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ARTICLE

## Comparison of Riboflavin-Derived Flavinium Salts Applied to Catalytic H<sub>2</sub>O<sub>2</sub> Oxidations

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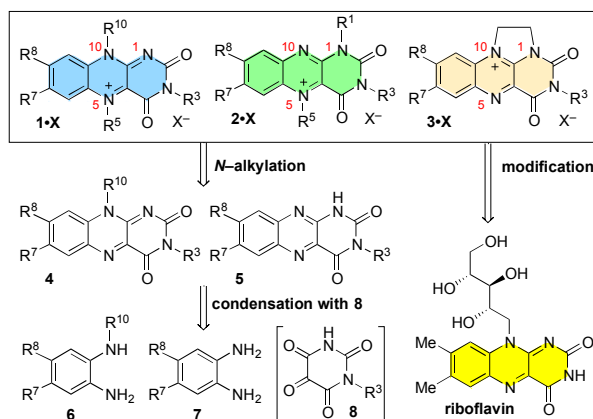
A series of flavinium salts, 5-ethylisoalloxazinium, 5-ethylalloxazinium, and 1,10-ethylene-bridged alloxazinium triflates, were prepared from commercially available riboflavin. This study presents a comparison between their optical and redox properties, and their catalytic activity in H<sub>2</sub>O<sub>2</sub> oxidations of sulfide, tertiary amine, and cyclobutanone. Reflecting the difference between the  $\pi$ -conjugated ring structures, the flavinium salts displayed very different redox properties, with reduction potentials in the order of: 5-ethylisoalloxazinium > 5-ethylalloxazinium > 1,10-ethylene-bridged alloxazinium. A comparison of their catalytic activity revealed that 5-ethylisoalloxazinium triflate specifically oxidises sulfide and cyclobutanone, and 5-ethylalloxazinium triflate smoothly oxidises tertiary amine. 1,10-Bridged alloxazinium triflate, which can be readily obtained from riboflavin in large quantities, showed moderate catalytic activity for the H<sub>2</sub>O<sub>2</sub> oxidation of sulfide and cyclobutanone.

### Introduction

Flavinium salts have previously been developed by mimicking the functions of flavin-dependent monooxygenases.<sup>1</sup> Recently, flavinium salts have drawn much attention for their unique biomimetic organocatalytic properties, which promote various metal-free oxidative transformations.<sup>2</sup> The flavinium catalysts generally require O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub> as easily available, inexpensive, and minimally polluting terminal oxidants to carry out chemoselective oxidative reactions under mild conditions, such as the oxidation of sulfides,<sup>3,4</sup> amines,<sup>5,6</sup> ketones,<sup>7</sup> aldehydes,<sup>8,9</sup> boronic acids,<sup>10</sup> thiols,<sup>4a</sup> metal complex,<sup>11</sup> and other functional groups<sup>12,13</sup>, as well as asymmetric oxidations.<sup>14</sup> In addition, multiple catalytic systems based on flavinium catalysis have been explored gradually by combining metals,<sup>15</sup> biocatalysts,<sup>16</sup> and organocatalysts.<sup>17</sup> Therefore, the flavinium-catalysed system has emerged as a promising tool for environmentally friendly transformations, and may fulfil the increasing demand for green sustainable chemistry.

Flavinium catalysts are commonly classified into three

types: 5-alkylisoalloxaziniums (**1**), 5-alkylalloxaziniums (**2**), and 1,10-bridged alloxaziniums (**3**), based on the difference between their conjugated systems (Fig. 1).<sup>2e,f</sup> Because flavinium cations (**1–3**) can be prepared by *N*-alkylation of neutral flavins (**4** and **5**), a series of artificial flavins has been synthesized through a flavin ring formation reaction mainly by using a condensation reaction between 1,2-diaminobenzenes (**6** and **7**) and alloxanes (**8**) (Fig. 1).<sup>3c,4b,8a,14b,f,h,18,19</sup>



**Fig. 1** Three types of flavinium salts; 5-alkylisoalloxaziniums (**1·X**), 5-alkylalloxaziniums (**2·X**), and 1,10-bridged alloxaziniums (**3·X**).

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<sup>‡</sup>Electronic Supplementary Information (ESI) available: Cyclic voltammograms and <sup>1</sup>H and <sup>13</sup>C NMR charts. See DOI: 10.1039/x0xx00000x

Naturally occurring riboflavin (vitamin B<sub>2</sub>), one of the most important bioactive compounds, is synthesised by microbial fermentation, and thus is obtained commercially with low-cost. Because of its abundance and because the use of riboflavin can avoid the multiple synthetic manipulations for the synthesis of the flavin ring skeleton, some chemists have attempted to synthesise semi-synthetic flavinium catalysts by the modification of riboflavin. However, very few examples of riboflavin-derived 7,8-dimethylflavinium catalysts have been reported.<sup>3k,m,7b,13b,d,e</sup> In particular, 1,10-bridged 7,8-dimethylalloxazinium catalysts have not previously been developed except for in our recent reports,<sup>17a</sup> although analogous 1,10-bridged alloxaziniums have recently been applied to various reactions.<sup>3g,h,n,o,6,8b,13c,14h,16,17a,18a,20</sup>

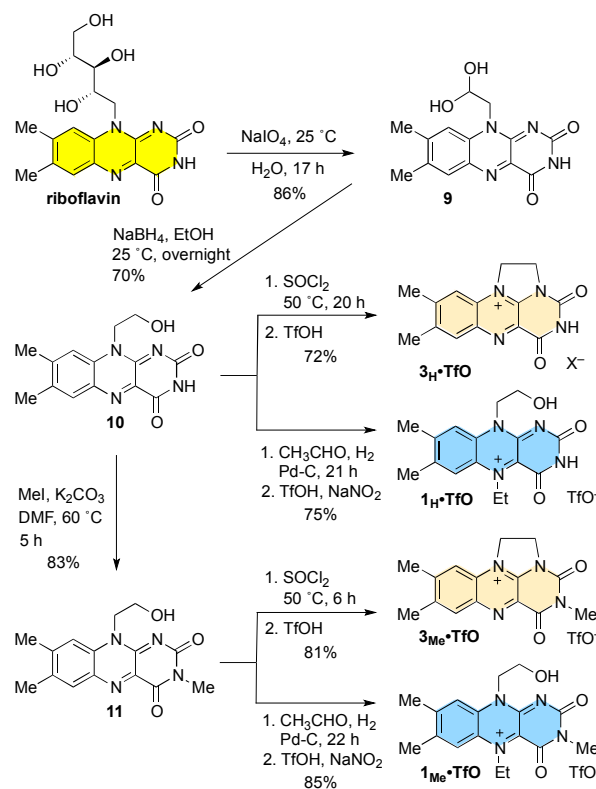
In this study, three types of 7,8-dimethylflavinium catalysts were synthesised from naturally occurring riboflavin: 5-ethyl-7,8-dimethylisoalloxazinium (**1**·TfO), 5-ethylalloxazinium (**2**·TfO), and 1,10-ethylenealloxazinium triflates (**3**·TfO). Their optical and redox properties were investigated, and their catalytic activity was analysed in several oxidations using H<sub>2</sub>O<sub>2</sub> as a terminal oxidant to compare the three types of flavinium salts. The results are expected to provide insight into the possibility and application of riboflavin-derived flavinium catalysts. Despite the obvious synthetic advantage of the 7,8-dimethylflavinium skeleton, little attention has been given to the systematic study on the property differences and catalytic activity between **3** and **1/2**, although the difference between **1** and **2** has been well examined previously.<sup>2e,3j</sup>

## Results and discussion

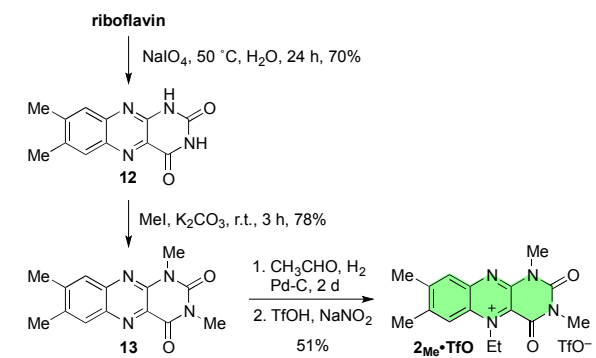
### Synthesis of riboflavin-derived flavinium salts

As shown in Schemes 1 and 2, a series of flavinium triflates (**1**–**3**·TfO) was synthesized from riboflavin. Through oxidation with NaIO<sub>4</sub> at 25 °C followed by the reduction of **9** with NaBH<sub>4</sub>, 10-(2-hydroxyethyl)-7,8-dimethylisoalloxazine (**10**) can be readily in large quantities (>10 g) obtained from riboflavin.<sup>4d,21</sup> Due to the ease of synthesis and the possibility to obtain **10** in large quantities, it is employed as a key synthetic intermediate of flavinium salts (Scheme 1). Intramolecular cyclisation of **10** with SOCl<sub>2</sub> and subsequent treatment with TfOH afforded 1,10-ethylene-bridged alloxazinium triflate (**3**<sub>H</sub>·TfO)<sup>17a</sup> in 72% yield. Because of facile intramolecular cyclisation, **3**<sub>H</sub>·TfO was readily synthesised and obtained on the gram scale. Reductive N<sup>5</sup>-ethylation of **10** with CH<sub>3</sub>CHO, followed by oxidation with NaNO<sub>2</sub> and TfOH, gave 5-ethylisoalloxazinium triflate (**1**<sub>H</sub>·TfO) in 75% yield. To investigate the substitution effect of the N<sup>3</sup>-position, 3-methylated 1,10-ethylene-bridged alloxazinium triflate (**3**<sub>Me</sub>·TfO) and 5-ethylisoalloxazinium triflate (**1**<sub>Me</sub>·TfO)<sup>4d</sup> were synthesised in 81 and 85% yields, respectively, from 10-(2-hydroxyethyl)-3,7,8-trimethylisoalloxazine (**11**), prepared by the methylation of **9** with MeI. Interestingly, when the oxidation of riboflavin with NaIO<sub>4</sub> was carried out at 50

°C, alloxazine (**12**) was obtained in 70% yield (Scheme 2). In contrast, the same oxidation gave **9** in 86% yield at 25 °C (Scheme 1). After N<sup>1</sup>- and N<sup>3</sup>-dimethylation of **12**, reductive N<sup>5</sup>-ethylation of **13** and subsequent oxidation with NaNO<sub>2</sub> and TfOH successfully afforded 5-ethylalloxazinium triflate (**2**<sub>Me</sub>·TfO) in 51% yield. It is noteworthy that 1,10-ethylene-bridged alloxazinium triflates (particularly **3**<sub>H</sub>·TfO) could be synthesised through the most facile synthetic pathway through which upscaling can be readily carried out.



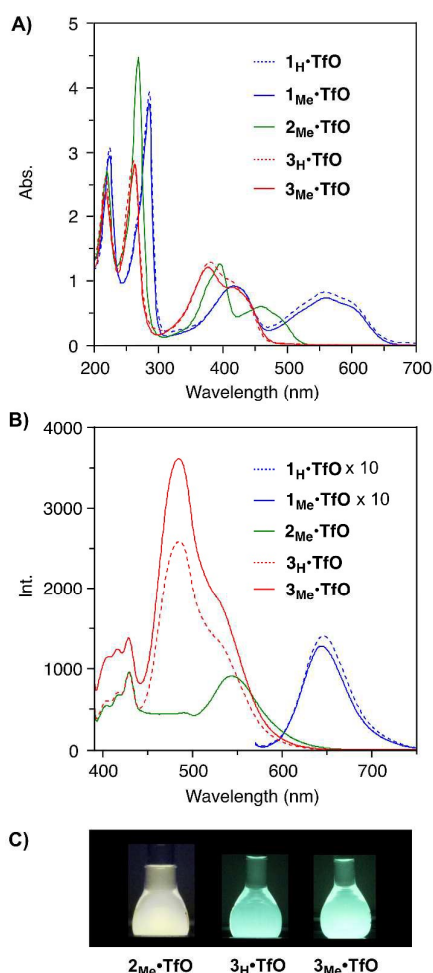
**Scheme 1** Synthesis of 1,10-ethylene-bridged alloxazinium triflates (**3**<sub>H</sub>·TfO and **3**<sub>Me</sub>·TfO) and 5-ethylisoalloxazinium triflates (**1**<sub>H</sub>·TfO and **1**<sub>Me</sub>·TfO) from riboflavin.



**Scheme 2** Synthesis of 5-ethylalloxazinium triflate (**2**<sub>Me</sub>·TfO) from riboflavin.

## Optical properties of flavinium salts

To explore the optical properties of the flavinium salts, their absorption and fluorescence spectra were measured from a CH<sub>3</sub>CN-salt solution (Fig. 2 and Table 1). The isoalloxazinium triflates (**1<sub>H</sub>**·TfO and **1<sub>Me</sub>**·TfO) gave rise to the typical absorption signals centred at around 420 and 560 nm, assigned to the  $\pi$ - $\pi^*$  transitions of the  $\pi$ -conjugated isoalloxazinium ring (Fig. 2A).<sup>22</sup> In comparison with **1<sub>H</sub>**·TfO and **1<sub>Me</sub>**·TfO, **2<sub>Me</sub>**·TfO presented blue-shifted absorption signals at 395 and 460 nm. The  $\pi$ -conjugated system of the isoalloxazinium ring includes its imide moiety, whereas the  $\pi$ -conjugation of the alloxazinium ring does not extend to the imide moiety. Therefore, the



**Fig. 2** (A) Absorption spectra of 0.1 mM **1<sub>H</sub>**·TfO, **1<sub>Me</sub>**·TfO, **2<sub>Me</sub>**·TfO, **3<sub>H</sub>**·TfO, and **3<sub>Me</sub>**·TfO in CH<sub>3</sub>CN measured at 25 °C. (B) Fluorescence spectra of 0.20 μM **1<sub>H</sub>**·TfO, **1<sub>Me</sub>**·TfO, **2<sub>Me</sub>**·TfO, **3<sub>H</sub>**·TfO, and **3<sub>Me</sub>**·TfO in CH<sub>3</sub>CN measured at 25 °C (**1<sub>H</sub>**·TfO and **1<sub>Me</sub>**·TfO:  $\lambda_{\text{Ex}}$  = 560 nm; **2<sub>Me</sub>**·TfO, **3<sub>H</sub>**·TfO, and **3<sub>Me</sub>**·TfO:  $\lambda_{\text{Ex}}$  = 380 nm). (C) Photographs of 0.1 mM **2<sub>Me</sub>**·TfO, **3<sub>H</sub>**·TfO, and **3<sub>Me</sub>**·TfO in CH<sub>3</sub>CN under UV light ( $\lambda_{\text{Ex}}$  = 365 nm)

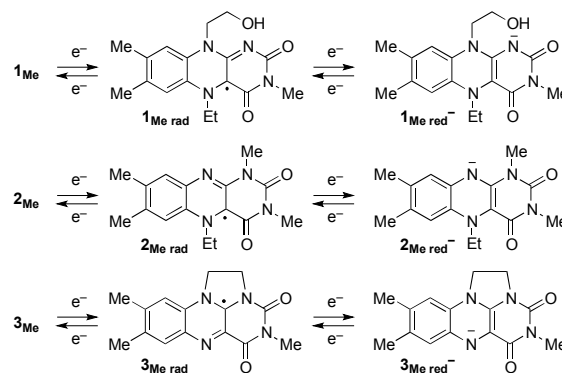
Entry	Flavinium	Absorption	Fluorescence
		$\lambda_{\text{max}}$ (log $\epsilon$ ) <sup>a</sup> , nm	$\lambda_{\text{F,max}}$ <sup>a,b</sup> , nm
1	<b>1<sub>H</sub></b> ·TfO	559 (3.91), 417 (3.96), 286 (4.59), 224 (4.49)	648
2	<b>1<sub>Me</sub></b> ·TfO	560 (3.87), 416 (3.96), 285 (4.58), 224 (4.47)	645
3	<b>2<sub>Me</sub></b> ·TfO	460 (3.78), 395 (4.10), 268 (4.65), 220 (4.44)	545
4	<b>3<sub>H</sub></b> ·TfO	380 (4.11), 261 (4.46), 218 (4.42)	486
5	<b>3<sub>Me</sub></b> ·TfO	376 (4.09), 263 (4.46), 218 (4.38)	485

<sup>a</sup> In CH<sub>3</sub>CN. <sup>b</sup> Excitation wavelength ( $\lambda_{\text{Ex}}$ ) was 560 nm for **1<sub>H</sub>**·TfO and **1<sub>Me</sub>**·TfO, and 380 nm for **2<sub>Me</sub>**·TfO, **3<sub>H</sub>**·TfO, and **3<sub>Me</sub>**·TfO.

relatively narrow conjugated system of **2<sub>Me</sub>**·TfO presumably results in the blue-shift. The absorption spectra of **3<sub>H</sub>**·TfO and **3<sub>Me</sub>**·TfO were not equivalent to that of **2<sub>Me</sub>**·TfO, although they possess the similar alloxazinium ring structure, and the absorption signals were further blue-shifted to around 260 and 380 nm maybe due to the difference of the cation delocalisation within the conjugated ring system. As a result, **1<sub>H</sub>**·TfO and **1<sub>Me</sub>**·TfO were purple, while **2<sub>Me</sub>**·TfO, **3<sub>H</sub>**·TfO, and **3<sub>Me</sub>**·TfO appeared yellow. The CH<sub>3</sub>CN solution of **1<sub>H</sub>**·TfO and **1<sub>Me</sub>**·TfO exhibited very weak fluorescence ( $\lambda_{\text{Fmax}}$  = 648 and 645 nm, respectively) upon excitation at 560 nm (Fig. 2B). In contrast to the isoalloxazinium salts, the alloxazinium salts provided strong fluorescence signals upon excitation at 380 nm; **2<sub>Me</sub>**·TfO showed blue-shifted, yellow fluorescence ( $\lambda_{\text{Fmax}}$  = 545 nm) and **3<sub>H</sub>**·TfO and **3<sub>Me</sub>**·TfO displayed strong yellowish-green fluorescence ( $\lambda_{\text{Fmax}}$  = 486 and 485 nm, respectively) (Fig. 2C).

## Redox property of flavinium salts

To investigate the redox activity, the reduction potentials



**Scheme 3** Redox reactions of flavinium cations.

of the synthesized flavinium salts were determined by cyclic voltammetry (CV) in a solution of CH<sub>3</sub>CN containing Bu<sub>4</sub>NClO<sub>4</sub> (0.1 M); the results are summarised in Table 2. The obtained voltammograms exhibit two reversible reduction peaks, which correspond to the two-electron reduction of flavinium salts (Scheme 3).<sup>4b,22</sup> Among the three *N*<sup>3</sup>-substituted flavinium salts, **1**<sub>Me</sub>·TfO showed the most positive potentials, with reduction potentials (*E*<sub>1</sub> and *E*<sub>2</sub>) of 0.263 and −0.365 V vs SCE, followed in order by **2**<sub>Me</sub>·TfO and **3**<sub>Me</sub>·TfO (Table 2, entries 2, 3, and 5, respectively). The first and second reductions of **3**<sub>Me</sub>·TfO (−0.255 and −1.25 V vs SCE) were largely unfavourable in comparison with those of **1**<sub>Me</sub>·TfO. Therefore, the LUMO orbital of **1**<sub>Me</sub> seems to be stabilized rather than those of **2**<sub>Me</sub> and **3**<sub>Me</sub>, and **1**<sub>Me</sub>·TfO is more electrophilic than **2**<sub>Me</sub>·TfO and

**3**<sub>Me</sub>·TfO. The *N*<sup>3</sup>-unsubstituted flavinium salts, **1**<sub>H</sub>·TfO and **3**<sub>H</sub>·TfO, showed comparatively positive reduction potentials to the corresponding *N*<sup>3</sup>-substituted **1**<sub>Me</sub>·TfO and **3**<sub>Me</sub>·TfO because of the lack of an electronegative methyl substituent (entries 1 and 4). Although the two reversible reduction peaks were observed for *N*<sup>3</sup>-substituted flavinium salts,<sup>4b,22</sup> the second reduction peaks of the *N*<sup>3</sup>-unsubstituted **1**<sub>H</sub>·TfO and **3**<sub>H</sub>·TfO (*E*<sub>2</sub> = −0.256 and −0.725 V, respectively) were likely irreversible (Fig. S1). The irreversible peaks would result from the complex formation of the flavin radical or reduced forms.<sup>23</sup> These results indicated that the redox activity of the flavinium salts can be significantly regulated by the initial modification of riboflavin.

Table 2. Reduction potentials of flavinium triflates<sup>a</sup>

Entry	Flavinium	<i>E</i> <sub>c</sub> <sup>p</sup> (V vs SCE) <sup>b</sup>	<i>E</i> <sub>a</sub> <sup>p</sup> (V vs SCE) <sup>b</sup>	<i>E</i> <sub>1</sub> (V vs SCE) <sup>b</sup>	<i>E</i> <sub>2</sub> (V vs SCE) <sup>b</sup>
1	<b>1</b> <sub>H</sub> ·TfO	0.246, -0.372	0.315, -0.140	0.281	-0.256
2	<b>1</b> <sub>Me</sub> ·TfO	0.231, -0.397	0.295, -0.332	0.263	-0.365
3	<b>2</b> <sub>Me</sub> ·TfO	-0.058, -0.818	0.007, -0.755	-0.026	-0.787
4	<b>3</b> <sub>H</sub> ·TfO	-0.236, -0.748	-0.170, -0.702	-0.203	-0.725
5	<b>3</b> <sub>Me</sub> ·TfO	-0.291, -1.28	-0.219, -1.23	-0.255	-1.25

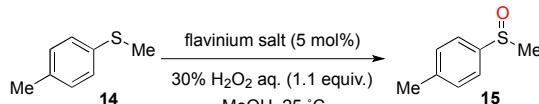
<sup>a</sup> The redox potentials of the flavins were measured by cyclic voltammetry at a scan rate of 100 mV/s in tetrabutylammonium perchlorate (0.1 M) containing CH<sub>3</sub>CN. [b] The electrochemical potentials (*E*<sub>1</sub> and *E*<sub>2</sub>) of each flavinium were determined by the relationship  $E = (E_c^p + E_a^p)/2$  relative to SCE.

Table 3. Catalytic activities of flavinium salts for H<sub>2</sub>O<sub>2</sub> oxidation of various substrates<sup>a</sup>

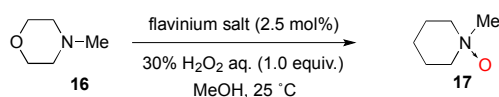
Sulfide <sup>a</sup>				Tertiary amine <sup>b</sup>				Cyclobutanone <sup>c</sup>			
Entry	Catalyst	<i>v</i> <sub>obs</sub> (μmol/h)	<i>v</i> <sub>obs</sub> / <i>v</i> <sub>0</sub>	Entry	Catalyst	<i>v</i> <sub>obs</sub> (μmol/h)	<i>v</i> <sub>obs</sub> / <i>v</i> <sub>0</sub>	Entry	Catalyst	<i>v</i> <sub>obs</sub> (μmol/h)	<i>v</i> <sub>obs</sub> / <i>v</i> <sub>0</sub>
1	None	2.3 <sup>d</sup> (= <i>v</i> <sub>0</sub> )	—	1	None	6.2 (= <i>v</i> <sub>0</sub> )	—	1	None	0.80 <sup>a</sup> (= <i>v</i> <sub>0</sub> )	—
2	<b>1</b> <sub>H</sub> ·TfO	>1.9 × 10 <sup>2d</sup>	>83	2	<b>1</b> <sub>Me</sub> ·TfO	56 <sup>d</sup>	9.1	2	<b>1</b> <sub>Me</sub> ·TfO	>1.2 × 10 <sup>2</sup>	>1.5 × 10 <sup>2</sup>
3	<b>1</b> <sub>Me</sub> ·TfO	>2.2 × 10 <sup>2d</sup>	>98	3	<b>2</b> <sub>Me</sub> ·TfO	5.8 × 10 <sup>2</sup>	94	3	<b>2</b> <sub>Me</sub> ·TfO	5.3	8.6
4	<b>2</b> <sub>Me</sub> ·TfO	4.7 <sup>d</sup>	2.1	4	<b>3</b> <sub>H</sub> ·TfO	10	1.7	4	<b>3</b> <sub>H</sub> ·TfO	13	16
5	<b>3</b> <sub>H</sub> ·TfO	13 <sup>d</sup>	5.6	5	<b>3</b> <sub>Me</sub> ·TfO	>93 <sup>e</sup>	>15 <sup>e</sup>	5	<b>3</b> <sub>Me</sub> ·TfO	—	—
6	<b>3</b> <sub>Me</sub> ·TfO	4.8 <sup>d</sup>	2.2								

<sup>a</sup> Conditions: **14** (0.1 M), flavinium salt (5 mol%), diethylene glycol diethyl ether (0.5 equiv, internal standard), 30% H<sub>2</sub>O<sub>2</sub> aq. (1.1 equiv), and MeOH at 25 °C. <sup>b</sup> Conditions: **16** (0.5 M), flavinium salt (2.5 mol%), mesitylene (0.5 equiv, internal standard), 30% H<sub>2</sub>O<sub>2</sub> aq. (1.0 equiv), and CD<sub>3</sub>OD at 25 °C. <sup>c</sup> Conditions: **18** (0.1 M), flavinium salt (5 mol%), 1,1,2,2-tetrachloroethane (0.5 equiv, internal standard), 30% H<sub>2</sub>O<sub>2</sub> aq. (1.1 equiv), and MeOH at 25 °C. <sup>d</sup> Average of two runs. <sup>e</sup> Decomposition of the catalyst presumably occurred.

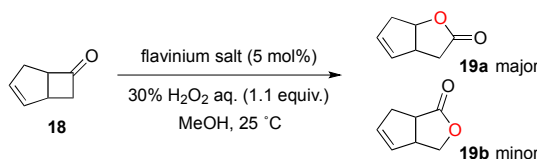
#### oxidation of sulfide



#### oxidation of amine



#### Baeyer-Villiger oxidation of cyclobutanone

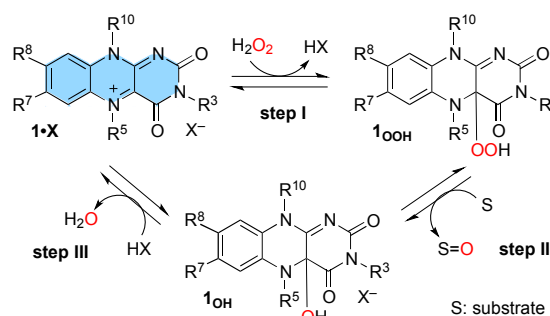




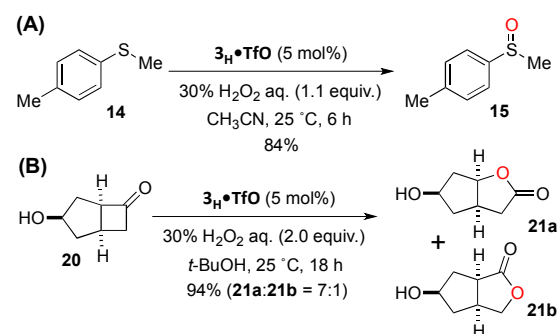
### Catalytic activity

To gain insight into the influence of structural difference of the riboflavin-derived flavinium salts on their catalytic activity, the flavinium triflates were compared on the basis of flavinium-catalysed oxidations of sulfide, amine, and cyclobutanone in the presence of  $\text{H}_2\text{O}_2$  (Table 3). The initial rates of these reactions were determined both with and without the catalyst ( $v_{\text{obs}}$  and  $v_0$ , respectively). The enhancement in the reaction rate in the presence of a flavinium catalyst, relative to that of the non-catalysed process ( $v_{\text{obs}}/v_0$ ), was calculated for each of the flavinium triflates. In the oxidation of sulfide (14), the isoalloxazininium salts ( $1_{\text{H}}\cdot\text{TfO}$  and  $1_{\text{Me}}\cdot\text{TfO}$ ) showed significantly higher activities than that of the alloxazininium salts ( $2_{\text{Me}}\cdot\text{TfO}$ ,  $3_{\text{H}}\cdot\text{TfO}$ , and  $3_{\text{Me}}\cdot\text{TfO}$ ). The reaction mechanism of flavinium-catalysed  $\text{H}_2\text{O}_2$  oxidation is shown in Scheme 4.<sup>2,3a</sup> The flavinium salt ( $\text{FI}^+\cdot\text{X}$ ) undergoes a reaction with  $\text{H}_2\text{O}_2$  to form  $\text{HX}$  and oxidatively active hydroperoxyflavin ( $\text{FI}_{\text{OOH}}$ ) (step I), which is responsible for the oxygenation of various substrates. Through the transfer of oxygen to the substrates,  $\text{FI}_{\text{OOH}}$  is converted to a hydroxy adduct ( $\text{FI}_{\text{OH}}$ ) (step II), and then  $\text{H}_2\text{O}$  elimination of  $\text{FI}_{\text{OH}}$  with  $\text{HX}$  affords  $\text{FI}^+\cdot\text{X}$  (step III), which is the rate-limiting step of the 5-alkylated isoalloxazininium catalysts ( $1_{\text{H}}\cdot\text{TfO}$  and  $1_{\text{Me}}\cdot\text{TfO}$ ).<sup>3a</sup> As revealed by the electrochemical measurements,  $1_{\text{H}}\cdot\text{TfO}$  and  $1_{\text{Me}}\cdot\text{TfO}$  were more electrophilic than  $2_{\text{Me}}\cdot\text{TfO}$ ,  $3_{\text{H}}\cdot\text{TfO}$  and  $3_{\text{Me}}\cdot\text{TfO}$ . The relatively higher activity of  $1_{\text{H}}\cdot\text{TfO}$  and  $1_{\text{Me}}\cdot\text{TfO}$  can be explained by their electrophilic character which enhances the smooth generation of the oxidatively active  $\text{FI}_{\text{OOH}}$  from  $\text{FI}^+$  in the presence of  $\text{H}_2\text{O}_2$ . As Cibulka and coworkers reported,<sup>2e,3j</sup> the alloxazininium salts are less electrophilic than the isoalloxazininium salts, and much more difficult to react with  $\text{H}_2\text{O}_2$ . Therefore,  $\text{H}_2\text{O}_2$  addition seems to be the rate-limiting step of  $2_{\text{Me}}\cdot\text{TfO}$ ,  $3_{\text{H}}\cdot\text{TfO}$ , and  $3_{\text{Me}}\cdot\text{TfO}$  (step I). This is supported by the revelation of a slightly lower activity of the more electronegative  $\text{N}^3$ -methylated  $3_{\text{Me}}\cdot\text{TfO}$  than that of the corresponding  $\text{N}^3$ -unsubstituted  $3_{\text{H}}\cdot\text{TfO}$ .

In the  $\text{N}$ -oxidation of tertiary amine (16), the most efficient catalyst was  $2_{\text{Me}}\cdot\text{TfO}$ , followed in order by  $3_{\text{Me}}\cdot\text{TfO}$ ,  $1_{\text{Me}}\cdot\text{TfO}$ , and  $3_{\text{H}}\cdot\text{TfO}$ , because the basic condition can accelerate the rate-limiting  $\text{H}_2\text{O}_2$  addition step of  $2_{\text{Me}}$  (step I).<sup>2e,3j</sup>  $\text{N}$ -Oxidation with  $3_{\text{Me}}\cdot\text{TfO}$  rapidly decelerated before reaching the 10% yield, presumably owing to the decomposition of the catalyst under basic conditions.<sup>3h</sup> The Baeyer-Villiger oxidation of cyclobutanone (18) was also conducted using  $1_{\text{Me}}\cdot\text{TfO}$ ,  $2_{\text{Me}}\cdot\text{TfO}$ , and  $3_{\text{H}}\cdot\text{TfO}$ . Because the reaction conditions were neutral like that of sulfoxidation, the order of the most efficient catalyst ( $1_{\text{Me}}\cdot\text{TfO} > 3_{\text{H}}\cdot\text{TfO} > 2_{\text{Me}}\cdot\text{TfO}$ ) was identical to that of the sulfoxidation of 14. In conclusion,  $1\cdot\text{TfO}$  displayed outstanding activity for oxidation under neutral conditions, while  $2\cdot\text{TfO}$  favoured oxidation under basic conditions. Contrary to  $1\cdot\text{TfO}$



Scheme 4. Catalytic cycle of the flavinium-catalysed  $\text{H}_2\text{O}_2$  oxidation, illustrated using simple  $1\cdot\text{X}$ .



Scheme 5 (A) Sulfoxidation of 14 and (B) Baeyer-Villiger oxidation of 20, catalysed by  $3_{\text{H}}\cdot\text{TfO}$  in the presence of  $\text{H}_2\text{O}_2$ .

and  $2\cdot\text{TfO}$ ,  $3\cdot\text{TfO}$  showed moderate catalytic activity for  $\text{H}_2\text{O}_2$  oxidations tested in this study. However,  $3_{\text{H}}\cdot\text{TfO}$  is more readily synthesised on a large scale from riboflavin. Therefore, we confirmed the availability of  $3_{\text{H}}\cdot\text{TfO}$  in the catalytic sulfoxidation and Baeyer-Villiger reactions with  $\text{H}_2\text{O}_2$  (Scheme 5). Although  $3_{\text{H}}\cdot\text{TfO}$  showed a lower catalytic activity than  $1\cdot\text{TfO}$ , the chemoselective sulfoxidation of 14 was efficiently performed by 5 mol% of  $3_{\text{H}}\cdot\text{TfO}$ , yielding the corresponding sulfoxide without overoxidation to sulfone (Scheme 5A). The Baeyer-Villiger oxidation of 20 was also promoted to give the corresponding lactones (21a and 21b) in good yield (Scheme 5B).

### Conclusions

We synthesized 5-ethylisoalloxazininium ( $1\cdot\text{TfO}$ ), 5-ethylalloxazininium ( $2\cdot\text{TfO}$ ), and 1,10-ethylene alloxazininium triflates ( $3\cdot\text{TfO}$ ) from commercially available riboflavin in three or four steps. Their redox properties and catalytic activity were largely different from each other depending on the  $\pi$ -conjugated ring structures, although these flavinium salts possess the same 7,8-dimethyl substituents originating from riboflavin. These results indicated that simple modification of riboflavin can provide unique flavin compounds with diverse

functionalities, which are useful in a wide variety of applications. This information would be useful for designing further efficient redox organocatalysts with high accessibility, as well as for developing novel riboflavin-containing functional materials.<sup>24</sup>

## Experimental

**Large scale synthesis of 9.** Sodium periodate (159 g, 0.74 mol) was added to a suspension of riboflavin (100 g, 0.27 mol) in water (4.0 L) in five portions, and the mixture was stirred at ca. 25 °C for 17 h. The yellow precipitate was collected by filtration, washed with water (700 mL), MeOH (700 mL), and diethyl ether (400 mL), and dried under reduced pressure to give **9** (69.0 g, 86%) as a yellow powder. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  3180br (OH), 1723s (NCO), 1656s (NCO), 1578s (NCO), 1546s (NCO).  $\delta\text{H}$  (500 MHz; TFA-*d*; r.t.) 8.49 (s, 1H, ArH), 8.04 (s, 1H, ArH), 7.16 (dd, 1H, *J* = 3.0, 7.0 Hz, CH), 5.68 (dd, *J* = 7.0, 15 Hz, 1H, CHH), 5.44 (dd, *J* = 2.5, 15 Hz, 1H, CHH), 2.90 (s, 3H, CH<sub>3</sub>), 2.79 (s, 3H, CH<sub>3</sub>). The spectral properties of **9** were in good agreement with the reported data.<sup>4d</sup>

**Large scale synthesis of 10.** To a suspension of **9** (25.0 g, 83 mmol) in Solmix AP-7 (8.7 L, 85:5:10 EtOH/2-propanol/1-propanol), NaBH<sub>4</sub> (5.15 g, 0.14 mol) was added in five portions, and the mixture was stirred at 25 °C overnight. After adding water (1.7 L), the resulting precipitate was collected by filtration, washed with methanol (1.7 L) and diethyl ether (0.8 L), and then suspended in MeOH (280 mL). After evaporation of the solvents, the residue was washed with water (0.3 L) and dried in vacuo to afford **10** (16.7 g, 70%) as a yellow powder. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  3225br (OH), 1712s (NCO), 1672s (NCO), 1578s (NCO), 1547s (NCO).  $\delta\text{H}$  (400 MHz; DMSO-*d*<sub>6</sub>; r.t.) 11.33 (s, 1H, -CONHCO-), 7.89 (s, 2H, ArH), 4.95 (t, *J* = 5.8 Hz, 1H, OH), 4.69 (t, *J* = 5.8 Hz, 2H, CH<sub>2</sub>), 3.80 (m, 2H, CH<sub>2</sub>), 2.53-2.45 (3H, CH<sub>3</sub>, overlapped with DMSO-*d*<sub>5</sub>), 2.40 (s, 3H, CH<sub>3</sub>). The spectral properties of **10** were in good agreement with the reported data.<sup>4d</sup>

**Large scale synthesis of 3<sub>H</sub>•TfO.** A mixture of **10** (7.08 g, 25 mmol) and SOCl<sub>2</sub> (43.0 mL, 0.59 mol) was stirred at 50 °C for 20 h under molecular nitrogen. The resulting yellow precipitate was collected by filtration, washed with CH<sub>2</sub>Cl<sub>2</sub> (350 mL), and purified by reprecipitation from formic acid (42 mL) by diethyl ether (800 mL). After a collection by filtration, the crude product was washed with 6% aqueous HCl (14 mL x 2) and dissolved into 1.5% aqueous HCl (640 mL). After solvent evaporation under reduced pressure, the resulting residue was redissolved into 1.5% aqueous HCl (640 mL) and lyophilized to obtain the chloride salt of **3<sub>H</sub>** (**3<sub>H</sub>•Cl**, 5.80 g) as a yellow powder. To exchange the counter anion, TfOH (479  $\mu\text{L}$ , 5.4 mmol) was added to a solution of **3<sub>H</sub>•Cl** (1.50 g, 4.9 mmol) in

MeOH (500 mL), and the resulting mixture was dried by evaporation. The residue was then washed with diethyl ether (250 mL) and dried in vacuo to obtain **3<sub>H</sub>•TfO** (1.92 g, 72%) as a yellow powder. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1744br (NCO), 1629s (NCO), 1602s (NCO).  $\delta\text{H}$  (500 MHz; DMSO-*d*<sub>6</sub>; r.t.) 12.75 (s, 1H, NH), 8.38 (s, 1H, ArH), 8.12 (s, 1H, ArH), 5.31 (t, *J* = 9.5 Hz, 2H, CH<sub>2</sub>), 4.64 (t, *J* = 9.3 Hz, 2H, CH<sub>2</sub>), 2.66 (s, 3H, CH<sub>3</sub>), 2.56 (s, 3H, CH<sub>3</sub>). The spectral properties of **3<sub>H</sub>•TfO** were in good agreement with the reported data.<sup>17a</sup>

**Synthesis of 1<sub>H</sub>•TfO.** Acetaldehyde (3.00 mL, 54 mmol) was added to a mixture of **10** (552 mg, 1.9 mmol), 10% Pd-C (41.2 mg, 0.039 mmol), conc. HCl (3.0 mL), EtOH (32 mL), and water (32 mL), and the mixture was stirred at room temperature for 21 h under molecular hydrogen. The reaction mixture was filtered through a pad of Celite under nitrogen, and the filtrate solvents were evaporated under reduced pressure. After successive addition of 2 M aqueous TfOH (4.00 mL, 8.0 mmol), NaNO<sub>2</sub> (612 mg, 8.9 mmol), and NaOTf (3.10 g, 19 mmol), the mixture was stirred at room temperature for 30 min. The resulting purple precipitate was collected by filtration, washed with cold water (40 mL) and diethyl ether (40 mL x 2) to give **1<sub>H</sub>•TfO** (672 mg, 75%) as a purple powder. mp 195.9-196.7 °C. Elemental analysis: Found: C, 43.7; H, 4.2; N, 11.9. Calc. for C<sub>17</sub>H<sub>19</sub>F<sub>3</sub>N<sub>4</sub>O<sub>6</sub>S: C, 44.0; H, 4.1; N, 12.1%. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1702s (NCO), 1675s (NCO), 1597s (NCO), 1545vs (NCO).  $\delta\text{H}$  (400 MHz; CD<sub>3</sub>CN; r.t.) 9.96 (br s, 1H, NH), 8.17 (s, 1H, ArH), 8.12 (s, 1H, ArH), 6.08 (br s, 2H, CH<sub>2</sub>), 4.94 (t, *J* = 5.4 Hz, 2H, CH<sub>2</sub>), 4.04 (t, *J* = 5.5 Hz, 2H, CH<sub>2</sub>), 2.62 (s, 3H, CH<sub>3</sub>), 2.56 (s, 3H, CH<sub>3</sub>), 1.75 (t, *J* = 7.1 Hz, 3H, CH<sub>3</sub>).  $\delta\text{C}$  (126 MHz; CD<sub>3</sub>CN; r.t.) 156.90, 153.94, 153.28, 152.12, 143.52, 138.01, 132.19, 127.27, 124.84 (q, *J* = 353 Hz, CF<sub>3</sub>), 121.31, 120.20, 58.88, 53.34, 51.10, 21.54, 20.26, 15.35. The corresponding molecular ion peak was not detected in the HRMS spectrum for **1<sub>H</sub>•TfO**.

**Synthesis of 11.** To a mixture of **10** (2.99 g, 11 mmol), K<sub>2</sub>CO<sub>3</sub> (7.41 g, 58 mmol), and DMF (300 mL) was added MeI (3.40 mL, 55 mmol), and the mixture was stirred at 60 °C for 5 h under molecular nitrogen. After most of the solvents was removed under reduced pressure, 0.3 M aqueous HCl (0.30 L) was added to the residue and the mixture was stirred for 30 min. The resulting powder was collected by filtration and washed with hexane (100 mL). A part of the crude product (558 mg/2.78 g) was washed with water (50 mL) and dried in vacuo to give **11** (527 mg, 83%) as a yellow powder. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  3422br (OH), 1698s (NCO), 1644s (NCO), 1582s (NCO), 1550s (NCO).  $\delta\text{H}$  (500 MHz; DMSO-*d*<sub>6</sub>; r.t.) 7.94 (s, 1H, ArH), 7.92 (s, 1H, ArH), 4.97 (t, *J* = 6.0 Hz, 1H, OH), 4.71 (t, *J* = 6.0 Hz, 2H, CH<sub>2</sub>), 3.81 (m, 2H, CH<sub>2</sub>), 3.27 (s, 3H, CH<sub>3</sub>), 2.54-2.45 (3H, CH<sub>3</sub>, overlapped with DMSO-*d*<sub>5</sub>), 2.40 (s, 3H, CH<sub>3</sub>). The spectral properties of **11** were in good agreement with the reported data.<sup>4d</sup>

**Synthesis of 1<sub>Me</sub>•TfO.** Acetaldehyde (2.80 mL, 50 mmol) was added to a mixture of **11** (507 mg, 1.7 mmol), 10% Pd/C (73.5 mg, 0.069 mmol), conc. HCl (2.7 mL), EtOH (32 mL), and H<sub>2</sub>O (32 mL), and the mixture was stirred at room temperature for 22 h under molecular hydrogen. The reaction mixture was filtered through a pad of Celite under nitrogen, and the filtrate solvents were evaporated under reduced pressure. After successive addition of 2 M aqueous TfOH (2.50 mL, 5.0 mmol), TfONa (2.70 g, 16 mmol), and NaNO<sub>2</sub> (574 mg, 8.3 mmol) at 0 °C, the mixture was stirred for 15 min. An additional 2 M aqueous TfOH (2.50 mL, 5.0 mmol) was added to this, and the resulting purple precipitate was collected by filtration, washed with cold water (10 mL x 2) and diethyl ether (20 mL x 3), and dried under reduced pressure to give **1<sub>Me</sub>•TfO** (687 mg, 85%) as a purple powder. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1712s (NCO), 1650vs (NCO), 1600s (NCO), 1559vs (NCO).  $\delta\text{H}$  (400 MHz; CD<sub>3</sub>CN; r.t.) 8.19 (s, 1H, ArH), 8.12 (s, 1H, ArH), 6.08 (br, 2H, CH<sub>2</sub>), 4.96 (br, 2H, CH<sub>2</sub>), 4.04 (t,  $J$  = 5.6 Hz, 2H, CH<sub>2</sub>), 3.42 (s, 3H, CH<sub>3</sub>), 2.62 (s, 3H, CH<sub>3</sub>), 2.57 (s, 3H, CH<sub>3</sub>), 1.79 (t,  $J$  = 7.2 Hz, 3H, CH<sub>3</sub>). The spectral properties of **1<sub>Me</sub>•TfO** were in good agreement with the reported data.<sup>4d</sup>

**Synthesis of 3<sub>Me</sub>•TfO.** A mixture of **11** (700 mg, 2.3 mmol) and SOCl<sub>2</sub> (4.20 mL, 58 mmol) was stirred at 50 °C for 6 h. The solvent was removed under reduced pressure, and the residue was washed with diethyl ether (50 mL x 4) and dried in vacuo to afford orange powder (796 mg). After some of the crude product (529 mg) was dissolved in water (300 mL), the aqueous layer was washed with CHCl<sub>3</sub> (150 mL x 3) and lyophilized to obtain the chloride salt of **3<sub>Me</sub>•Cl** (457 mg) as an orange powder. To exchange the counter anion, TfOH (22.9  $\mu\text{L}$ , 0.26 mmol) was added to a solution of **3<sub>Me</sub>•Cl** (74.5 mg, 0.23 mmol) in MeOH (47 mL), and the resulting mixture was dried by evaporation. The resulting residue was washed with diethyl ether (47 mL), dried in vacuo, and dissolved in water (10 mL), and lyophilized to obtain **3<sub>Me</sub>•TfO** (88.1 mg, 81%) as a yellow powder. mp 164 °C (dec). IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1747s (NCO), 1703s (NCO), 1636s (NCO), 1610s (NCO).  $\delta\text{H}$  (500 MHz; DMSO-*d*<sub>6</sub>; r.t.) 8.43 (s, 1H, ArH), 8.15 (s, 1H, ArH), 5.34 (t,  $J$  = 9.3 Hz, 2H, CH<sub>2</sub>), 4.71 (t,  $J$  = 9.3 Hz, 2H, CH<sub>2</sub>), 3.41 (s, 3H, CH<sub>3</sub>), 2.67 (s, 3H, CH<sub>3</sub>), 2.57 (s, 3H, CH<sub>3</sub>).  $\delta\text{C}$  (126 MHz; DMSO-*d*<sub>6</sub>; r.t.) 157.91, 152.49, 147.15, 142.56, 142.49, 139.13, 131.74, 131.19, 127.81, 121.06 (q,  $J$  = 317 Hz, CF<sub>3</sub>) 117.26, 50.62, 45.81, 28.95, 21.27, 19.76. HRMS (ESI+):  $m/z$  calcd for C<sub>15</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub> (M - TfO<sup>-</sup>), 283.1190; found, 283.1192.

**Synthesis of 12.**<sup>17b</sup> Sodium periodate (4.77 g, 22 mmol) was added to a suspension of riboflavin (3.00 g, 8.0 mmol) in water (120 mL), and the mixture was stirred at 50 °C for 24 h. The brown precipitate was collected by filtration, washed with water (180 mL), MeOH (130 mL), and diethyl ether (20 mL), and dried in vacuo to give **12** (1.34 g, 70%) as a yellow powder. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1699br (NCO), 1577s (NCO), 1485s (NCO).

$\delta\text{H}$  (500 MHz; DMSO-*d*<sub>6</sub>; r.t.) 11.82 (s, 1H, -CONHCO-), 11.66 (s, 1H, -CONHC-), 7.91 (s, 1H, ArH), 7.70 (s, 1H, ArH), 2.49 (s, 3H, ArCH<sub>3</sub>), 2.46 (s, 3H, ArCH<sub>3</sub>). The spectral properties of **12** were in good agreement with the reported data.<sup>3i</sup>

**Synthesis of 13.**<sup>17b</sup> A mixture of **12** (4.00 g, 17 mmol), K<sub>2</sub>CO<sub>3</sub> (11.8 g, 86 mmol), and methyl iodide (2.40 mL, 39 mmol) in dry DMF (150 mL) was stirred for 3 h at room temperature. After most of the solvent was evaporated under reduced pressure at 50 °C, water (200 mL) was added to the residue, and the crude mixture was extracted with CHCl<sub>3</sub> (700 mL). The organic layer was washed with brine (200 mL) and dried over MgSO<sub>4</sub>, filtrated, and evaporated to dryness. No further purification was required in order to obtain **13** (3.48 g, 78%) as a yellow solid. IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1720s (NCO), 1677s (NCO), 1556s (NCO).  $\delta\text{H}$  (400 MHz; CDCl<sub>3</sub>; r.t.) 8.07 (s, 1H, ArH), 7.79 (s, 1H, ArH), 3.81 (s, 3H, NCH<sub>3</sub>), 3.60 (s, 3H, NCH<sub>3</sub>), 2.54 (s, 3H, ArCH<sub>3</sub>), 2.51 (s, 3H, ArCH<sub>3</sub>). The spectral properties of **12** were in good agreement with the reported data.<sup>8a</sup>

**Synthesis of 2<sub>Me</sub>•TfO.**<sup>17b</sup> Acetaldehyde (8.50 mL, 0.15 mol) was added to a mixture of **13** (1.02 g, 3.7 mmol), 10% Pd-C (400 mg), H<sub>2</sub>O (12.5 mL), and acetic acid (125 mL), and the mixture was stirred for 2 days under molecular hydrogen. The reaction mixture was filtered through a pad of Celite under molecular nitrogen, and the filtrate solvents were evaporated under reduced pressure. After successive addition of 2 M aqueous TfOH solution (10 mL, 20 mmol), TfONa (5.07 g, 30 mmol), and NaNO<sub>2</sub> (1.07 g, 16 mmol), the mixture was stirred under air at 0 °C for 30 min. The resulting purple precipitate was collected by filtration, washed with cold water (10 mL) and diethyl ether (200 mL) to give the crude product (1.11 g). The product (680 mg) was then purified by the reprecipitation from CH<sub>3</sub>Cl to diethyl ether to give **2•TfO** (533 mg, 51%) as a yellow powder. mp 171 °C (dec). IR (KBr):  $\nu_{\text{max}}/\text{cm}^{-1}$  1728s (NCO), 1685s (NCO), 1666s (NCO).  $\delta\text{H}$  (500 MHz; CDCl<sub>3</sub>; r.t.) 8.10 (s, 1H, ArH), 8.05 (s, 1H, ArH), 6.12 (br, 1H, N<sup>+</sup>CHHCH<sub>3</sub>), 5.34 (br, 1H, N<sup>+</sup>CHHCH<sub>3</sub>), 3.85 (s, 3H, 1-NCH<sub>3</sub>), 3.57 (s, 3H, 3-NCH<sub>3</sub>), 2.68 (s, 3H, ArCH<sub>3</sub>), 2.61 (s, 3H, ArCH<sub>3</sub>), 1.85 (t,  $J$  = 7.2 Hz, 3H, NCH<sub>2</sub>CH<sub>3</sub>).  $\delta\text{C}$  (126 MHz; CDCl<sub>3</sub>; r.t.) 155.27, 149.25, 148.70, 148.62, 147.25, 146.10, 129.13, 128.95, 120.01 (q,  $J$  = 320 Hz, CF<sub>3</sub>), 119.63, 117.40, 51.57, 30.88, 30.01, 21.76, 20.65, 15.23. HRMS (ESI-TOF)  $m/z$ : [M - TfO]<sup>+</sup> calcd for C<sub>17</sub>H<sub>19</sub>F<sub>3</sub>N<sub>4</sub>O<sub>5</sub>S, 299.1503, found, 299.1503.

**Cyclic voltammetry.** Cyclic voltammograms were collected using an electrochemical analyzer model 1210B (BAS, Tokyo, Japan) with a conventional three-electrode cell employing a Pt working electrode, a Pt counter electrode, and a Ag/Ag<sup>+</sup> reference electrode (BAS, Tokyo, Japan). The electrochemical analysis of flavinium salts were carried out in acetonitrile (1.0 mM) containing Bu<sub>4</sub>NClO<sub>4</sub> (0.1 M) at a sweep rate of 100 mV/s at 25 °C under nitrogen atmosphere. The electrochemical



potentials were converted into values relative to SCE using standard redox couple  $\text{Fc}/\text{Fc}^+$  according to the previously reported method,<sup>12c</sup> and were calculated as the mean of cathodic and anodic peak potentials [ $E = (E_p^c + E_p^a)/2$ ].

**Comparison of flavinium catalysts in sulfoxidation of 14.** A 30% aqueous  $\text{H}_2\text{O}_2$  solution (24.9 mg, 0.22 mmol) was added to a mixture of **14** (27.6 mg, 0.20 mmol), flavinium salt (0.01 mmol), and diethylene glycol diethyl ether (16.2 mg, 0.10 mmol, internal standard) in MeOH (2.0 mL), and the reaction mixture was stirred at 25 °C. The reaction was monitored by GC, and the yield of **15** was calculated based on the calibration curves using diethylene glycol diethyl ether as an internal standard. These results are summarised in Fig. S2 and Table 3.

**Comparison of flavinium catalysts in N-oxidation of 16.** A 30% aqueous  $\text{H}_2\text{O}_2$  solution (45.3 mg, 0.40 mmol) was added to a mixture of **16** (40.5 mg, 0.40 mmol), flavinium salt (0.01 mmol), and mesitylene (24.0 mg, 0.20 mmol, internal standard) in  $\text{CD}_3\text{OD}$  (0.8 mL), and the reaction mixture was stirred at 25 °C. The reaction was monitored by  $^1\text{H}$  NMR, and the yield of **17** was calculated using an internal standard. These results are summarised in Fig. S3 and Table 3.

**Comparison of flavinium catalysts in Baeyer-Villiger oxidation of 18.** A 30% aqueous  $\text{H}_2\text{O}_2$  solution (45.3 mg, 0.40 mmol) was added to a mixture of **18** (21.6 mg, 0.20 mmol), flavinium salt (0.01 mmol), and 1,1,2,2-tetrachloroethane (16.8 mg, 0.10 mmol, internal standard) in MeOH (2.0 mL), and the reaction mixture was stirred at 25 °C. The reaction was monitored by GC, and the total yield of **19a** and **19b** was calculated based on the calibration curves using 1,1,2,2-tetrachloroethane as an internal standard. These results are summarised in Fig. S4 and Table 3.

**Sulfoxidation of 14 catalyzed by  $3_{\text{H}}\bullet\text{TfO}$ .** A 30% aqueous  $\text{H}_2\text{O}_2$  solution (112  $\mu\text{L}$ , 1.1 mmol) was added to a mixture of **14** (138 mg, 1.0 mmol),  $3_{\text{H}}\bullet\text{TfO}$  (21.0 mg, 0.050 mmol) in MeCN (1.0 mL), and the reaction mixture was stirred at 25 °C for 6 h. After an addition of sat. aqueous  $\text{NaSO}_3$  (1.0 mL) and  $\text{CHCl}_3$  (20 mL), the organic layer was washed with water (10 mL x 2) and brine (10 mL), dried over  $\text{MgSO}_4$ , and filtered. After the solvent was removed by evaporation, the residue was purified by column chromatography ( $\text{SiO}_2$ , hexane/ethyl acetate = 4/1 to 1/3, v/v) to give **15** (130 mg, 84%) as a white solid. The spectral properties of **15** were in good agreement with the reported data.<sup>4d</sup>

**Baeyer-Villiger oxidation of 20 catalyzed by  $3_{\text{H}}\bullet\text{TfO}$ .** A 30% aqueous  $\text{H}_2\text{O}_2$  solution (102  $\mu\text{L}$ , 1.0 mmol) was added to a mixture of **20** (63.1 mg, 0.50 mmol),  $3_{\text{H}}\bullet\text{TfO}$  (10.5 mg, 0.026 mmol) in *t*-BuOH (0.5 mL), and the reaction mixture was stirred at 25 °C for 18 h. The yields of **21a** and **21b** were

determined to be 82 and 12%, respectively, by  $^1\text{H}$  NMR using 1,1,2,2-tetrachloroethane as an internal standard. The spectral properties of **21a**<sup>25a</sup> and **21b**<sup>25b</sup> were in good agreement with the reported data.

## Conflicts of interest

There are no conflicts to declare.

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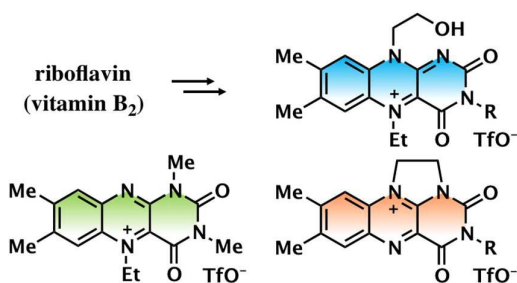
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## Table of contents



A series of flavinium salts were prepared from commercially available riboflavin, and their optical and redox properties and their catalytic activity were compared.