **3**, which recombine to form preferentially a C-O bond to yield the desired lactone **4**. (Scheme-2).



Scheme-2

With a view to enhance the efficiency and gain some mechanistic insight, the progress of phototransformation was examined by varying different reaction parameters e.g. (i) solvent effect, (ii) concentration effect, (iii) wavelength effect, (iv) quenching study and (v) sensitization study.

(i) Solvent effect : The diones e.g **3c** and **3e** were chosen to examine the solvent effect. Thus, the solution of above compounds (0.1 mol dm^{-3}) with similar concentration in a variety of dry solvents e.g acetonitrile,

benzene, cyclohexane, ethanol, methanol, isopropanol and n-hexane was irradiated separately at 300 *nm* for 2h and the formation of γ-alkylidene γ-butyrolactones was monitored by GC. The GC yields in these solvents were 90%, 98%, 94%, 92%, 93%, 93% and 94% respectively. A slightly better yield of product was obtained in benzene as solvent. One of the purposes of employing H-donating solvents e.g. cyclohexane, ethanol, isopropanol and n-hexane was to trap the intermediate biradicals during photolysis. However, surprisingly, no trapping products could be observed indicating that either the phototransformation is of highly concerted nature or the biradicals formed are extremely short lived. This behavior, as well as the absence of recombination products of the postulated short lived biradicals[12] with each other might be due to a "cage effect".[13]

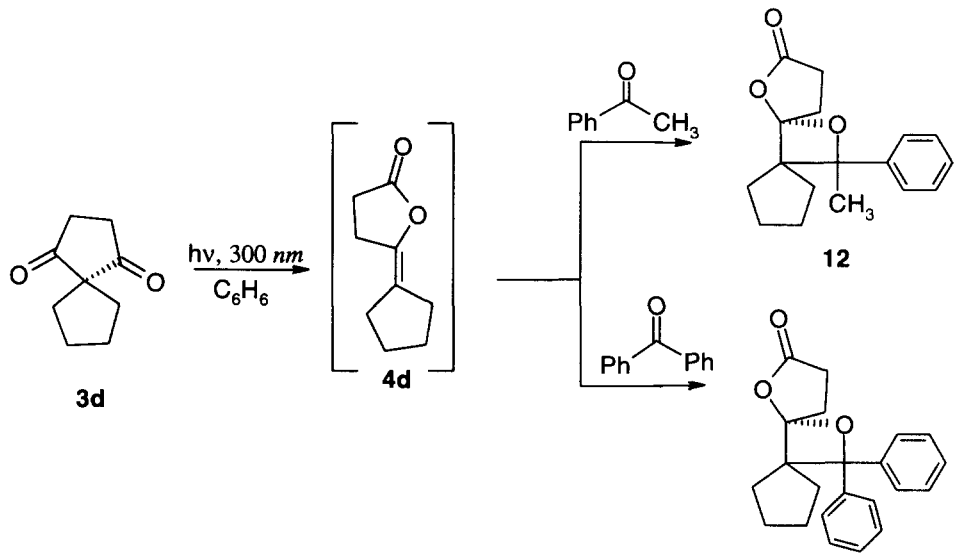
(ii) Concentration effect **:** The optimum concentration of the solvent was found to be 0.1mol dm^{-3}. Though the reaction was accelerated with a little higher concentration of the solvent (0.12 mol dm^{-3}); there was no appreciable effect in the formation of γ-alkylidene γ-butyrolactone.

(iii) Wavelength effect **:** The spiro dione **3e** was photolysed separately at different wavelength e.g 254, 300, 350 *nm* respectively. The formation of photoproduct was detected only at 300 *nm* irradiation. However at 254 *nm*, the formation of butyrolactone **4e** (25% conversion by GC) was observed as the only product after 24 h of irradiation in optimum concentration.

(iv) Quenching study **:** The substrates **3c** and **3e** were chosen for quenching experiment in order to determine the multiplicity of excited states. The dienes such as piperylene and 1,3-cyclohexadiene were used separately as quencher of triplet state. Thus one equivalent of **3c** or **3e** and five equivalent of dienes (piperylene or 1,3-cyclohexadiene) were irradiated under the identical photochemical conditions. The reaction was monitored by TLC and GC which showed the formation of only rearranged product **4c** or **4e**. The increased amount of quenchers e.g 10 or 20 equivalents has no effect on the formation of photoproduct. Thus, similar to the photolysis in H-atom donating solvent, from quenching studies as well, the reaction appears to go *via* a short lived singlet manifold.

(v) Sensitization study **:** The quenching and solvent effect studies gave indication that the excited state formed during photolysis is not only of highly concerted nature, but of singlet manifold as well. To verify further the nature of excited state multiplicity, sensitization studies were carried out with standard triplet sensitizers e.g acetophenone and benzophenone etc. Compound **3d** in the presence of sensitizers such as acetophenone and benzophenone furnished highly efficient chemo- and regio selective oxetane **12** and **13** respectively, (Scheme-3).

While there are many useful methods for oxetane formation, including ring expansion,[14] ring contraction[15a] and alkylation,[15b] the synthesis from the quenching of photochemically excited carbonyl compounds and alkenes is perhaps the most direct and flexible one.[16] Some of the reported syntheses of oxetane involve intermolecular[17] and intramolecular[17] [2+2] cycloaddition with enol ethers and carbonyl compounds which provided substituted oxetanes with modest to good regioselectivity leading mainly to the corresponding 3-alkoxy oxetanes.[18] Bach[19] has reported an elegant regio- and diastereoselective synthesis of oxetane by [2+2] cycloaddition of benzaldehyde and substituted trimethylsilyl enol ethers.



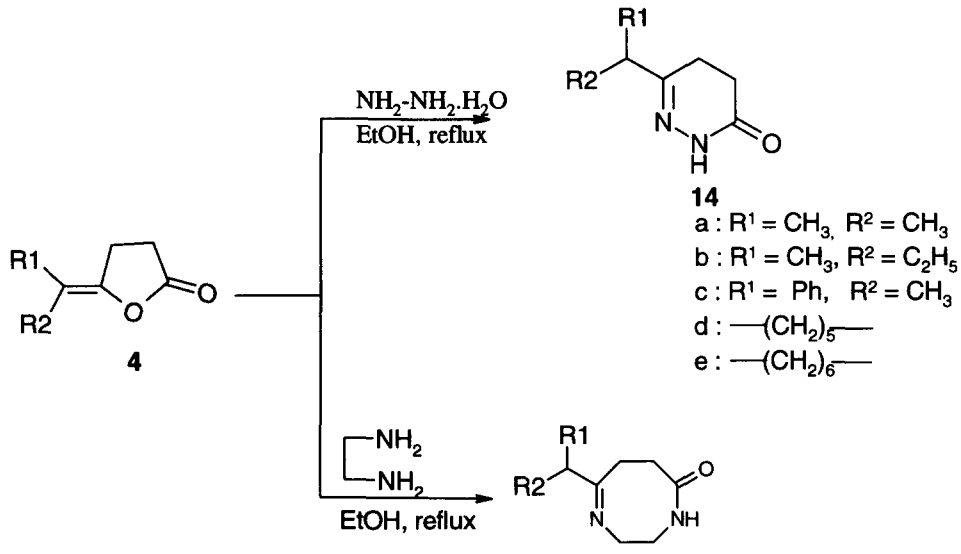
Scheme-3

On the contrary, we observed only one regio- and chemoselective oxetane formation during the irradiation of spirodiones with appropriate sensitizers as discussed above. The generality of oxetane formation was established with additional sensitizers such as acetone and benzaldehyde as well. The structures of various oxetanes were confirmed on the basis of chemical, analytical and spectroscopic evidence.[8]

γ-Alkylidene γ-butyrolactones are synthetically and biologically useful compounds. The synthetic potential of these lactones was further extended for the construction of biologically useful pyridazinones and diazocinones. Substituted pyridazinones and 1,4-diazocinones are known to possess a wide variety of biological activities.[20] In general these compounds do not occur in nature. Pyridazinone derivatives have been found to exhibit hypotensive, antihypertensive, amoebacidal, antibacterial, antitumour, antiviral and antimalarial activities, whereas diazocinones are useful as anthelmintic, germicidal and adrenolytic agents.[21,22]

In general pyridazinones and diazocinones are prepared from 1,4-ketoacids,[20] 1,4-diketone, 1,2-dicarbonyl compounds, anhydrides and lactones.[2] Thus, when a mixture of compound **4** and hydrazine hydrate or 1,2-diaminoethane was heated in refluxing ethanol for 2 h, the desired 6-alkyl-4,5-dihydro-3(2H)-

pyridazinone **14** and 8-alkyl-2,3,6,7-tetrahydro-1,4-diazocin-5(4H)-one **15** were obtained in almost quantitative yields (Scheme-**4**). The structures of these compounds were established based on chemical, analytical and spectroscopic evidence.[8]



Scheme-4

In summary, the efficient phototransformation of a variety of spirodiones to γ-butyrolactones has been demonstrated. During sensitization studies of phototransformation of spirodiones with a variety of sensitizers, a highly efficient chemo- and regioselective formation of oxetane was noteworthy. Finally, the application of γ-alkylidene γ-butyrolactones to biologically relevant pyridazinone and 1,4-diazocinone derivatives has been established.

EXPERIMENTAL SECTION

General information : Metling points were determined with a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer model 683 grating infrared spectrometer. Proton and ^{13}C NMR spectra were recorded on a various FT-80A, Bruker WH-90 FT NMR and Bruker AC-200 NMR spectrometers. The chemical shifts are reported in parts per million (δ) with tetramethyl silane as internal standard. Mass spectra were obtained with a Finnigan MAT-1020B-70-eV mass spectrometer. Elemental analyses were carried out on a Carlo Erba CHNS-O analyzer.

The various spirodiones (**3a-f**) utilized in our studies were prepared according to the literature procedure.[5] The physical and spectroscopic data for compounds **3a-b**,[6] **3c**,[5] **3d-f**[7] were in agreement with those described in the literature.

Experimental procedure for the preparation of γ-alkylidene γ-butyrolactones (4a-f) : The spirodione **3** (0.05-0.1 mol dm^{-3}) was dissolved in dry benzene in pyrex tube and the solution was degassed by bubbling with nitrogen for 15 min. Subsequently, the degassed solution was stoppered and irradiated at 300 *nm* (Rayonet photoreactor) for 2 to 4 h. The progress of the reaction was followed by TLC and/or GC. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using pet.ether : acetone mixture as eluent to get pure γ-alkylidene γ-butyrolactones **4** in excellent yields.

[(1,1-Dimethyl) γ-methylidene] γ-butyrolactone (4a) : Elution using 2% acetone in pet.ether gave the product as colorless liquid in 92% yield. IR ν_{max} / cm^{-1}(Neat) : 2980, 2920, 1800, 1725, 1460, 1300, 1200, 1140; ^{1}H-NMR ($CDCl_3$) δ : 1.68 (s, 3H), 1.76 (s, 3H), 2.63-2.77 (m, 2H), 2.78-2.82 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ : 175.22 (s), 142.43 (s), 106.30 (s), 27.91 (t), 22.79 (t), 17.16 (t), 16.55 (t); MS (*m/z*, rel. int %): M^+ 126 (26%), 115 (72), 111 (34), 70 (58), 59 (30), 55 (100), 43 (78); Anal. calcd for $C_7H_{10}O_2$ (126.15) : C, 66.64; H, 7.99. Found : C, 66.40; H, 7.81.

(Z : E, 3 :2)-[(1-Ethyl-1-methyl) γ-methylidene] γ-butyrolactone (4b) : Elution using 2% acetone in pet.ether during column chromatography gave **4b** as a colorless liquid in 95% yield. IR ν_{max} / cm^{-1}(Neat) : 1795, 1710, 1450, 1380, 1295, 1265, 1180, 1130; ^{1}H-NMR ($CDCl_3$) δ : 0.79-1.33 (m, 3H), 1.55-2.32 (m, 5H), 2.48-2.95 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ : 174.71 (s), 174.10 (s), 142.10 (s), 141.50 (s) , 111.67 (d), 111.57 (s), 27.40 (t), 27.09 (t), 24.16 (t), 24.00 (t), 23.39 (t), 22.53 (t), 22.17 (q), 14.11 (q), 13.35 (q), 11.47 (q); MS (*m/z*, rel. int %): M^+ 140 (44%), 125 (100), 97 (23), 69 (20); Anal. calcd for $C_8H_{12}O_2$ (140.18) : C, 68.54; H, 8.63. Found : C, 68.32; H, 8.84.

(E)-[(1-Methyl-1-phenyl) γ-methylidene] γ-butyrolactone (4c) : Elution with 2% acetone in pet.ether gave **4c** as a colorless liquid in 38% yield. IR ν_{max} / cm^{-1}(Neat) : 1805, 1695, 1610, 1500, 1460, 1320, 1200, 1150, 1080; ^{1}H-NMR ($CDCl_3$) δ : 2.1 (m, 3H), 2.51-3.06 (m, 4H), 7.15-7.5 (m, 5H); ^{13}C-NMR ($CDCl_3$) δ : 174.45 (s), 145.21 (s), 139.42 (s), 128.11 (d) , 127.50 (d), 126.57 (d), 113.14 (s), 27.98 (t), 24.60 (t), 16.69 (q); MS (*m/z*, rel. int %) : M^+ 188 (100%), 160 (13), 145 (38), 132 (20), 117 (14), 105 (24), 104 (48), 103 (24); Anal. calcd for $C_{12}H_{12}O_2$ (188.22) : C, 76.57; H, 6.43. Found : C, 76.29; H, 6.24.

(Z)-[(1-Methyl-1-phenyl) γ-methylidene] γ-butyrolactone (4c) : Elution using 3% acetone in pet.ether during column chromatography and subsequent recrystallization from n-hexane afforded the product as a colorless solid in 58% yield. M. P : 78°C; IRν_{max} / cm^{-1}(Nujol) : 1800, 1700, 1600, 1450, 1225, 1140; ^{1}H-NMR ($CDCl_3$) δ : 2.0 (m, 3H), 2.62-3.22 (m, 4H), 7.2-7.67 (m, 5H); ^{13}C-NMR ($CDCl_3$) δ : 174.74 (s), 143.92 (s), 127.62 (d), 127.44 (d) , 127.21 (s), 126.25 (d), 109.78 (s), 26.90 (t), 24.03 (t), 16.49 (q); MS(*m/z*, rel. int %) : M^+ 188 (100%), 160 (20), 145 (52), 132 (38), 117 (23), 105 (36), 104 (90), 103 (42); Anal. calcd for $C_{12}H_{12}O_2$ (188.22) : C, 76.57; H, 6.43. Found : C, 76.71; H, 6.53.

γ-Cyclopentylidene γ-butyrolactones (4d) : Elution using 2% acetone in pet.ether during the column chromatography and subsequent recrystallization from n-hexane afforded the product as a colorless solid in 96% yield. M. P : 45 °C; IRν_{max} / cm^{-1}(Nujol) : 1806, 1726, 1490, 1390, 1150, 1120; ^{1}H-NMR ($CDCl_3$) δ : 1.55-2.55 (m, 8H), 2.61-2.9 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ : 175.07 (s), 139.45 (s), 116.88 (s), 28.14 (t), 27.74 (t), 26.37 (t), 26.24 (t), 26.00 (t), 23.41 (t); MS (*m/z*, rel. int %) : M^+ 152 (100%), 124 (37), 111 (24), 96 (25), 68 (15); Anal. calcd for $C_9H_{12}O_2$ (152.19) : C, 71.02; H, 7.95. Found : C, 70.91; H, 8.23.

γ-Cyclohexylidene γ-butyrolactone (4e) : Elution using 2% acetone in pet.ether during column chromatography and subsequent recrystallization from n-hexane afforded the product as a colorless solid in 98% yield. M. P. : 76 °C; IRν_{max} / cm^{-1}(Nujol) : 1790, 1710, 1495, 1215, 1185, 1135, 1120; ^{1}H-NMR ($CDCl_3$) δ : 1.30-2.38 (m, 10H), 2.52-3.0 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ : 174.85 (s), 139.55 (s), 114.27 (s), 27.56 (t), 27.34 (t), 26.71 (t), 26.36 (t), 26.12 (t), 25.93 (t), 22.21 (t); MS (*m/z*, rel. int %) : M^+ 166 (100%), 137 (36), 124 (25), 111 (35), 109 (20), 85 (14), 67 (12); Anal. calcd for $C_{10}H_{14}O_2$ (166.21) : C, 72.28; H, 8.49. Found : C, 72.26; H, 8.61.

γ-Cyclododecylidene γ-butyrolactone (4f) : Elution using 2% acetone in pet.ether during column chromatography and subsequent recrystallization from n-hexane afforded **4f** as a colorless solid in 92% yield. M. P. : 79°C; IRν_{max} / cm^{-1}(Nujol) : 1800, 1705, 1230, 1140; ^{1}H-NMR ($CDCl_3$) δ : 1.20-1.65 (m, 18H), 1.86-2.32 (m, 4H) 2.6-2.91 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ : 175.33 (s), 143.64 (s), 114.86 (s), 28.01 (t), 27.82 (t), 26.48 (t), 24.95 (t), 24.21 (t), 24.01 (t), 23.65 (t), 23.34 (t), 22.99 (t), 22.68 (t); MS(*m/z*, rel. int %) : M^+ 250 (74), 195 (8), 151 (22), 137 (23), 125 (88), 111 (54), 95 (55), 91 (32), 79 (54), 67 (64), 55 (100), 53 (33); Anal. calcd for $C_{16}H_{26}O_2$ (250.37) : C, 76.75; H, 10.47. Found : C, 76.53; H, 10.26.

Experimental procedure for the synthesis of oxetanes : Nitrogen gas was bubbled through a solution of γ-cyclopentylidene γ-butyrolactone **3d** (0.05-0.1 mol dm^{-3}) in dry benzene containing 2-5 equiv. of one of the sensitizers (acetophenone or benzophenone) in pyrex tube for 15 min. The solution was then photolysed at 300

nm (Rayonet photoreactor) for 4 to 6 h. The progress of the reaction was monitored by TLC. After the reaction was complete, benzene was removed under diminished pressure and residue was purified by silica gel column chromatography using acetone : pet.ether mixture as eluent to get oxetane in >95% yield. During column chromatography, excess sensitizer 80-90% was recovered.

Oxetane 12 : Elution using 3% acetone in pet.ether followed by recrystallization from n-hexane afforded **12** as colorless solid in 95% yield. M. P. 154-155°C; IRν_{max} / cm^{-1}(Nujol) : 1775, 1610, 1500, 1460, 1380, 1260, 1215, 1170, 1055, 1040, 955, 930, 900; ^{1}H-NMR ($CDCl_3$) δ : 1.13-1.75 (m, 8H), 1.84 (s, 3H), 2.14-2.93 (m, 4H), 7.20-7.45 (m, 5H); ^{13}C-NMR ($CDCl_3$) δ : 175.45 (s), 144.01 (s), 128.20 (d), 127.12 (d), 124.39 (d), 116.39 (s), 88.43 (s), 59.86 (s), 31.61 (t), 30.69 (t), 28.99 (t), 28.03 (t), 26.00 (q), 23.77 (t); MS (*m/z*, rel. int %) : 228 (3), 172 (22), 157 (21), M$^+$-$PhCOCH_3$ 152 (59), 151 (100), 142 (12), 129 (14), 124 (12), 115 (5), 105 (7), 77 (4); Anal. calcd for $C_{17}H_{20}O_3$ (272.33) : C, 74.97; H, 7.34. Found : C, 74.90; H, 7.23.

Oxetane 13 : Elution using 3% acetone in pet.ether followed by recrystallization from n-hexane afforded **13** as a colorless solid in 96% yield. M. P. 114-116°C; IRν_{max} / cm^{-1}(Nujol) : 1795, 1610, 1505, 1460, 1430, 1325, 1275, 1190, 1155, 1090, 1050, 1030, 985, 950, 915; ^{1}H-NMR ($CDCl_3$) δ : 1.40-2.10 (m, 8H), 2.17-2.64 (m, 3H), 2.78-3.00 (m, 1H), 7.15-7.45 (m, 6H), 7.48-7.65 (m, 4H); ^{13}C-NMR ($CDCl_3$) δ : 175.20 (s), 142.76 (s), 142.52 (s), 128.00 (d), 127.88 (d), 127.09 (d), 126.14 (d), 125.70 (d), 115.38 (s), 88.95 (s), 62.32 (s), 31.63 (t), 31.30 (t), 31.03 (t), 27.97 (t), 23.35 (t); MS (*m/z*, rel. int %) : 234 (8), 183 (27), 165 (9), M$^+$-Ph_2CO 152 (100), 105 (9), 97 (9), 77 (12); Anal. calcd for $C_{22}H_{22}O_3$ (334.40) : C, 79.01; H, 6.63. Found : C, 79.42; H, 6.64.

***Experimental procedure for the preparation of 6-alkyl-4,5-dihydro-3(2H) pyridazinones* 14 *and 8-alkyl-2,3,6,7-tetrahydro-1,4-diazocin 5(4H) ones* 15.**

A mixture of γ-alkylidene γ-butyrolactone (0.1mol), hydrazine hydrate or ethylene diamine (0.1mol) in dry ethanol (20ml) was heated under reflux for 2 h. The solvent was removed under reduced pressure and solid obtained was recrystallized from ethanol to get pure product in excellent yield.

6-Isopropyl-4,5-dihydro-3(2H) pyridazinone (14a) : Colorless solid; Yield : 93%; IRν_{max} / cm^{-1}(Nujol) : 3320-3200, 1680, 1650, 1470, 1440. ^{1}H-NMR ($CDCl_3$) δ : 1.14-1.20 (d, 6H), 2.37-2.52 (m, 4H), 2.54-2.69 (m, 1H), 8.50 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ : 168.10 (s), 160.16 (s), 34.97 (d), 26.33 (t), 22.41 (t), 19.45 (q); MS (*m/z*, rel. int %) : M$^+$ 140 (76), 125 (90), 112 (100), 97 (31), 83 (35), 69 (76), 55 (64), 43 (75), 40 (58), 38 (30); Anal. calcd for $C_7H_{12}N_2O$ (140.17) : C, 59.98; H, 8.63, N, 19.98. Found : C, 59.71; H, 8.21 N, 19.62.

6-Isobutyl-4,5-dihydro-3(2H) pyridazinone (14b) : Colorless viscous liquid; Yield : 93%. IRν_{max} / cm^{-1}($CHCl_3$) : 3250, 1680, 1530, 1440. ^{1}H-NMR ($CDCl_3$) δ : 0.85-1.00 (t, 3H), 1.13 (d, 3H), 1.35-1.65 (m, 2H),

1.75-1.89 (m, 1H), 2.35-2.50 (m, 4H), 8.50 (s, 1H); MS (*m/z*, rel. int %) : M^+ 154 (38), 139 (34), 126 (100), 125 (82), 112 (46), 97 (27), 83 (42), 55 (49), 43 (36), 41 (61), 39 (31); Anal. calcd for : $C_8H_{14}N_2O$ (154.19) : C, 62.31; H, 9.15; N, 18.16. Found : C, 62.13; H, 8.91; N, 18.41.

6-Benzyl-1'-methyl-4,5-dihydro-3(2H) pyridazinone (14c) : Colorless solid; Yield : 92%; M. P. : 135°C; IRν_{max} / cm^{-1}(Nujol), : 3300-3250, 1680, 1640, 1610, 1500, 1390; ^{1}H-NMR ($CDCl_3$) δ : 1.50 (d, 3H), 2.25-2.40 (m, 4H), 3.6-3.77 (q, 1H), 7.17-7.46 (m, 5H), 8.50 (s, 1H); MS (*m/z*, rel. int %) : M^+ 202 (100), 187 (35), 131 (33), 115 (36), 105 (63), 91 (97), 77 (53), 55 (34); Anal. calcd for : $C_{12}H_{14}N_2O$ (202.23) : C, 71.27, H, 6.98; N, 13.85. Found : C, 71.01; H, 7.11; N, 13.51.

6-Cyclopentyl-4,5-dihydro-3(2H) pyridazinone (14d) : Colorless solid; Yield : 94%; M. P. : 72°C; IRν_{max} /cm^{-1} (Nujol) : 3880-3220, 1680, 1460, 1440; ^{1}H-NMR ($CDCl_3$) δ : 1.47-1.98 (m, 8H), 2.30-2.55 (m, 4H), 2.65-2.80 (m, 1H), 8.35 (s, 1H); MS (*m/z*, rel. int %) : M^+ 166 (24%), 137 (8), 125 (100), 95 (8), 67 (7), 55 (7); Anal. calcd for $C_9H_{14}N_2O$ (166.20) : C, 65.04; H, 8.49; N, 16.85. Found : C, 64.93; H, 8.21; N, 16.41.

6-Cyclohexyl-4,5-dihydro-3(2H) pyridazinone (14e) : Colorless crystalline solid; Yield : 95%; M. P. : 105°C; IRν_{max} / cm^{-1}(Nujol) : 3300-3250, 1690, 1680, 1640; ^{1}H-NMR ($CDCl_3$) δ : 1.10-1.47 (m, 5H), 1.63-1.97 (m, 5H), 2.15-2.35 (m, 1H), 2.40-2.58 (m, 4H), 8.75 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ : 167.50 (s), 159.19 (s), 44.84 (d), 29.81 (t), 26.37 (t), 25.85 (t), 25.79 (t), 23.04 (t); MS (*m/z*, rel. int %) : M^+ 180 (47%), 165 (5), 151 (12), 139 (15), 125 (100), 112 (79), 55 (15); Anal. calcd for : $C_9H_{16}N_2O$ (180.23) : C, 66.64; H, 8.95; N, 15.54. Found : C, 66.41; H, 8.61; N, 15.32.

8-Isopropyl-2,3,6,7-tetrahydro-1,4-diazocin-5(4H)-one (15a) : Light yellow solid; Yield : 79%; M. P. : 114 - 116°C; IRν_{max} / cm^{-1}(Nujol) : 3300, 1680, 1400; ^{1}H-NMR ($CDCl_3$) δ : 0.9-1.05 (t, 6H), 1.55-1.76 (m, 1H), 1.83-2.00 (m, 1H), 2.27-2.55 (m, 2H), 2.58-3.00 (m, 2H), 3.10-3.25 (m, 2H), 3.72-3.85 (m, 1H), 6.22 (s, 1H); MS (*m/z*, rel. int %) : M^+-C_3H_7 125 (100), 97 (2), 56 (5), 44 (9); Anal. calcd for : $C_9H_{16}N_2O$ (168.22) : C, 64.26; H, 9.59; N, 16.64. Found : C, 64.02; H, 9.21; N, 16.21.

8-Cyclopentyl-2,3,6,7-tetrahydro-1,4-diazocin-5(4H)-one (15b) : Light yellow viscous liquid; Yield : 82%; IRν_{max} / cm^{-1}(Neat) : 3300, 1680, 1400, 1280, 1120; ^{1}H-NMR ($CDCl_3$) δ :1.45-2.05 (m, 8H), 2.15-2.81 (m, 5H), 2.85-3.05 (m, 1H), 3.07-3.35 (m, 2H), 3.65-4.00 (m, 1H), 6.45 (s, 1H); MS (*m/z*, rel. int %) : M^+ -C_5H_9, 125 (100), 67 (5), 56 (6); Anal. calcd for : $C_{11}H_{18}N_2O$ (194.22) : C, 68.02; H, 9.34; N, 14.42. Found : C, 68.31; H, 9.41; N, 14.21.

8-Cyclohexyl-2,3,6,7-tetrahydro-1,4-diazocin-5(4H)-one (15c) : Yellow solid; Yield : 80%; M. P. : 121°C; IRν_{max}/cm^{-1}(Nujol) : 3500-3200, 1680; ^{1}H-NMR ($CDCl_3$) δ : 0.9-1.35 (m, 4H), 1.42-2.12 (m, 6H), 2.25-2.55 (m, 4H), 2.60-3.00 (m, 2H), 3.05-3.30 (m, 2H), 3.68-3.85 (m, 1H), 6.62 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ : 177.63 (s), 89.37 (s), 46.71 (t), 43.99 (d), 42.53 (t), 34.46 (t), 30.00 (t), 27.72 (t), 27.51 (t), 26.56 (t), 26.51 (t), 26.54 (t); MS (*m/z*, rel. int %) : M^+ - C_6H_{11} 125 (100), 55 (10), 45 (10); Anal. calcd for : $C_{12}H_{20}N_2O$ (208.28) : C, 69.20; H, 9.68; N, 13.44. Found : C, 69.61; H, 9.32; N, 13.10.

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