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Syntheses and regiochemistry of enol addition to 9-phenyl-9*H*-xanthen-9-ol

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Abstract

Regioselective C–C bond formation of 9-phenyl-9*H*-xanthen-9-ol **1** with various enolizable ketones **I–X** in an acidic (HBr) medium, obtained by the reaction of 1,1′-(ethane-1,2-diyl)dipyridinium bistribromide (EDPBT) with ketone is observed. Except for ketone, 4-methyl-pentan-2-one **VII** in all other cases examined the attack to xanthenyl carbocation is from the thermodynamically stable enolizable side of the unsymmetrical ketones. In the case of 3-methyl-butan-2-one **VIII** the equilibrium is in favor of the more stable enolizable ketone, which has large steric factor, hence no reaction was observed during its addition to alcohol **1**.

1. Introduction

Xanthene derivatives are useful pharmaceuticals such as muscarinic receptor antagonist,[1a] cancer chemotherapy,[1b] trypanothione reductase inhibitor,[1c] chemosensitizers against chloroquine-resistant *Plasmodium falciparum*,[1d] nonpeptidic inhibitors,[1e] mGluR1 enhancer,[1f,g] and CCR1 antagonist.[1h,i] They are also useful as dyes,[2a,b] photosensitizers,[2c–e] ligand for asymmetric catalysis[3] and have the propensity to form inclusion compounds with various aromatic compounds and form self assembled superstructures.[4] Thus, syntheses of xanthene derivatives are of immense interest. Various multi carbon homologations **1a–1j** of 9-phenyl-9*H*-xanthen-9-ol **1** were obtained through a C–C bond formation by reacting it with various enolizable ketones in an acidic medium. Here we report the syntheses of various enol additions to xanthene. In addition to their syntheses we were interested in factors responsible for the regiochemistry of various addition products.

Tetrabutylammonium tribromide in an organic medium is an excellent source of anhydrous HBr, which has been utilized for various important organic transformations in our laboratory.[5] Recently we have developed 1,2-dipyridiniumditribromide-ethane (DPTBE), which is found to be superior to all known organicammonium tribromides.[6] This compound is renamed as 1,1′-(ethane-1,2-diyl)dipyridinium bistribromide (EDPBT) and is an excellent catalyst for acylation of alcohols using acetic anhydrides and reagent for the formation of thiazolylidene derivatives and 1,4-dithiins.[7]

2. Results and discussion

In an attempt to acetylate 9-phenyl-9*H*-xanthen-9-ol **1** employing acetic anhydride in acetone and 1,1′-(ethane-1,2-diyl)-dipyridinium bistribromide (EDPBT) as catalyst[7a] gave no trace of acetylated product, rather an unusual three-carbon homologation **1a** was observed (Table 1, Scheme 1). Being buoyant by this result we focused our attention to synthesize various xanthene analogues. Reaction of xanthydrol, thioxanthydrol, and 9,10-dihydro-10-methyl-9-acrydenol with *N*-vinylacetamide or ethylvinylether as acetaldehyde anion equivalents has been reported.[8] Formation of the product 1-(9-phenyl-9*H*-xanthen-9-yl)-propan-2-one **1a** could be explained through a carbocation intermediate, obtained by the initial reaction of tertiary alcohol **1** with HBr generated by the reaction of EDPBT with acetone, which undergoes nucleophilic attack by the enolized acetone (Scheme 1). In this reaction acetic anhydride acts as a dehydrating agent by reacting

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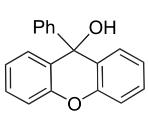
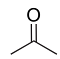
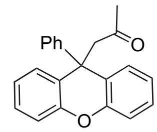
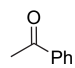
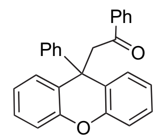
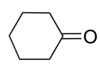
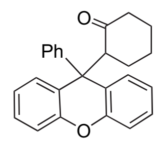
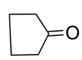
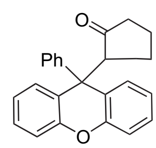
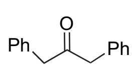
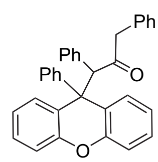
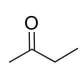
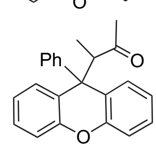
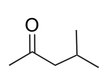
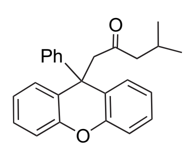
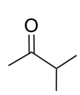
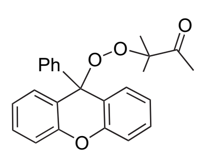
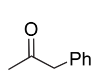
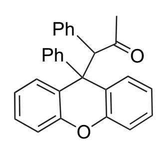
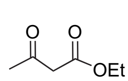
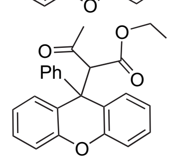
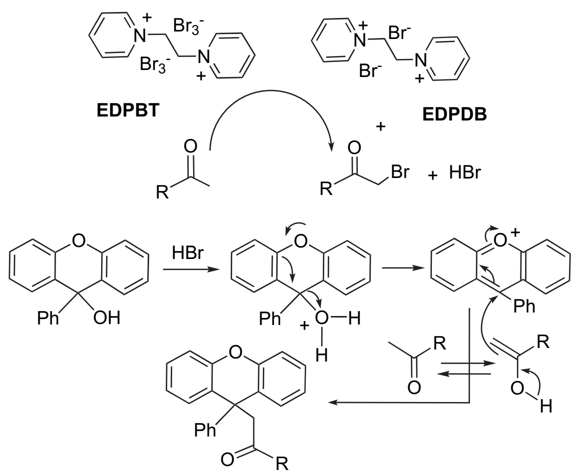
Table 1
C–C bond formation at the tertiary carbon of 9-phenyl-9*H*-xanthen-9-ol with ketones[a]

Substrate	Ketone	Product[b]	Time (h)	Yield[c] (%)
 (**1**)	 (**I**)	 (**1a**)	12	87
	 (**II**)	 (**1b**)	24	81
	 (**III**)	 (**1c**)	18	80
	 (**IV**)	 (**1d**)	18	77
	 (**V**)	 (**1e**)	24	72
	 (**VI**)	 (**1f**)	24	79
	 (**VII**)	 (**1g**)	24	60
	 (**VIII**)	 (**1h**)[d]	12	35
	 (**IX**)	 (**1i**)	24	78
	 (**X**)	 (**1j**)	12	75

[a] Reactions were monitored by TLC.
[b] Products were characterized by IR, ^{1}H, ^{13}C NMR.
[c] Yields of the isolated product.
[d] Obtained due to the contamination of hydroperoxide.

with the water generated in the reaction medium to yield acetic acid, which further facilitates the reaction by making the medium further acidic.



Scheme 1. Proposed mechanism of C–C bond formation.

The scope of the reaction was extended further by replacing acetone with other enolizable ketones such as acetophenone **II**, which gave **1b** as the exclusive product (Table 1). Cyclic aliphatic ketones such as cyclohexanone **III** and cyclopentanone **IV** gave the corresponding addition products **1c** and **1d**, respectively, in good yields in a relatively shorter reaction time.

Other symmetrical ketone, 1,3-diphenyl-propan-2-one **V** also gave the expected product **1e** (Table 1).

In the case of ketone **II** the enolization is possible only from one side and in all other cases (**III–V**) due to their symmetrical nature the same enol is formed whether enolization is from the left side or from the right.

Reaction of an unsymmetrical ketone such as butan-2-one **VI**, under a similar condition gave 3-(9-phenyl-9*H*-xanthen-9-yl)-butan-2-one **1f** as the sole product, which was obtained through the attack of methylene carbon rather than methyl carbon. In spite of the steric hindrance, the regioselectivity of the product is governed by the formation of a stable enol, giving 3-(9-phenyl-9*H*-xanthen-9-yl)-butan-2-one **1f** exclusively. This observation is, however, inconsistent with the observation made by others, where the product obtained is by the attack of the methyl carbon of butan-2-one.[9] The difference in the observed regiochemistry may be due to difference in the xanthene system, 1,8-dimethoxy-9*H*-xanthene-9-ol instead of 9-phenyl-9*H*-xanthen-9-ol **1**. Interestingly, kinetically controlled enol addition product 4-methyl-1-(9-phenyl-9*H*-xanthen-9-yl)-pentan-2-one **1g** was observed when unsymmetrical and one side sterically hindered ketone, 4-methyl-pentan-2-one **VII**, was used (Table 1). In this case even though enolization is expected to favor toward a thermodynamically stable form, the attack is possible only from the less hindered enolizable side, due to the large steric hindrance caused by the adjacent isopropyl group (Fig. 1). The single crystal XRD structure of the product **1g** is reported, which exhibits interesting C–H···O type hydrogen bonding network.[4c]

However, neither of the above observations has been manifested during the reaction of 3-methyl-butan-2-one **VIII** with **1** under an identical condition. X-ray crystallographic analysis of product showed a molecular oxygen insertion (Fig. 2) from the more hindered side of the enolized ketone **VIII** giving the

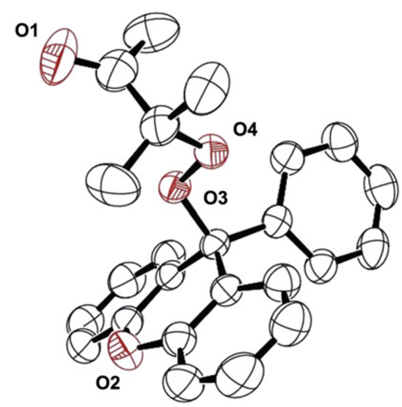


Figure 2. An ORTEP view with the atomic numbering scheme of **1h**.

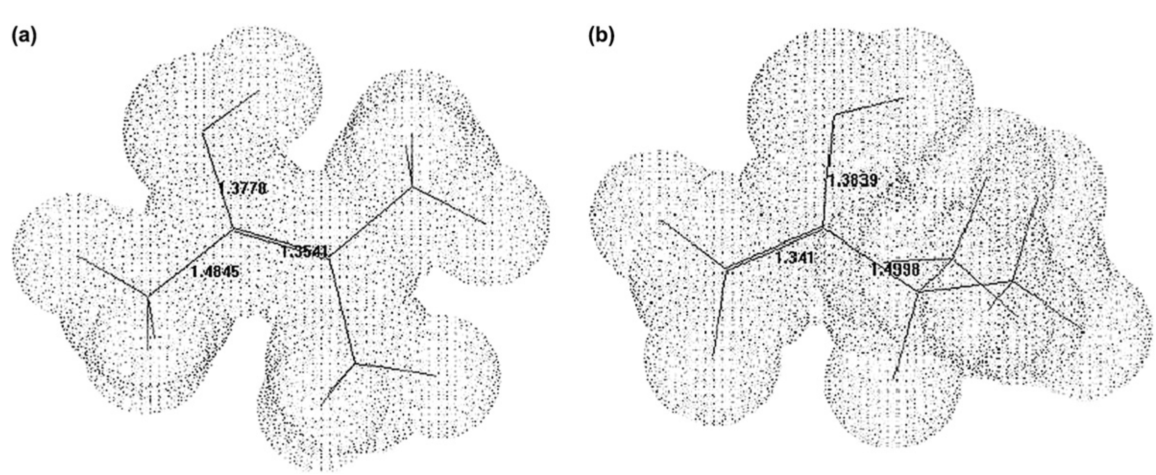


Figure 1. View showing the steric environment in ketone **VII**. (a) Enolization towards more substituted side; (b) enolization towards less substituted side.

molecular oxygen inserted product **1h**. This can be explained only if the reaction goes via a radical mechanism. No signal for the radical could be detected when reaction was continuously monitored by EPR spectrometer. It was found that formation of the product **1h** was due to the contamination of corresponding hydroperoxide obtained by a radical auto-oxidation at the tertiary carbon of **VIII**. When reaction was performed with a freshly distilled ketone under a nitrogen atmosphere no reaction occurred even after three days. This is because enolization is expected to favor exclusively[10] toward the more substituted enol, which is sterically unfavorable for the attack on xanthenyl carbocation. No kinetically controlled enol addition product was observed due to the great stability of the highly substituted enol in **VIII**.[10]

Two other unsymmetrical ketones viz. 1-phenyl-propan-2-one **IX** and ethyl acetoacetate **X** were reacted with **1**, giving the products **1i** and **1j**, respectively (Table 1). The regiochemistry of the product obtained corresponds to the attack by the thermodynamically stable enol (Table 1). Ketone 1-phenyl-propan-2-one **IX** gives exclusive thermodynamically controlled product **1i** whereas ketone 4-methyl-pentan-2-one **VII** yielded kinetically controlled product **1g**. In the case of ketone **IX** the steric factor exhibited by a flat phenyl ring is presumably much less compared to **VII** having an isopropyl group with three tetrahedral carbon atoms, thereby giving entirely kinetically controlled product.

3. Conclusion

In conclusion, we have achieved multi carbon homologations of xanthene **1** through a C–C bond formation by various enolizable ketones in an acidic medium. In most cases the regiochemistry of the product is governed by the attack of thermodynamically stable enol. But when the steric factor dominates as is the case with 4-methyl-pentan-2-one **VII** product obtained is via a kinetically controlled enol attack. With further increase in steric hindrance as in 3-methyl-butan-2-one **VIII** no reaction takes place.

4. Experimental

4.1. General

All the reagents were commercial grade and purified according to the established procedures. Organic extracts were dried over anhydrous sodium sulfate. Solvents were removed in a rotary evaporator under reduced pressure. Silica gel (60–120 mesh size) was used for the column chromatography. Reactions were monitored by TLC on silica gel 60 GF254 (0.25 mm). NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 with tetramethylsilane as the internal standard for ^{1}H NMR (400 MHz) and $CDCl_3$ or DMSO-d_6 solvents as internal standard for ^{13}C NMR (100 MHz). IR spectra were recorded in KBr or neat. GC–MS were recorded using a capillary column (30×0.25 mm×0.25 mμ) in EI mode. HRMS spectra were recorded in WATERS LC-MS/MS System, Q-Tof Premier™. Crystal Data were collected with Bruker Smart Apex-II CCD diffractometer using graphite monochromated Mo Kα radiation (λ=0.71073 Å) at 298 K. Cell parameters were retrieved using SMART software and refined with SAINT on all observed reflections. Data reduction was performed with the SAINT software and corrected for Lorentz and polarization effects. Absorption corrections were applied with the program SADABS. The structure was solved by direct methods implemented in SHELX-97 program and refined by full-matrix least-squares methods on F^2. All non-hydrogen atomic positions were located in difference Fourier maps and refined anisotropically. The hydrogen atoms were placed in their geometrically generated positions. All the colorless crystals were isolated in rectangular shape from ethyl acetate and hexane mixture (8:2) at room temperature.

4.2. General procedure

To 9-phenyl-9*H*-xanthen-9-ol (1.37 g, 5 mmol) in ketone (5 mL) were added EDPBT (166 mg, 0.25 mmol) and acetic anhydride (945 μL, 10 mmol). After the addition of the EDPBT the color of the reaction mixture turned to red, intensity of which increased after some time. Progress of the reaction was monitored by TLC. Toward the completion of the reaction the color intensity faded. The reaction mixture was concentrated and admixed with ethyl acetate [product **1d** was extracted with CH_2Cl_2 (2×25 mL)]. Organic layer was washed subsequently with saturated sodium bicarbonate solution (2×5 mL) and water (2×5 mL). The product was dried over anhydrous Na_2SO_4 and crystallized from a mixture of ethyl acetate/hexane (8:2) to yield the desired product. In the case of **1d** it was separated over neutral alumina column using ethyl acetate/hexane as the eluent.

4.3. Spectral data

4.3.1. 1-(9-Phenyl-9H-xanthen-9-yl)-propan-2-one (*1a*)

White solid, mp 139–140 °C. R_f=0.47 (EtOAc/hexane 2:98). IR (KBr): 3058, 3027, 2960, 2930, 1711, 1603, 1568, 1481, 1450, 1301, 1255, 1158, 1122, 1030, 892, 753, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.72 (s, 3H), 3.51 (s, 2H), 6.81 (d, 2H, J=7.6 Hz), 6.89 (t, 3H, J=7.6 Hz), 7.07 (d, 2H, J=8 Hz), 7.15 (t, 3H, J=7.6 Hz), 7.25–7.27 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.3, 44.7, 55.8, 116.1, 122.9, 126.2, 126.5, 127.8, 128.0, 128.8, 148.9, 150.4, 205.3. HRMS (ESI): $(MH)^+$, found: 315.3906, $C_{22}H_{18}O_2$ requires: 315.3909.

4.3.2. 1-Phenyl-2-(9-phenyl-9H-xanthen-9-yl)-ethanone (*1b*)

White solid, mp 186–188 °C. R_f=0.65 (EtOAc/hexane 2:98). IR (KBr): 3065, 3038, 2951, 2891, 1685, 1598, 1571, 1484, 1451, 1352, 1310, 1257, 1222, 1181, 1126, 1098, 1040, 974, 889, 774, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.12 (s, 2H), 6.84 (m, 3H), 7.09 (m, 4H), 7.31 (m, 9H), 7.70 (d, 2H, J=7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.3, 50.6, 116.4, 123.1, 126.6, 127.5, 127.9, 128.1, 128.4, 128.6, 129.0, 132.8, 137.6, 149.3, 151.2, 196.7. HRMS (ESI): $(MH)^+$, found: 377.4613, $C_{27}H_{20}O_2$ requires: 377.4617.

*4.3.3. rac-2-(9-Phenyl-9H-xanthen-9-yl)-cyclohexanone (**1c**)*

White solid, mp 181–183 °C. R_f=0.51 (EtOAc/hexane 2:98). IR (KBr): 3066, 3031, 2930, 2857, 1711, 1596, 1571, 1475, 1440, 1308, 1276, 1240, 1124, 1095, 1035, 876, 758, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.54 (m, 3H), 1.80 (m, 1H), 1.98 (m, 1H), 2.15 (m, 1H), 2.23 (m, 1H), 2.33 (m, 1H), 3.48 (dd, 1H, J_1=5 Hz, J_2=12.8 Hz), 6.68 (d, 1H, J=8 Hz), 6.86 (m, 2H), 7.05 (m, 2H), 7.15 (m, 5H), 7.23 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.2, 28.4, 30.8, 44.3, 49.4, 61.4, 115.7, 116.0, 122.5, 126.0, 127.2, 127.7, 127.8, 127.9, 129.7, 130.1, 132.0, 147.1, 151.5, 151.8, 209.4. HRMS (ESI): $(MH)^+$, found: 355.4550, $C_{25}H_{22}O_2$ requires: 355.4555.

*4.3.4. rac-2-(9-Phenyl-9H-xanthen-9-yl)-cyclopentanone (**1d**)*

White solid, mp 146–148 °C. R_f=0.65 (EtOAc/hexane 2:98). IR (KBr): 3056, 3031, 2964, 2878, 1736, 1598, 1572, 1477, 1444, 1403, 1305, 1239, 1153, 1097, 1039, 889, 754, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.66 (m, 4H), 2.18 (br s, 2H), 3.36 (t, 1H, J=9.2 Hz), 6.67 (d, 1H, J=8 Hz), 6.87 (t, 2H, J=8 Hz), 6.93 (d, 1H, J=8 Hz), 7.09 (m, 3H), 7.20 (m, 2H), 7.27 (t, 2H, J=8 Hz), 7.37 (d, 2H, J=8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.3, 27.6, 41.1, 49.9, 58.4, 115.8, 116.1, 123.0, 123.3, 126.3, 127.5, 127.7, 128.3, 129.6, 130.5, 131.8, 146.5, 150.1, 151.9, 216.1. HRMS (ESI): $(MH)^+$, found: 341.4284, $C_{24}H_{20}O_2$ requires: 341.4287.

*4.3.5. 1,3-Diphenyl-1-(9-phenyl-9H-xanthen-9-yl)-propan-2-one (**1e**)*

White solid, mp 141–143 °C. R_f=0.69 (EtOAc/hexane 2:98). IR (KBr): 3060, 3030, 2884, 1722, 1600, 1573, 1477, 1444, 1311, 1280, 1245, 1098, 1037, 753, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.46 (d, 1H, J=14.8 Hz), 3.59 (d, 1H, J=14.8 Hz), 4.69 (s, 1H), 6.17 (d, 2H, J=7.2 Hz), 6.57 (d, 1H, J=8 Hz), 6.69 (dd, 3H, J_1=8 Hz, J_2=15.6 Hz), 6.86 (t, 2H, J=7.2 Hz), 6.97 (t, 2H, J=8 Hz), 7.02–7.39 (m, 12H), 7.62 (d, 1H, J=8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 50.5, 67.7, 115.3, 115.7, 121.8, 122.8, 126.3, 127.1, 127.6, 127.8, 128.0, 128.3, 128.5, 128.7, 129.4, 129.5, 129.7, 130.0, 131.1, 133.7, 134.4, 146.4, 151.2, 152.9, 204.8. HRMS (ESI): $(MH)^+$, found: 467.5857, $C_{34}H_{26}O_2$ requires: 467.5861.

*4.3.6. rac-3-(9-Phenyl-9H-xanthen-9-yl)-butan-2-one (**1f**)*

White solid, mp 142–143 °C. R_f=0.48 (EtOAc/hexane 2:98). IR (KBr): 3071, 3033, 2929, 2870, 1701, 1603, 1571, 1484, 1441, 1363, 1305, 1278, 1245, 1183, 1045, 938, 902, 871, 761, 717 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14 (d, 3H, J=6.8 Hz), 1.53 (s, 3H), 3.80 (q, 1H), 6.72 (dd, 1H, J=1.6, 7.6 Hz), 6.78 (dd, 1H, J=1.6, 8 Hz), 6.98 (m, 2H), 7.06 (m, 1H), 7.14 (m, 3H), 7.31 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.6, 31.5, 50.1, 55.2, 116.1, 116.4, 116.7, 122.1, 123.2, 123.3, 124.3, 126.5, 126.6, 127.6, 128.0, 128.2, 128.3, 128.5, 128.6, 129.2, 130.0, 130.2, 131.7, 147.0, 150.5, 152.3, 210.5. HRMS (ESI): $(MH)^+$, found: 329.4171, $C_{23}H_{20}O_2$ requires: 329.4177.

*4.3.7. 4-Methyl-1-(9-phenyl-9H-xanthen-9-yl)-pentan-2-one (**1g**)*

White solid, mp 194–196 °C. R_f=0.57 (EtOAc/hexane 2:98). IR (KBr): 3050, 3037, 2966, 2879, 1711, 1603, 1578, 1486, 1450, 1404, 1368, 1312, 1260, 1235, 1126, 1062, 1040, 890, 750, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.63 (d, 6H, J=5.2 Hz), 1.56 (br s, 1H), 1.85 (d, 2H), 3.46 (s, 2H), 6.78 (d, 2H, J=8 Hz), 6.88 (t, 3H, J=7.6 Hz), 7.06 (d, 2H, J=8 Hz), 7.14 (m, 4H), 7.26 (d, 2H, J=4.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.4, 24.2, 44.8, 53.2, 55.1, 116.1, 122.8, 126.2, 126.7, 127.7, 128.0, 128.2, 128.8, 149.1, 150.5, 207.0. HRMS (ESI): $(MH)^+$, found: 357.4709, $C_{25}H_{24}O_2$ requires: 357.4713.

*4.3.8. 3-Methyl-3-(9-phenyl-9H-xanthen-9-yl-peroxy)-butan-2-one (**1h**)*

White solid, mp 125–128 °C. R_f=0.55 (EtOAc/hexane 2:98). IR (KBr): 3054, 3036, 2996, 2983, 2927, 1710, 1601, 1573, 1476, 1449, 1352, 1319, 1293, 1251, 1219, 1164, 1156, 979, 935, 878, 765, 755, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (s, 6H), 2.05 (s, 3H), 6.99 (t, 2H, J=6.8 Hz), 7.07 (d, 2H, J=8 Hz), 7.20 (t, 3H, J=8.4 Hz), 7.31 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 24.1, 86.9, 116.0, 122.4, 122.6, 127.1, 127.5, 127.6, 129.4, 130.8, 143.7, 151.7, 210.8. HRMS (ESI): $(MNa)^+$, found: 397.4255, $C_{24}H_{24}O_4Na$ requires: 397.4252.

*4.3.9. rac-1-Phenyl-1-(9-phenyl-9H-xanthen-9-yl)-propan-2-one (**1i**)*

White solid, mp 185–188 °C. R_f=0.67 (EtOAc/hexane 2:98). IR (KBr): 3076, 3054, 3021, 2884, 1711, 1599, 1572, 1476, 1443, 1347, 1319, 1305, 1281, 1242, 1149, 1122, 1031, 880, 864, 770, 749, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.05 (s, 3H), 4.60 (s, 1H), 6.17 (d, 2H, J=7.2 Hz), 6.67 (d, 2H, J=8 Hz), 6.73 (d, 1H, J=8 Hz), 6.88 (t, 1H, J=8 Hz), 6.95 (t, 2H, J=7.6 Hz), 7.05 (m, 2H), 7.18 (m, 2H), 7.28 (m, 5H), 7.64 (d, 1H, J=8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.9, 52.7, 68.8, 115.0, 115.5, 121.6, 122.6, 123.4, 126.2, 127.4, 127.5, 127.6, 127.8, 128.1, 129.1, 129.8, 130.5, 133.6, 134.2, 146.4, 150.9, 152.7, 205.4. HRMS (ESI): $(MH)^+$, found: 391.4878, $C_{28}H_{22}O_2$ requires: 391.4885.

*4.3.10. rac-3-Oxo-2-(9-phenyl-9H-xanthen-9-yl)-butyric acid ethyl ester (**1j**)*

White solid, mp 125–128 °C. R_f=0.35 (EtOAc/hexane 2:98). IR (KBr): 3056, 3033, 2992, 2940, 1726, 1717, 1602, 1574, 1481, 1446, 1357, 1308, 1284, 1260, 1217, 1042, 1016, 906, 876, 763, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.08 (t, 3H, J=7.8 Hz), 1.80 (s, 3H), 3.97 (dq, 2H J_1=7.2 Hz, J_2=1.2 Hz), 4.61 (s, 1H), 6.86 (d, 1H, J=7.6 Hz), 6.92 (q, 2H, J=8 Hz), 7.01 (d, 1H, J=8 Hz), 7.10 (d, 2H, J=8 Hz), 7.21 (m, 3H), 7.28 (t, 2H, J=6.4 Hz), 7.36 (d, 2H, J=6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$):

δ 13.8, 31.2, 61.4, 67.8, 115.8, 116.2, 122.4, 122.8, 125.7, 126.4, 127.6, 128.4, 129.6, 130.6, 131.8, 151.2, 151.3, 167.6, 201.2. HRMS (ESI): $(MH)^+$, found: 385.4281, $C_{25}H_{20}O_4$ requires: 385.4277.

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