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# Substituent-Controlled Electrocyclization of 2,4-Dienones: Synthesis of 2,3,6-Trisubstituted 2*H*-Pyran-5-carboxylates and Their Transformations

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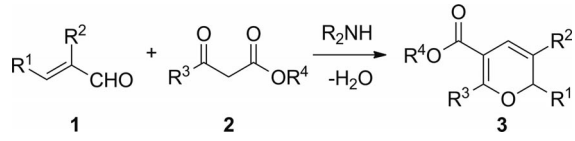
A facile access to 2,3,6-trisubstituted 2*H*-pyran-5-carboxylates is developed by employing 2-alkyl-2-enals as reactants with acetoacetates. The reaction involves Knoevenagel condensation followed by a 6π-electrocyclization, in which the presence of the C2 alkyl substituent in the enals favors the formation of (*E*)-Knoevenagel adducts for the ensuing electrocyclization. The resulting 2*H*-pyrans are hydrogenated to form 3,4-dihydro-2*H*-pyrans and converted into the endoperoxides by singlet-oxygen cycloaddition.

## Introduction

The pyran moiety is common to a wide range of natural products, and therefore, development of an efficient access to this class of substructures is a continuous challenge in relation to the syntheses of biologically relevant compounds.[1] In particular, the 1,2-addition of 1,3-dicarbonyl compounds to 2-alkenylimminiums followed by electrocyclization of the resulting 2,4-dienone system is one of the most versatile approaches to 2*H*-pyrans.[2] However, this iminium-based strategy for the synthesis of 2*H*-pyrans has only been successful when using 1,3-dicarbonyls with a highly enolizable structure, such as cyclohexane-1,3-diones,[3] 4-hydroxycoumarin,[4] and 4-hydroxypyrones,[5] as the reactants. In addition to iminium activation, Lewis[6] and Brønsted acid[7] catalyzed protocols were recently developed to dictate the synthesis of the same 2*H*-pyran structure. 2*H*-Pyrans have been synthesized by $Ag^{I}$-catalyzed isomerization of propargyl vinyl ethers.[8]

On the other hand, acyclic acetoacetates and their analogues as nucleophiles have suffered from poor yields[9a] or low product selectivity due to the competitive formation of Knoevenagel adducts under less equilibrating conditions with a carboxylate[9b] or hydroxide[9c] base. Furthermore, the 1,4-addition rather than the 1,2-addition of acetoacetates to the iminium of 2-alkenals is favored when the sterically congested pyrrolidine catalyst is employed as demonstrated by Jørgensen et al. for their performance during the high enantioselective synthesis of cyclohexane derivatives.[10] Alternative method for the synthesis of Knoevenagel adducts from 2-enals has been developed by Paquette et al. using the indium-catalyzed addition of 4-bromo-3-methoxycrotonate.[11]

In our approach to poly-substituted 2*H*-pyrans **3**, we employed an iminium activation strategy[12] for the tandem reaction of acetoacetates **2** and 2-alkenals **1**. Thus, we now describe that enals **1** with a C2 alkyl substituent undergo 1,2-addition with **2** and subsequent 6π-electrocyclization[13] of the resulting 2,4-dienones to efficiently form poly-substituted 2*H*-pyran-5-carboxylates (Scheme 1). Furthermore, we examined transformations of the resulting oxygen heterocycles to form 3,4-dihydro-2*H*-pyran derivatives by hydrogenation and 3,6-peroxy-3,6-dihydro-2*H*-pyrans by cycloaddition of singlet oxygen.




Scheme 1. Formation of poly-substituted 2*H*-pyran-5-carboxylates.

## Results and Discussion

We employed 2-ethyl-2-hexenal (**1a**) and methyl acetoacetate (**2a**) as the reactants to test the reaction. As shown in Table 1, the desired reaction is realized with secondary amines such as piperidine (Table 1, entries 1–10)[14] and *N*-methylhomopiperazine (Table 1, entry 14), affording the desired 2*H*-pyran-5-carboxylate **3a**. Consequently, the reaction was optimized by varying the amount of piperidine (0.2–2.0 equiv.), by changing the kind of acid catalysts, and by performing the reaction without acid catalyst in THF for 24 h. As shown in Table 1, entry 4, the best result was obtained by using two equiv. of piperidine and acetic acid

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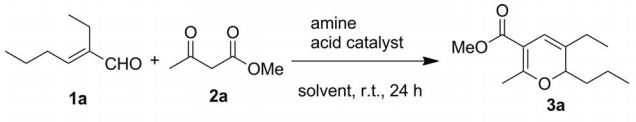
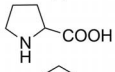
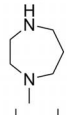
(ca. 20 mol-%). Increasing the amount of piperidine increased the yield significantly (Table 1, entries 1–3) and AcOH was favorable as an acid catalyst (Table 1, entries 5–7). In contrast, five-membered amines such as pyrrolidine (Table 1, entry 11) and proline (Table 1, entry 12) were of no use.

Table 1. Optimization of reaction conditions by varying amines and acid catalysts.[a]



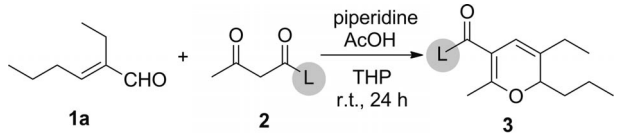

| Entry | Amine (equiv.) | Acid catalyst (mol-%) | Solvent | Yield (%)[b] |
|---|---|---|---|---|
| 1 | piperidine (0.2) | AcOH (20) | THF | 18 |
| 2 | piperidine (0.5) | AcOH (20) | THF | 29 |
| 3 | piperidine (1.0) | AcOH (20) | THF | 52 |
| 4 | piperidine (2.0) | AcOH (20) | THF | 61 |
| 5 | piperidine (2.0) | PPTS (20) | THF | 59 |
| 6 | piperidine (2.0) | *p*TsOH (20) | THF | 55 |
| 7 | piperidine (2.0) | -- | THF | 43 |
| 8 | **piperidine (2.0)** | **AcOH (20)** | **THP** | **71** |
| 9 | piperidine (2.0) | AcOH (20) | $CH_2Cl_2$ | 60 |
| 10 | piperidine (2.0) | AcOH (20) | toluene | 59 |
| 11 |  (2.0) | AcOH (20) | THF | 2~3 |
| 12 |  (2.0) | AcOH (20) | THF | no reaction |
| 13 |  (2.0) | AcOH (20) | THF | no reaction |
| 14 |  (2.0) | AcOH (20) | THF | 48 |
| 15 |  (2.0) | AcOH (20) | THF | no reaction |
| 16 | $Et_3N$ (2.0) | AcOH (20) | THF | no reaction |
| 17 | TMG (2.0) | AcOH (20) | THF | 2 |
| 18 | DBU (2.0) | AcOH (20) | THF | 3 |

[a] Reactions were carried out using **1a** (1.0 mmol) and **2a** (1.5 mmol) in the presence of amine and acid catalyst in solvent (2 mL) at room temperature for 24 h. PPTS = pyridinium *p*-toluenesulfonate, *p*TsOH = *p*-toluenesulfonic acid, THP = tetrahydropyran, TMG = 1,1,3,3-tetramethylguanidine, DBU = 1,5-diazabicyclo[5.4.0]undec-5-ene. [b] Yields are based on the isolated products.

As a result of screening the solvent effect, we found that the yield of **3a** was improved to 71% by use of THP for 24 h, compared with other solvents such as THF (61%), $CH_2Cl_2$ (60%), and toluene (59%) (Table 1, entries 4, 8–10).

Subsequently, we examined the effect of acyl substituents L of **2** by varying the substituents from common alkoxy groups to either electron-withdrawing ones, namely, trifluoroethoxy and 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO),[15] or electron-donating ones, namely, $R^1R^2N$ (Table 2). As shown in Table 2, entries 1–4, moderate yields were obtained with common alkoxy groups or the electron-withdrawing nature of $CF_3CH_2O$, whereas no reactions occurred when using electron-releasing acyl substituents (Table 2, entries 6 and 7). Methyl (**2a**) and allyl esters (**2c**) showed good performances with respect to the yield (Table 2, entries 1 and 3).

Table 2. Effect of acyl substituent L of **2** on the condensation and electrocyclization reaction.[a]




| Entry | 2 | L | 3 | Yield (%)[b] |
|---|---|---|---|---|
| 1 | **2a** | $OCH_3$ | **3a** | 71 |
| 2 | **2b** | O-*t*Bu | **3b** | 64 |
| 3 | **2c** | O-allyl | **3c** | 65 |
| 4 | **2d** | $OCH_2CF_3$ | **3d** | 57 |
| 5 | **2e** |  | **3e** | 33 |
| 6 | **2f** | $N[CH_2CH_2]_2O$ | **3f** | – |
| 7 | **2g** | N(OMe)Me | **3g** | – |

[a] Reactions were carried out using **1a** (1.0 mmol) and **2** (1.5 mmol) in the presence of piperidine (2.0 mmol) and AcOH (0.2 mmol) in THP (2 mL) at room temperature for 24 h. [b] Yields are based on the isolated products.

These results can be explained by taking the enolizability of the acetoacetic derivatives and the existence of hydrogen bonding in the enol form into account. Thus, acetoacetic derivatives with electron-donating substituents are less likely to form an enol form, whereas those with an electron-withdrawing acyl substituent can invoke the enol form, although slightly stabilized by internal hydrogen-bonding, which is favorable for ensuing Knoevenagel condensation. On the other hand, increased reactivity was found with cyclic keto esters (see below), since the enol form is a major tautomer and lacks internal hydrogen bonding (Figure 1).[16]

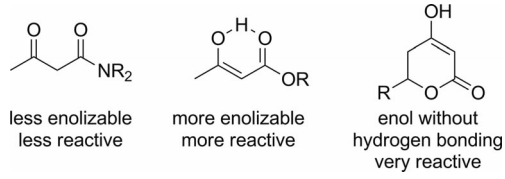
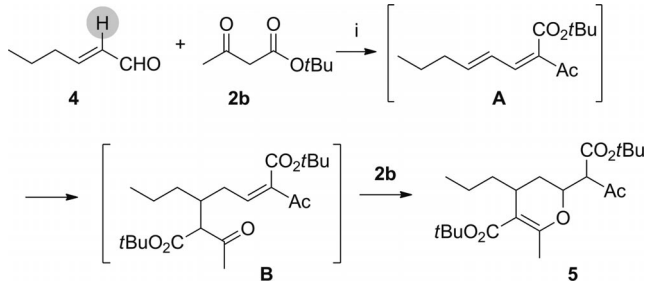



Figure 1. Acyclic and cyclic acetoacetic derivatives.

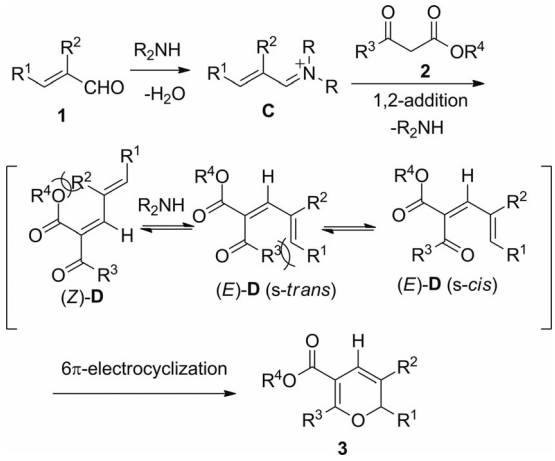
In contrast to the smooth formation of **3a** from **1a**, the reaction of 2-hexenal (**4**), which lacks an alkyl substituent at the C2 position, with *tert*-butyl acetoacetate (**2b**) using a piperidine catalyst led to the three-component coupling product **5** as the major product (40%) (Scheme 2). The formation of **5** can be explained by Michael addition of another molecule of acetoacetate **2b** adding to the δ position of the initially formed Knoevenagel adducts **A** followed by cyclization of the enol of **B** to form **5**. Thus, the presence of an alkyl substituent at the C2 position is indispensable for the smooth formation of the 2*H*-pyran structure.




Scheme 2. Reaction conditions: (i) **2b** (1.5 equiv.), piperidine (2.0 equiv.), AcOH (20 mol-%), THP, room temperature, 24 h, 40%.

Since condensation and cyclization invoked the installation of a substituent on the C2 of the 2-enals **1**, the reaction mechanism for **3** can be proposed as that described in Scheme 3. Thus, the Knoevenagel condensation of iminium **C** and **2** would lead to dienones **D**. Among them, dienone (*E*)-**D**, which has the requisite configuration for the ensuing electrocyclization, would be favored for steric reasons through the amine-catalyzed equilibration of (*Z*)-**D** and (*E*)-**D**. Eventually, the *s-cis* conformer of (*E*)-**D** undergoes spontaneous 6π-electrocyclization to form the 2*H*-pyran **3**.[2]




Scheme 3. Proposed mechanism for the 1,2-addition through iminium activation followed by 6π-electrocyclization.

In the next stage, different kinds of acyl groups, $R^3$, of the β-keto ester counterpart were employed to gain insight into the steric effect of $R^3$ on the *s-cis* or *s-trans* conformers of (*E*)-D in the proposed mechanism (Scheme 3). As shown in Table 3, the cyclohexanoyl- and phenylthioacetylacetates **6** and **8** produced the corresponding 2*H*-pyrans **7** and **9** in 66–70% yield (Table 3, entries 1 and 2), whereas benzoylacetate (**10**) resulted in the desired 2*H*-pyrans **11** in a lower yield (39%; Table 3, entry 3). The condensation of **1a** with the cyclic keto ester **12** proceeded promptly to give the bicyclic 2*H*-pyrans **13** in 69% yield (Table 3, entry 4).

Table 3. Scope of condensation and electrocyclization reactions of enals and keto esters.

| Entry | Enal | Keto ester | Product[a] | Yield (%)[b] |
|---|---|---|---|---|
| 1 | **1a** | **6** | **7** | 70 |
| 2 | **1a** | **8** | **9** | 66 |
| 3 | **1a** | **10** | **11** | 39 |
| 4 | **1a** | **12** | **13** | 69 |
| 5 | **1b** | **2a** | **14** | 76 |
| 6 | **1c** | **2a** | **15** | 63 |
| 7 | **1d** | **2a** | **16** | 72 |
| 8 | **1e** | **2a** | **17** | 44 |
| 9 | **1f** | **2a** | **18** | 60 |
| 10 | **1g** | **2a** | **19** | 30 |
| 11 | **1h** | **2a** | **20** | 42 |

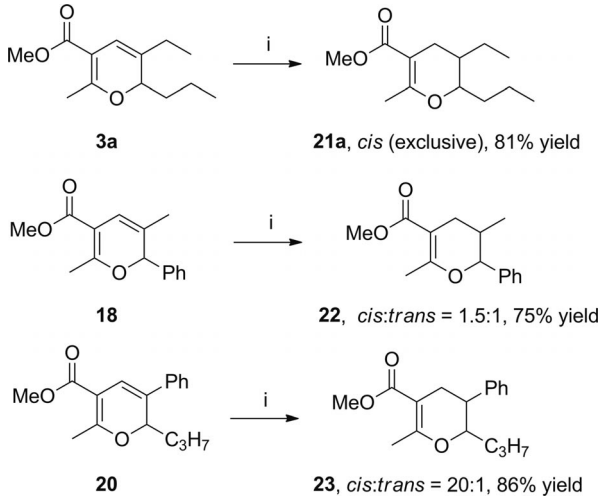
[a] Carried out by the reaction of enal (**1**, 1.0 mmol) and keto esters (1.5 mmol) with piperidine (2.0 mmol) and AcOH (0.2 mmol) in THP (2 mL) for 24–48 h. [b] Yield of isolated and fully characterized products.

The present method was applied to other enals, the results of which are shown in Table 3. Thus, acyclic **1b** and **1c** (Table 3, entries 5 and 6), cyclic **1d** and **1e** (Table 3, entries 7 and 8), and aryl-substituted derivatives **1f** and **1h**[17] (Table 3, entries 9 and 11) were successfully combined with acetoacetate **2a**, giving the corresponding 2*H*-pyrans **14**–**18** and **20** in moderate to good yields. In contrast to **1f**, the reaction of 3-(2-furyl)-2-methyl-2-propenal (**1g**) and **2a** terminated at the Knoevenagel condensation stage of the pro-

cess, forming the corresponding (*Z*) adduct **19**, presumably due to the difficulty of amine-catalyzed equilibration between (*E*) and (*Z*) adducts (Table 3, entry 10). The result in Table 3, entry 11, shows that an aryl group can be used as a steric executing factor to produce the 3-phenyl-2*H*-pyran **20**, although in a slightly decreased yield (42%; Table 3, entry 11).

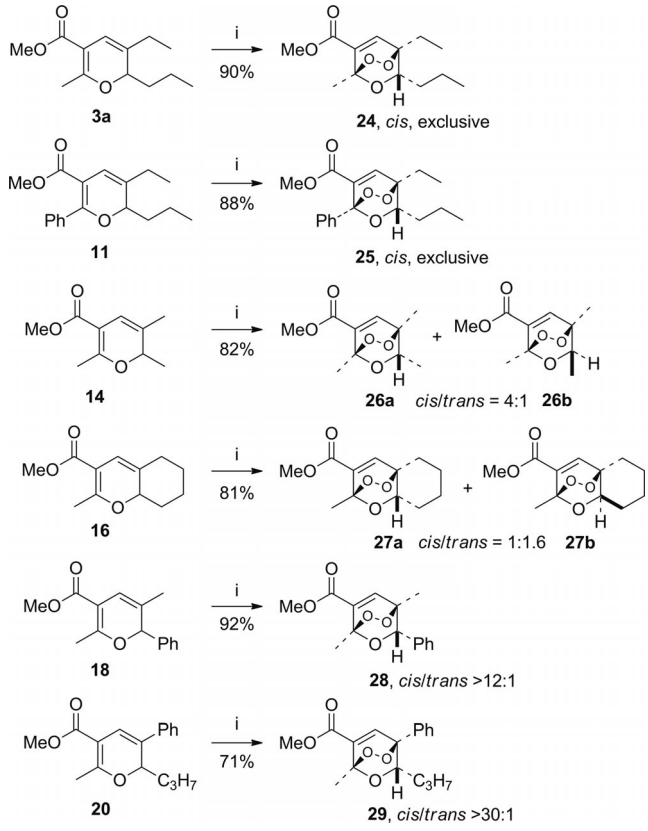
Due to the instability of the resulting 2*H*-pyran-5-carboxylates on standing, selected compounds **3a**, **18**, and **20** were hydrogenated to form the corresponding 3,4-dihydro-2*H*-pyran-5-carboxylates **21a**, **22**, and **23**, the structures of which and the ratio of 2,3-*cis* or 2,3-*trans* stereoisomers were determined on the basis of $^1$H NMR spectroscopic analyses (Scheme 4). In general, the hydrogenation occurred selectively on a double bond at the C3,4 positions[8] and the *cis* isomers were predominant in the C2 alkyl derivatives, namely, **21a** and **23**, whereas the C2 phenyl derivative **18** produced a mixture of *cis*/*trans* isomers **22**.[18]




Scheme 4. Hydrogenation of 2*H*-pyran-5-carboxylates: (i) $H_2$, Pd/C, THF.

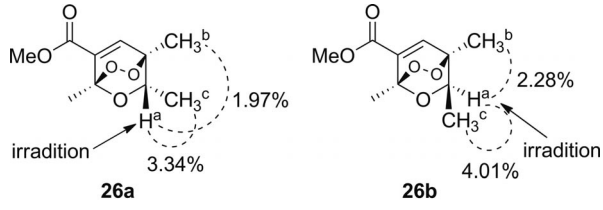
Stimulated by recent interest in endoperoxides as valuable organic intermediates, radical initiators, and oxidants,[19] we attempted the preparation of the bridged 1,2,4-trioxane structures by cycloaddition of singlet oxygen on the obtained 2*H*-pyran-5-carboxylates (Scheme 5).[20] Thus, irradiation of **14** with a 250 W halogen lamp in the presence of rose bengal under oxygen bubbling afforded the desired endoperoxide **26** in 82% yield as an inseparable mixture of stereoisomers in a ratio of 4:1. Similarly, photooxidation of compounds **3a**, **11**, **16**, **18**, and **20** under the same conditions as those described above afforded the corresponding endoperoxides **24**, **25**, **27**, **28**, and **29** in moderate to good yields. In general, 2,3-*cis* isomers formed predominantly, that is, **24**, **25**, **28**, and **29**, whereas the formation of mixtures of *cis*/*trans* isomers with reversed isomer ratios were found with the conversions of **14** into **26** and **16** into **27**.

The *cis*/*trans* stereochemistry of endoperoxide **26** was determined on the basis of NOE experiments (Figure 2). Namely, the *trans* adduct **26b** (minor isomer) showed a




Scheme 5. Photooxidation of 2*H*-pyran-5-carboxylates: (i) $O_2$, rose bengal, *hv*, MeOH, –78 °C.

larger NOE between $H^c$ and $CH_3{}^b$ than that of the *cis* adduct **26a** (major isomer), indicating a *cis* relationship between $CH_3{}^c$ and $CH_3{}^b$ of **26a**. Furthermore, the chemical shift of the $H^a$ of the *cis* adduct **26a** appeared more downfield presumably due to the deshielding effect of the adjacent peroxy group, compared with that of the *trans* adduct **26b**; these results supported the assigned structure.



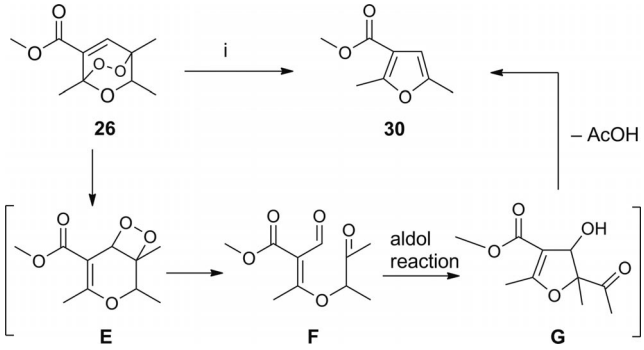

| **26a** (major isomer) | **26b** (minor isomer) |
|---|---|
| $H^a$, $\delta$ 4.26 ppm | $H^a$, $\delta$ 3.60 ppm |
| $CH_3{}^c$, $\delta$ 0.98 ppm | $CH_3{}^c$, $\delta$ 1.42 ppm |

Figure 2. Characteristic $^1$H NMR spectroscopic data and observed NOE of **26**.

Subsequently, we examined further transformation of endoperoxide **26** into versatile intermediates. Thus, acid treatment of **26** with *p*TsOH in the presence of $Ph_3P$ afforded furan **30** in 65% yield, the formation of which could be ascribed to the rearrangement of endoperoxide **26** into 1,2-

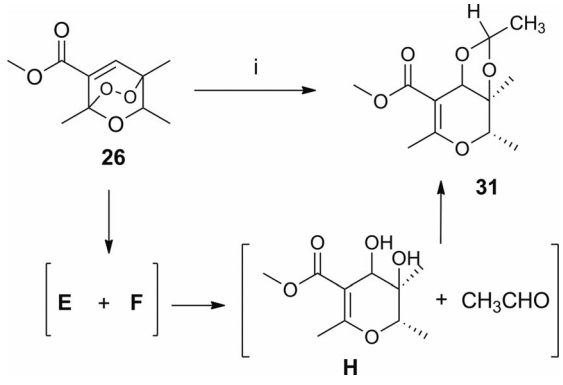
  

dioxide **E**, subsequent ring cleavage of **E**, the formation of **F**, followed by continuous intramolecular aldol reaction of **F**, and elimination of acetic acid from **G** (Scheme 6).[21]




Scheme 6. Acid treatment of endoperoxide **26**: (i) *p*TsOH, $Ph_3P$, $CH_2Cl_2$, 65%.

On the other hand, treatment of **26** with a Lewis acid such as $Cu(OTf)_2$ (OTf = triflate) afforded the acetal **31** in 27% yield. Formation of **31** can be explained by an interconversion reaction of 1,2-dioxide **E** and the α-oxyketone group of **F**, producing diol **H** and acetaldehyde as a result of intermolecular reduction and oxidation, which was followed by acetalization, leading to **31** (Scheme 7).




Scheme 7. Lewis acid treatment of endoperoxide **26**: (i) $Cu(OTf)_2$, $CH_2Cl_2$, 27%.

## Conclusions

We developed a new access to poly-substituted 2*H*-pyran-5-carboxylates from simple 2-alkyl-2-enals and 3-keto esters, performed only by treatment with piperidine/acetic acid. The reaction was improved by examining the effect of the acyl substituent, the amine base, the C2 substituent of the enals, and the alkanoyl group of the keto esters. The success of the reaction is dependent on the presence of a C2 substituent on the enals. 2*H*-Pyran-5-carboxylates were photooxidized to give endoperoxides, which showed interesting reactivities upon acid treatments.

## Experimental Section

**Preparation of Methyl 3-Ethyl-6-methyl-2-propyl-2*H*-pyran-5-carboxylate (3a). Typical Procedure:** Piperidine (170 mg, 2.0 mmol) and AcOH (12 mg, 0.2 mmol) were consecutively added at room temperature to a solution of **1a** (126 mg, 1.0 mmol) and **2a** (175 mg, 1.5 mmol) in THP (2 mL). The resulting mixture was stirred and the reaction was continued until the aldehyde was no longer detectable by TLC monitoring, which took about 24 h. The reaction was quenched with the addition of an aqueous solution of $NH_4Cl$ and was extracted with AcOEt. The crude product was purified by column chromatography ($SiO_2$, hexane/AcOEt 30:1 v/v) to give **3a** as a colorless oil (160 mg, 71%). $R_f$ = 0.70 (hexane/AcOEt 7:1 v/v). IR (neat): $\tilde{\nu}$ = 2960, 2939, 2874, 1710, 1658, 1597, 1462, 1437, 1381, 1365, 1329, 1274, 1263, 1240, 1228, 1190, 1172, 1149, 1080, 1057, 1030, 958, 779 $cm^{-1}$. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 0.93 (t, $J$ = 7.3 Hz, 3 H), 1.09 (t, $J$ = 7.3 Hz, 3 H), 1.38 (m, 2 H), 1.52 (m, 1 H), 1.73 (m, 1 H), 1.96 (m, 1 H), 2.05 (m, 1 H), 2.27 (s, 3 H), 3.73 (s, 3 H), 4.59 (dd, $J$ = 9.5, 2.9 Hz, 1 H), 6.07 (s, 1 H) ppm. $^{13}C$ NMR (150.8 MHz, $CDCl_3$): $\delta$ = 11.7, 13.9, 18.2, 19.5, 25.3, 34.3, 51.1, 78.8, 104.2, 113.7, 130.6, 163.3, 167.1 ppm. This product was too unstable for successful element analysis or HRMS.

**Methyl 3-Ethyl-6-methyl-2-propyl-3,4-dihydro-2*H*-pyran-5-carboxylate (21a):** 10% Pd/C (15 mg) at room temperature was added to a solution of **3a** (112 mg, 0.5 mmol) in THF (3 mL) . The mixture was stirred overnight in a flask equipped with a balloon of $H_2$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography ($SiO_2$, hexane/AcOEt 30:1 v/v) to give **21a** as a colorless oil (92 mg, 81%). $R_f$ = 0.74 (hexane/AcOEt 7:1 v/v). IR (neat): $\tilde{\nu}$ = 2961, 2872, 1711, 1624, 1460, 1433, 1379, 1265, 1244, 1231, 1188, 1107, 1071, 1020, 951, 939, 767 $cm^{-1}$. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 0.93 (m, 6 H), 1.13–1.40 (m, 3 H), 1.51–1.71 (m, 4 H), 1.90–2.03 (m, 1 H), 2.21 (m, 3 H), 2.33–2.43 (m, 1 H), 3.68 (s, 3 H), 4.01 (m, 1 H) ppm. $^{13}C$ NMR (150.8 MHz, $CDCl_3$): $\delta$ = 11.0 + 12.0, 14.0 + 14.1, 18.2 + 19.2, 20.1 + 20.2, 22.0 + 24.3, 25.3 + 25.7, 30.7 + 34.3, 36.1 + 36.2, 50.90 + 50.91, 78.7 + 79.6, 99.76 + 99.78, 164.0 + 164.3, 169.2 + 169.3 ppm. $C_{13}H_{22}O_3$ (226.32): calcd. C 68.99, H 9.80; found C 68.95, H 9.98.

**Photooxidation of 3a, Preparation of the *cis*-Methyl 1-Ethyl-4-methyl-6-propyl-2,3,5-trioxabicyclo[2.2.2]oct-7-ene-8-carboxylate (24):** Compound **3a** (224 mg, 1.0 mmol) and rose bengal (15 mg) were dissolved in MeOH (10 mL) and cooled to –78 °C in a 50 mL round-bottomed flask before being irradiated with a 250 W halogen lamp under bubbling with oxygen for 4 h. The solution was warmed to room temperature and the solvent was removed in vacuo to afford a pink residue, which was purified by column chromatography ($SiO_2$, hexane/AcOEt 10:1 v/v) to give **24** as a white solid (231 mg, 90%). $R_f$ = 0.50 (hexane/AcOEt 5:1 v/v). IR (KBr): $\tilde{\nu}$ = 2961, 2878, 1728, 1626, 1460, 1433, 1381, 1333, 1275, 1206, 1140, 1123, 1101, 1071, 1049, 964, 926, 854, 818, 745, 679 $cm^{-1}$. $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 0.89 (t, $J$ = 7.2 Hz, 3 H), 1.03 (m, 1 H), 1.04 (t, $J$ = 7.2 Hz, 3 H), 1.30 (m, 2 H), 1.45 (m, 1 H), 1.76 (s, 3 H), 1.79 (m, 1 H), 1.92 (m, 1 H), 3.81 (s, 3 H), 4.20 (dd, $J$ = 10.2, 2.4 Hz, 1 H), 7.17 (s, 1 H) ppm. $^{13}C$ NMR (150.8 MHz, $CDCl_3$): $\delta$ = 6.8, 13.9, 18.0, 19.6, 24.8, 33.3, 51.9, 76.8, 78.7, 97.0, 136.4, 138.9, 162.5 ppm. $C_{13}H_{20}O_5$ (256.30): calcd. C 60.92, H 7.87; found C 61.22, H 7.69.

**Methyl 2,5-Dimethylfuran-3-carboxylate (30):** *p*TsOH (7 mg, 0.2 equiv.) and $Ph_3P$ (68 mg, 0.26 mmol) were added to a solution of **26** (43 mg, 0.2 mmol) in $CH_2Cl_2$ (1.5 mL) . The mixture was stirred at room temperature overnight. The solvent was removed in vacuo and the residue was purified by column chromatography ($SiO_2$, hexane/AcOEt 40:1 v/v) to give **30** as a colorless oil (20 mg, 65%). $R_f$ = 0.82 (hexane/AcOEt 5:1 v/v). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 2.25 (s, 3 H), 2.53 (s, 3 H), 3.81 (s, 3 H), 6.21 (s, 1 H)

ppm. $^{13}C$ NMR (150.8 MHz, $CDCl_3$): $\delta$ = 13.2, 13.6, 51.2, 106.1, 113.7, 149.9, 157.7, 164.8 ppm.

**Methyl 2,3a,4,6-Tetramethyl-4,7a-dihydro-3a*H*-[1,3]dioxolo[4,5-*c*]-pyran-7-carboxylate (31):** $Cu(OTf)_2$ (15 mg, 0.2 equiv.) was added to a solution of **26** (43 mg, 0.2 mmol) in $CH_2Cl_2$ (1.5 mL) . The mixture was stirred at room temperature overnight. The solvent was removed and the residue was purified by column chromatography ($SiO_2$, hexane/AcOEt 40:1 v/v) to give **31** as a white solid (13 mg, 27%). $R_f$ = 0.54 (hexane/AcOEt 5:1 v/v). $^1H$ NMR (600 MHz, $CDCl_3$): $\delta$ = 0.98 (s, 3 H), 1.30 (d, $J$ = 4.8 Hz, 3 H), 1.36 (d, $J$ = 6.6 Hz, 3 H), 2.26 (s, 3 H), 3.75 (s, 3 H), 4.40 (s, 1 H), 4.98 (q, $J$ = 6.6 Hz, 1 H), 5.48 (q, $J$ = 5.4 Hz, 1 H) ppm. $^{13}C$ NMR (150.8 MHz, $CDCl_3$): $\delta$ = 12.7, 14.1, 17.9, 20.3, 51.4, 70.9, 72.0, 76.5, 101.3, 101.5, 167.4, 168.8 ppm.

**Supporting Information** (see footnote on the first page of this article): Detailed experimental procedures and product characterization.

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