

# Synthesis of 6*H*-Dibenzo[*b,d*]pyran-6-ones Using the Inverse Electron Demand Diels–Alder Reaction

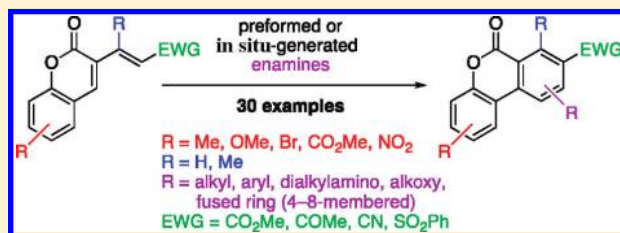
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## Supporting Information

**ABSTRACT:** A set of coumarin-fused electron-deficient 1,3-dienes was synthesized, which differ in the nature of the electron-withdrawing group (EWG) at the terminus of the diene unit and (when EWG = CO<sub>2</sub>Me) the nature and position of substituents. These dienes reacted with the enamine derived from cyclopentanone and pyrrolidine to afford the corresponding cyclopenteno-fused 6*H*-dibenzo[*b,d*]pyran-6-ones, most likely via a domino inverse electron demand Diels–Alder (IEDDA)/elimination/transfer hydrogenation sequence. The parent diene (EWG = CO<sub>2</sub>Me, no substituents) was reacted with a range of electron-rich dienophiles (mostly enamines) to afford the corresponding 6*H*-dibenzo[*b,d*]pyran-6-ones or their nondehydrogenated precursors, which were aromatized upon treatment with a suitable oxidant. The enamines could either be synthesized prior to the reaction or generated in situ. The syntheses of 30 dibenzopyranones are reported.



## INTRODUCTION

A variety of natural products feature a 6*H*-dibenzo[*b,d*]pyran-6-one (1) core, including fasciculiferol (2),<sup>1,2</sup> alternariol (3),<sup>3</sup> autumariol (4),<sup>4</sup> autumnariniol (5),<sup>4</sup> altenuisol (6),<sup>5</sup> and ellagic acid (7).<sup>6,7</sup> (Figure 1). A closely related structure, 6*H*-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (8), is common to several bactericidal and antitumor natural products such as the gilvocarcins (9),<sup>8–15</sup> the ravidomycins (10),<sup>16–19</sup> the chrysomycins (11),<sup>20,21</sup> and arnottin I (12).<sup>22,23</sup> Furthermore, dibenzopyranones have served as intermediates in the synthesis of cannabinoids<sup>24–27</sup> and other pharmaceutically interesting compounds, for example, progesterone, androgen, and glucocorticoid receptor agonists,<sup>28–30</sup> endothelial proliferation inhibitors,<sup>31</sup> and antidiabetic agents.<sup>32</sup>

Numerous approaches to the synthesis of 6*H*-dibenzo[*b,d*]pyran-6-ones have been reported. These can be broadly classified according to the bonds formed during the key step(s) as follows: approaches that involve (1) biaryl bond formation followed by lactonization,<sup>33–40</sup> (2) construction of an ester or ether followed by intramolecular biaryl bond formation,<sup>41–43</sup> (3) a cyclization to form the C ring (or B and C rings), with or without a subsequent aromatization,<sup>27,44–57</sup> (4) rearrangement of spirocyclic compounds,<sup>58–60</sup> (5) biomimetic syntheses of alternariol derivatives,<sup>61–65</sup> and (6) miscellaneous methods.<sup>66,67</sup> In category 3, enediyne cycloaromatization,<sup>44–46</sup> ruthenium-catalyzed [2+2+2] cycloaromatization,<sup>27</sup> 6π electrocyclic ring closure,<sup>47</sup> condensations involving chromones<sup>48</sup> and coumarins<sup>49–51</sup> bearing electron-withdrawing groups, and the Diels–Alder reaction<sup>52–57</sup> have been exploited. Of these methods, the Diels–Alder reaction arguably offers the greatest potential for

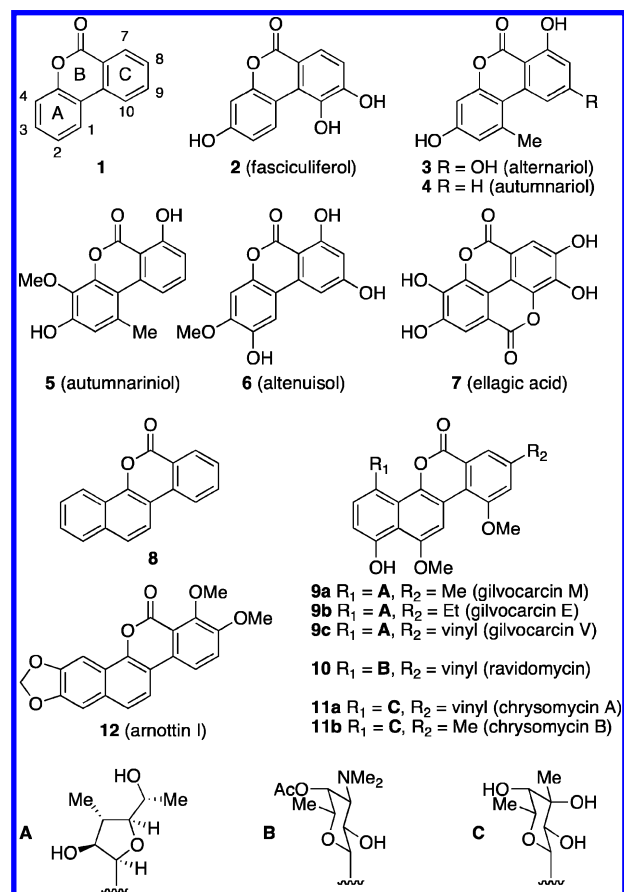
diversity-oriented synthesis. An existing coumarin system can be designed to function as either a diene or a dienophile in either the normal or inverse electron demand version of the reaction. For the normal Diels–Alder reaction, coumarin-based dienophiles<sup>53–55</sup> and a diene<sup>52</sup> have been reported. Our group communicated the only example of a coumarin-based diene (13) to be used as a substrate in an inverse electron demand Diels–Alder (IEDDA)-based synthesis of C-ring-functionalized 6*H*-dibenzo[*b,d*]pyran-6-ones<sup>56</sup> 14 (Scheme 1) and, more recently, an application of this methodology in the total synthesis of urolithin M7 (15).<sup>68</sup> Reported herein are the details of an exploration of the scope and limitations of this methodology.

## RESULTS AND DISCUSSION

As reported earlier,<sup>56</sup> coumarin-fused diene 13 was synthesized in a single step from salicylaldehyde (16) and dimethyl glutaconate (17) (Scheme 2). This involves a transesterification and a vinylogous Knoevenagel condensation, although the order of events is unclear. An important feature of diene 13 is that the electron-withdrawing groups on the diene unit have a 1,3 relationship,<sup>69</sup> as do the electron-donating groups on Danishefsky's diene.<sup>70</sup> However, the synthesis of diene 13 is not easily modified to allow for the incorporation of a variety of other electron-withdrawing groups at the terminus of the diene system. Accordingly, an alternative and more general approach

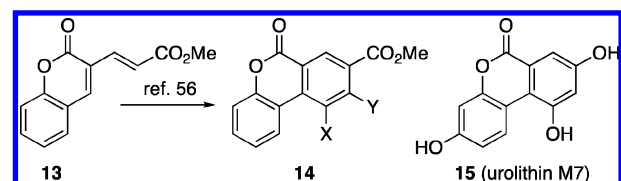
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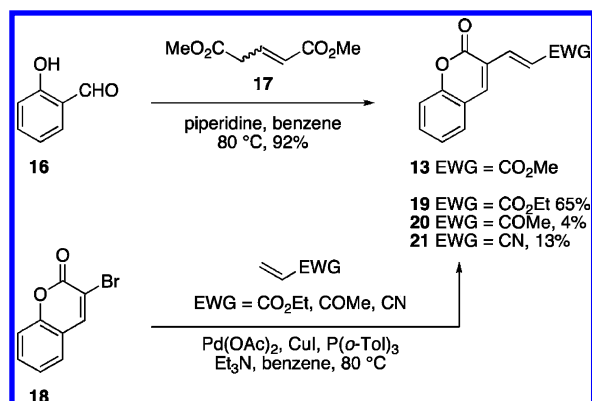


**Figure 1.** Structures of 6H-dibenzo[*b,d*]pyran-6-one (1), 6H-benzo[*d*]naphtho[1,2-*b*]pyran-6-one (8), and some natural products possessing these core structures.

### Scheme 1



### Scheme 2

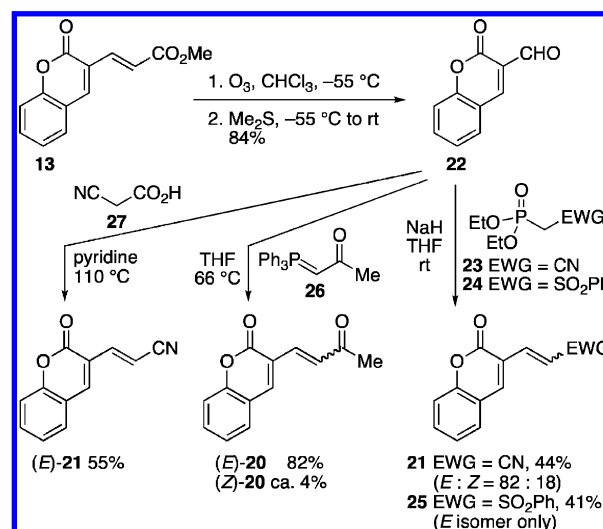


to the synthesis of a family of electron-deficient, coumarin-fused dienes was sought.

The use of 3-bromocoumarin (18)<sup>71</sup> as a common starting material in the Heck reaction with various electron-deficient

alkenes was identified as a promising route (Scheme 2). After some optimization, good results were obtained using ethyl acrylate. Diene 19 was obtained in 65% yield. However, the use of these conditions with methyl vinyl ketone or acrylonitrile afforded dienes 20 and 21 in very poor yield. Faced with the prospect of reoptimizing the Heck reaction for each electron-deficient alkene, another approach was investigated. This involved the use of the Horner–Wadsworth–Emmons reaction to generate the electron-deficient diene system, which had been used successfully for other electron-deficient dienes (Scheme

### Scheme 3



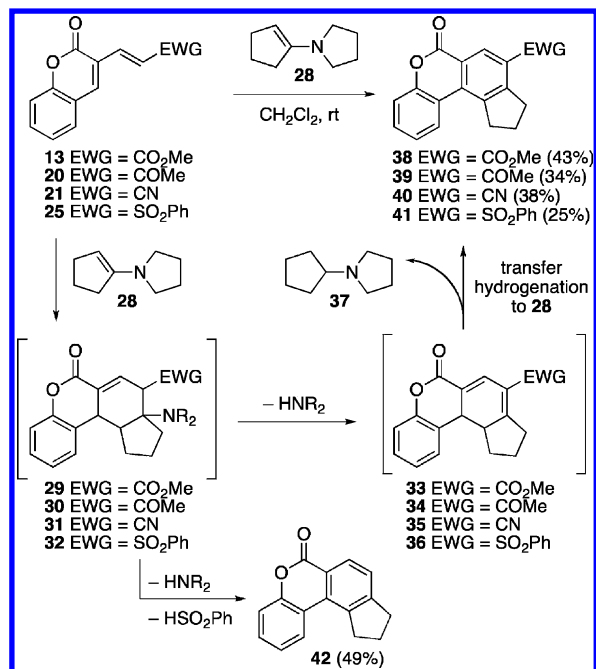
3).<sup>69,72–74</sup> Thus, access to multigram quantities of 3-formylcoumarin (22) was required, and this was achieved by ozonolysis of diene 13. At 84%, the yield of this reaction is somewhat better than that reported by Triggle et al. for the oxidative cleavage of 19 using OsO<sub>4</sub>/NaIO<sub>4</sub> (70%).<sup>75</sup>

Aldehyde 22 was reacted with phosphonates 23<sup>76</sup> and 24<sup>77</sup> to afford dienes 21 and 25 in modest yield. In the case of cyanodiene 21, an inseparable mixture of geometric isomers favoring the *E* isomer (82:18 by <sup>1</sup>H NMR analysis) was obtained. On the other hand, only the *E* isomer of the corresponding sulfone 25 was isolated. Methyl ketone 20 was synthesized using a Wittig reaction between 3-formylcoumarin (22) and ylide 26.<sup>78</sup> Both geometric isomers were produced, and the *E* isomer could be isolated in 82% yield using flash chromatography. A 9:1 mixture of (*Z*)-20/(*E*)-20 (4%) was also isolated. Finally, isomerically pure cyanodiene (*E*)-21 was synthesized via decarboxylative Knoevenagel condensation of 22 with cyanoacetic acid (27). Attempts to generate the corresponding nitrodiene using a Henry reaction of 22 with nitromethane were unsuccessful.

The investigation of the IEDDA chemistry of dienes 13, (*E*)-20, (*E*)-21, and 25 commenced with the reaction of 13 with ethyl vinyl ether. Although ethyl vinyl ether is a relatively weak dienophile, it had been found to react with a related electron-deficient diene at 80 °C.<sup>69</sup> However, 13 was unreactive toward ethyl vinyl ether (TLC analysis) after heating for 4 d at 120 °C (sealed tube) or under catalysis by Yb(OTf)<sub>3</sub>,<sup>79</sup> Eu(hfc)<sub>3</sub>,<sup>79</sup> or silica gel.<sup>80</sup> Partial aromatic character (even a small amount) in the pyranone ring would be expected to decrease the Diels–Alder reactivity. In view of the lower reactivity of 13, a more reactive dienophile was employed. Indeed, the enamine (28)

derived from cyclopentenone and pyrrolidine reacted smoothly with diene **13** in dichloromethane at ambient temperature to afford dibenzopyranone **38** in 43% yield (Scheme 4). Under the same conditions, dienes (*E*)-**20**, (*E*)-**21**, and **25** provided the corresponding dibenzopyranones **39–41** (25–38%).

Scheme 4



The products presumably arise from a formal IEDDA reaction<sup>81</sup> to afford adducts **29–32**, followed by 1,2-elimination to give cyclohexadienes **33–36**<sup>82</sup> and a dehydrogenation (Scheme 4). Disproportionation products have been observed in intramolecular IEDDA reactions of a related heterodiene,<sup>83</sup> but none were observed in any of these reactions. Transfer hydrogenation<sup>84</sup> to enamine **28** (giving amine **37**) is therefore a more likely pathway for the dehydrogenation of **33–36** to afford **38–41**. Support for this notion is presented at the end of this article. For dienes **13**, (*E*)-**20**, and (*E*)-**21**, no intermediates or byproducts were isolated or observed (TLC analysis) during the course of these reactions. However, diene **25** gave rise to the formation of dibenzopyranone **42** (49%), which lacks the sulfonyl group, in addition to **41**. Allylic sulfones are known to undergo 1,4-elimination of benzenesulfonic acid;<sup>85</sup> therefore, it seems likely that **42** is formed by a 1,4-elimination of benzenesulfonic acid from **32** followed by a 1,2-elimination of pyrrolidine.<sup>86</sup>

Diene **13** was then reacted with a series of enamines, whereby the outcome depended on the nature of the dienophile (Table 1). The use of enamines **43**, **45**, **47**, and **49**,<sup>87</sup> which are derived from acyclic carbonyl compounds or cyclic ketones with a ring size of 5, led to the formation of functionalized dibenzopyranones **44**, **46**, **48**, and **50** in 43–64% yield (Table 1, entries 1–4). As before, no intermediates or byproducts were isolated or observed (TLC analysis) during the course of these reactions.

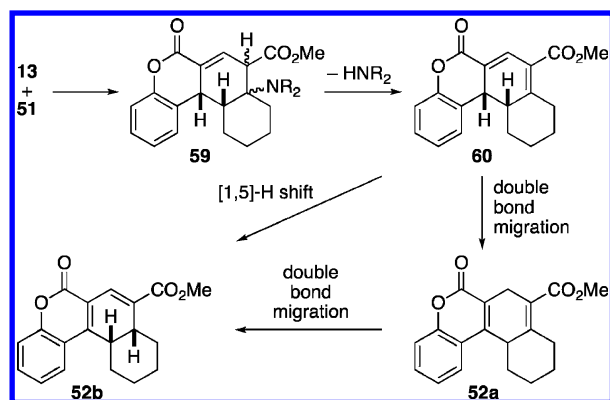
Enamines **51** and **53**, which are derived from cyclic ketones with a ring size of  $\geq 6$ , gave products that had not undergone dehydrogenation (Table 1, entries 5,6). In the case of enamine **51**, cyclohexadienes **52a** (82%) and **52b** (4%) were isolated. The structures of both products were determined by single-

Table 1. Results of IEDDA-Driven Domino Reactions of Diene **13** with Enamines

Entry	Enamine	Product	Yield (%)
1	<b>43</b>	<b>44</b>	64
2	<b>45</b>	<b>46</b>	43
3	<b>47</b>	<b>48</b>	55
4	<b>49</b>	<b>50</b>	48
5	<b>51</b>	<b>52a</b> , <b>52b</b>	82, 4
6	<b>53</b>	<b>54</b>	80
7	<b>55</b>	<b>56</b>	15
8	<b>57</b>	<b>58</b>	56

crystal X-ray diffraction studies (Supporting Information). Although neither product corresponds to diene **33** in the proposed mechanism (Scheme 4), plausible pathways for their formation based on this mechanism can be put forward (Scheme 5). Following cycloaddition<sup>81</sup> of **13** and **51** to afford adduct **59**, and subsequent elimination of pyrrolidine to give **60**, diene **52a** could arise from a double bond migration that leads to the re-establishment of the coumarin system.<sup>88</sup> A subsequent double bond migration would afford diene **52b**, which was determined to have *cis* relative stereochemistry. AM1 calculations predicted that **52b** and its *trans* isomer are within 1 kcal/mol of each other; therefore, it does not seem likely that this process would give only the *cis* isomer. On the other hand, diene **52b** could be the product of a [1,5]-H shift<sup>89</sup> of diene **60**. If this is the case, then the *cis* relative stereochemistry in **52b** can be traced back to the precursor diene **60** as well as cycloaddition to **59**. If the cycloaddition to **59** is concerted, then it must have proceeded through a

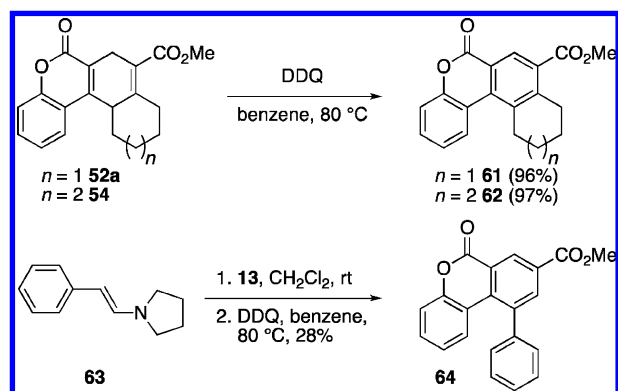
Scheme 5



transition state in which the  $\text{NR}_2$  group of the dienophile is exo to the diene. If it is a stepwise reaction, then the first step (conjugate addition) occurs with complete diastereoselectivity. Unfortunately, these considerations can only be applied to the 4% of the starting material that ended up as **52b**. The lack of any relative stereochemical relationships in **52a** precludes meaningful commentary about the nature of the cycloaddition. Enamine **53** gave only the 1,4-cyclohexadiene **54**, also in good yield (80%).

The failure of the reactions involving enamines **51** and **53** to undergo dehydrogenation is likely a consequence of strain in the dibenzopyranone products **61** and **62**, which were synthesized in high yield by the reactions of **52a** and **54** with DDQ (Scheme 6). AM1-calculated structures of **61** and **62**

Scheme 6



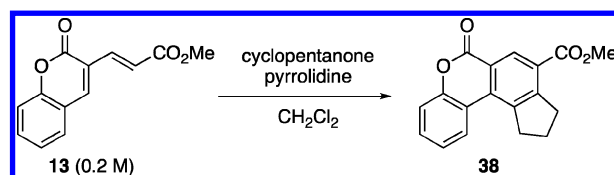
have twisted structures (Supporting Information). The average deviations from 0 or 180° of torsion angles around the biaryl bond are ~21°. By comparison, compounds **38**, **44**, and **46** were calculated to have essentially planar dibenzopyranone systems. Dibenzopyranone **64**, which was calculated to be twisted to a similar extent as **52a** and **54**, also required a two-step synthesis (Scheme 6). Enamine **63** reacted with diene **13** to afford a mixture of at least three unaromatized products ( $^1\text{H}$  NMR analysis), which could not be separated chromatographically. Treatment of this mixture with DDQ afforded **64**, but the overall yield (28%) was low.

Cyclooctanone-derived enamine **55** was essentially unreactive toward **13** at room temperature but reacted at reflux in dichloromethane to afford dibenzopyranone **56** in just 15% yield (Table 1, entry 7). The AM1-calculated structure of **56** is also twisted. Presumably, the elevated temperature facilitated

the transfer hydrogenation. Enamine **57**, which cannot give an aromatized product according to the proposed mechanism, reacted with diene **13** to give cyclohexadiene **58** (56%) (Table 1, entry 8). This compound is the product of a domino IEDDA/1,2-elimination/[1,5]-H shift sequence. As for **52b**, successive double bond migrations could replace the [1,5]-H shift.<sup>89</sup>

In considering the further extension of the methodology, the synthesis of the required enamines in reasonably pure form was identified as a potential problem.<sup>90</sup> As such, attention was turned to the possibility of generating the enamines in situ. Moreover, the proposed mechanism for dibenzopyranone formation involves the elimination of the secondary amine used to generate the enamine; therefore, the opportunity to perform these reaction organocatalytically also presented itself.

A system consisting of diene **13**, cyclopentanone, pyrrolidine, and 4 Å molecular sieves was chosen for optimization (Table

Table 2. Optimization of the Synthesis of **38** Using In-Situ-Generated Enamine **28**

entry	cyclopentanone (equiv)	pyrrolidine (equiv)	conditions	isolated yield (%)
1	1.5	0.2	rt, 45 min, 4 Å MS	63
2	1.5	0.05	rt, 24 h, 4 Å MS	37
3	2.0	0.2	rt, 20 min, 4 Å MS	42
4	2.0	0.5	rt, 15 min, 4 Å MS	56
5	5.0	0.5	rt, 15 min, 4 Å MS	66
6	5.0	0.5	0 °C, 45 min, 4 Å MS	59
7	5.0	0.5	40 °C, 45 min, 4 Å MS	15
8	5.0	0.5	rt, 15 min, MgSO <sub>4</sub>	74

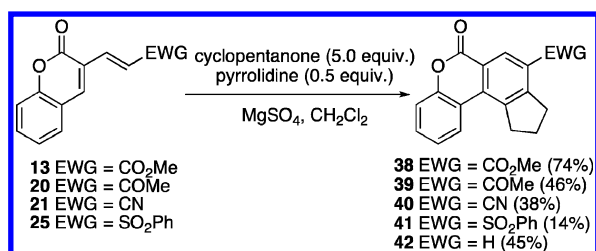
2). The initial experiment using 1.5 equiv of cyclopentanone and 0.2 equiv of pyrrolidine afforded dibenzopyranone **38** in 63% yield after a 45 min reaction (Table 2, entry 1), which was already significantly better than when preformed enamine **28** was employed (43%). Upon lowering the proportion of pyrrolidine to 0.05 equiv (Table 2, entry 2), **38** was again generated, but the reaction had not proceeded to completion after 24 h. The use of 2.0 equiv of cyclopentanone (Table 2, entries 3,4) resulted in the consumption of diene **13** within 15–20 min, but the yields were somewhat lower. A further increase in the proportion of cyclopentanone to 5.0 equiv raised the yield to 66% (Table 2, entry 5). Variation of the temperature from 0 to 40 °C (Table 2, entries 5–7) had only a small effect on the yield, the best yield being obtained at room temperature. Finally, changing the drying agent from 4 Å molecular sieves to  $\text{MgSO}_4$  improved the yield of **38** to 74% (Table 2, entry 8).

Using the best conditions for the synthesis of **38**, dienes (*E*)-**20**, (*E*)-**21**, and **25** were converted into the corresponding dibenzopyranones **39–41** in yields that matched or exceeded



those obtained using preformed enamine **28** (Scheme 7). In the case of sulfone-bearing diene **25**, the byproduct **42** (45%) was

Scheme 7



again produced along with **41** (14%). The product distribution was similar to that obtained using preformed enamine **28**.

Diene **13** was then reacted with a series of ketones under conditions for the in situ generation of enamines (Table 3). The use of 2-indanone (**65**) resulted in the formation of dibenzopyranone **48** in substantially better yield than that when preformed enamine **47** was employed (81 versus 55%) (Table 3, entry 1). The reaction with cyclohexanone (**66**) proceeded slowly at room temperature (Table 3, entry 2), but the outcome was similar to that obtained when using preformed enamine **51**. Upon moving to cycloheptanone (**67**),<sup>91</sup> no reaction occurred at room temperature. However, performing the reaction in acetonitrile at reflux afforded dibenzopyranone **62** in 46% yield (Table 3, entry 3). In this case, the use of preformed enamine **53** is the better option. Analogous behavior was observed for acetophenone (**68**), which reacted in acetonitrile at reflux to give dibenzopyranone **44** (74 versus 64% from **43**) (Table 3, entry 4).

Owing to their expense or problems associated with the synthesis of the corresponding enamines, the remaining ketones were used only in the in situ method. Only 1.5 equiv of expensive ketones (Table 3, entries 6–11) were employed. Acetone (**69**) and cyclobutanone (**71**) reacted at room temperature to afford dibenzopyranones **70** (66%) and **72** (26%) (Table 3, entries 5,6). The latter reaction was considerably slower and lower yielding, but it provided a novel entry to a benzocyclobutene system, which could serve as a precursor to an electron-deficient *ortho*-xylylene. Like cyclohexanone (**66**), tetrahydro-4*H*-thiopyran-4-one (**73**) and *N*-methyl-4-piperidone (**75**) reacted at room temperature, albeit significantly faster, to afford mixtures of nondehydrogenated products (**74a,b** and **76a,b**, respectively) in good yield (Table 3, entries 7,8). Products **74a** (78%) and **74b** (11%) could be separated by flash chromatography. However, chromatographic separation of **76a** and **76b** (80% combined, 71:9 by  $^1\text{H}$  NMR analysis) was more difficult, and only **76a** (44%) could be obtained in pure form. The relative stereochemistry in the minor products was not established unambiguously, but by analogy to **52b**, a *cis* relationship would be expected.

The reaction involving tetrahydro-4*H*-pyran-4-one (**77**) appeared to have stalled after 24 h and gave a chromatographically separable mixture of diene **13** (18% recovery), **78a** (40%), and an unexpected byproduct **79** (32%) (Table 3, entry 9). A product analogous to **52b**, **74b**, and **76b** was not isolated. The structure of **79** was determined using a single-crystal X-ray diffraction experiment (Supporting Information). Its formation can be explained by a diastereoselective conjugate addition of the enamine **86** to the convex face of **78a**, followed by an

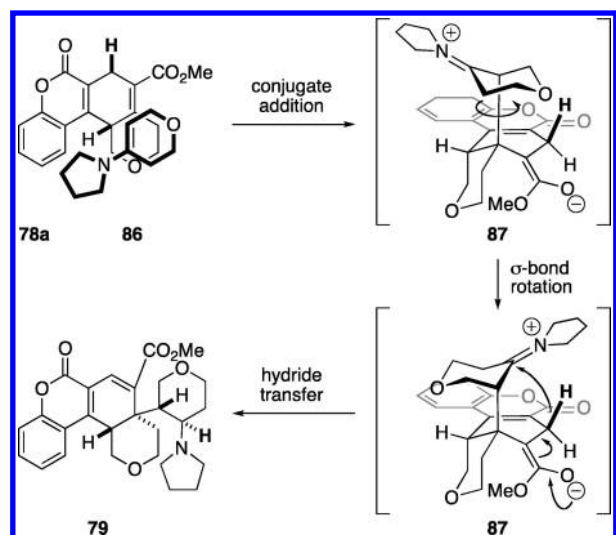
Table 3. Results of Reactions of Diene **13** with In-Situ Generated Enamines

Entry	Ketone	Conditions	Product(s)	Yield (%)
1	<b>65</b>	$\text{CH}_2\text{Cl}_2$ , rt, 3 h	<b>48</b>	81
2	<b>66</b>	$\text{CH}_2\text{Cl}_2$ , rt, 5 d	<b>52a</b> + <b>52b</b>	74, 8
3	<b>67</b>	$\text{CH}_3\text{CN}$ , 82 °C, 24 h	<b>62</b>	46
4	<b>68</b>	$\text{CH}_3\text{CN}$ , 82 °C, 24 h	<b>44</b>	74
5	<b>69</b>	$\text{CH}_2\text{Cl}_2$ , rt, 1 h	<b>70</b>	66
6	<b>71</b>	$\text{CH}_2\text{Cl}_2$ , rt, 48 h	<b>72</b>	26
7	X = S, <b>73</b>	$\text{CH}_2\text{Cl}_2$ , rt, 24 h	<b>74a</b> , <b>74b</b>	79, 11
8	X = NMe, <b>75</b>	$\text{CH}_2\text{Cl}_2$ , rt, 5 h	<b>76a</b> , <b>76b</b>	80 (71:9)
9	<b>77</b>	$\text{CH}_2\text{Cl}_2$ , rt, 24 h	<b>78a</b> , <b>79</b>	40, 32
10	<b>80</b>	$\text{CH}_2\text{Cl}_2$ , rt, 24 h	<b>81</b>	15
11	<b>82</b>	$\text{CH}_2\text{Cl}_2$ , rt, 3 d	<b>83</b>	17
12	<b>84</b>	$\text{CH}_2\text{Cl}_2$ , rt, 1.5 h	<b>85</b>	59

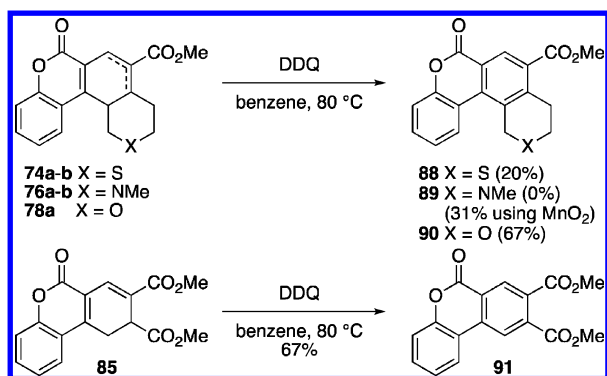
intramolecular hydride transfer in the resulting intermediate **87** (Scheme 8).<sup>92</sup> Alternatively, conjugate addition could occur to a diene analogous to **33**, which looks to be a much better Michael acceptor, followed by a similar intramolecular hydride transfer. Whatever the case, it is not obvious why this side reaction occurs with ketone **77** and not with ketones **66**, **73**, and **75**.

More hindered ketones **80** and **82** reacted at room temperature, but they afforded the corresponding dibenzopyranones **81** and **83** in just 15 and 17% yield, respectively. Finally, methyl pyruvate (**84**) (10 equiv) was used, and despite the electron-withdrawing ester group, it reacted relatively quickly at room temperature to afford the nonaromatized product **85** in 59% yield. This compound and the other nonaromatized products (**74a,b**, **76a,b**, and **78a**) were reacted with DDQ with the intention of producing the corresponding aromatized

Scheme 8



Scheme 9



products **88–91** (Scheme 9). Whereas dibenzopyranones **90** and **91** were isolated in reasonably good yield, the systems with more oxidation-sensitive S and N atoms were obtained in 20 and 0% yield, respectively. An alternative aromatization using  $\text{MnO}_2$  afforded dibenzopyranone **89** in 31% yield.

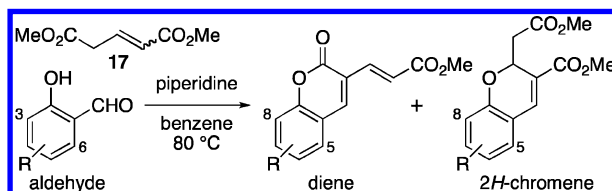
Some of the yields obtained using the in situ method were in excess of 50%, which would be the theoretical limit if transfer hydrogenation to the enamine were solely responsible for the dehydrogenation step. Clearly, one or more other mechanisms

for dehydrogenation must be available, such as transfer hydrogenation to the ketone, which is present in excess.

To demonstrate that A-ring substituted dibenzopyranones are also accessible using the IEDDA-based approach, a series of salicylaldehydes was reacted with dimethyl glutaconate (**17**) to afford the corresponding coumarin-fused dienes (Table 4). Aldehydes **92**, **94**, **96**, **98**, and **101** were synthesized by Skattebol formylation<sup>93</sup> of the corresponding phenols, whereas aldehydes **104** and **107** were synthesized by Duff formylation<sup>94,95</sup> of the corresponding phenols. The methyl-substituted salicylaldehydes **92**, **94**, and **96** reacted smoothly to afford dienes **93**, **95**, and **97** in 72–80% yield (Table 4, entries 1–3). Salicylaldehydes **98**, **101**, and **104** also afforded the desired dienes **99**, **102**, and **105**, but the yields were slightly lower (65–71%) and the 2*H*-chromenes **100**, **103**, and **106** were also formed in 15–25% yield (Table 4, entries 4–6). In the case of 5-nitrosalicylaldehyde (**107**), diene **108** was obtained in only 26% yield, and 2*H*-chromene **109** was the major product (72%). In contrast to the diene products, which arise from a combination of vinylogous Knoevenagel condensation and transesterification, the 2*H*-chromene products arise from a combination of vinylogous Knoevenagel condensation and conjugate addition. The order of events and the factors influencing the product distribution are, at this time, unclear.

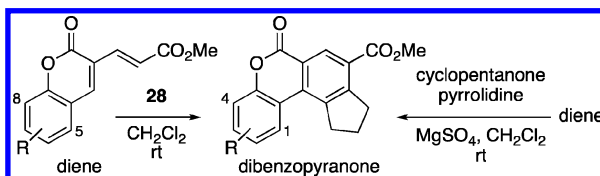
The dienes were reacted with **28** using both the preformed enamine and the method involving its generation in situ (Table 5). In the case of the parent diene **13**, it had already been found that the in situ method gave a much better yield of dibenzopyranone **38** (Table 5, entry 1). This was also the case for dienes **93**, **95**, **97**, and **99**, but the superiority of the in situ method was less pronounced (Table 5, entries 2–5). For dienes **102**, **105**, and **108**, better yields were obtained using preformed **28** (Table 5, entries 6–8). Overall, the yields using preformed **28** were more consistent than when using the in situ method. In both instances, nitro-substituted diene **108** stood out as the poorest-yielding example.

As a further example of the scope of the methodology, salicylaldehyde (**16**) was reacted with dimethyl 3-methylglutaconate (**117**) to afford diene **118** (55%), which bears a methyl group on the diene unit (see Scheme 10). Reaction of **118** with preformed enamine **28** gave dibenzopyranone **119** (67%), in which the newly formed aromatic ring is hexasubstituted. Generation of the enamine in situ gave a 44% yield of **119**.

Table 4. Results of Reactions of Dimethyl Glutaconate (**17**) with Salicylaldehydes

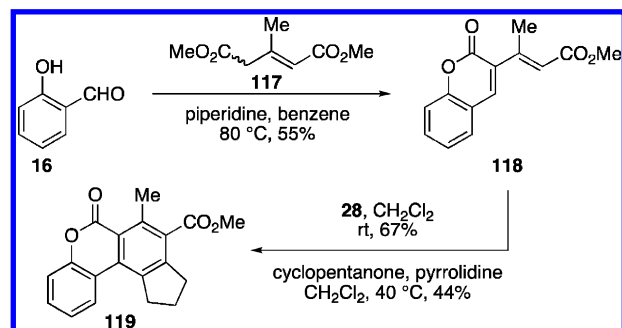
entry	aldehyde	diene (% yield)	2 <i>H</i> -chromene (% yield)
1	<b>92</b> R = 5-Me	<b>93</b> R = 6-Me (78)	
2	<b>94</b> R = 4-Me	<b>95</b> R = 7-Me (80)	
3	<b>96</b> R = 3-Me	<b>97</b> R = 8-Me (72)	
4	<b>98</b> R = 5-OMe	<b>99</b> R = 6-OMe (71)	<b>100</b> R = 6-OMe (19)
5	<b>101</b> R = 5-Br	<b>102</b> R = 6-Br (65)	<b>103</b> R = 6-Br (25)
6	<b>104</b> R = 5-CO <sub>2</sub> Me	<b>105</b> R = 6-CO <sub>2</sub> Me (66)	<b>106</b> R = 6-CO <sub>2</sub> Me (15)
7	<b>107</b> R = 5-NO <sub>2</sub>	<b>108</b> R = 6-NO <sub>2</sub> (26)	<b>109</b> R = 6-NO <sub>2</sub> (72)

Table 5. Results of Reactions of Enamine 28 with Coumarin-Fused Electron Deficient Dienes

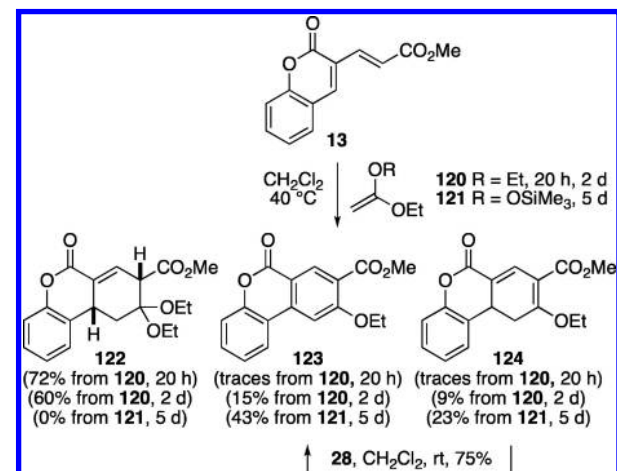


entry	diene	dibenzopyranone	% yield (preformed 28)	% yield in situ (28)
1	13 R = H	38 R = H	43	74
2	93 R = 6-Me	110 R = 2-Me	47	50
3	95 R = 7-Me	111 R = 3-Me	51	57
4	97 R = 8-Me	112 R = 4-Me	48	54
5	99 R = 6-OMe	113 R = 2-OMe	51	64
6	102 R = 6-Br	114 R = 2-Br	51	35
7	105 R = 6-CO <sub>2</sub> Me	115 R = 2-CO <sub>2</sub> Me	41	34
8	108 R = 6-NO <sub>2</sub>	116 R = 2-NO <sub>2</sub>	24	22

Scheme 10



Scheme 11



Whereas ethyl vinyl ether was found to be unreactive toward diene 13, ketene acetals **120**<sup>96</sup> and **121**<sup>97</sup> reacted slowly at reflux in dichloromethane (see Scheme 11). In the case of **120**, IEDDA adduct **122** was isolated in 72% yield after 20 h of reaction. Upon extending the reaction time to 48 h, **122** (60%) was still the major product, but dibenzopyranone **123** (15%) and cyclohexadiene **124** (9%) were also isolated. As for most of the reactions with enamines described above, the formation of dibenzopyranone **123** can be explained by a sequential IEDDA/elimination/transfer hydrogenation process. Diene **124** appears simply to be the result of a sequential IEDDA/elimination sequence. A 5 d reaction using ketene acetal **121** afforded only **123** (43%) and **124** (23%), both of which are

follow-on products from **122**. The relative stereochemistry in **122** was established using an X-ray crystal structure determination (Supporting Information). While it is fully consistent with a concerted cycloaddition, it does not rule out a completely stereoselective stepwise mechanism. The much slower rate of elimination in adduct **122** than that in the corresponding enamine adducts (e.g., **29**, Scheme 4) is likely due to the absence of an organic base. In the reactions involving enamines, pyrrolidine (a 2° amine), adducts such as **29** (a 3° amine) and the enamines themselves (3° amines) are present.

In an attempt to use diene **124** as an IEDDA substrate, it was reacted with enamine **28** at room temperature. However, no products arising from cycloaddition were observed. Instead, dibenzopyranone **123** was isolated in 75% yield after a 3 h reaction. It thus appears that transfer hydrogenation is indeed a facile process. The presence of 1-cyclopentylpyrrolidine (**37**) in the reaction mixture was supported by GC-MS analysis (*m/z* = 139) of an extract of a (neutralized) acid wash of a reaction between **124** and **28**, for which independently synthesized **37**<sup>98</sup> was used as a standard.

## CONCLUSIONS

Twelve coumarin-fused electron-deficient dienes were synthesized, and they reacted with a variety of preformed and/or in-situ-generated enamines. When the enamine was derived from an acyclic carbonyl compound or a cyclic ketone with a ring size of ≤5, 6*H*-dibenzo[*b,d*]pyran-6-ones were obtained from room-temperature reactions. When the enamine was derived from a cyclic ketone with a ring size of ≥6, dihydro-6*H*-dibenzo[*b,d*]pyran-6-ones were obtained, unless a reaction temperature of >40 °C was employed, in which case, the aromatized products were generated. The dihydro-6*H*-dibenzo[*b,d*]pyran-6-one products could be dehydrogenated to afford the corresponding 6*H*-dibenzo[*b,d*]pyran-6-ones. A total of 30 6*H*-dibenzo[*b,d*]pyran-6-ones were synthesized, including one in which the newly formed six-membered ring was hexasubstituted. The reactions presumably commence with a formal IEDDA reaction. The question of whether this step is concerted or stepwise could not be addressed generally, but the few pieces of evidence pertaining to the mechanism of the cycloaddition step were fully consistent with a concerted cycloaddition. Nevertheless, a stepwise mechanism cannot yet be excluded.



## ■ EXPERIMENTAL SECTION

**General Methods.** General methods have been published elsewhere.<sup>99</sup>

**Methyl (E)-3-(2-Oxo-2H-chromen-3-yl)acrylate (13).**<sup>56</sup> To a magnetically stirred solution of salicylaldehyde (**16**) (0.44 mL, 4.1 mmol) and dimethyl glutaconate (**17**) (0.57 mL, 4.1 mmol) in benzene (25 mL) was added piperidine (0.20 mL, 2.0 mmol) in one portion, and the resulting mixture was heated at reflux with azeotropic removal of water for 4 h. Upon cooling to room temperature, a white precipitate formed, which was isolated by suction filtration. The filter cake was washed with cool benzene (25 mL) to afford **17** (0.58 g, 62%) as a white solid. The filtrate was concentrated under reduced pressure and subjected to flash chromatography on silica gel (3% ethyl acetate/dichloromethane) to afford a second batch of **17** (0.29 g, 30%, total = 0.87 g, 92%): mp 176–178 °C; IR (nujol)  $\nu$  = 1727 (s)  $\text{cm}^{-1}$ ; UV–vis (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 315 (3.62), 290 (3.63) nm; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.88 (s, 1H), 7.59–7.55 (m, 3H), 7.35–7.30 (m, 2H), 7.10 (d,  $J$  = 15.3 Hz, 1H), 3.82 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 167.2 (0), 159.0 (0), 153.5 (0), 143.5 (1), 138.0 (1), 132.8 (1), 128.5 (1), 124.8 (1), 123.2 (1), 122.2 (0), 118.9 (0), 116.6 (1), 51.8 (3); EI-MS  $m/z$  (%) 230 ( $M^+$ , 16), 171 (100); Anal. Calcd for  $\text{C}_{13}\text{H}_{10}\text{O}_4$ : C, 67.82; H, 4.38. Found: C, 67.71; H, 4.27.

**Ethyl (E)-3-(2-Oxo-2H-chromen-3-yl)acrylate (19).** A mixture of 3-bromocoumarin (1.00 g, 5.18 mmol), ethyl acrylate (0.84 mL, 7.70 mmol),  $\text{Pd}(\text{OAc})_2$  (46 mg, 0.20 mmol), tri-*o*-tolylphosphine (94 mg, 0.31 mmol), CuI (35 mg, 0.18 mmol), and triethylamine (3.58 mL, 25.8 mmol) in benzene (10 mL) was heated at reflux for 4 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature, and aqueous 1 M HCl solution (20 mL) was added. The resulting mixture was extracted with chloroform, and the combined organic extracts were dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed under reduced pressure, and the residue was subjected to flash chromatography on silica gel (chloroform). The product was triturated with ether (2  $\times$  5 mL) to afford **19** as a cream-colored solid (0.82 g, 65%): mp 120–121 °C; IR (powder)  $\nu$  = 2978 (w), 1708 (s), 1604 (m), 1165 (s)  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.88 (s, 1H), 7.60–7.54 (m, 2H), 7.57 (d,  $J$  = 16.1 Hz, 1H), 7.36 (d,  $J$  = 8.3 Hz, 1H), 7.33–7.30 (m, 1H), 7.10 (d,  $J$  = 15.9 Hz, 1H), 4.27 (q,  $J$  = 7.1 Hz, 2H), 1.34 (t,  $J$  = 7.1 Hz, 3H); <sup>13</sup>C NMR (500 MHz)  $\delta$  166.9, 159.1, 153.5, 143.4, 137.8, 132.9, 128.5, 124.8, 123.8, 122.4, 119.0, 116.7, 60.8, 14.3; APCI(+)–MS  $m/z$  (%) 245 ( $[M + 1]^+$ , 12), 200 (14), 199 (100); HRMS (APCI(+)) calcd for  $\text{C}_{14}\text{H}_{13}\text{O}_4$ : 245.0814; found: 245.0815.

**3-Formyl-2-oxo-2H-chromene (22).** Ozone was bubbled through a –55 °C (dry ice/acetone bath) solution of diene **13** (3.00 g, 13.0 mmol) for 50 min, at which time the solution had become dark blue. Nitrogen gas was then bubbled through the solution for 30 min, and the temperature was allowed to rise to –30 °C. Dimethyl sulfide (3.5 mL, 48 mmol) was added in one portion, and the temperature was allowed to rise slowly to room temperature. The resulting mixture was stirred at room temperature for 16 h and concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (2.5% ethyl acetate/dichloromethane) to afford aldehyde **22** (1.90 g, 84%) as a white solid: mp 132–134 °C (lit.<sup>100</sup> mp: 131–132 °C); IR (nujol)  $\nu$  = 1737 (s), 1692 (s), 1609 (s)  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 10.27 (s, 1H), 8.43 (s, 1H), 7.72–7.68 (m, 2H), 7.42–7.37 (m, 2H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 187.7, 160.1, 155.5, 145.6, 135.0, 130.8, 125.3, 121.8, 118.2, 117.1; EI-MS  $m/z$  (%) 174 ( $M^+$ , 21), 146 (100).

**(E)-4-(2-Oxo-2H-chromen-3-yl)but-3-en-2-one (20).** To a magnetically stirred solution of aldehyde **22** (2.59 g, 14.9 mmol) in THF (75 mL) was added ylid **26**<sup>78</sup> (4.73 g, 14.9 mmol) in one portion, and the resulting mixture was heated at reflux for 2 h. The reaction was cooled to room temperature and then concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (3% ethyl acetate/dichloromethane) to afford diene **20** (2.61 g, 82%) as a white solid: mp 157–158 °C; IR (nujol)  $\nu$  = 1704 (s), 1661 (s), 1603 (m)  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.94 (s, 1H), 7.61–7.57 (m, 2H), 7.47 (d,  $J$  = 15.9 Hz, 1H), 7.36 (d,  $J$  = 8.3 Hz,

1H), 7.33 (t,  $J$  = 8.1 Hz, 1H), 7.29 (d,  $J$  = 15.9 Hz, 1H), 2.40 (s, 3H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 198.3 (0), 159.3 (0), 153.6 (0), 143.3 (1), 135.9 (1), 133.0 (1), 130.8 (1), 128.5 (1), 124.9 (1), 122.5 (0), 119.0 (0), 116.7 (1), 28.6 (3); GC-MS  $m/z$  (%) 214 ( $M^+$ , 4), 171 (100); HRMS (EI) calcd for  $\text{C}_{13}\text{H}_{10}\text{O}_3$ : 214.0629; found: 214.0607.

**(E)-3-(2-Oxo-2H-chromen-3-yl)acrylonitrile (21).** A mixture of aldehyde **22** (264 mg, 1.51 mmol) and cyanoacetic acid (**27**) (141 mg, 1.66 mmol) was heated at 110 °C, and then, pyridine (4.0 mL) was added dropwise over 30 s. The resulting mixture was stirred at 110 °C for 8 min and then cooled to room temperature. The reaction mixture was dissolved in dichloromethane (20 mL), washed with aqueous 1 M HCl solution, dried over  $\text{MgSO}_4$ , and concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (dichloromethane) to afford diene **21** (164 mg, 55%) as a light yellow solid: mp 170–172 °C; IR (nujol)  $\nu$  = 2215 (m), 1724 (s), 1606 (s)  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.85 (s, 1H), 7.66–7.62 (m, 1H), 7.59 (d,  $J$  = 7.7 Hz, 1H), 7.39–7.35 (m, 2H), 7.20 (d,  $J$  = 16.4 Hz, 1H), 6.86 (d,  $J$  = 16.4 Hz, 1H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 158.6 (0), 153.5 (0), 144.8 (1), 143.9 (1), 133.7 (1), 128.8 (1), 125.1 (1), 121.0 (0), 118.5 (0), 118.0 (0), 116.7 (1), 102.8 (1); GC-MS  $m/z$  (%) 197 ( $M^+$ , 100); HRMS (EI) calcd for  $\text{C}_{12}\text{H}_7\text{NO}_2$ : 197.0476; found: 197.0493.

**(E)-1-(Phenylsulfonyl)-2-(2-oxo-2H-chromen-3-yl)ethene (25).** To a stirred 0 °C slurry of 60% sodium hydride (0.449 g, 11.2 mmol) in anhydrous THF (50 mL) was added dropwise a solution of phosphonate **24**<sup>77</sup> (3.11 g, 11.2 mmol) in anhydrous THF (10 mL), and the resulting clear solution was stirred for 15 min at 0 °C. A solution of aldehyde **22** (1.63 g, 9.35 mmol) in anhydrous THF (50 mL) was then added dropwise. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature for 24 h. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel (dichloromethane) to afford **25** (1.20 g, 41%) as a white solid: mp 205–206 °C; <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.96–7.94 (m, 3H), 7.79 (d,  $J$  = 15.1 Hz, 1H), 7.65–7.56 (m, 5H), 7.51 (d,  $J$  = 14.7 Hz, 1H), 7.36–7.33 (m, 2H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 158.6 (0), 153.7 (0), 146.5 (1), 140.2 (0), 135.4 (1), 133.7 (1), 133.5 (1), 133.0 (1), 129.4 (1), 128.8 (1), 127.8 (1), 125.1 (1), 120.4 (0), 118.7 (0), 116.7 (1); EI-MS  $m/z$  (%) 312 ( $M^+$ , 2), 171 (100). HRMS (EI) calcd for  $\text{C}_{17}\text{H}_{12}\text{O}_4\text{S}$ : 312.0456; found: 312.0434.

**Standard Procedure A (for IEDDA Reactions Using Preformed Enamines).** To a magnetically stirred, room-temperature solution of the diene (4.34 mmol) in dichloromethane (25 mL) was added neat enamine (6.51 mmol) dropwise, and the resulting solution was stirred at room temperature for the amount of time indicated. The disappearance of the starting material was monitored by TLC. The solvent was then removed under reduced pressure, and the residue was subjected to flash chromatography on silica gel (4% ethyl acetate/dichloromethane, unless otherwise stated) to afford the product(s).

**Standard Procedure B (for IEDDA Reactions Using in Situ-Generated Enamines).** To a magnetically stirred, room-temperature solution of the diene (4.34 mmol), the ketone (21.7 mmol for inexpensive ketones or 6.5 mmol for expensive ketones), and  $\text{MgSO}_4$  (1.00 g, 8.31 mmol) in dichloromethane (25 mL) was added pyrrolidine (0.18 mL, 2.2 mmol). The mixture was stirred at room temperature, and the disappearance of the diene was monitored by TLC. When the diene had been consumed, the  $\text{MgSO}_4$  was removed by gravity filtration. The filtrate was washed with aqueous 1 M HCl solution, dried over  $\text{MgSO}_4$ , and concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel to afford the product(s).

**Standard Procedure for the Synthesis of Enamines.** A magnetically stirred solution of the ketone (0.10 mol), pyrrolidine (0.15 mol for most ketones; 1.5 mol for aryl ketones), and benzene (200 mL) was heated at reflux with azeotropic removal of water until the appropriate volume of water had been removed from the reaction mixture. The reaction mixture was cooled to room temperature and then concentrated under reduced pressure. The residue was subjected to vacuum distillation to afford the enamine.



**Benzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (38).** Using standard procedure A (3 h), **38** (0.65 g, 43%) was obtained as a white solid: mp 231–232 °C; IR (nujol)  $\nu$  = 1721 (s), 1600 (m)  $\text{cm}^{-1}$ ; UV-vis (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 335 (3.85), 322 (3.84), 303 (3.92), 285 (4.14), 276 (4.08) nm;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.91 (s, 1H), 8.20 (d,  $J$  = 7.9 Hz, 1H), 7.52–7.49 (m, 1H), 7.37–7.32 (m, 2H), 3.94 (s, 3H), 3.48–3.43 (m, 4H), 2.28 (quint,  $J$  = 7.7 Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 166.0 (0), 160.9 (0), 155.3 (0), 151.9 (0), 141.8 (0), 134.4 (0), 132.0 (1), 130.7 (1), 126.8 (1), 126.6 (0), 124.3 (1), 120.4 (0), 118.8 (0), 117.9 (1), 52.1 (3), 35.3 (2), 33.6 (2), 24.9 (2); EI-MS  $m/z$  (%) 294 ( $\text{M}^+$ , 100); Anal. Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_4$ : C, 73.46; H, 4.79. Found: C, 73.19; H, 4.67. Using standard procedure B (15 min), **38** (0.95 g, 74%) was obtained as a white solid.

**8-Acetylbenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one (39).**<sup>56</sup> Using standard procedure A (12 h, scaled down by a factor of 3.1, chloroform used for chromatography), **39** (0.13 g, 34%) was obtained as a white solid: mp 220–223 °C; IR (powder)  $\nu$  = 1720 (s), 1603 (m), 1184 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.83 (s, 1H), 8.26 (d,  $J$  = 8.1 Hz, 1H), 7.56 (t,  $J$  = 7.7 Hz, 1H), 7.44 (d,  $J$  = 8.2 Hz, 1H), 7.39 (t,  $J$  = 7.7 Hz, 1H), 3.49 (t,  $J$  = 7.5 Hz, 2H), 3.44 (t,  $J$  = 7.8 Hz, 2H), 2.73 (s, 3H), 2.28 (quint,  $J$  = 7.7 Hz, 2H);  $^{13}\text{C}$  NMR (500 MHz)  $\delta$  = 198.6, 161.2, 154.4, 152.0, 142.3, 134.6, 133.5, 131.3, 130.9, 126.9, 124.5, 120.3, 118.9, 118.0, 35.1, 33.9, 28.3, 25.2; ESI-(+)-MS  $m/z$  (%) 279 ( $[\text{M} + 1]^+$ , 100), 171 (15); HRMS (EI) calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_3$ : 278.0943; found: 278.0947. Using standard procedure B (5 h, scaled down by a factor of 3.1, chloroform used for chromatography), **39** (0.18 g, 46%) was obtained as a white solid.

**8-Cyanobenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one (40).** Using standard procedure A (3 h, scaled down by a factor 2.8, chloroform used for chromatography), **40** (0.15 g, 38%) was obtained as a white solid: mp 301–304 °C; IR (powder)  $\nu$  = 2220 (w), 1724 (s), 1594 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.62 (s, 1H), 8.21 (d,  $J$  = 8.0 Hz, 1H), 7.60 (t,  $J$  = 7.6 Hz, 1H), 7.45 (d,  $J$  = 8.2 Hz, 1H), 7.41 (t,  $J$  = 7.6 Hz, 1H), 3.59 (t,  $J$  = 7.3 Hz, 2H), 3.31 (t,  $J$  = 7.6 Hz, 2H), 2.40 (quint,  $J$  = 7.5 Hz, 2H);  $^{13}\text{C}$  NMR (500 MHz)  $\delta$  = 160.0, 155.9, 152.0, 141.4, 135.3, 133.7, 131.6, 126.8, 124.7, 121.2, 118.3, 118.2, 116.7, 109.3, 36.0, 32.8, 24.7; ESI-(+)-MS  $m/z$  (%) 262 ( $[\text{M} + 1]^+$ , 100), 263 (15), 284 (20); HRMS (EI) calcd for  $\text{C}_{17}\text{H}_{11}\text{NO}_2$ : 261.0790; found: 261.0793. Using standard procedure B (3 h, scaled down by a factor 2.8, chloroform used for chromatography), **40** (0.15 g, 38%) was obtained as a white solid.

**8-(Phenylsulfonyl)benzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one (41) and benzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one (42).** To a magnetically stirred solution of diene **25** (312 mg, 1.00 mmol) in dichloromethane (5.75 mL) was added enamine **28** (206 mg, 1.50 mmol) dropwise, and the resulting mixture was stirred for 5 min at room temperature. The mixture was diluted with dichloromethane (20 mL), washed with aqueous 1 M HCl solution (20 mL), dried over  $\text{MgSO}_4$ , and concentrated under reduced pressure. The residue was subjected to flash chromatography (dichloromethane) to afford **42** (116 mg, 49%,  $R_f$  (30% ethyl acetate/hexanes) = 0.80) as a white solid and then **41** (92.3 mg, 25%,  $R_f$  (30% ethyl acetate/hexanes) = 0.40) as a white solid. **41**: mp 285–286 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 9.04 (s, 1H), 8.18 (d,  $J$  = 8.7 Hz, 1H), 7.98 (d,  $J$  = 8.0 Hz, 2H), 7.62 (t,  $J$  = 7.4 Hz, 1H), 7.57–7.53 (m, 3H), 7.42 (d,  $J$  = 8.6 Hz, 1H), 7.36 (t,  $J$  = 7.5 Hz, 1H), 3.46 (t,  $J$  = 7.5 Hz, 2H), 3.28 (t,  $J$  = 7.8 Hz, 2H), 2.26 (quint,  $J$  = 7.8 Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 160.3 (0), 152.1 (0), 151.4 (0), 143.3 (0), 140.4 (0), 137.5 (0), 135.7 (0), 133.6 (1), 131.4 (1), 130.4 (1), 129.3 (1), 128.1 (1), 126.9 (1), 124.5 (1), 121.2 (0), 118.3 (0), 118.1 (1), 35.4 (2), 32.2 (2), 25.0 (2); APCI-(+)-MS  $m/z$  (%) 377 ( $[\text{M} + 1]^+$ , 100); HRMS (EI) calcd for  $\text{C}_{22}\text{H}_{16}\text{O}_4\text{S}$ : 376.0769; found: 376.0767. **42**: mp 165–166 °C; IR (nujol)  $\nu$  = 1723 (s), 1712 (s), 1598 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.30 (d,  $J$  = 7.3 Hz, 1H), 8.17 (d,  $J$  = 7.1 Hz, 1H), 7.48–7.45 (m, 2H), 7.38 (d,  $J$  = 7.4 Hz, 1H), 7.34–7.30 (m, 1H), 3.46 (t,  $J$  = 7.4 Hz, 2H), 3.08 (t,  $J$  = 7.8 Hz, 2H), 2.36–2.24 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 161.8 (0), 153.7 (0), 151.4 (0), 139.5 (0), 131.7 (0), 129.7 (1), 129.6 (1), 126.4 (1), 125.1 (1), 124.1 (1), 120.2 (0), 119.6 (0), 117.7 (1), 35.4

(2), 33.0 (2), 25.1 (2); EI-MS  $m/z$  (%) 236 ( $\text{M}^+$ , 100); HRMS (EI) calcd for  $\text{C}_{16}\text{H}_{12}\text{O}_2$ : 236.0837; found: 236.0835. Using standard procedure B (4 h, scaled down by a factor 3.1, dichloromethane used for chromatography), **41** (0.05 g, 14%) was obtained as a white solid, and **42** (0.10 g, 45%) was obtained as a white solid.

**9-Phenyl-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (44).**<sup>56</sup> Using standard procedure A (3 h), **44** (0.90 g, 64%) was obtained as a white solid: mp 195–196 °C; IR (nujol)  $\nu$  = 1738 (s), 1719 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 8.81 (s, 1H), 8.03–8.01 (m, 2H), 7.56–7.31 (m, 8H), 3.74 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 166.9 (0), 160.0 (0), 151.8 (0), 148.7 (0), 139.8 (0), 136.5 (0), 132.7 (1), 131.4 (1), 131.1 (0), 128.2 (1), 128.1 (1), 124.7 (1), 124.2 (1), 123.2 (1), 119.6 (0), 117.8 (1), 117.1 (0), 52.3 (3); GC-MS  $m/z$  (%) 330 ( $\text{M}^+$ , 81), 299 (100); Anal. Calcd for  $\text{C}_{22}\text{H}_{14}\text{O}_4$ : C, 76.36; H, 4.27. Found: C, 76.20; H, 4.10. For the in situ method, a modification of standard procedure B was used. To a solution of diene **13** (1.00 g, 4.34 mmol), acetophenone (2.53 mL, 21.7 mmol), and  $\text{MgSO}_4$  (1.00 g, 83 mmol) in  $\text{CH}_3\text{CN}$  (25 mL) was added pyrrolidine (0.18 mL, 2.17 mmol) dropwise, and the mixture was heated at reflux for 12 h. The mixture was cooled to room temperature, and  $\text{MgSO}_4$  was removed by gravity filtration. The filtrate was washed with aqueous 1 M HCl solution, dried over  $\text{MgSO}_4$ , and concentrated under reduced pressure to leave an oily solid. Hexanes (2 mL) was added to this material, and after manual agitation for 5 min, the hexanes solution was decanted into another flask. The solid residue that remained was subjected to flash chromatography on silica gel (4% ethyl acetate/dichloromethane) to afford **44** (1.06, 74%) as a white solid.

**Benzo[b]-9H-fluoreno[2,1-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (46).** Using standard procedure A (3 h), **46** (635 mg, 43%) was obtained as a white solid: mp 256–257 °C; IR (nujol)  $\nu$  = 1741 (s), 1720 (s), 1599 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.89 (s, 1H), 8.42 (d,  $J$  = 7.3 Hz, 1H), 8.32 (d,  $J$  = 7.0 Hz, 1H), 7.70 (d,  $J$  = 7.7 Hz, 1H), 7.60–7.59 (m, 1H), 7.49–7.43 (m, 4H), 4.39 (s, 2H), 4.08 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.6 (0), 160.9 (0), 152.0 (0), 147.3 (0), 144.8 (0), 140.0 (0), 137.8 (0), 133.5 (0), 132.4 (1), 130.9 (1), 129.3 (1), 127.4 (1), 127.1 (0), 126.6 (1), 125.4 (1), 124.7 (1), 124.5 (1), 119.5 (0), 118.6 (0), 118.3 (1), 52.8 (3), 39.8 (2); EI-MS  $m/z$  (%) 342 ( $\text{M}^+$ , 98), 283 (100); HRMS (EI) calcd for  $\text{C}_{22}\text{H}_{14}\text{O}_4$ : 342.0891; found: 342.0903.

**Benzo[b]-9H-fluoreno[3,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (48).** Using standard procedure A (24 h), **48** (0.82 g, 55%) was obtained as a white solid: mp 206–208 °C; IR (nujol)  $\nu$  = 1745 (s), 1720 (s), 1607 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.87 (s, 1H), 8.51–8.49 (m, 1H), 8.17 (d,  $J$  = 8.2 Hz, 1H), 7.60 (d,  $J$  = 7.4 Hz, 1H), 7.54–7.50 (m, 1H), 7.40–7.35 (m, 2H), 7.28–7.23 (m, 2H), 4.34 (s, 2H), 3.99 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 165.5 (0), 160.8 (0), 153.4 (0), 151.2 (0), 144.7 (0), 139.2 (0), 138.8 (0), 134.1 (0), 131.5 (1), 130.5 (1), 128.2 (1), 127.2 (1), 126.3 (0), 126.0 (1), 125.1 (1), 123.3 (1), 121.9 (0), 117.7 (1), 117.6 (0), 52.2 (3), 39.2 (2); EI-MS  $m/z$  (%) 342 ( $\text{M}^+$ , 100); HRMS (EI) calcd for  $\text{C}_{22}\text{H}_{14}\text{O}_4$ : 342.0891; found: 342.0902. Using standard procedure B (3 h), **48** (1.21 g, 81%) was obtained as a white solid.

**9-(1-Piperidinyl)-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (50).**<sup>56</sup> Using standard procedure A (18 h), **50** (0.71 g, 48%) was obtained as a white solid: mp 130–131 °C; IR (nujol)  $\nu$  = 1718 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.68 (s, 1H), 7.99 (d,  $J$  = 6.9 Hz, 1H), 7.48 (t,  $J$  = 8.5 Hz, 1H), 7.47 (s, 1H), 7.30–7.34 (m, 2H), 3.93 (s, 3H), 3.26–3.28 (m, 4H), 1.76–1.81 (m, 4H), 1.66–1.71 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.3 (0), 160.6 (0), 156.6 (0), 152.1 (0), 138.1 (0), 135.6 (1), 131.1 (0), 124.3 (1), 122.9 (1), 122.7 (0), 117.9 (1), 117.7 (0), 111.7 (0), 108.6 (1), 52.8 (2), 52.3 (3), 25.6 (2), 24.0 (2); EI-MS  $m/z$  (%) 337 ( $\text{M}^+$ , 44), 322 (100); HRMS (EI) calcd for  $\text{C}_{20}\text{H}_{19}\text{NO}_4$ : 337.1313; found: 337.1314.

**Benzo[b]-3,5,6,7,8a-hexahydronaphthaleno[2,1-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (52a) and (8aS\*,12aR\*)-Benzo[b]-4a,5,6,7,8,8a-hexahydronaphthaleno[2,1-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (52a).** Using standard procedure A (3 h), **52a** (1.09 g, 82%,  $R_f$  (4% ethyl acetate/dichloromethane) = 0.45) was obtained as a white solid, and **52b** (0.05 g, 4%,  $R_f$  (4% ethyl acetate/dichloromethane) = 0.55) was obtained as a white solid. **52a**:

mp 168.5–170 °C; IR (nujol)  $\nu$  = 1711 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 7.55 (d,  $J$  = 7.6 Hz, 1H), 7.49–7.44 (m, 1H), 7.35–7.25 (m, 2H), 3.79 (s, 3H), 3.79–3.75 (m, 1H), 3.59–3.48 (m, 2H), 3.32 (dd,  $J$  = 23.4, 5.3 Hz, 1H), 2.40–2.35 (m, 1H), 2.08–1.79 (m, 4H), 1.59–1.40 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 167.4 (0), 160.3 (0), 152.5 (0), 148.6 (0), 145.0 (0), 130.3 (1), 123.9 (1), 123.4 (1), 119.5 (0), 117.9 (0), 117.4 (0), 116.9 (1), 51.2 (3), 42.1 (1), 36.4 (2), 31.7 (2), 29.0 (2), 26.7 (2), 26.5 (2); EI-MS  $m/z$  (%) 310 ( $\text{M}^+$ , 59), 251 (100); Anal. Calcd for  $\text{C}_{19}\text{H}_{18}\text{O}_4$ : C, 73.53; H, 5.85. Found: C, 73.36; H, 6.04. **52b**: mp 209.5–211 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 7.70 (dd,  $J$  = 8.7, 2.7 Hz, 1H), 7.63 (d,  $J$  = 3.1 Hz, 1H), 7.58–7.52 (m, 1H), 7.37–7.31 (m, 2H), 3.83 (s, 3H), 3.24–3.18 (m, 1H), 3.08–3.05 (m, 1H), 2.29–2.86 (m, 1H), 1.78–1.70 (m, 2H), 1.60–1.37 (m, 4H), 1.28–1.19 (m, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 167.4 (0), 159.5 (0), 153.9 (0), 152.8 (0), 132.6 (0), 132.1 (1), 130.0 (1), 124.6 (1), 124.2 (1), 120.3 (0), 117.8 (0), 117.5 (1), 51.8 (3), 37.1 (1), 34.4 (1), 25.6 (2), 24.9 (2), 22.4 (2); EI-MS  $m/z$  (%) 310 ( $\text{M}^+$ , 54), 251 (100); Anal. Calcd for  $\text{C}_{19}\text{H}_{18}\text{O}_4$ : C, 73.53; H, 5.85. Found: C, 73.47; H, 5.76. Using standard procedure B (5 d), **52a** (0.99 g, 74%) was obtained as a white solid, and **52b** (0.11 g, 8%) was obtained as a white solid.

**Compound 54**. Using standard procedure A (3 h), **54** (1.13 g, 80%) was obtained as a white solid: mp 135–136 °C; IR (nujol)  $\nu$  = 1703 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.58 (dd,  $J$  = 8.4, 1.2 Hz, 1H), 7.52–7.49 (m, 1H), 7.35 (dd,  $J$  = 8.2, 1.3 Hz, 1H), 7.34–7.30 (m, 1H), 3.86–3.81 (m, 2H), 3.79 (s, 3H), 3.58–3.52 (m, 1H), 3.21–3.26 (m, 1H), 2.34–2.37 (m, 1H), 2.07–2.11 (m, 1H), 1.95–1.99 (m, 1H), 1.79–1.88 (m, 3H), 1.66–1.69 (m, 1H), 1.36–1.42 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.3 (0), 160.7 (0), 153.1 (0), 150.7 (0), 148.8 (0), 130.7 (1), 124.2 (1), 123.1 (1), 122.2 (0), 120.2 (0), 117.8 (0), 117.3 (1), 51.5 (3), 42.4 (1), 35.4 (2), 33.5 (2), 28.3 (2), 27.2 (2), 26.7 (2), 25.5 (2); EI-MS  $m/z$  (%) 324 ( $\text{M}^+$ , 84), 293 (100); Anal. Calcd for  $\text{C}_{20}\text{H}_{20}\text{O}_4$ : C, 74.06; H, 6.21. Found: C, 73.80; H, 6.27.

**Compound 56**. To a magnetically stirred solution of diene **13** (500 mg, 2.17 mmol) in dichloromethane (25 mL) was added 1-(1-pyrrolidinyl)cyclooctene (1.12 g, 6.51 mmol) dropwise, and the resulting solution was heated at reflux for 48 h. The reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography on silica gel (dichloromethane) to afford **56** (108 mg, 15%) as a white solid: mp 153–155 °C; IR (nujol)  $\nu$  = 1733 (s), 1719 (s), 1606 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz, 333 K)  $\delta$  = 8.76 (s, 1H), 8.27 (dd,  $J$  = 8.4, 1.1 Hz, 1H), 7.51–7.47 (m, 1H), 7.38 (dd,  $J$  = 8.5, 1.2 Hz, 1H), 7.34–7.31 (m, 1H), 3.94 (s, 3H), 3.39–3.34 (m, 2H), 3.29–3.24 (m, 2H), 2.07–2.02 (m, 2H), 1.98–1.93 (m, 2H), 1.70–1.65 (m, 2H), 1.47–1.40 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125.8 MHz, 333 K)  $\delta$  = 167.8, 161.0, 152.0, 149.5, 140.3, 135.6, 132.2, 130.7, 130.3, 127.8, 124.0, 121.1, 118.9, 118.4, 52.2, 31.4, 31.1, 29.4, 28.9, 27.2, 26.0; EI-MS  $m/z$  (%) 336 ( $\text{M}^+$ , 100); HRMS (EI) calcd for  $\text{C}_{21}\text{H}_{20}\text{O}_4$ : 336.1360; found: 336.1368.

**10,10-Dimethyl-9,10-dihydro-6H-dibenzo[b,d]pyran-6-one (58)**.<sup>56</sup> Using standard procedure A (3 h), **58** (0.69 g, 56%) was obtained as a white solid: mp 139–141 °C; IR (nujol)  $\nu$  = 1717 (s)  $\text{cm}^{-1}$ ; UV–vis  $\lambda_{\text{max}}$  (log  $\epsilon$ ) (MeOH) 308 (3.29), 288 (3.35) nm;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 8.04 (d,  $J$  = 8.3 Hz, 1H), 7.48–7.45 (m, 1H), 7.37 (dd,  $J$  = 8.2, 1.1 Hz, 1H), 7.31–7.26 (m, 1H), 6.72 (t,  $J$  = 1.7 Hz, 1H), 3.82 (s, 3H), 3.47 (d,  $J$  = 1.6 Hz, 2H), 1.73 (s, 6H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 166.7 (0), 160.7 (0), 152.7 (0), 149.5 (0), 145.3 (1), 130.2 (1), 126.7 (1), 123.4 (1), 122.0 (0), 120.7 (0), 117.8 (1), 117.6 (0), 51.8 (3), 37.8 (0), 28.26 (3), 25.5 (2); EI-MS  $m/z$  (%) 284 ( $\text{M}^+$ , 6), 269 (100); Anal. Calcd for  $\text{C}_{17}\text{H}_{16}\text{O}_4$ : C, 71.82; H, 5.67. Found: C, 71.82; H, 5.74.

**Benzo[b]-5,6,7,8-tetrahydronaphthaleno[2,1-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (61)**. To a magnetically stirred solution of **52a** (0.62 g, 2.0 mmol) in benzene (100 mL) was added DDQ (0.50 g, 2.2 mmol) in one portion, and the resulting mixture was heated at reflux for 24 h. The reaction mixture was cooled to room temperature and gravity filtered, and the filtrate was concentrated under reduced pressure. The residue was subjected to flash

chromatography on silica gel (2% ethyl acetate/dichloromethane) to afford **61** (0.59 g, 96%) as a white solid: mp 163–164 °C; IR (nujol)  $\nu$  = 1721 (s)  $\text{cm}^{-1}$ ; UV–vis (MeOH)  $\lambda_{\text{max}}$  (log  $\epsilon$ ) = 334 (3.36), 322 (3.42), 283 (3.85) nm;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 8.71 (s, 1H), 8.27 (d,  $J$  = 8.2 Hz, 1H), 7.52–7.46 (m, 1H), 7.39–7.28 (m, 2H), 3.93 (s, 3H), 3.31–3.27 (m, 4H), 1.92–1.66 (m, 4H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 167.0 (0), 160.9 (0), 151.6 (0), 145.9 (0), 136.9 (0), 136.3 (0), 130.7 (0), 130.2 (1), 129.9 (1), 128.3 (1), 123.6 (1), 119.6 (0), 118.5 (0), 117.8 (1), 52.2 (3), 32.6 (2), 28.5 (2), 22.6 (2), 21.7 (2); EI-MS  $m/z$  (%) 308 ( $\text{M}^+$ , 100); Anal. Calcd for  $\text{C}_{19}\text{H}_{16}\text{O}_4$ : C, 74.01; H, 5.23. Found: C, 73.98; H, 5.08.

**Compound 62**. To a magnetically stirred solution of **54** (0.50 g, 1.5 mmol) in benzene (25 mL) was added DDQ (0.35 g, 1.5 mmol) in one portion, and the resulting mixture was heated at reflux for 72 h. The reaction mixture was cooled to room temperature, and the tan precipitate was removed by suction filtration. The filtrate was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (3% ethyl acetate/dichloromethane) to afford **62** (0.48 g, 97%) as a white solid: mp 151–152 °C; IR (nujol)  $\nu$  = 1720 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.61 (s, 1H), 7.96 (dd,  $J$  = 7.7, 1.3 Hz, 1H), 7.50–7.47 (m, 1H), 7.39 (dd,  $J$  = 8.4, 1.2 Hz, 1H), 7.32–7.29 (m, 1H), 3.94 (s, 3H), 3.36–3.34 (m, 2H), 3.28–3.26 (m, 2H), 1.98–1.97 (m, 4H), 1.86–1.84 (m, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 168.0 (0), 161.1 (0), 151.8 (0), 151.6 (0), 141.8 (0), 135.5 (0), 131.3 (1), 130.3 (0), 129.6 (0), 127.6 (1), 123.9 (1), 120.2 (0), 118.8 (0), 118.0 (1), 52.4 (3), 31.5 (2), 31.0 (2), 26.7 (2), 26.3 (2); EI-MS  $m/z$  (%) 322 ( $\text{M}^+$ , 100); Anal. Calcd for  $\text{C}_{20}\text{H}_{18}\text{O}_4$ : C, 74.52; H, 5.63. Found: C, 74.37; H, 5.60. Using standard procedure B, **62** (0.65 g, 46%) was obtained as a white solid.

**10-Phenyl-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (64)**. To a magnetically stirred solution of diene **13** (1.00 g, 4.34 mmol) in dichloromethane (25 mL) was added 2-phenyl-1-(1-pyrrolidinyl)ethene (**63**) (1.62 g, 8.68 mmol) dropwise, and the resulting mixture was stirred at room temperature for 15 min. The reaction mixture was washed with aqueous 1 M HCl solution, dried over  $\text{MgSO}_4$ , and concentrated under reduced pressure. To the residue was added benzene (50 mL) and DDQ (536 mg, 2.36 mmol). The resulting mixture was heated at reflux for 48 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford **64** (408 mg, 28%) as a white solid: mp 188–189 °C; IR (nujol)  $\nu$  = 1740 (s), 1728 (s), 1603 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 9.12 (d,  $J$  = 2.1 Hz, 1H), 8.27 (d,  $J$  = 2.1 Hz, 1H), 7.53–7.50 (m, 3H), 7.39–7.33 (m, 4H), 7.13–7.11 (m, 1H), 6.87–6.84 (m, 1H), 3.98 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 165.4 (0), 160.8 (0), 151.9 (0), 141.2 (0), 140.3 (0), 138.4 (1), 136.1 (0), 131.5 (1), 131.0 (1), 129.6 (0), 129.4 (1), 128.7 (1), 128.4 (1), 128.1 (1), 123.6 (1), 123.0 (0), 117.9 (1), 117.7 (0), 52.6 (3); EI-MS  $m/z$  (%) 330 ( $\text{M}^+$ , 100); Anal. Calcd for  $\text{C}_{21}\text{H}_{14}\text{O}_4$ : C, 76.36; H, 4.27. Found: C, 76.01; H, 4.20.

**9-Methyl-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (70)**. Using standard procedure B (inexpensive ketone, 1 h),<sup>101</sup> **70** (0.769 g, 66%) was obtained as a white solid: mp 216–217 °C; IR (neat)  $\nu$  = 1715 (s), 1608 (m), 1310 (m), 1240 (m), 1186 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  = 8.09 (s, 1H), 8.05 (dd,  $J$  = 6.3, 2.4 Hz, 1H), 7.93 (s, 1H), 7.54–7.49 (m, 1H), 7.37–7.33 (m, 2H), 3.95 (s, 3H), 2.78 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  = 166.2 (0), 160.4 (0), 151.9 (0), 147.5 (0), 137.0 (0), 133.5 (1), 131.4 (1), 130.0 (0), 124.7 (1), 124.6 (1), 123.2 (1), 118.9 (0), 117.9 (1), 117.0 (0), 52.2 (3), 22.5 (3); EI-MS  $m/z$  (%) 268 ( $\text{M}^+$ , 71), 237 (100); Anal. Calcd for  $\text{C}_{16}\text{H}_{12}\text{O}_4$ : C, 71.64; H, 4.51. Found: C, 71.58; H, 4.40.

**Compound 72**. Using standard procedure B (expensive ketone, 48 h, scaled down by a factor of 2), **72** (0.16 g, 26%) was obtained as a white solid: mp 245–246 °C; IR (nujol)  $\nu$  = 1723 (s), 1611 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.84 (s, 1H), 7.84 (d,  $J$  = 7.5 Hz, 1H), 7.52–7.49 (m, 1H), 7.35–7.31 (m, 2H), 3.94 (s, 3H), 3.60 (s, 4H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 165.0 (0), 161.0 (0), 155.3 (0), 151.9 (0), 140.8 (0), 133.0 (0), 131.6 (1), 131.3 (1), 125.8 (1), 125.3 (0), 124.6 (1), 119.9 (0), 117.5 (1), 117.3 (0), 52.1 (3), 32.1



(2), 31.0 (2); EI-MS  $m/z$  (%) 280 (100,  $M^+$ ); HRMS (EI) calcd for  $C_{17}H_{12}O_4$ : 280.0735; found: 280.0736.

**Benzo[b]-6,8a-dihydroisothiochromano[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (74a) and Benzo[b]-4a,8a-dihydroisothiochromano[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (74b).** Using standard procedure B (expensive ketone, 24 h), **74a** (1.13 g, 79%) was obtained as a white solid, and **74b** (0.16 g, 11%) was obtained as a white solid. **74a**: mp 212–214.5 °C; IR (nujol)  $\nu$  = 1706 (s), 1605 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.63 (d,  $J$  = 7.2 Hz, 1H), 7.53 (t,  $J$  = 7.7 Hz, 1H), 7.38 (d,  $J$  = 9.0 Hz, 1H), 7.35 (t,  $J$  = 8.1 Hz, 1H), 4.10–4.04 (m, 2H), 3.81 (s, 3H), 3.72–3.67 (m, 1H), 3.39–3.33 (m, 1H), 3.08–3.01 (m, 2H), 2.90–2.87 (m, 1H), 2.80–2.75 (m, 1H), 2.40–2.35 (m, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 167.3 (0), 160.4 (0), 153.0 (0), 145.5 (0), 143.3 (0), 131.0 (1), 124.6 (1), 123.4 (1), 121.2 (0), 120.2 (0), 117.5 (1), 117.3 (0), 51.8 (3), 44.5 (1), 37.2 (2), 34.4 (2), 32.0 (2), 27.0 (2); EI-MS  $m/z$  (%) 328 ( $M^+$ , 26), 269 (93), 61 (100); HRMS (EI) calcd for  $C_{18}H_{16}O_4S$ : 328.0768; found: 328.0750. **74b**: mp 199–200 °C; IR (nujol)  $\nu$  = 1719 (s), 1708 (s), 1608 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.74 (dd,  $J$  = 8.2, 1.1 Hz, 1H), 7.70 (d,  $J$  = 2.6 Hz, 1H), 7.60–7.57 (m, 1H), 7.39–7.36 (m, 2H), 3.84 (s, 3H), 3.59–3.54 (m, 1H), 3.31–3.27 (m, 1H), 3.22–3.20 (m, 1H), 2.89 (t,  $J$  = 12.7 Hz, 1H), 2.68 (td,  $J$  = 13.4, 2.3 Hz, 1H), 2.49–2.46 (m, 1H), 2.25–2.22 (m, 1H), 2.07–2.01 (m, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.8 (0), 159.1 (0), 154.0 (0), 150.4 (0), 132.6 (1), 131.4 (0), 131.1 (1), 124.9 (1), 124.1 (1), 117.8 (0), 117.6 (1), 117.2 (0), 52.0 (3), 38.1 (1), 34.1 (1), 26.4 (2), 25.0 (2), 24.3 (2); EI-MS  $m/z$  (%) 328 ( $M^+$ , 68), 223 (85), 61 (100); HRMS (EI) calcd for  $C_{18}H_{16}O_4S$ : 328.0768; found: 328.0767.

**11-Methylbenzo[b]-1,2,3,4,6,8a-hexahydroisoquinolinono[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (76a) and 11-Methylbenzo[b]-1,2,3,4,4a,8a-hexahydroisoquinolino[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (76b).** Using standard procedure B (expensive ketone, 5 h, chromatography using 5% MeOH/dichloromethane), **76a** (0.63 g, 44%) and a mixture of **76a** and **76b** (0.50 g, 36%, 27: 9) were obtained (combined yield = 1.13 g, 80%, 71: 9) as white solids. Compound **76a**: mp 122–123 °C, IR (nujol)  $\nu$  = 1713 (s), 1668 (m), 1607 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.71 (dd,  $J$  = 7.5, 1.3 Hz, 1H), 7.52–7.49 (m, 1H), 7.36 (d,  $J$  = 7.7 Hz, 1H), 7.33 (t,  $J$  = 7.7 Hz, 1H), 3.99 (m, 1H), 3.81 (s, 3H), 3.79–3.75 (m, 1H), 3.61–3.48 (m, 2H), 3.44–3.41 (m, 1H), 3.17–3.14 (m, 1H), 2.35 (s, 3H), 2.34–2.31 (m, 1H), 2.23–2.18 (m, 1H), 2.06 (t,  $J$  = 11.0 Hz, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 167.4 (0), 160.4 (0), 152.8 (0), 145.7 (0), 142.4 (0), 130.8 (1), 124.3 (1), 123.7 (1), 121.0 (0), 119.3 (0), 117.6 (0), 117.4 (1), 62.7 (2), 57.9 (2), 51.7 (3), 45.2 (3), 41.3 (1), 31.0 (2), 27.1 (2); EI-MS  $m/z$  (%) 325 ( $M^+$ , 52), 281 (100); HRMS (EI) calcd for  $C_{19}H_{19}O_4N$ : 325.1313; found: 325.1315.

**Benzo[b]-6,8a-dihydroisochromano[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (78a) and Compound 79.** Using standard procedure B (expensive ketone, 24 h), **78a** (0.43 g, 40%) was obtained as a white solid, and **79** (0.65 g, 32%) was obtained as a white solid. **78a**: mp 188–189.5 °C; IR (nujol)  $\nu$  = 1712 (s), 1608 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.72 (dd,  $J$  = 7.3, 1.3 Hz, 1H), 7.53–7.50 (m, 1H), 7.36 (dd,  $J$  = 8.3, 1.3 Hz, 1H), 7.35–7.32 (m, 1H), 4.52 (dd,  $J$  = 10.8, 3.9 Hz, 1H), 4.27–4.24 (m, 1H), 3.98–3.95 (m, 1H), 3.84–3.81 (m, 1H), 3.81 (s, 3H), 3.64–3.48 (m, 3H), 3.34 (t,  $J$  = 10.2 Hz, 1H), 2.42–2.39 (m, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 167.2 (0), 160.3 (0), 152.7 (0), 144.7 (0), 140.3 (0), 131.0 (1), 124.4 (1), 123.6 (1), 121.5 (0), 119.3 (0), 117.5 (0), 117.4 (1), 73.9 (2), 70.9 (2), 51.7 (3), 43.1 (1), 33.0 (2), 27.1 (2); EI-MS  $m/z$  (%) 312 ( $M^+$ , 33), 253 (100); HRMS (EI) calcd for  $C_{18}H_{16}O_5$ : 312.0997; found: 312.1006. **79**: mp 286–287 °C;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.85 (s, 1H), 7.77 (d,  $J$  = 7.4 Hz, 1H), 7.71–7.67 (m, 1H), 7.46–7.67 (m, 2H), 4.51 (dd,  $J$  = 14.2, 3.8 Hz, 1H), 4.29 (t,  $J$  = 12.2 Hz, 1H), 4.01–3.95 (m, 2H), 3.87 (s, 3H), 3.85–3.76 (m, 4H), 3.53–3.47 (m, 2H), 3.36 (t,  $J$  = 10.9 Hz, 1H), 3.29 (t,  $J$  = 11.9 Hz, 1H), 2.77–2.73 (m, 1H), 2.68 (d,  $J$  = 14.1 Hz, 1H), 2.48–2.23 (m, 5H), 2.02–1.84 (m, 4H);  $^{13}C$  NMR ( $CDCl_3$ , 125.8 MHz)  $\delta$  = 167.9 (0), 158.3 (0), 154.3 (0), 149.1 (0), 134.2 (1), 132.8 (0), 132.6 (1), 125.8 (1), 124.1 (1), 118.1 (1), 117.7 (0), 117.4 (0), 65.4 (2), 65.3 (2), 62.8 (1), 62.3 (2),

62.0 (2), 53.9 (2), 53.6 (2), 52.7 (3), 42.3 (0), 40.7 (1), 38.6 (1), 28.7 (2), 26.4 (2), 23.4 (2), 23.3 (2); EI-MS  $m/z$  (%) 465 ( $M^+$ , 5), 464 (6), 347 (2), 252 (3), 223 (3), 154 (46), 153 (47), 110 (44), 97 (100).

**Compound 81.** Using standard procedure B (expensive ketone, 24 h, reflux, scaled down by a factor of 2), **81** (107 mg, 15%) was obtained as a white solid: mp 230–231 °C; IR (nujol)  $\nu$  = 1727 (s), 1715 (s), 1598 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 8.87 (s, 1H), 8.30 (d,  $J$  = 7.9 Hz, 1H), 7.53–7.50 (m, 1H), 7.40–7.36 (m, 2H), 4.43 (m, 1H), 4.27 (m, 1H), 3.97 (s, 3H), 2.25–2.17 (m, 2H), 1.78–1.75 (m, 1H), 1.68–1.66 (m, 1H), 1.48–1.44 (m, 1H), 1.38–1.34 (m, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.1 (0), 161.1 (0), 158.4 (0), 151.7 (0), 144.6 (0), 131.5 (0), 131.0 (1), 130.7 (1), 126.4 (1), 124.5 (1), 123.9 (0), 119.4 (0), 118.6 (0), 118.0 (1), 52.1 (3), 48.6 (2), 43.9 (1), 42.9 (1), 25.8 (2), 25.0 (2); EI-MS  $m/z$  (%) 320 ( $M^+$ , 51), 292 (100); HRMS (EI) calcd for  $C_{20}H_{16}O_4$ : 320.1048; found: 320.1063.

**9-Methylbenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (83).** Using standard procedure B (3 d, scaled down by a factor of 2), **83** (114 mg, 17%) was obtained as a white solid: mp 206–207 °C; IR (nujol)  $\nu$  = 1726 (s), 1716 (s), 1606 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 8.99 (s, 1H), 8.26 (d,  $J$  = 8.3 Hz, 1H), 7.55–7.52 (m, 1H), 7.41 (dd,  $J$  = 8.3, 1.1 Hz, 1H), 7.37 (t,  $J$  = 7.7 Hz, 1H), 4.14–4.11 (m, 1H), 3.96 (s, 3H), 3.58–3.40 (m, 2H), 2.35–2.30 (m, 1H), 2.11–2.07 (m, 1H), 1.29 (d,  $J$  = 7.1 Hz, 3H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 165.8 (0), 161.0 (0), 160.3 (0), 152.0 (0), 140.8 (0), 134.8 (0), 132.6 (1), 130.8 (1), 127.0 (1), 125.3 (0), 124.3 (1), 120.6 (0), 118.9 (0), 118.0 (1), 52.1 (3), 39.0 (1), 33.4 (2), 33.1 (2), 20.3 (3); EI-MS  $m/z$  (%) 308 ( $M^+$ , 100); HRMS (EI) calcd for  $C_{19}H_{16}O_4$ : 308.1049; found: 308.1049.

**9,10-Dihydro-6H-dibenzo[b,d]pyran-6-one-8,9-dicarboxylic Acid Dimethyl Ester (85).** To a magnetically stirred solution of diene **13** (502 mg, 2.18 mmol), methyl pyruvate (2.00 mL, 22.1 mmol), and  $MgSO_4$  (500 mg, 4.15 mmol) in dichloromethane (12.5 mL) was added pyrrolidine (1.63 mL, 19.5 mmol) dropwise, and the resulting mixture was stirred at room temperature for 1.5 h. The reaction mixture was diluted with dichloromethane (25 mL), washed with aqueous 1 M HCl solution, dried over  $MgSO_4$ , and concentrated under reduced pressure. The crude yellow oil was then subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford **85** (400 mg, 59%) as a yellow solid: mp 130–134 °C; IR (nujol)  $\nu$  = 1728 (s), 1712 (s), 1605 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.87 (s, 1H), 7.78–7.76 (m, 1H), 7.60–7.56 (m, 1H), 7.38–7.33 (m, 2H), 4.08 (dd,  $J$  = 10.1, 2.6 Hz, 1H), 3.89–3.83 (m, 4H), 3.65 (s, 3H), 3.05 (dd,  $J$  = 18.0, 7.7 Hz, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 171.9 (0), 166.0 (0), 158.8 (0), 153.4 (0), 147.7 (0), 132.7 (1), 130.4 (1), 126.9 (0), 124.7 (1), 124.7 (1), 118.6 (0), 118.3 (0), 117.2 (1), 52.6 (3), 52.2 (3), 36.3 (1), 26.0 (2); EI-MS  $m/z$  (%) 314 ( $M^+$ , 8), 255 (100); HRMS (EI) calcd for  $C_{17}H_{14}O_6$ : 314.0789; found: 314.0801.

**Benzo[b]isothiochromano[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (88).** To a magnetically stirred solution of **74a** (200 mg, 0.61 mmol) in benzene (10 mL) was added DDQ (140 mg, 0.61 mmol) in one portion, and the resulting mixture was heated at reflux for 48 h. The reaction was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford **88** (39 mg, 20%) as a white solid: mp 150–152 °C; IR (nujol)  $\nu$  = 1721 (s), 1607 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 8.85 (s, 1H), 8.00 (d,  $J$  = 8.1 Hz, 1H), 7.55–7.52 (m, 1H), 7.44 (dd,  $J$  = 8.2, 1.4 Hz, 1H), 7.37–7.34 (m, 1H), 4.26 (s, 2H), 3.97 (s, 3H), 3.60 (t,  $J$  = 6.2 Hz, 2H), 3.01 (t,  $J$  = 6.7 Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.8 (0), 160.8 (0), 151.8 (0), 147.4 (0), 136.9 (0), 134.6 (0), 131.0 (1), 130.9 (1), 129.9 (0), 128.0 (1), 124.3 (1), 120.3 (0), 118.3 (1), 117.8 (0), 52.6 (3), 27.5 (2), 26.6 (2), 25.8 (2); EI-MS  $m/z$  (%) 326 ( $M^+$ , 74), 311 (100); HRMS (EI) calcd for  $C_{18}H_{14}SO_2$ : 326.0613; found: 326.0620.

**11-Methylbenzo[b]-1,2,3,4,6,8a-hexahydroisoquinolinono[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (89).** To a magnetically stirred solution of **76a** and **76b** (220 mg, 0.68 mmol) in toluene (25 mL) was added manganese dioxide (62.3 mg, 0.72 mmol) in one

portion, and the resulting mixture was heated at reflux for 12 h. The reaction mixture was cooled to room temperature and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (5% methanol/dichloromethane) to afford **89** (68.3 mg, 31%) as a yellow solid: mp 165–168 °C; IR (nujol)  $\nu$  = 1720 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.89 (s, 1H), 8.02 (d,  $J$  = 8.3 Hz, 1H), 7.55–7.52 (m, 1H), 7.43 (dd,  $J$  = 6.7, 1.2 Hz, 1H), 7.38–7.35 (m, 1H), 4.07 (s, 2H), 3.93 (s, 3H), 3.50 (t,  $J$  = 6.3 Hz, 2H), 2.81 (t,  $J$  = 6.4 Hz, 2H), 2.58 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 166.5 (0), 160.9 (0), 151.9 (0), 143.7 (0), 135.6 (0), 134.4 (0), 131.3 (1), 130.7 (1), 130.0 (0), 128.2 (1), 124.1 (1), 120.0 (0), 118.3 (1), 118.2 (0), 60.6 (2), 52.3 (3), 51.8 (2), 46.3 (3), 29.3 (2); EI-MS  $m/z$  (%) 323 ( $\text{M}^+$ , 18), 293 (96), 222 (100); Anal. Calcd for  $\text{C}_{19}\text{H}_{17}\text{NO}_4$ : C, 70.58; H, 5.30; N, 4.33. Found: C, 70.39; H, 5.62; N, 4.38.

**Benzo[b]isochromano[7,8-d]-6H-pyran-6-one-carboxylic Acid Methyl Ester (90).** To a magnetically stirred solution of **78a** (151 mg, 0.48 mmol) in benzene (50 mL) was added DDQ (109 mg, 0.48 mmol) in one portion, and the resulting mixture was heated at reflux for 24 h. The reaction mixture was then cooled to room temperature, diluted with benzene (25 mL), and gravity filtered to remove the light brown precipitate. The filtrate was concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford **90** (101 mg, 67%) as a white solid: mp 216–217 °C; IR (nujol)  $\nu$  = 1723 (s), 1705 (s), 1598 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.94 (s, 1H), 7.78 (d,  $J$  = 7.7 Hz, 1H), 7.57–7.53 (m, 1H), 7.44 (d,  $J$  = 7.9 Hz, 1H), 7.38–7.35 (m, 1H), 5.28 (s, 2H), 4.08 (t,  $J$  = 6.1 Hz, 2H), 3.95 (s, 3H), 3.47 (t,  $J$  = 6.0 Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 166.2 (0), 160.7 (0), 151.9 (0), 142.8 (0), 135.1 (0), 134.8 (0), 131.6 (1), 131.0 (1), 129.9 (0), 128.0 (1), 124.4 (1), 120.1 (0), 118.4 (1), 117.9 (0), 70.0 (2), 64.5 (2), 52.3 (3), 28.3 (2); EI-MS  $m/z$  (%) 310 ( $\text{M}^+$ , 84), 251 (100); Anal. Calcd for  $\text{C}_{18}\text{H}_{14}\text{O}_5$ : C, 69.67; H, 4.55. Found: C, 69.54; H, 4.75.

**6H-Dibenzo[b,d]pyran-6-one-8,9-dicarboxylic Acid Dimethyl Ester (91).** To a magnetically stirred solution of **85** (60 mg, 0.19 mmol) in benzene (5.0 mL) was added DDQ (44 mg, 0.19 mmol) in one portion, and the resulting mixture was heated at reflux for 48 h. The reaction mixture was cooled to room temperature, filtered through a plug of Celite, and concentrated under reduced pressure. The residue was then subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford **91** (40 mg, 67%) as a white solid: mp 151–152 °C; IR (nujol)  $\nu$  = 1728 (s), 1714 (s), 1612 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.83 (s, 1H), 8.33 (s, 1H), 8.08 (d,  $J$  = 7.5 Hz, 1H), 7.59–7.55 (m, 1H), 7.40–7.37 (m, 2H), 4.00 (s, 3H), 3.97 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.5 (0), 165.7 (0), 159.6 (0), 151.9 (0), 138.6 (0), 137.4 (0), 132.2 (1), 132.1 (1), 130.4 (0), 125.0 (1), 123.4 (1), 122.4 (1), 122.3 (0), 118.0 (1), 116.6 (0), 53.2 (3), 52.9 (3); EI-MS  $m/z$  (%) 312 ( $\text{M}^+$ , 80), 281 (100); Anal. Calcd for  $\text{C}_{17}\text{H}_{12}\text{O}_6$ : C, 65.39; H, 3.87. Found: C, 65.13; H, 3.93.

**Methyl (E)-3-(6-Methyl-2-oxo-2H-chromen-3-yl)acrylate (93).** To a magnetically stirred solution of 5-methylsalicylaldehyde (**92**)<sup>93</sup> (5.40 g, 40.0 mmol) and dimethyl glutaconate (**17**) (5.58 mL, 40.0 mmol) in benzene (50 mL) was added piperidine (1.96 mL, 20.0 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 1 h. The mixture was cooled to room temperature, whereupon a white precipitate formed. Suction filtration afforded **93** (6.78 g, 70%) as a white solid. The filtrate was concentrated under reduced pressure, and the residue was taken up in dichloromethane (100 mL), washed with aqueous 1 M HCl solution, and washed with water. The organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The residue was recrystallized from 95% ethanol to afford another batch of **93** (0.78 g, 8%) (total yield: 7.56 g, 78%); mp 176–177 °C; IR (nujol)  $\nu$  = 1723 (s), 1710 (s), 1603 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.81 (s, 1H), 7.55 (d,  $J$  = 16.3 Hz, 1H), 7.38 (dd,  $J$  = 8.4, 1.9 Hz, 1H), 7.32 (s, 1H), 7.23 (d,  $J$  = 9.0 Hz, 1H), 7.09 (d,  $J$  = 15.7 Hz, 1H), 3.81 (s, 3H), 2.42 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.3 (0), 159.2 (0), 151.7 (0), 143.5 (1), 138.2 (1), 134.5 (0), 134.0 (1), 128.2 (1), 123.0 (1),

122.0 (0), 118.7 (0), 116.3 (1), 51.8 (3), 20.7 (3); EI-MS  $m/z$  (%) 244 ( $\text{M}^+$ , 21), 185 (100); Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{O}_4$ : C, 68.85; H, 4.95. Found: C, 68.67; H, 4.83.

**Methyl (E)-3-(7-Methyl-2-oxo-2H-chromen-3-yl)acrylate (95).** To a magnetically stirred solution of 4-methylsalicylaldehyde (**94**)<sup>93</sup> (1.29 g, 10.8 mmol) and dimethyl glutaconate (**17**) (1.51 mL, 10.8 mmol) in benzene (16 mL) was added piperidine (0.53 mL, 5.4 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 1 h. The reaction was cooled to room temperature, whereupon a white precipitate formed. Suction filtration afforded **95** (1.86 g, 71%). The filtrate was concentrated under reduced pressure. The residue was taken up in dichloromethane (100 mL), washed with aqueous 1 M HCl solution, and washed with water (50 mL). The organic layer was dried over  $\text{MgSO}_4$  and then concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (4% ethyl acetate/dichloromethane) to afford a second batch of **95** (0.23 g, 9%) (total yield: 2.09 g, 80%); mp 222–223 °C; IR (nujol)  $\nu$  = 1713 (s), 1616 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.84 (s, 1H), 7.56 (d,  $J$  = 16.3 Hz, 1H), 7.43 (d,  $J$  = 8.3 Hz, 1H), 7.16–7.12 (m, 2H), 7.08 (d,  $J$  = 15.7 Hz, 1H), 3.81 (s, 3H), 2.48 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.5 (0), 159.3 (0), 153.7 (0), 144.6 (0), 143.6 (1), 138.3 (1), 128.2 (1), 126.1 (1), 122.6 (1), 121.1 (0), 116.8 (1), 116.6 (0), 51.8 (3), 22.0 (3); GC-MS  $m/z$  (%) 244 ( $\text{M}^+$ , 20), 185 (100); HRMS (EI) calcd for  $\text{C}_{14}\text{H}_{12}\text{O}_4$ : 244.0735; Found: 244.0735.

**Methyl (E)-3-(8-Methyl-2-oxo-2H-chromen-3-yl)acrylate (97).** To a magnetically stirred solution of 3-methylsalicylaldehyde (**96**)<sup>93</sup> (2.71 g, 19.8 mmol) and dimethyl glutaconate (**17**) (3.5 mL, 20 mmol) in benzene (30 mL) was added piperidine (1.0 mL, 9.9 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 1 h. The reaction mixture was cooled to room temperature, whereupon a white precipitate formed. Suction filtration afforded **97** (0.54 g, 11%) as a white solid. The filtrate was concentrated under reduced pressure. The residue was taken up in dichloromethane (50 mL), washed with aqueous 1 M HCl solution, and washed with water. The organic layer was dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. The residue was subjected to flash chromatography on silica gel (dichloromethane) to afford a second batch of **97** (2.95 g, 61%) (total yield: 3.49 g, 72%); mp 131–132 °C; IR (nujol)  $\nu$  = 1725 (s), 1712 (s), 1600 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.85 (s, 1H), 7.55 (d,  $J$  = 16.0 Hz, 1H), 7.41 (d,  $J$  = 6.9 Hz, 1H), 7.38 (d,  $J$  = 7.8 Hz, 1H), 7.20 (t,  $J$  = 7.9 Hz, 1H), 7.08 (d,  $J$  = 15.5 Hz, 1H), 3.81 (s, 3H), 2.44 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.2 (0), 159.0 (0), 151.8 (0), 143.9 (1), 138.1 (1), 134.1 (1), 126.2 (1), 126.0 (0), 124.3 (1), 122.8 (1), 121.7 (0), 118.5 (0), 51.7 (3), 15.2 (3); EI-MS  $m/z$  (%) 244 ( $\text{M}^+$ , 16), 185 (100); Anal. Calcd for  $\text{C}_{14}\text{H}_{12}\text{O}_4$ : C, 68.85; H, 4.95. Found: C, 68.39; H, 4.91.

**Methyl (E)-3-(6-Methoxy-2-oxo-2H-chromen-3-yl)acrylate (99) and Methyl (6-Methoxy-3-(methoxycarbonyl)-2H-chromen-2-yl)-acetate (100).** To a magnetically stirred solution of 5-methoxysalicylaldehyde (**98**)<sup>93</sup> (4.00 g, 26.3 mmol) and dimethyl glutaconate (**17**) (3.7 mL, 26 mmol) in benzene (75 mL) was added piperidine (1.3 mL, 13 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 2 h. The reaction mixture was cooled to room temperature, whereupon a yellow precipitate formed. Suction filtration (filter cake was washed with cold benzene (2  $\times$  40 mL)) afforded **99** (4.89 g, 71%) as a white solid. The filtrate was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford **100** (1.32 g, 19%) as a yellow solid. **99**: mp 202–203 °C; IR (nujol)  $\nu$  = 1729 (s), 1713 (s), 1634 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.82 (s, 1H), 7.57 (d,  $J$  = 15.7 Hz, 1H), 7.28 (d,  $J$  = 8.8 Hz, 1H), 7.17–7.09 (m, 2H), 6.95 (d,  $J$  = 2.8 Hz, 1H), 3.87 (s, 3H), 3.82 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125.8 MHz)  $\delta$  = 167.4 (0), 159.2 (0), 156.3 (0), 148.1 (0), 143.3 (1), 138.1 (1), 123.3 (1), 122.6 (0), 121.0 (1), 119.3 (0), 117.7 (1), 110.0 (1), 55.9 (3), 51.9 (3); EI-MS  $m/z$  (%) 260 ( $\text{M}^+$ , 39), 201 (100); HRMS (EI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{12}\text{O}_5$ : 260.0684; found: 260.0709. **100**: mp 66–67 °C; IR (nujol)  $\nu$  = 1745 (s), 1699 (s), 1640 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500



(MHz)  $\delta$  = 7.46 (s, 1H), 6.84 (dd,  $J$  = 9.0, 3.0 Hz, 1H), 6.80 (d,  $J$  = 8.8 Hz, 1H), 6.70 (d,  $J$  = 3.1 Hz, 1H), 5.67 (dd,  $J$  = 10.5, 3.4 Hz, 1H), 3.82 (s, 3H), 3.77 (s, 3H), 3.71 (s, 3H), 2.78 (dd,  $J$  = 15.1, 9.9 Hz), 2.54 (dd,  $J$  = 14.9, 3.2 Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 170.2 (0), 164.7 (0), 154.4 (0), 146.3 (0), 133.5 (1), 124.8 (0), 120.4 (0), 118.3 (1), 117.9 (1), 112.8 (1), 70.5 (1), 55.7 (3), 52.0 (3), 51.8 (3), 38.1 (2); EI-MS  $m/z$  (%) 292 ( $\text{M}^+$ , 9), 219 (100); HRMS (EI)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{16}\text{O}_6$ : 292.0946; found: 292.0975.

**Methyl (E)-3-(6-Bromo-2-oxo-2H-chromen-3-yl)acrylate (102)**  
**Methyl (6-Bromo-3-(methoxycarbonyl)-2H-chromen-2-yl)acetate (103).** To a magnetically stirred solution of 4-bromosalicylaldehyde (**101**)<sup>93</sup> (2.50 g, 12.4 mmol) and dimethyl glutaconate (**17**) (1.75 mL, 12.4 mmol) in benzene (20 mL) was added piperidine (0.61 mL, 6.2 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 1 h. The reaction mixture was cooled to room temperature, whereupon a white precipitate formed. Suction filtration (filter cake washed with cold benzene (2  $\times$  25 mL)) afforded **102** (2.12 g, 55%). The filtrate was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford a second batch of **102** (0.38 g, 10%) (total yield: 2.50 g, 65%) and **103** (1.32 g, 25%) as a white solid. **102**: mp 210–211 °C; IR (nujol)  $\nu$  = 1740 (s), 1707 (s), 1630 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.78 (s, 1H), 7.68 (d,  $J$  = 1.4 Hz, 1H), 7.66 (dd,  $J$  = 8.7, 2.5 Hz, 1H), 7.55 (d,  $J$  = 15.9 Hz, 1H), 7.24 (d,  $J$  = 9.4 Hz, 1H), 7.12 (d,  $J$  = 15.8 Hz, 1H), 3.82 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.1 (0), 158.3 (0), 152.3 (0), 141.9 (1), 137.5 (1), 135.5 (1), 130.6 (1), 124.2 (1), 123.5 (0), 120.4 (0), 118.4 (1), 117.4 (0), 51.9 (3); GC-MS  $m/z$  (%) 310 ( $\text{M}^+$   $^{81}\text{Br}$ , 16), 308 ( $\text{M}^+$   $^{79}\text{Br}$ , 16), 249 (100); HRMS (EI) calcd for  $\text{C}_{13}\text{H}_9\text{O}_4^{79}\text{Br}$ : 307.9683; found: 307.9671. **103**: mp 77–79 °C; IR (nujol)  $\nu$  = 1727 (s), 1693 (s), 1632 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.40 (s, 1H), 7.34 (dd,  $J$  = 8.5, 2.3 Hz, 1H), 7.28 (d,  $J$  = 3.0 Hz, 1H), 6.76 (d,  $J$  = 8.9 Hz, 1H), 5.72 (dd,  $J$  = 9.7, 3.2 Hz, 1H), 3.83 (s, 3H), 3.71 (s, 3H), 2.77 (dd,  $J$  = 15.6, 9.6 Hz, 1H), 2.59 (dd,  $J$  = 15.5, 3.2 Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 169.9 (0), 164.3 (0), 151.7 (0), 134.9 (1), 132.1 (1), 131.0 (1), 125.3 (0), 121.7 (0), 118.9 (1), 113.9 (0), 70.9 (1), 52.1 (3), 51.9 (3), 38.5 (2); EI-MS  $m/z$  (%) 342 ( $\text{M}^+$   $^{81}\text{Br}$ , 6), 340 ( $\text{M}^+$   $^{79}\text{Br}$ , 6), 267 (100); HRMS (EI) calcd for  $\text{C}_{14}\text{H}_{13}\text{O}_5^{79}\text{Br}$ : 339.9945; found: 339.9916.

**Methyl (E)-3-(6-(Methoxycarbonyl)-2-oxo-2H-chromen-3-yl)acrylate (105) and Methyl (3,6-bis(methoxycarbonyl)-2H-chromen-2-yl)acetate (106).** To a magnetically stirred solution of methyl 3-formyl-hydroxybenzoate (**104**)<sup>94,95</sup> (508 mg, 2.8 mmol) and dimethyl glutaconate (**17**) (0.39 mL, 2.8 mmol) in benzene (10 mL) was added piperidine (0.14 mL, 1.4 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 2 h. The reaction mixture was cooled to room temperature, whereupon a white precipitate formed. Suction filtration (filter cake washed with cold benzene (2  $\times$  10 mL)) afforded **105** (0.22 g, 28%) as a white solid. The filtrate was concentrated under reduced pressure, and the residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to afford a second batch of **105** (0.31 g, 38%) (total yield: 0.53 g, 66%) and **106** (0.13 g, 15%) as a white solid. **105**: mp 233–234 °C; IR (nujol)  $\nu$  = 1748 (s), 1720 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.27 (d,  $J$  = 2.0 Hz, 1H), 8.23 (dd,  $J$  = 9.4, 2.0 Hz, 1H), 7.90 (s, 1H), 7.57 (d,  $J$  = 15.6 Hz, 1H), 7.40 (d,  $J$  = 9.3 Hz, 1H), 7.13 (d,  $J$  = 15.7 Hz, 1H), 3.97 (s, 3H), 3.83 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 167.1 (0), 165.4 (0), 158.3 (0), 156.2 (0), 142.9 (1), 137.5 (1), 133.6 (1), 130.5 (1), 127.0 (0), 124.1 (1), 123.2 (0), 118.7 (0), 116.9 (1), 52.6 (3), 52.0 (3); EI-MS  $m/z$  (%) 288 ( $\text{M}^+$ , 14), 229 (100); HRMS (EI) calcd for  $\text{C}_{15}\text{H}_{12}\text{O}_6$ : 288.0633; found: 288.0616. **106**: mp 126–127 °C; IR (nujol)  $\nu$  = 1737 (s), 1692 (s), 1609 (s)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 7.95 (dd,  $J$  = 8.3, 2.0 Hz, 1H), 7.91 (s, 1H), 7.87 (d,  $J$  = 2.0 Hz, 1H), 6.90 (d,  $J$  = 8.8 Hz, 1H), 5.79 (dd,  $J$  = 9.6, 3.3 Hz, 1H), 3.90 (s, 3H), 3.84 (s, 3H), 3.71 (s, 3H), 2.79 (dd,  $J$  = 15.5, 9.6 Hz, 1H), 2.65 (dd,  $J$  = 14.7, 3.7 Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 169.9 (0), 166.1 (0), 164.4 (0), 156.6 (0), 133.9 (1), 132.8 (1), 130.6 (1), 124.6 (0), 124.0 (0), 119.5 (0), 117.1 (1), 71.5 (1), 52.2 (3), 52.1 (3), 51.9

(3), 39.1 (2); GC-MS  $m/z$  (%) 320 ( $\text{M}^+$ , 5), 247 (100). HRMS (EI) calcd for  $\text{C}_{16}\text{H}_{16}\text{O}_7$ : 320.0896; found: 320.0903.

**Methyl (E)-3-(6-Nitro-2-oxo-2H-chromen-3-yl)acrylate (108) methyl (3-(Methoxycarbonyl)-6-nitro-2H-chromen-2-yl)acetate (109).** To a magnetically stirred solution of 5-nitrosalicylaldehyde (**108**)<sup>94,95</sup> (2.85 g, 17.0 mmol) and dimethyl glutaconate (**17**) (2.40 mL, 17.0 mmol) in benzene (60 mL) was added piperidine (0.84 mL, 8.5 mmol) dropwise, and the resulting mixture was heated at reflux with azeotropic removal of water for 30 min. During this time, a white solid formed in the reaction mixture. The reaction mixture was cooled to room temperature and suction filtered, and the filter cake was washed with cold benzene (2  $\times$  25 mL) to afford **108** (1.22 g, 26%) as a white solid. The filtrate was concentrated under reduced pressure, and then, the residue was subjected to flash chromatography on silica gel (5% ethyl acetate/dichloromethane) to give **109** (3.83 g, 72%) as a white solid. **108**: mp 210–211 °C; IR (nujol)  $\nu$  = 1768 (s), 1697 (s), 1611 (m), 1208 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.68–8.67 (m, 2H), 8.47 (dd,  $J$  = 9.5, 3.1 Hz, 1H), 7.68 (d,  $J$  = 9.2 Hz, 1H), 7.54 (d,  $J$  = 15.9 Hz, 1H), 6.97 (d,  $J$  = 16.0 Hz, 1H), 3.76 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 166.2 (0), 158.0 (0), 156.6 (0), 143.7 (0), 143.2 (1), 137.6 (1), 127.4 (1), 124.8 (1), 123.0 (0), 122.7 (1), 119.2 (0), 117.8 (1), 51.9 (3); EI-MS  $m/z$  (%) 275 ( $\text{M}^+$ , 14), 216 (100); HRMS (EI) calcd for  $\text{C}_{13}\text{H}_9\text{NO}_6$ : 275.0430; found: 275.0435. **109**: mp 143–144 °C; IR (nujol)  $\nu$  = 1729 (s), 1697 (s), 1612 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.16 (dd,  $J$  = 9.0, 2.5 Hz, 1H), 8.09 (d,  $J$  = 2.5 Hz, 1H), 7.52 (s, 1H), 6.96 (d,  $J$  = 9.0 Hz, 1H), 5.85 (dd,  $J$  = 9.6, 3.2 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H), 2.80 (dd,  $J$  = 15.4, 10.0 Hz, 1H), 2.71 (dd,  $J$  = 15.4, 3.8 Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 169.5 (0), 163.9 (0), 158.0 (0), 142.3 (0), 131.6 (1), 127.8 (1), 126.0 (0), 124.3 (1), 119.7 (0), 117.5 (1), 72.2 (1), 52.4 (3), 52.0 (3), 39.3 (2); EI-MS  $m/z$  (%) 307 ( $\text{M}^+$ , 5), 247 (100); HRMS (EI) calcd for  $\text{C}_{14}\text{H}_{13}\text{NO}_7$ : 307.0691; found: 307.0677.

**2-Methylbenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (110).** Using standard procedure A (3 h), **110** (0.63 g, 47%) was obtained as a white solid: mp 258–260 °C; IR (nujol)  $\nu$  = 1724 (s), 1715 (s),  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.94 (s, 1H), 7.99 (s, 1H), 7.31 (d,  $J$  = 8.3 Hz, 1H), 7.27 (d,  $J$  = 7.6 Hz, 1H), 3.95 (s, 3H), 3.49–3.43 (m, 4H), 2.47 (s, 3H), 2.28 (quint,  $J$  = 7.6 Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 166.1 (0), 161.2 (0), 155.2 (0), 150.0 (0), 141.7 (0), 134.6 (0), 133.8 (0), 132.1 (1), 131.6 (1), 126.9 (1), 126.5 (0), 120.5 (0), 118.5 (0), 117.6 (1), 52.1 (3), 35.4 (2), 33.6 (2), 25.0 (2), 21.4 (3); EI-MS  $m/z$  (%) 308 ( $\text{M}^+$ , 100); HRMS (EI) calcd. for  $\text{C}_{19}\text{H}_{16}\text{O}_4$ : 308.1048; found: 308.1034. Using standard procedure B (2 h, scaled down by a factor of 2.1, chloroform used for chromatography), **110** (0.32 g, 50%) was obtained as a white solid.

**3-Methylbenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (111).** Using standard procedure A (3 h), **111** (0.68 g, 51%) was obtained as a white solid: mp 268–269 °C; IR (nujol)  $\nu$  = 1720 (s), 1623 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.90 (s, 1H), 8.06 (d,  $J$  = 8.1 Hz, 1H), 7.16–7.13 (m, 2H), 3.94 (s, 3H), 3.43 (t,  $J$  = 7.7 Hz, 4H), 2.45 (s, 3H), 2.27 (quint,  $J$  = 7.7 Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 166.1 (0), 161.2 (0), 155.1 (0), 151.9 (0), 141.7 (0), 141.3 (0), 134.6 (0), 132.0 (1), 126.6 (1), 126.2 (0), 125.4 (1), 120.0 (0), 118.0 (1), 116.2 (0), 52.0 (3), 35.2 (2), 33.6 (2), 24.9 (2), 21.3 (3); GC-MS  $m/z$  (%) 308 ( $\text{M}^+$ , 100); HRMS (EI)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{16}\text{O}_4$ : 308.1048; found: 308.1064. Using standard procedure B (2 h, scaled down by a factor of 4.3, chloroform used for chromatography), **111** (0.18 g, 57%) was obtained as a white solid.

**4-Methylbenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (112).** Using standard procedure A (3 h), **112** (0.65 g, 48%) was obtained as a white solid: mp 228–229 °C; IR (nujol)  $\nu$  = 1718 (s), 1193 (m)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  = 8.82 (s, 1H), 7.97 (d,  $J$  = 7.9 Hz, 1H), 7.32 (d,  $J$  = 7.6 Hz, 1H), 7.19 (t,  $J$  = 7.8 Hz, 1H), 3.93 (s, 3H), 3.39 (t,  $J$  = 7.6 Hz, 4H), 2.44 (s, 3H), 2.24 (quint,  $J$  = 7.7 Hz, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  = 165.9 (0), 160.8 (0), 155.0 (0), 150.0 (0), 141.7 (0), 134.7 (0), 132.1 (1), 131.8 (1), 126.9 (0), 126.3 (0), 124.5 (1), 123.6 (1), 120.1 (0), 118.3 (0), 52.0 (3), 35.4 (2), 33.5 (2), 24.8 (2), 16.2 (3);

GC-MS  $m/z$  (%) 308 ( $M^+$ , 100); HRMS (EI) calcd for  $C_{19}H_{16}O_4$ : 308.1049; found: 308.1045. Using standard procedure B (2 h, scaled down by a factor of 3.5, chloroform used for chromatography), **112** (0.20 g, 54%) was obtained as a white solid.

**2-Methoxybenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (113).** Using standard procedure A (3 h), **113** (0.72 g, 51%) was obtained as a light orange solid: mp 244–245 °C; IR (nujol)  $\nu$  = 1719 (s), 1703 (s), 1600 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 8.86 (s, 1H), 7.71 (d,  $J$  = 2.9 Hz, 1H), 7.34 (d,  $J$  = 9.0 Hz, 1H), 7.09 (dd,  $J$  = 9.0, 2.0 Hz, 1H), 3.95 (s, 3H), 3.90 (s, 3H), 3.51–3.44 (m, 4H), 2.29 (quint,  $J$  = 7.5 Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.1 (0), 161.2 (0), 155.9 (0), 155.2 (0), 146.2 (0), 141.7 (0), 134.4 (0), 132.2 (1), 126.8 (0), 120.6 (0), 119.3 (0), 118.6 (1), 116.8 (1), 111.3 (1), 55.8 (3), 52.1 (3), 35.2 (2), 33.6 (2), 25.0 (2); GC-MS  $m/z$  (%) 324 ( $M^+$ , 100); HRMS (EI) calcd for  $C_{19}H_{16}O_5$ : 324.0997; found: 324.1024. Using standard procedure B (3 h, scaled down by a factor of 2.3), **113** (0.40 g, 64%) was obtained as a white solid.

**2-Bromobenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (114).** Using standard procedure A (3 h, scaled down by a factor of 2.0), **114** (0.41 g, 51%) was obtained as a white solid: mp 262–263 °C; IR (nujol)  $\nu$  = 1731 (s), 1716 (s)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 8.95 (s, 1H), 8.33 (d,  $J$  = 1.5 Hz, 1H), 7.61 (dd,  $J$  = 8.6, 2.2 Hz, 1H), 7.29 (d,  $J$  = 8.6 Hz, 1H), 3.96 (s, 3H), 3.47 (t,  $J$  = 7.7 Hz, 4H), 2.31 (quint,  $J$  = 7.8 Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.3 (0), 160.8 (0), 156.1 (0), 151.3 (0), 142.4 (0), 133.9 (1), 133.6 (0), 132.6 (1), 129.9 (1), 127.8 (0), 121.0 (0), 120.8 (0), 120.0 (1), 117.6 (0), 52.7 (3), 35.6 (2), 34.0 (2), 25.4 (2); EI-MS  $m/z$  (%) 374 ( $M^+$   $^{81}Br$ , 97), 372 ( $M^+$   $^{79}Br$ , 100); Anal. Calcd for  $C_{18}H_{13}O_4Br$ : C, 57.53; H, 3.50. Found: C, 57.93; H, 3.51; HRMS (EI) calcd for  $C_{18}H_{13}O_4Br$ : 371.9996; found: 371.9991. Using standard procedure B (2 h, scaled down by a factor of 2), **114** (0.22 g, 35%) was obtained as a white solid.

**Benzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-2,8-dicarboxylic Acid Dimethyl Ester (115).** Using standard procedure A (3 h), **115** (0.62 g, 41%) was obtained as a white solid: mp > 300 °C; IR (nujol)  $\nu$  = 1731 (s), 1706 (s), 1666 (s), 1586 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 9.00–8.99 (m, 2H), 8.19 (dd,  $J$  = 8.2, 2.2 Hz, 1H), 7.46 (d,  $J$  = 7.9 Hz, 1H), 4.00 (s, 3H), 3.97 (s, 3H), 3.59 (t,  $J$  = 7.4 Hz, 2H), 3.49 (t,  $J$  = 7.9 Hz, 2H), 2.33 (quint,  $J$  = 7.3 Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.1 (0), 166.0 (0), 160.4 (0), 155.8 (0), 154.9 (0), 142.2 (0), 133.7 (0), 132.2 (1), 131.7 (1), 129.1 (1), 127.3 (0), 126.4 (0), 120.3 (0), 118.8 (0), 118.1 (1), 52.5 (3), 52.2 (3), 35.2 (2), 33.7 (2), 25.0 (2); GC-MS  $m/z$  (%) 352 ( $M^+$ , 100); HRMS (EI) calcd for  $C_{20}H_{16}O_6$ : 352.0947; found: 352.0946. Using standard procedure B (2 h, scaled down by a factor of 3.1, chloroform used for chromatography), **115** (0.17 g, 34%) was obtained as a white solid.

**2-Nitrobenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (116).** Using standard procedure A (1.5 h), **116** (0.19 g, 24%) was obtained as a white solid: mp 272–273 °C; IR (nujol)  $\nu$  = 1753 (s), 1729 (s), 1599 (m), 1529 (s), 1354 (s)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 9.22 (d,  $J$  = 2.8 Hz, 1H), 9.00 (s, 1H), 8.41 (dd,  $J$  = 8.9, 2.7 Hz, 1H), 7.54 (d,  $J$  = 9.0 Hz, 1H), 3.98 (s, 3H), 3.60 (t,  $J$  = 7.3 Hz), 3.52 (t,  $J$  = 8.2 Hz), 2.37 (quint,  $J$  = 7.7 Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 165.7 (0), 159.6 (0), 156.4 (0), 155.7 (0), 144.1 (0), 142.5 (0), 132.5 (0), 132.3 (1), 128.2 (0), 125.6 (1), 122.9 (1), 120.3 (0), 119.3 (0), 119.0 (1), 52.4 (3), 35.1 (2), 33.7 (2), 25.0 (2); EI-MS  $m/z$  (%) 339 ( $M^+$ , 100); Anal. Calcd for  $C_{18}H_{13}NO_6$ : C, 63.72; H, 3.86; N, 4.13. Found: C, 63.37; H, 3.72; N, 4.05. Using standard procedure B (2 h, scaled down by a factor of 4.8, 1:49 methanol/chloroform used for chromatography), **116** (0.070 g, 22%) was obtained as a pale yellow solid.

**Methyl (E)-3-(2-Oxo-2H-chromen-3-yl)but-2-enoate (118).** To a magnetically stirred solution of salicylaldehyde **16** (1.24 mL, 11.6 mmol) and dimethyl 3-methylglutaconate (**117**) (1.83 mL, 11.6 mmol) in benzene (43 mL) was added piperidine (0.57 mL, 5.8 mmol) dropwise, and the resulting mixture was heated at reflux for 45 h. The mixture was cooled to room temperature, whereupon a white precipitate formed. This precipitate was isolated by suction filtration,

and the filter cake was washed with cold 95% ethanol (25 mL) to afford **118** (1.55, 55%) as a white solid: mp 163–164.5 °C; IR (nujol)  $\nu$  = 1699 (s), 1609 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 7.74 (s, 1H), 7.57–7.52 (m, 2H), 7.35–7.29 (m, 2H), 6.44 (d,  $J$  = 1.2 Hz, 1H), 3.77 (s, 3H), 2.53 (d,  $J$  = 1.5 Hz, 3H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 166.7 (0), 159.1 (0), 153.6 (0), 150.1 (0), 140.1 (1), 132.2 (1), 129.8 (0), 128.2 (1), 124.6 (1), 120.8 (1), 118.8 (0), 116.5 (1), 51.3 (3), 17.7 (3); GC-MS  $m/z$  (%) 244 ( $M^+$ , 23), 185 (100); HRMS (EI) calcd for  $C_{14}H_{12}O_4$ : 244.0735; found: 244.0750.

**7-Methylbenzo[b]-2,3-dihydro-1H-indeno[5,4-d]-6H-pyran-6-one-8-carboxylic Acid Methyl Ester (119).** Using standard procedure A (3 h, scaled by a factor of 2.0), **119** (0.45 g, 67%) was obtained as a white solid: mp 174–175 °C;  $^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  = 8.15 (d,  $J$  = 8.2 Hz, 1H), 7.48–7.45 (m, 1H), 7.34 (dd,  $J$  = 8.3, 1.3 Hz, 1H), 7.29 (t,  $J$  = 7.4 Hz, 1H), 3.97 (s, 3H), 3.47 (t,  $J$  = 7.1, 2H), 3.03 (t,  $J$  = 7.7 Hz, 2H), 2.81 (s, 3H), 2.22 (quint,  $J$  = 7.6 Hz, 2H);  $^{13}C$  NMR ( $CDCl_3$ , 125 MHz)  $\delta$  = 169.3 (0), 160.3 (0), 151.5 (0), 149.8 (0), 140.1 (0), 138.0 (0), 134.3 (0), 132.8 (0), 130.1 (1), 126.7 (1), 123.8 (1), 119.3 (0), 119.2 (0), 117.2 (1), 52.4 (3), 36.1 (2), 32.3 (2), 25.1 (2), 20.7 (3); GC-MS  $m/z$  (%) 308 ( $M^+$ , 100); HRMS (EI) calcd for  $C_{19}H_{16}O_4$ : 308.1048; found: 308.1039. Using standard procedure B (8 h, scaled down by a factor of 2.1) **119** (0.28 g, 44%) was obtained as a white solid.

**9,9-Diethoxy-8,9,10,10a-tetrahydro-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (122), 9-Ethoxy-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (123), and 9-Ethoxy-10,10a-dihydro-6H-dibenzo[b,d]pyran-6-one-8-carboxylic Acid Methyl Ester (124).** To a solution of diene **13** (0.40 g, 1.74 mmol) in dichloromethane (8 mL) was added 1,1-diethoxyethene (1.15 g, 9.91 mmol), and the resulting mixture was heated at reflux 20 h. The reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure, and the residue was subjected to flash chromatography on silica gel (dichloromethane) to give **122** (0.43 g, 72%) as a pale yellow solid: mp 151–154 °C; IR (powder)  $\nu$  = 1738 (s), 1649 (w), 1201 (s)  $cm^{-1}$ ;  $^1H$  NMR ( $CD_2Cl_2$ , 500 MHz)  $\delta$  = 7.32–7.27 (m, 2H), 7.20–7.17 (m, 1H), 7.01–7.05 (m, 1H), 6.89 (dd,  $J$  = 5.3, 3.2 Hz, 1H), 3.89 (m, 1H), 3.80–3.78 (m, 1H), 3.67–3.61 (m, 2H), 3.66 (s, 3H), 3.59–3.53 (m, 2H), 2.77 (ddd,  $J$  = 13.0, 5.7, 1.8 Hz, 1H), 2.34 (dd,  $J$  = 13.0, 11.1 Hz, 1H), 1.18 (t,  $J$  = 7.0 Hz, 3H), 1.17 (t,  $J$  = 7.0 Hz, 3H);  $^{13}C$  NMR (300 MHz,  $CD_2Cl_2$ )  $\delta$  = 169.5, 163.0, 150.7, 136.3, 130.0, 128.6, 125.4, 125.0, 124.4, 117.3, 99.2, 56.6, 56.1, 52.7, 50.2, 33.2, 30.7, 15.4, 15.3; APCI(–)-MS  $m/z$  (%) 346 ( $M^+$ , 5), 345 (40), 300 (15), 299 (100); HRMS (APCI(+)) calcd for  $C_{19}H_{23}O_6$ : 347.1495; found: 347.1497. Upon extending the reaction time to 2 d, compounds **122** (0.36 g, 60%) **123** (0.078 g, 15%), and **124** (0.047 g, 9%) were obtained. **123**: mp 218–220 °C; IR (powder)  $\nu$  = 1711 (s), 1608 (m)  $cm^{-1}$ ;  $^1H$  NMR ( $CD_2Cl_2$ , 500 MHz)  $\delta$  = 8.70 (s, 1H), 8.06 (dd,  $J$  = 7.9, 1.6 Hz, 1H), 7.57–7.54 (m, 2H), 7.39–7.33 (m, 2H), 4.34 (q,  $J$  = 7.0 Hz, 2H), 3.91 (s, 3H), 1.55 (t,  $J$  = 6.9 Hz, 3H);  $^{13}C$  NMR (500 MHz)  $\delta$  = 165.3, 163.3, 160.4, 152.6, 139.7, 135.1, 131.9, 124.9, 123.6, 122.6, 118.2, 117.8, 113.9, 104.7, 65.7, 52.5, 14.7; EI-MS  $m/z$  (%) 299 ( $[M + 1]^+$ , 100), 267 (60); HRMS (APCI(+)) calcd for  $C_{17}H_{15}O_5$ : 299.0919; found: 299.0917. **124**: mp 177–180 °C; IR (powder)  $\nu$  = 1703 (s), 1618 (m), 1520 (s)  $cm^{-1}$ ;  $^1H$  NMR ( $CD_2Cl_2$ , 500 MHz)  $\delta$  = 7.91 (d,  $J$  = 3.4 Hz, 1H), 7.32–7.26 (m, 2H), 7.18–7.15 (m, 1H), 7.07–7.05 (m, 1H), 4.41–4.35 (m, 1H), 4.27–4.21 (m, 1H), 4.16 (ddd,  $J$  = 18.8, 7.6, 3.3 Hz, 1H), 3.75 (s, 3H), 3.35 (dd,  $J$  = 17.2, 7.6 Hz, 1H), 2.63 (dd,  $J$  = 18.8, 16.9 Hz, 1H), 1.44 (t,  $J$  = 7.0 Hz, 3H);  $^{13}C$  NMR (300 MHz,  $CD_2Cl_2$ )  $\delta$  = 171.4, 164.0, 161.3, 150.8, 141.1, 129.0, 125.9, 124.5, 121.8, 117.7, 111.8, 106.7, 63.3, 51.5, 32.2, 31.2, 15.1; EI-MS  $m/z$  (%) 301 ( $[M + 1]^+$ , 100), 241 (55), 323, (50), 269 (40); HRMS (EI) calcd for  $C_{17}H_{16}O_5$ : 300.0998; found: 300.1006.

## ■ ASSOCIATED CONTENT

### ● Supporting Information

$^1H$  NMR and  $^{13}C$  NMR spectra for compounds **13**, **19–22**, **25**, **38–42**, **44**, **46**, **48**, **50**, **52a,b**, **54**, **56**, **58**, **61**, **62**, **64**, **70**, **72**, **74a,b**, **76a**, **78a**, **79**, **81**, **83**, **85**, **88–91**, **93**, **95**, **97**, **99**, **100**,



102, 103, 105, 106, 108, 109, 110–116, 118, 119, and 122–124. CIFs for compounds 52a, 52b, 79, and 122. Experimental details for X-ray crystallography and views of compounds 52a, 52b, 79, and 122 in the crystal. Calculated torsion angles in compounds 38, 44, 46, 48, 56, 61, 62, and 64. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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