

# Photocyclization of 2-(alkylthio)ethyl benzoylacetates *via* remote proton transfer following charge-transfer interaction between excited ketone carbonyl and thioether chromophore

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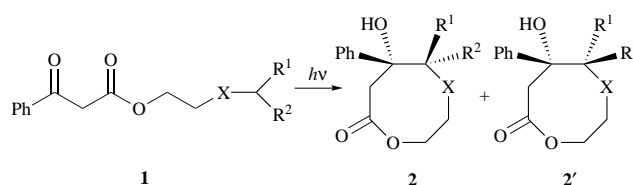
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Upon irradiation, 2-(alkylthio)ethyl benzoylacetates **1a–d** undergo photocyclization to give eight-membered thia lactones **2**. No photoreactivity is observed for 2-(benzylsulfonyl)ethyl benzoylacetate **1e** the sulfur atom of which lacks lone pairs able to serve as donor electrons. The photocyclization takes place *via* 1,9-proton transfer following intramolecular charge-transfer interaction between the sulfur atom and the excited carbonyl group.

The photochemical behaviour of organic compounds having two distinct functional groups separated by a long molecular chain has attracted much attention.<sup>1–4</sup> Lack of conformational mobility in such compounds may limit their photoreactivity. Dienes are widely used as energy-transfer quenchers in the Stern–Volmer analysis of triplet excited-state molecules and the rate of the intermolecular quenching is usually assumed to be diffusion controlled.<sup>5</sup> The intramolecular quenching process is imposed by the length of a molecular chain. A specific geometry is required for efficient intramolecular quenching of triplet ketones by an olefin chromophore.<sup>6</sup> Amines quench triplet ketones by a charge-transfer (CT) process and the intramolecular CT quenching occurs in amino ketones.<sup>7–12</sup> The CT quenching requires some degree of orbital overlap between the electron donor and acceptor for sufficient electron transfer.<sup>13</sup> We have reported the photocyclization of 2-(dialkylamino)ethyl esters of  $\beta$ - and  $\gamma$ -oxo acids in which there is CT interaction between the excited carbonyl group and amine nitrogen connected by five and six atoms, respectively.<sup>14–19</sup> Sulfides act as efficient CT quenchers,<sup>20–22</sup> but are generally inefficient reducing agents for excited ketones in contrast to amines;<sup>21,22</sup> 2-(dialkylamino)propiophenones undergo photocyclization to give cyclopropanols<sup>23</sup> from 1,3-biradicals generated *via* proton transfer following the intermolecular CT interaction, but 2-(alkylthio)propiophenones show no photoreactivity because of lack of a proton transfer process.<sup>24</sup> However, there are some reports of photocyclization *via* remote proton transfer through the intramolecular CT interaction between excited carbonyl and sulfide sulfur.<sup>25–28</sup> In these cases remote hydrogen migrates as proton. Remote proton transfer to carbonyl oxygen may generally occur from remote sulfide carbon and this may be characteristic in the photochemistry of ketones containing a sulfur atom. We report here the photocyclization of 2-(alkylthio)ethyl benzoylacetates *via* intramolecular CT interaction between an excited ketone carbonyl and the thioether chromophore followed by 1,9-proton transfer.

## Results and discussion

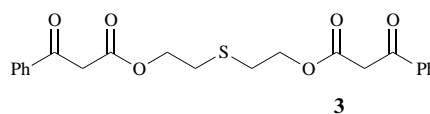
Irradiation of 2-(benzylthio)ethyl benzoylacetate **1a** in benzene under nitrogen with a 450-W high pressure mercury lamp through a Pyrex filter gave the eight-membered thia lactone **2a** (33%). The structure of **2a** was elucidated on the basis of spectral evidence and elemental analysis. Irradiation of the alkylthioethyl esters **1b–d** also gave the corresponding eight-membered thia lactones **2b–d**. As expected, thia lactone isomers having *cis*- and *trans*-phenyl or methyl groups near to the 6-



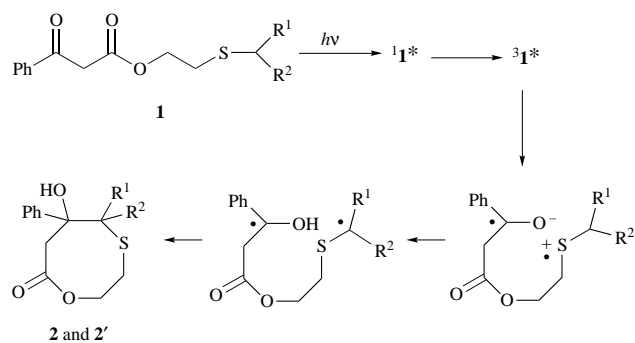
	R <sup>1</sup>	R <sup>2</sup>	X	Yield (%)	
				2	2'
a	Ph	H	S	65	
b	Me	Me	S	44	
c	Me	H	S	29	26
d	H	H	S	35	
e	Ph	H	SO <sub>2</sub>	0	

Scheme 1

phenyl group were formed in the photoreaction of **1a** and **1c**, respectively, and although individual isomers could not be isolated for **1c** a single isomer, **2a**, was obtained for **1a**, no other being detected. A compound which was quite insoluble in ordinary solvents was also obtained in the photoreaction of **1a**, but in no other reaction. This compound was not an isomer of **2a** since the mass number of its parent peak was 414. The IR spectrum of this compound showed peaks at 3400 and 1675  $\text{cm}^{-1}$  and we have tentatively identified it as bis[2-(benzoyl-acetoxy)ethyl] sulfide **3**.



Analysis using MOPAC was performed for the *cis*- and *trans*-thia lactones expected to be formed from **1a** in order both to establish the structure of **2a** and to explain the absence of the second isomer. Eight-membered thia lactones show a transannular electronic interaction between the carbonyl group and sulfur, with their C=O stretching absorptions at rather lower wavenumbers than those for normal lactone carbonyl,<sup>29</sup> whilst substituents on the ring affect the strength of the interaction.<sup>14b,30</sup> The S...C=O bond distances in the optimized structures having *cis*- and *trans*-configurations were 3.73 and 3.36 Å, respectively. The thia lactone **2a** was thought to be the *cis*-isomer since its C=O stretching absorption appeared at 1740  $\text{cm}^{-1}$ , a value close to that of the aza lactone which was produced from 2-dibenzylaminoethyl benzoylacetate and has a *cis*-configuration and a longer N...C=O distance.<sup>14b,30</sup> Thus, the



Scheme 2

thia lactone absent in the photoreaction of **1a** would be the isomer **2a'** having a *trans*-configuration. Heats of formation for **2a** and **2a'** were calculated as  $-58.1$  and  $-54.6$  kcal mol $^{-1}$ , respectively. These results indicate that the *cis*-isomer **2a** is more stable than the *trans*-isomer **2a'** although the reverse is generally true in small ring compounds. This may be explained in terms of the conformation of the eight-membered ring. The most stable ring conformation for an eight-membered ring is a boat-chair form.<sup>31</sup> The optimized structures of **2a** and **2a'** also have boat-chair like ring conformation. In boat-chair forms the two neighbouring phenyl groups have a dihedral angle quite different from that in small ring compounds.<sup>30</sup> The dihedral angles of Ph-C(5)-C(6)-Ph in **2a** and **2a'** were 60.1 and 54.5°, respectively. The deviation from the ideal dihedral angle of 0° in the *cis*-conformation decreases the repulsive interaction between the phenyl groups whilst that in the *trans*-configuration increases it. The ring conformation should determine the deviation of the dihedral angles whilst formations should reflect the stability of the configuration of substituents and the conformation of the eight-membered ring. The structures of cyclic transition states producing **2a** and **2a'** should resemble those of the thia lactone. This would account for the lack of the formation of **2a'** in the photoreaction of **1a**. Dealkylation occurs in the photoreaction of some ethers<sup>32</sup> and *N,N*-dialkylamines.<sup>33,34</sup> The benzyl radical is stabilized by delocalization, so that the debenzoylation from the biradical intermediate might occur faster than cyclization to give the unstable isomer **2a'**. Heat of formations for the thia lactone **2c** and **2c'** were comparable ( $-94.5$  kcal mol $^{-1}$  for **2c** and  $-93.6$  for **2c'**). This would account for the lack of a severe stereoselectivity in the photoreaction of **1c**; the ratio of **2c**:**2c'** = 29:26. The ratio in cyclobutanol formation in the Type II reaction of alkyl phenyl ketones is generally less than 30%.<sup>35</sup>

The quantum yield for disappearance of **1a** was 0.05. Since the photoreaction was effectively quenched with 2,5-dimethylhexa-2,4-diene, it proceeds from the triplet excited state of **1a**. The sulfone **1e** was stable upon irradiation, the fully oxidized sulfur atom present having no remaining lone pairs to serve as donor electrons, no CT interaction being expected by such an electron-deficient centre.<sup>27</sup> This suggests that the photoreaction of **1** takes place *via* the charge-transfer intermediate from the  $n, \pi^*$  triplet state.

The photoreaction of **1a** occurred in both benzene and acetonitrile. The Stern-Volmer quenching for the formation of **2a** in acetonitrile showed a linear relationship. The  $kq\tau$  value was determined to be  $3.7 \times 10^2$  mol $^{-1}$  dm $^3$ . The lifetime  $\tau$  of the triplet state of **1a** and the rate constant  $kr$  were calculated to be  $3.7 \times 10^{-8}$  s and  $2.7 \times 10^7$  s $^{-1}$ , respectively, assuming a diffusion-controlled rate for  $kq$  ( $1 \times 10^{10}$  mol dm $^{-3}$  s $^{-1}$ ).<sup>36</sup> The rate constant is comparable to that of valerophenone ( $14 \times 10^7$  s $^{-1}$ )<sup>37</sup> and that of 2-dibenzylaminoethyl benzoylacetate ( $14 \times 10^7$  s $^{-1}$ ) which undergoes photocyclization *via* a charge-transfer intermediate.<sup>14b</sup> This supports the idea of intervention of the charge-transfer intermediate in the photoreaction of **1a**. The rate of the elementary process of charge-transfer inter-

action itself should be much faster than that of the bimolecular quenching process. The process involving the conformational change leading to suitable conformations for the interaction is presumed to be the rate-determining step. In keto sulfides, PhCO(CH $_2$ ) $_n$ SBu ( $n = 5$ ) is reported to be an upper limit for the CT interaction.<sup>29</sup> As the carbonyl group and the sulfur atom in **1a** is connected by 5 atoms, efficient CT interaction in **1a** may be due to an increase in population of suitable conformations for the CT interaction because of the presence of the ester group in the long molecular chain. The difference in the  $kr$  values of **1a** and that of the corresponding 2-dibenzylaminoethyl ester would reflect the higher ionization potential of sulfides over dialkylamines.<sup>20</sup>

## Experimental

IR spectra were recorded with a JASCO IR Report-100 spectrometer, and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured with a JEOL JNM-EX400 spectrometer using tetramethylsilane as an internal standard. An Ushio 450-W high-pressure mercury lamp was used as an irradiation source. The 2-benzoylacetates **1a-d** were prepared by esterification of ethyl benzoylacetate and the corresponding thio alcohols.

### Preparation of 2-(benzylsulfonyl)ethyl benzoylacetate **1e**

The benzoylacetate **1a** (0.81 g, 2.6 mmol) in a 100-cm $^3$  three-necked flask was dissolved in acetic acid (3 cm $^3$ ). Hydrogen peroxide (30%, 1 cm $^3$ , 8.9 mmol) was then added dropwise to the solution. The mixture was heated at 100 °C for 20 min and then cooled and extracted with ethyl acetate. The extract was dried (Na $_2$ SO $_4$ ) and concentrated to give a pale yellow solid, recrystallization of which from hexane-dichloromethane gave **1e** as a colourless solid (0.153 g, 0.44 mmol, 17%); mp 101–102 °C (Found: C, 62.6; H, 5.3. C $_{18}$ H $_{18}$ O $_5$ S requires C, 62.41; H, 5.24%);  $\nu_{\text{max}}$ (KBr)/cm $^{-1}$  1745, 1690, 1310 and 1120;  $\delta_{\text{H}}$  3.20 (2H, t,  $J$  6.2, SCH $_2$ ), 4.05 (2H, s, CH $_2$ Ph), 4.23 (1.8H, s, COCH $_2$ ), 4.48 (2H, t,  $J$  6.2, OCH $_2$ ), 5.69 (0.1H, s, C=CH), 7.1–8.0 (10H, m, ArH) and 12.35 (0.1H, s, OH).

### General procedure for the preparative photolysis of **1**

A benzene solution of **1** (*ca.* 0.04 mol dm $^{-1}$ ) was irradiated under nitrogen with a 450-W high-pressure mercury lamp through a Pyrex filter. After concentration of the reaction mixture by removal of the solvent, the residue was chromatographed on a silica-gel column. Elution with hexane-ethyl acetate gave **2** and/or **2'**. In the case of **1a**, insoluble material was filtered off and the filtrate was concentrated and chromatographed. The insoluble material was recrystallized from a large quantity of acetone.

6-Hydroxy-5,6-diphenyl-1-oxa-4-thiacyclooctan-8-one **2a**. Mp 173–173.5 °C (Found: C, 68.8; H, 5.7. C $_{18}$ H $_{18}$ O $_3$ S requires C, 68.76; H, 5.77%);  $\nu_{\text{max}}$ (KBr)/cm $^{-1}$  3520 and 1740;  $\delta_{\text{H}}$  2.67 (1H, d,  $J$  11.7, COCHH), 2.93 (1H, dd,  $J$  15.2 and 2.9, SCHH), 3.24 (1H, d,  $J$  11.7, COCHH), 3.40 (1H, ddd,  $J$  15.2, 11.5 and 4.4, SCHH), 4.24 (1H, s, OH), 4.27 (1H, dd,  $J$  11.7 and 4.4, OCHH), 4.46 (1H, s, CHPh), 5.12 (1H, ddd,  $J$  11.7, 11.5 and 2.9, OCHH) and 6.9–7.4 (10H, m, ArH);  $\delta_{\text{C}}$  39.1 (t), 51.0 (t), 63.5 (d), 66.6 (t), 82.2 (s), 125.2 (d, 2C), 126.4 (d), 126.6 (d), 127.5 (d, 2C), 127.7 (d, 2C), 127.9 (d, 2C), 142.4 (s), 143.8 (s) and 173.5 (s);  $m/z$  (EI) 314 (M $^+$ ).

The compound insoluble in ordinary solvents. Mp 181.5–183.5 °C (Found: C, 63.9; H, 5.9, C $_{22}$ H $_{22}$ O $_6$ S requires C, 63.75; H, 5.35%);  $\nu_{\text{max}}$ (KBr)/cm $^{-1}$  3400 and 1675;  $m/z$  (EI) 414 (M $^+$ ). The NMR spectrum of this compound could not be measured because of quite low solubility in chloroform, benzene, methanol or acetone. This compound was tentatively identified as bis[2-(benzoylacetoxo)ethyl] sulfide **3**.

6-Hydroxy-5,5-dimethyl-6-phenyl-1-oxa-4-thiacyclooctan-8-one **2b**. Mp 98–99 °C (Found: C, 63.10; H, 6.92. C $_{14}$ H $_{18}$ O $_3$ S requires C, 63.13; H, 6.81%);  $\nu_{\text{max}}$ (KBr)/cm $^{-1}$  3490 and 1725;

$\delta_{\text{H}}$  1.03 (3H, s, CH<sub>3</sub>), 1.64 (3H, s, CH<sub>3</sub>), 2.44 (1H, d,  $J$  11.8, COCHH), 2.75 (1H, dd,  $J$  3.1 and 15.4, SCHH), 3.33 (1H, ddd,  $J$  4.4, 11.6 and 15.4, SCHH) 3.46 (1H, d,  $J$  11.8, COCHH), 4.19 (1H, dd,  $J$  4.4 and 11.0, OCHH), 4.23 (1H, s, OH), 4.92 (1H, ddd,  $J$  3.1, 11.6 and 11.0, OCHH) and 7.2–7.6 (5H, m, ArH);  $\delta_{\text{C}}$  23.6 (q), 29.6 (q), 34.8 (t), 44.8 (t), 56.7 (s), 66.5 (t), 83.5 (s), 126.2 (d), 127.3 (d, 2C), 127.7 (d, 2C), 142.5 (s) and 174.2 (s).

6-Hydroxy-5-methyl-6-phenyl-1-oxa-4-thiacyclooctan-8-ones **2c** and **2c'**. These thia lactones could not be separated. The yields of **2c** (29%) and **2c'** (26%) were determined on the basis of <sup>1</sup>H NMR spectral measurements. Mp 107.0–109.0 °C (Found: C, 62.05; H, 6.40. C<sub>13</sub>H<sub>16</sub>O<sub>3</sub>S requires C, 61.88; H, 6.39%);  $\nu_{\text{max}}$ (KBr)/cm<sup>-1</sup> 3470, 1730 and 1700sh; **2c**  $\delta_{\text{H}}$  0.96 (3H, d,  $J$  7.2, CH<sub>3</sub>), 2.59 (2H, ABq,  $J$  18.5 and 11.9, COCH<sub>2</sub>), 2.5–3.7 (3H, m, CHCH<sub>3</sub> and SCH<sub>2</sub>), 4.14 (1H, s, OH), 4.24 (1H, dd,  $J$  7.5 and 3.1, OCHH) 5.01 (1H, ddd,  $J$  4.0, 7.5 and 10.1, OCHH) and 7.2–7.5 (5H, m, ArH); **2c'**  $\delta_{\text{H}}$  1.29 (3H, d,  $J$  7.2, CH<sub>3</sub>), 2.59 (2H, ABq,  $J$  18.5 and 11.9, COCH<sub>2</sub>), 2.5–3.7 (3H, m, CHCH<sub>3</sub> and SCH<sub>2</sub>), 4.14 (1H, s, OH), 4.24 (1H, dd,  $J$  7.5 and 3.1, OCHH), 4.87 (1H, ddd,  $J$  4.0, 7.5 and 10.1, OCHH) and 7.2–7.5 (5H, m, ArH).

6-Hydroxy-6-phenyl-1-oxa-4-thiacyclooctan-8-one **2d**. Mp 135–135.5 °C (Found: C, 60.57; H, 5.92. C<sub>12</sub>H<sub>14</sub>O<sub>3</sub>S requires C, 60.48; H, 5.92%);  $\nu_{\text{max}}$ (KBr)/cm<sup>-1</sup> 3540 and 1750;  $\delta_{\text{H}}$  2.56 (1H, d,  $J$  11.7, COCHH), 2.82 (1H, dd,  $J$  14.7 and 2.9, 6-CHH), 2.97 (1H, d,  $J$  11.7, COCHH), 3.19 (1H, ddd,  $J$  14.7, 11.8 and 4.2, 6-CHH), 3.21 (1H, d,  $J$  15.1, 4-CH) 3.28 (1H, d,  $J$  15.1, 4-CHH), 3.93 (1H, s, OH), 4.23 (1H, dd,  $J$  11.4 and 4.2, OCHH), 4.99 (1H, ddd,  $J$  11.8, 11.4 and 2.9, OCHH) and 7.3–7.5 (5H, m, ArH).

#### Quantum yield determination

The benzoylacetate **1a** was dissolved in acetonitrile (*ca.* 0.05 mol dm<sup>-3</sup>) and the solution placed in 15 × 150-mm Pyrex culture tubes. In quenching experiments, each aliquot of solution also contained an appropriate concentration of 2,5-dimethylhexa-2,4-diene. The tubes were degassed by three freeze-pump-thaw cycles and then sealed. Irradiation was performed on a 'merry-go-round' apparatus with an Ushio 450-W high-pressure mercury lamp. The potassium chromate filter solution was used for isolation of the 313 nm line.<sup>38</sup> After the irradiation, an acetonitrile solution containing a known amount of phenanthrene, as a calibrant, was added to the solution. Analyses of the starting ester and products were performed using a Gasukuro Kogyo 570B high-pressure liquid chromatograph with a Model 511 single-wave UV detector (254 nm). An Inertsil ODS-2 column (4.6 × 150 mm) was used, with acetonitrile–water (*v/v* = 65:35) being used as the mobile phase (8 cm<sup>3</sup> min<sup>-1</sup>). Valerophenone was used as an actinometer.<sup>37</sup>

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