DOI: 10.1002/ejoc.201402478

Rapid and Structurally Diverse Synthesis of Multi-Substituted β-Keto Amide Derivatives Based on a Dioxinone Scaffold

Shinichiro Fuse,*[a] Hayato Yoshida,[a] Kazuya Oosumi,[a] and Takashi Takahashi[b]

Keywords: Combinatorial chemistry / Amides / Palladium / Cross-coupling / Dyes

A sequential diversification approach for the synthesis of various multi-substituted β-keto amide derivatives based on a simple and readily available dioxinone scaffold was developed. The process involves: (1) nucleophilic addition of the scaffold to an aldehyde, and a subsequent one-pot dehydration; (2) palladium-catalysed cross-coupling of the scaffold with either an arylboronic acid pinacol ester, or CO and an aliphatic amine; and (3) nucleophilic addition of either an aliphatic amine or an arylamine, or a hetero-Diels–Alder reaction of isocyanate/isothiocyanate, with an acylketene generated in situ from the dioxinone scaffold.

Introduction

Molecular scaffolds that allow orthogonal structural modifications are valuable in the synthesis of compound libraries for drug discovery and materials development.[1] For instance, many researchers have used modified monosaccharides as 3D scaffolds for drug discovery.[2] Rebek and co-workers have used cyclic pseudopeptide scaffolds containing three orthogonally protected amino groups.[3] Porco and co-workers have used a unique spiroacetal scaffold containing three appropriately protected reaction centres for natural-product-like compound library synthesis.[4] However, such typical non-sequential diversification approaches require extra synthetic steps such as deprotection and/or the introduction of activating groups, so they are not necessarily suitable for library synthesis. Sequential diversification approaches without the extra synthetic steps that do not contribute to structural diversification would be more valuable for rapid library construction. From this point of view, Itami and Yoshida have reported the elegant syntheses of various multi-substituted alkenes and pyrimidines using simple and readily available scaffolds.[1] Itami and co-workers also reported the synthesis of multi-aryl-substituted thiophenes.[5] We have also reported that simple and readily available aromatic scaffolds can be used in a sequential diversification approach for the rapid construction of libraries of rod-shaped liquid crystals,[6] resorcylic acid lactones,[7,8] near-infrared-absorbing dyes,[9] and D-π-A dyes for dye-sensitized solar cells.[10]

β-Keto amides and their derivatives make up an important class of compounds. They are frequently found in various biologically active compounds, such as growth hormone secretagogue **1**,[11] immunosuppressive agent **2**,[12] and a precursor **3** of a human gonadotropin-releasing hormone receptor antagonist[13,14] (Figure 1).

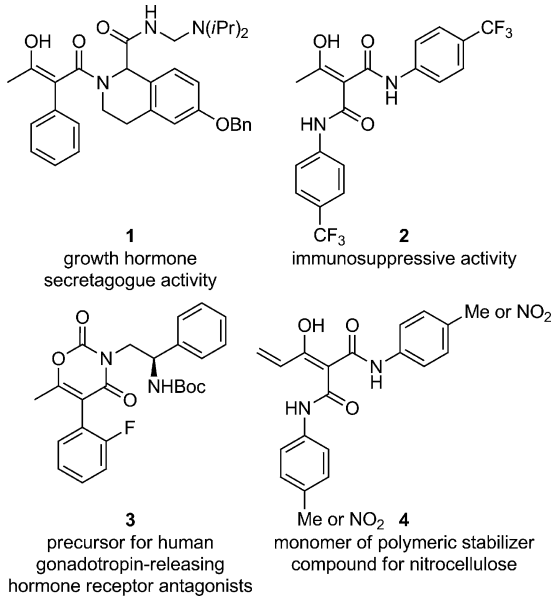


Figure 1. Structures of various useful compounds containing the β-keto amide motif. Boc = *tert*-butoxycarbonyl.

Moreover, the β-keto amide motif can be found in monomers used for the synthesis of polymeric stabilizers of nitrocellulose, such as **4**.[15] The development of useful scaffolds

[a] Department of Applied Chemistry, Tokyo Institute of Technology,
2-12-1, Ookayama, Meguro-ku, Tokyo 152-8552, Japan
E-mail: sfuse@apc.titech.ac.jp
http://www.apc.titech.ac.jp/~htanaka/index.html
[b] Yokohama College of Pharmacy,
601, Matana-cho, Totsuka-ku, Yokohama-shi 245-0066, Japan
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201402478.

has been important, as such compounds allow the rapid synthesis of structurally diverse β-keto amide derivatives and their analogues.

2,2-Dimethyl-1,3-dioxin-6-one was first reported by Carroll and Bader in 1953.[16] Dioxinone and its derivatives are useful in organic synthesis, because they are easily handled precursors of highly reactive acylketenes. Many elegant syntheses, including total syntheses of natural products, have been reported using this feature of dioxinones.[17–33] The dioxinones are also attractive as molecular scaffolds for assembling building blocks, because they provide multiple reaction centres for various chemical modifications.[17,23] In this paper, we report the rapid synthesis of structurally diverse multi-substituted β-keto amide derivatives using a sequential diversification approach based on a simple and readily available dioxinone scaffold **5**.

Results and Discussion

Scaffold **5**[34] is synthetically equivalent to compound **6**, which retains three reaction centres (Figure 2). Scaffold **5** can be readily prepared from commercially available 2,2-dimethyl-1,3-dioxin-6-one in one step (for details of the synthesis of **5**, see Supporting Information). We planned to carry out the nucleophilic addition of scaffold **5** to aldehydes, with subsequent dehydration and activation of the carbon–iodine bond under palladium-catalysed cross-coupling conditions. Finally, the acylketene would be generated in situ by a retro-Diels–Alder reaction, and the ketene would be attacked by various amines.

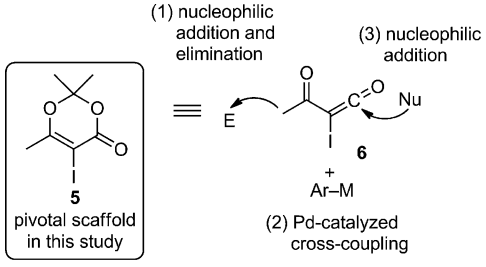
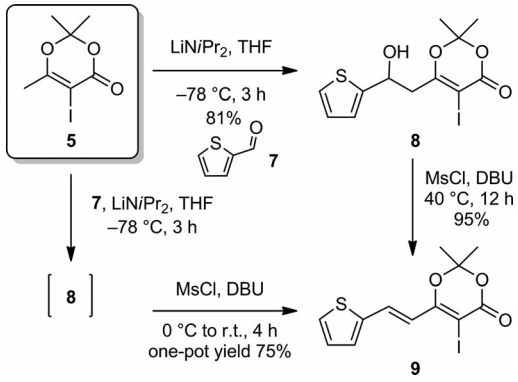


Figure 2. Dioxinone scaffold used in this study for the synthesis of various β-keto amide derivatives. E = electrophile, Nu = nucleophile, Ar–M = aryl–metal compounds.

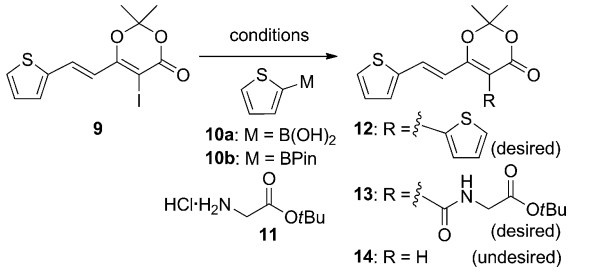
We began by examining the first step (Scheme 1). The nucleophilic addition of a simple 2,2-dimethyl-1,3-dioxin-6-one without iodine has been reported.[35] According to this report, the nucleophilic addition of scaffold **5** to 2-thiophenecarbaldehyde (**7**) was examined. In this reaction, the temperature was important. Gradual warming to room temperature resulted in a decrease in yield (to 27%) due to degradation of alcohol **8**. The subsequent elimination of the alcohol was achieved by converting alcohol **8** into the corresponding mesylate. The desired alkene (i.e., **9**) was obtained in an excellent yield. To improve the efficiency of this method, a one-pot reaction was carried out. To our delight, the desired product (i.e., **9**) was obtained in 75% yield based on **5**.



Scheme 1. Nucleophilic addition–elimination sequence for the synthesis of alkene **8**.

The second step was a palladium-catalysed cross-coupling reaction. A Suzuki–Miyaura coupling reaction between alkenyl iodide **9**[36,37] and 2-thienylboronic acid (**10a**) was optimized based on our previously developed conditions[7,10] (Table 1, Entries 1–4). Heating (80 °C) was neces-

Table 1. Optimization of the palladium-catalysed cross-coupling reactions of alkenyl iodide **9**. Pin = pinacolyl.



Entry	Substrate	Conditions[a]	Temperature	Base, solvent	Product, yield [%][b]
1	**10a**	A	room temp.	Na_2CO_3, toluene/H_2O	**9**, 53 **12**, 31
2	**10a**	A	50 °C	Na_2CO_3, toluene/H_2O	**9**, 15 **12**, 72
3	**10a**	A	80 °C	Na_2CO_3, toluene/H_2O	**12**, 84
4	**10b**	A	80 °C	Na_2CO_3, toluene/H_2O	**12**, 91
5	**11**	B	80 °C	DABCO, toluene	**13**, 71 **14**, 16
6	**11**	B	80 °C	DBU, toluene	**13**, 74 **14**, 12
7	**11**	B	80 °C	DBU, DMF	**13**, 82 **14**, 8

[a] Conditions A: $Pd_2(dba)_3$ (10 mol-%) (dba = dibenzylideneacetone), $CHCl_3$, Xantphos, 12 h; Conditions B: $Pd(OAc)_2$ (10 mol-%), [*t*Bu$_3$PH]BF$_4$, CO (15 atm), 80 °C, 24 h. [b] Isolated yield.

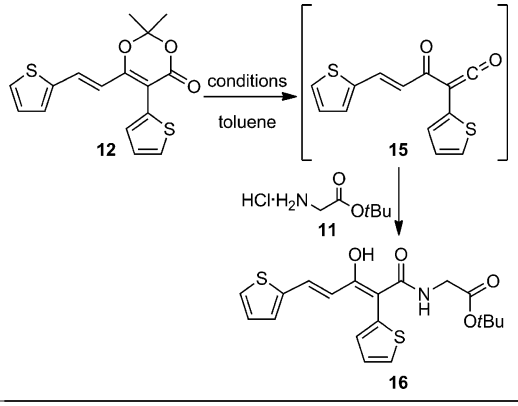
sary for the complete consumption of substrate **9** (Table 1, Entries 1–3). The use of a thiophene-2-boronic acid pinacol ester (**10b**) improved the yield of **12** (Table 1, Entry 4). Next, the carbonylative amidation of **9** with **11** was examined. The first trial using a combination of DABCO (1,4-diazabicyclo[2.2.2]octane) and toluene gave the desired product (i.e., **13**) in 71% yield, along with undesired product **14** (Table 1, Entry 5). The combination of DBU (1,8-diazabicycloundec-7-ene) and DMF suppressed the generation of **14** (8%), as shown in Table 1, Entry 7.

In the final step, the nucleophilic addition of amines to in situ generated ketene **15** by retro-Diels–Alder reaction was examined. Several heating conditions were examined to generate ketene **15** from **12** (Table 2). The best results were obtained using conventional reflux (in toluene) without using an additive (Table 2, Entry 3). Thus, a multi-substituted β-keto amide derivative **16** could be synthesized in high yield in only three steps (55% over three steps) from dioxinone scaffold **5**.

Various modifications of the acylketenes generated in situ from **12** or **13** are shown in Scheme 2. Nucleophilic addition of aliphatic amine **11** and arylamines **17**–**19** to the acylketene derived from **12** gave the desired α-aryl β-keto amide derivatives (i.e., **22**–**25**) in high yields. This is noteworthy, because a flexible and rapid synthesis of α-aryl β-keto amide derivatives has been hampered by limited substrate availability and/or limited substrate scope, despite the development of several methods.[38–43] The nucleophilic addition of aliphatic amine **11** to the acylketene derived from **13** also gave the desired product (i.e., **28**) in a satisfactory yield. Next, the hetero-Diels–Alder reaction of the acylketene derived from **12** with isocyanate **20**[44–46] or isothiocyanate **21**[47] was carried out, and the desired compounds (i.e., **26** and **27**) were obtained in moderate yields.

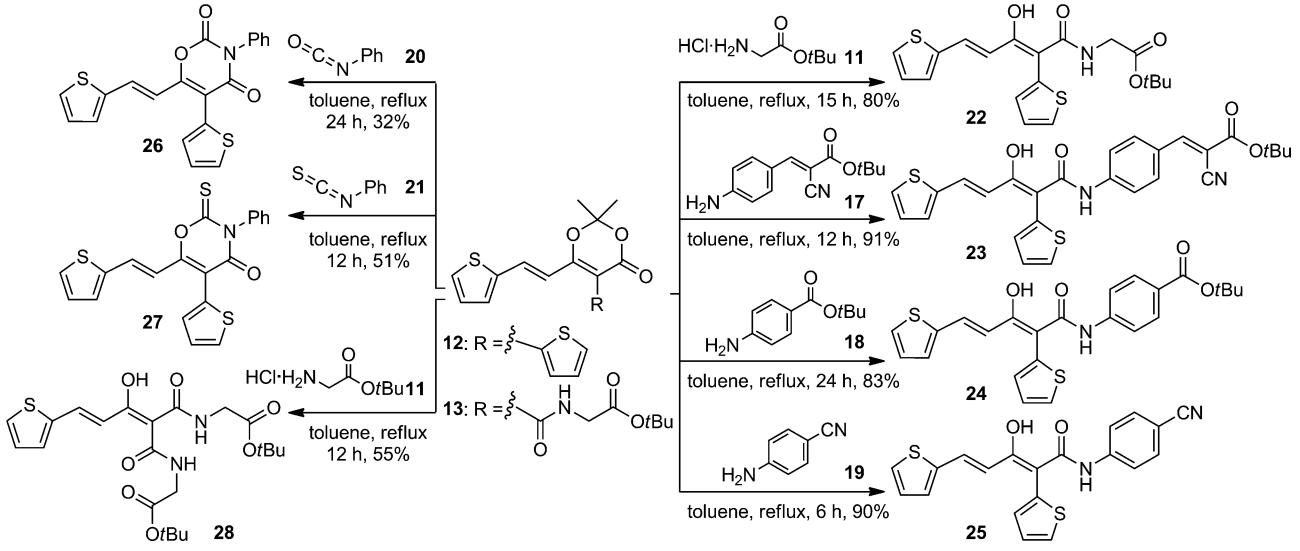
Finally, a potentially useful (donor-π-bridge)$_2$–acceptor dye **33** for dye-sensitized solar cells was designed based on the previous reports.[48,49] Dye **33** was synthesized according to our developed procedure in only three steps from scaffold **5**, as shown in Scheme 3. In the first step, nucleophilic addition of **5** to aldehyde **29** and subsequent elimination of the hydroxy group gave the desired product (i.e., **30**) in one pot in 73% yield. A subsequent Suzuki–Miyaura coupling between alkenyl iodide **30** and thiopheneboronic acid pinacol ester **31** gave the desired coupling product in 91% yield. Finally, nucleophilic addition of amine **11** to the in situ generated acylketene from **32** gave the desired product (i.e., **33**) in 74% yield.

Table 2. Optimization of the nucleophilic addition of amine **11** to in situ generated acyl ketene **15**. DIEA = diisopropylethylamine.

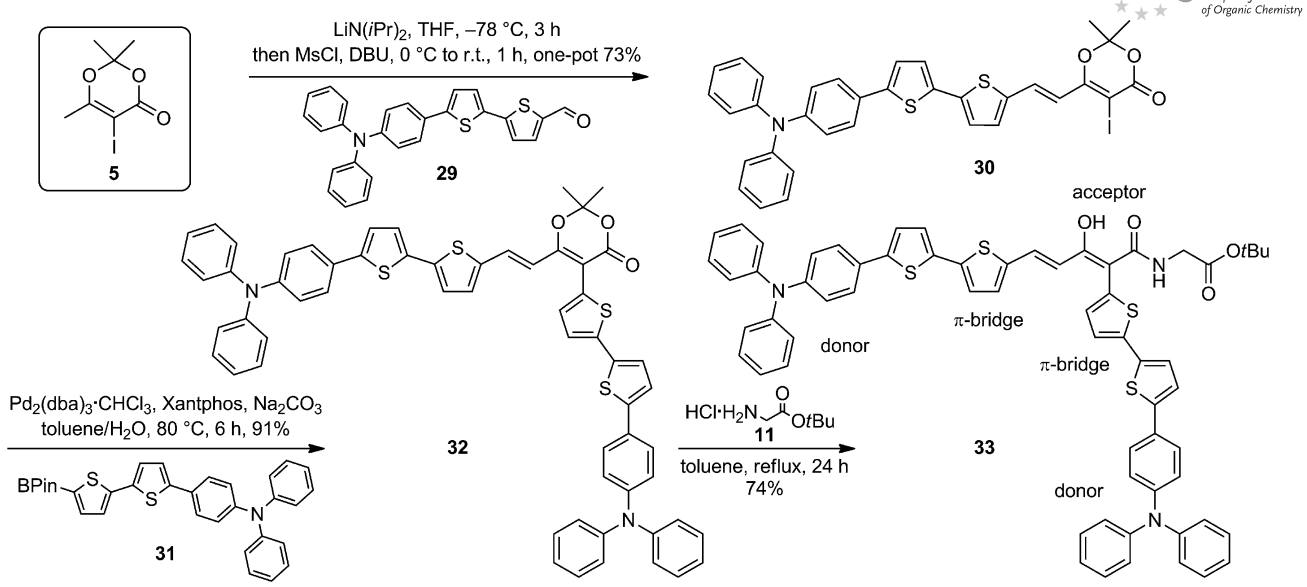


Entry	Additive	Conditions	Yield [%][a]
1	DIEA	reflux, 48 h	33
2	DIEA	microwaves (300 W), 140 °C, 1 h	72
3	–	reflux, 15 h	80
4	–	microwaves (300 W), 140 °C, 1 h	77

[a] Isolated yield.



Scheme 2. Synthesis of various β-keto amide derivatives.



Scheme 3. Synthesis of branched dye **33**.

Conclusions

We have successfully developed a sequential diversification approach for the synthesis of various multi-substituted β-keto amide derivatives based on a simple and readily available dioxinone scaffold. The first step, which gave high yields, was the nucleophilic addition of our pivotal dioxinone scaffold **5** to an aldehyde and a subsequent one-pot dehydration. The second step involved the palladium-catalysed cross-coupling reaction of the alkenyl iodide with either arylboronic acid pinacol esters or with CO and amines.

The third step involved the nucleophilic addition of amines or a hetero-Diels–Alder reaction of isocyanate or isothiocyanate with the acylketene generated in situ from the dioxinones. Our method paves the way for the practical synthesis of various useful and structurally diverse multi-substituted β-keto amide derivatives.

Experimental Section

General Remarks: NMR spectra were recorded with a JEOL model ECP-400 (400 MHz for ^{1}H, 100 MHz for ^{13}C) instrument in the indicated solvent. Chemical shifts are reported in units of parts per million (ppm) relative to the signal for internal tetramethylsilane (δ =0.00 ppm) for solutions in $CDCl_3$ (δ = 7.26 ppm for ^{1}H, δ = 77.0 ppm for ^{13}C). Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; br., broad. Coupling constants (*J*) are given in Hertz (Hz). IR spectra were recorded with a Perkin–Elmer Spectrum One FTIR spectrometer. IR data are given in cm^{-1}. Only the strongest and/or structurally important peaks are reported. HRMS (ESI-TOF) data were measured with a Waters LCT Premier™ XE instrument. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254). Plates were visualized with UV light, *p*-anisaldehyde solution, ceric sulfate or ethanolic phosphomolybdic acid (10%). Flash column chromatography was carried out on Silica Gel 60N, purchased from Kanto Chemical Co. Dry THF, dry CH_2Cl_2, and dry toluene were obtained using a Glasscontour solvent purification system.

(*E*)-5-Iodo-2,2-dimethyl-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (9): *n*BuLi (1.67 M in hexane; 0.350 mL, 0.592 mmol, 1.10 equiv.) was added dropwise to a solution of HN*i*Pr$_2$ (0.0900 mL, 0.646 mmol, 1.20 equiv.) in THF (1.00 mL) at –78 °C, and the reaction mixture was stirred at 0 °C under Ar for 30 min. A solution of 5-iodo-2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**5**; 144 mg, 0.538 mmol, 1.00 equiv.) in THF (0.500 mL) was added dropwise to the reaction mixture at –78 °C, and the resulting mixture was stirred at 0 °C for 30 min. A solution of thiophene-2-carbaldehyde (**7**; 0.100 mL, 1.08 mmol, 2.00 equiv.) in THF (0.500 mL) was added dropwise at –78 °C, and the reaction mixture was stirred at the same temperature under Ar for 3 h. MsCl (0.120 mL, 1.61 mmol, 3.00 equiv.) and DBU (0.400 mL, 2.69 mmol, 5.00 equiv.) were then added at –78 °C. The mixture was stirred at 0 °C for 4 h, then it was poured into HCl (1 M), and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel (0–10% ethyl acetate in hexane) to give (*E*)-5-iodo-2,2-dimethyl-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**9**; 146 mg, 0.401 mmol, 75%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 15.5 Hz, 1 H), 7.45 (d, *J* = 5.4 Hz, 1 H), 7.31 (d, *J* = 3.9 Hz, 1 H), 7.10 (dd, *J* = 3.9, 5.4 Hz, 1 H), 6.94 (d, *J* = 15.5 Hz, 1 H), 1.76 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1, 159.0, 140.0, 133.8, 130.9, 129.2, 128.4, 120.6, 106.4, 64.4, 25.0 ppm. IR (neat): $\tilde{\nu}$ = 1718, 1607, 1557, 1333, 1267, 1205, 1035 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{12}H_{12}IO_3S$ $[M + H]^+$ 362.9552; found 362.9552.

(*E*)-2,2-Dimethyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (12): To a solution of (*E*)-5-iodo-2,2-dimethyl-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**9**; 15.2 mg, 0.0420 mmol, 1.00 equiv.) and thiophene-2-boronic acid pinacol ester (**10b**; 17.6 mg, 0.0838 mmol, 2.00 equiv.) in toluene (0.25 mL) and H_2O (0.25 mL) were added $Pd_2(dba)_3$·$CHCl_3$ (3.8 mg, 0.0042 mmol, 0.10 equiv.), Xantphos (4.9 mg, 0.0084 mmol, 0.20 equiv.) and Na_2CO_3 (4.5 mg, 0.042 mmol, 1.0 equiv.) at room

temperature under Ar. After having been stirred at 80 °C for 12 h, the reaction mixture was poured into 1 M HCl, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and filtered. After removal of the solvent, the residue was purified by column chromatography on silica gel (0–10% ethyl acetate in hexane) to give (*E*)-2,2-dimethyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**12**; 12.1 mg, 0.038 mmol, 91%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, J = 15.5 Hz, 1 H), 7.44 (d, J = 1.5 Hz, 1 H), 7.36 (d, J = 5.3 Hz, 1 H), 7.21 (d, J = 3.4 Hz, 1 H), 7.10 (m, 2 H), 7.05 (dd, J = 3.9, 5.3 Hz, 1 H), 6.76 (d, J = 15.5 Hz, 1 H), 1.83 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.4, 159.2, 140.7, 132.6, 131.3, 129.9, 129.2, 128.4, 128.3, 127.5, 126.5, 117.6, 105.5, 102.7, 25.2 ppm. IR (neat): $\tilde{\nu}$ = 1716, 1608, 1388, 1335, 1278, 1207, 703 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{16}H_{15}O_3S_2$ $[M + H]^+$ 319.0463; found 319.0464.

***tert*-Butyl (*E*)-2-{2,2-Dimethyl-4-oxo-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxine-5-carboxamido}acetate (13):** (*E*)-5-Iodo-2,2-dimethyl-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**9**; 45.0 mg, 0.124 mmol, 1.00 equiv.) and glycine *tert*-butyl ester hydrochloride (**11**; 62.4 mg, 0.594 mmol, 3.00 equiv.) were suspended in DMF (1 mL) in a glass vessel. $Pd(OAc)_2$ (2.8 mg, 0.012 mmol, 0.10 equiv.), $[t\mathrm{Bu}_3\mathrm{PH}]BF_4$ (7.2 mg, 0.025 mmol, 0.20 equiv.), and DBU (55.6 μL, 0.594 mmol, 3.00 equiv.) were added under Ar. The vessel was placed in an autoclave, which was purged with CO three times before pressure (15 atm) was applied. The mixture was stirred at 80 °C for 24 h, then it was poured into HCl (1 M). The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel (0–25% ethyl acetate in hexane) to give *tert*-butyl (*E*)-2-{2,2-dimethyl-4-oxo-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxine-5-carboxamido}acetate (**13**; 40.1 mg, 0.102 mmol, 82%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.12 (br. s, 1 H), 8.03 (d, J = 15.5 Hz, 1 H), 7.66 (d, J = 15.9 Hz, 1 H), 7.45 (d, J = 5.3 Hz, 1 H), 7.34 (d, J = 3.4 Hz, 1 H), 7.08 (dd, J = 5.3, 3.4 Hz, 1 H), 4.08 (d, J = 5.3 Hz, 2 H), 1.79 (s, 6 H), 1.50 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 168.7, 163.3, 162.6, 140.7, 134.9, 131.3, 129.9, 128.3, 118.7, 105.4, 99.3, 81.9, 42.2, 28.0, 25.0 ppm. IR (neat): $\tilde{\nu}$ = 3340, 2980, 2939, 1740, 1705, 1647, 1603, 1547, 1372, 1352, 1276, 1228, 1156 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{24}NO_6S$ $[M + H]^+$ 394.1324; found 394.1326.

***tert*-Butyl 2-[(2*E*,4*E*)-3-Hydroxy-2,5-di(thiophen-2-yl)penta-2,4-dienamido]acetate (16):** Glycine *tert*-butyl ester hydrochloride (**11**; 99.5 mg, 0.594 mmol, 10.0 equiv.) was added to a solution of (*E*)-2,2-dimethyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**12**; 18.9 mg, 0.059 mmol, 1.00 equiv.) in toluene (0.600 mL) at room temperature in a sealed tube. The mixture was stirred at reflux for 15 h, then it was poured into HCl (1 M). The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel (0–9% ethyl acetate in hexane) to give *tert*-butyl 2-[(2*E*,4*E*)-3-hydroxy-2,5-di(thiophen-2-yl)penta-2,4-dienamido]acetate (**16**; 18.5 mg, 0.047 mmol, 80%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 14.7 (br. s, 1 H), 7.57 (d, J = 15.5 Hz, 1 H), 7.48 (dd, J = 5.3, 1.0 Hz, 1 H), 7.25 (d, J = 5.3 Hz, 1 H), 7.14 (dd, J = 5.3, 3.4 Hz, 1 H) 7.11 (d, J = 3.9 Hz, 1 H), 7.04 (dd, J = 3.4, 1.0 Hz, 1 H), 6.99 (dd, J = 5.3, 3.9 Hz, 1 H), 6.30 (d, J = 15.5 Hz, 1 H), 6.02 (t, J = 4.8 Hz, 1 H), 3.96 (d, J = 5.3 Hz, 2 H), 1.45 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 168.4, 167.2, 141.2, 134.7, 130.8, 129.5, 129.0, 128.3, 127.9, 127.6, 127.1, 119.5, 97.4, 82.4, 42.0, 28.0 ppm. IR (neat): $\tilde{\nu}$ = 3407, 2926, 1739, 1624, 1527, 1369, 1261, 1156, 703 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{19}H_{22}NO_4S_2$ $[M + H]^+$ 392.0990; found 392.0990.

General Procedure for the Nucleophilic Addition of Amines to In Situ Generated Ketene from the Dioxinone Scaffold: The amine (1.0–3.0 equiv.) was added to a solution of dioxinone (1.0 equiv.) in toluene at room temperature in a sealed tube. The mixture was stirred at reflux for the stated time, then it was poured into H_2O, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel to give the β-keto amide.

***tert*-Butyl (*E*)-2-Cyano-3-{4-[(2*E*,4*E*)-3-hydroxy-2,5-di(thiophen-2-yl)penta-2,4-dienamido]phenyl}acrylate (23):** Dioxinone **12** (15.4 mg, 48.4 μmol, 1.00 equiv.) and amine **17** (35.4 mg, 145 μmol, 3.00 equiv.) in toluene (0.5 mL), after 12 h, and purification by silica gel column chromatography (0–2% ethyl acetate in toluene) gave **23** (22.3 mg, 44.2 μmol, 91%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 14.6 (br. s, 1 H), 8.06 (s, 1 H), 7.94 (d, J = 8.7 Hz, 2 H), 7.64 (dd, J = 5.3, 1.0 Hz, 1 H), 7.55 (d, J = 8.7 Hz, 2 H), 7.42 (br. s, 1 H), 7.29 (d, J = 5.3 Hz, 1 H), 7.22 (dd, J = 5.3, 3.4 Hz, 1 H), 7.15 (d, J = 3.4 Hz, 1 H), 7.11 (dd, J = 3.4, 1.0 Hz, 1 H), 7.01 (dd, J = 5.3, 3.4 Hz, 1 H), 6.28 (d, J = 15.5 Hz, 1 H), 1.57 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 169.4, 161.6, 152.9, 141.4, 141.0, 134.2, 132.3, 131.4, 130.8, 129.7, 129.2, 128.1, 128.0, 127.7, 127.4, 119.9, 119.1, 116.0, 102.8, 97.6, 83.5, 27.9 ppm. IR (neat): $\tilde{\nu}$ = 3389, 2979, 2221, 1718, 1618, 1575, 1504, 1416, 1285, 1155, 838, 703 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{27}H_{25}N_2O_4S_2$ $[M + H]^+$ 505.1256; found 505.1273.

***tert*-Butyl 4-[(2*E*,4*E*)-3-Hydroxy-2,5-di(thiophen-2-yl)penta-2,4-dienamido]benzoate (24):** Dioxinone **12** (14.6 mg, 45.9 μmol, 1.00 equiv.) and amine **18** (26.6 mg, 138 μmol, 3.00 equiv.) in toluene (0.5 mL), after 24 h, and purification by silica gel column chromatography (0–8% ethyl acetate in toluene) gave **24** (14.7 mg, 38.1 μmol, 83%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 14.7 (br. s, 1 H), 7.93 (d, J = 8.7 Hz, 2 H), 7.64 (d, J = 15.5 Hz, 1 H), 7.56 (dd, J = 5.3, 1.4 Hz, 1 H), 7.46 (d, J = 8.7 Hz, 2 H), 7.35 (br. s, 1 H), 7.28 (d, J = 5.3 Hz, 1 H), 7.21 (dd, J = 5.3, 3.9 Hz, 1 H), 7.14 (d, J = 3.4 Hz, 1 H), 7.11 (dd, J = 3.4, 1.0 Hz, 1 H), 7.00 (dd, J = 5.3, 3.4 Hz, 1 H), 6.29 (d, J = 15.5 Hz, 1 H), 1.58 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 169.0, 165.2, 141.0, 140.8, 134.5, 131.4, 130.5, 129.5, 129.1, 128.2, 128.0 (×2), 127.7, 127.6, 119.2, 119.1, 97.7, 80.9, 28.2 ppm. IR (neat): $\tilde{\nu}$ = 3392, 2977, 1707, 1621, 1592, 1520, 1408, 1294, 1237, 1163, 1114, 703 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{24}H_{24}NO_4S_2$ $[M + H]^+$ 454.1147; found 454.1148.

(2*E*,4*E*)-*N*-(4-Cyanophenyl)-3-hydroxy-2,5-di(thiophen-2-yl)penta-2,4-dienamide (25): Dioxinone **12** (13.7 mg, 43.0 μmol, 1.00 equiv.) and amine **19** (15.2 mg, 129 μmol, 3.00 equiv.) in toluene (0.5 mL), after 6 h, and purification by silica gel column chromatography (0–15% ethyl acetate in toluene), gave **25** (14.7 mg, 38.8 μmol, 90%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 14.5 (br. s, 1 H), 7.65 (d, J = 15.5 Hz, 1 H), 7.59 (d, J = 8.7 Hz, 2 H), 7.57 (dd, J = 5.3, 1.0 Hz, 1 H), 7.54 (d, J = 8.7 Hz, 2 H), 7.36 (br. s, 1 H), 7.29 (d, J = 4.8 Hz, 1 H), 7.21 (dd, J = 5.3, 3.4 Hz, 1 H), 7.15 (d, J = 3.4 Hz, 1 H), 7.11 (dd, J = 3.4, 1.0 Hz, 1 H), 7.01 (dd, J = 5.3, 3.4 Hz, 1 H), 6.28 (d, J = 15.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 169.6, 141.2, 140.9, 134.1, 133.1, 131.5, 131.0, 129.8, 129.3, 128.1 (2×), 127.8, 119.9, 118.9, 118.7, 107.3, 97.4 ppm. IR (neat): $\tilde{\nu}$ = 3386, 2225, 1616, 1586, 1517, 1503, 1409,

1345, 1313, 1238, 838, 705 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{15}N_2O_2S_2$ $[M + H]^+$ 379.0575; found 379.0587.

(*E*)-3-Phenyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-2*H*-1,3-oxazine-2,4(3*H*)-dione (26): Phenyl isocyanate (**20**; 9.0 μL, 83 μmol, 2.5 equiv.) was added to a solution of (*E*)-2,2-dimethyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**12**; 11 mg, 33 μmol, 1.0 equiv.) in toluene (1.00 mL) at room temperature in a sealed tube. The mixture was stirred at reflux for 24 h, then it was concentrated in vacuo. The residue was purified by column chromatography on silica gel (0–5% ethyl acetate in hexane) to give (*E*)-3-phenyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-2*H*-1,3-oxazine-2,4(3*H*)-dione (**24**; 4.0 mg, 11 μmol, 32%) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 15.5 Hz, 1 H), 7.54 (d, *J* = 5.3 Hz, 1 H), 7.47 (d, *J* = 5.3 Hz, 1 H), 7.41 (d, *J* = 7.7 Hz, 2 H), 7.35–7.29 (m, 4 H), 7.16–7.08 (m, 3 H), 6.88 (d, *J* = 15.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.4, 137.2, 131.2, 130.5, 130.4, 129.9, 129.8, 129.5, 129.3, 129.2, 129.0, 128.7, 128.5, 128.0, 126.8, 124.5, 120.6, 114.9 ppm. IR (neat): $\tilde{\nu}$ = 2926, 1771, 1717, 1692, 1600, 1519, 1441, 1386, 1246, 1177, 755, 693 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{14}NO_3S_2$ $[M + H]^+$ 380.0415; found 380.0415.

(*E*)-3-Phenyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-2-thioxo-2*H*-1,3-oxazin-4(3*H*)-one (27): Phenyl isothiocyanate (**21**; 11 μL, 90 μmol, 2.5 equiv.) was added to a solution of (*E*)-2,2-dimethyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-4*H*-1,3-dioxin-4-one (**12**; 11 mg, 36 μmol, 1.0 equiv.) in toluene (1.00 mL) at room temperature in a sealed tube. The mixture was stirred at reflux for 12 h, then it was concentrated in vacuo. The residue was purified by column chromatography on silica gel (0–7% ethyl acetate in hexane) to give (*E*)-3-phenyl-5-(thiophen-2-yl)-6-[2-(thiophen-2-yl)vinyl]-2-thioxo-2*H*-1,3-oxazin-4(3*H*)-one (**25**; 7.2 mg, 18 μmol, 51%) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 15.5 Hz, 1 H), 7.57–7.49 (m, 5 H), 7.44 (d, *J* = 5.3 Hz, 1 H), 7.35–7.25 (m, 3 H), 7.17 (dd, *J* = 5.3, 3.9 Hz, 1 H), 7.11 (dd, *J* = 5.3, 3.9 Hz, 1 H), 6.89 (d, *J* = 15.5 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 140.4, 138.0, 133.5, 131.4, 130.6, 130.5, 129.8, 129.4, 129.3, 129.2, 129.0, 128.6, 127.8, 127.6, 126.8, 126.6, 114.4 ppm. IR (neat): $\tilde{\nu}$ = 2925, 1700, 1607, 1420, 1384, 1296, 1182, 707 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{20}H_{14}NO_2S_3$ $[M + H]^+$ 396.0187; found 396.0181.

Di-*tert*-butyl (*E*)-2,2′-[{2-[1-Hydroxy-3-(thiophen-2-yl)allylidene]-malonyl}bis(azanediyl)]diacetate (28): Dioxinone **13** (2.0 mg, 5.1 μmol, 1.00 equiv.) and amine **11** (0.9 mg, 5.1 μmol, 3.00 equiv.) in toluene (1.0 mL), after 12 h, and purification by silica gel column chromatography (0–15% ethyl acetate in toluene), gave **28** (1.3 mg, 2.8 μmol, 55%) as a pale yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.54 (br. s, 1 H), 7.74 (d, *J* = 15.5 Hz, 1 H), 7.36 (d, *J* = 5.3 Hz, 1 H), 7.32 (d, *J* = 3.4 Hz, 1 H), 7.18 (d, *J* = 15.5 Hz, 1 H), 7.05 (t, *J* = 4.3 Hz, 1 H), 6.21 (br. s, 1 H), 4.10 (d, *J* = 5.8 Hz, 2 H), 4.00 (d, *J* = 5.3 Hz, 2 H), 1.50 (s, 9 H), 1.48 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 170.7, 169.0, 168.6, 167.7, 140.8, 132.5, 130.0, 128.2, 128.1, 119.0, 100.9, 82.6, 82.3, 42.5, 42.0, 28.1, 28.0 ppm. IR (neat): $\tilde{\nu}$ = 3318, 2979, 2931, 1740, 1625, 1536, 1369, 1229, 1156 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{22}H_{31}N_2O_7S$ $[M + H]^+$ 467.1852; found 467.1861.

(*E*)-6-(2-{5′-[4-(Diphenylamino)phenyl]-(2,2′-bithiophen)-5-yl}vinyl)-5-iodo-2,2-dimethyl-4*H*-1,3-dioxin-4-one (30): *n*BuLi (1.67 M in hexane; 0.211 mL, 0.353 mmol, 1.44 equiv.) was added dropwise to a solution of $HNiPr_2$ (53.6 μL, 0.382 mmol, 1.56 equiv.) in THF (1.00 mL) at –78 °C, and the reaction mixture was stirred at 0 °C under Ar for 30 min. A solution of 5-iodo-2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (**5**; 78.7 mg, 0.294 mmol, 1.20 equiv.) in THF (0.500 mL) was added dropwise to the reaction mixture at –78 °C, and the resulting mixture was stirred at 0 °C for 30 min. A solution of 5′-[4-(diphenylamino)phenyl]-2,2′-bithiophene-5-carbaldehyde (**29**; 107 mg, 0.245 mmol, 1.00 equiv.) in THF (0.500 mL) was added dropwise at –78 °C, and the reaction mixture was stirred at the same temperature under Ar for 3 h. To the reaction mixture were added MsCl (56.9 μL, 0.735 mmol, 3.00 equiv.) and DBU (0.183 mL, 1.23 mmol, 5.00 equiv.) at 0 °C. The mixture was stirred at 0 °C to room temperature for 1 h, then it was poured into HCl (1 M). The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel (0–3% ethyl acetate in toluene) to give (*E*)-6-(2-{5′-[4-(diphenylamino)phenyl]-2,2′-bithiophen-5-yl}vinyl)-5-iodo-2,2-dimethyl-4*H*-1,3-dioxin-4-one (**30**; 123 mg, 0.179 mmol, 73%) as a red solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.7 Hz, 2 H), 7.40 (d, *J* = 15.5 Hz, 1 H), 7.26 (t, *J* = 8.2 Hz, 4 H), 7.20 (d, *J* = 3.9 Hz, 1 H), 7.16 (d, *J* = 3.9 Hz, 1 H), 7.13–7.09 (m, 6 H), 7.06 (d, *J* = 8.7 Hz, 2 H), 7.04 (t, *J* = 7.7 Hz, 2 H), 6.85 (d, *J* = 15.5 Hz, 1 H), 1.75 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1, 159.0, 147.7, 147.2, 144.8, 141.5, 138.2, 134.6, 133.5, 132.6, 129.3, 127.3, 126.4, 126.0, 124.7, 124.1, 123.3, 123.1, 123.0, 119.9, 106.3, 64.2, 25.0 ppm. IR (neat): $\tilde{\nu}$ = 2976, 1721, 1598, 1328, 1137, 982, 762 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{34}H_{27}NO_3S_2I$ $[M + H]^+$ 688.0477; found 688.0473.

(*E*)-5-{5′-[4-(Diphenylamino)phenyl]-2,2′-bithiophen-5-yl}-6-(2-{5′-[4-(diphenylamino)phenyl]-2,2′-bithiophen-5-yl}vinyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (32): (*E*)-6-(2-{5′-[4-(Diphenylamino)phenyl]-2,2′-bithiophen-5-yl}vinyl)-5-iodo-2,2-dimethyl-4*H*-1,3-dioxin-4-one (**30**; 154 mg, 0.225 mmol, 1.05 equiv.) and *N*,*N*-diphenyl-4-[5′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,2′-bithiophen-5-yl]-aniline (**31**; 115 mg, 0.214 mmol, 1.00 equiv.) were dissolved in toluene (2.00 mL) and H_2O (2.00 mL) at room temperature under Ar. $Pd_2(dba)_3{\cdot}CHCl_3$ (9.8 mg, 11 μmol, 0.050 equiv.), Xantphos (12.4 mg, 21.4 μmol, 0.100 equiv.), and Na_2CO_3 (22.7 mg, 0.214 mmol, 1.00 equiv.) were added. The mixture was stirred at 80 °C for 6 h, then it was poured into HCl (1 M). The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel (toluene) to give (*E*)-5-{5′-[4-(diphenylamino)phenyl]-2,2′-bithiophen-5-yl}-6-(2-{5′-[4-(diphenylamino)phenyl]-2,2′-bithiophen-5-yl}vinyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (**32**; 189 mg, 0.195 mmol, 91%) as a red solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.41 (m, 6 H), 7.28–7.25 (m, 8 H), 7.18–7.02 (m, 23 H), 6.77 (d, *J* = 15.5 Hz, 1 H), 1.83 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 159.0, 147.7, 147.4 (2×), 147.3, 144.6, 143.2, 140.9, 139.5, 139.1, 135.7, 134.9, 131.7, 131.6, 131.3, 129.8, 129.3, 129.3, 128.0, 127.4, 126.4, (2×), 125.8, 124.7, 124.7, 124.6, 124.1, 123.6, 123.3 (2×), 123.1, 123.0 (2×), 122.8, 116.9, 105.5, 102.7, 25.3 ppm. IR (neat): $\tilde{\nu}$ = 2926, 1717, 1593, 1494, 1451, 1384, 1279, 794, 755, 696 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{60}H_{45}N_2O_3S_4$ $[M + H]^+$ 969.2313; found 969.2311.

***tert*-Butyl 2-[(2*E*,4*E*)-2,5-Bis{5′-[4-(diphenylamino)phenyl]-(2,2′-bithiophen)-5-yl}-3-hydroxypenta-2,4-dienamido]acetate (33):** Glycine *tert*-butyl ester hydrochloride (**11**; 5.7 mg, 34 μmol, 3.0 equiv.) was added to a solution of (*E*)-5-{5′-[4-(diphenylamino)phenyl]-2,2′-bithiophen-5-yl}-6-(2-{5′-[4-(diphenylamino)phenyl]-2,2′-bithiophen-5-yl}vinyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (**32**; 11 mg, 11 μmol, 1.0 equiv.) in toluene (1.0 mL) at room temperature in a sealed tube. The mixture was stirred at reflux for 24 h, then it was

poured into H_2O. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried with $MgSO_4$, and filtered. The solvent was removed, and the residue was purified by column chromatography on silica gel (0–15% ethyl acetate in hexane) to give *tert*-butyl 2-[(2*E*,4*E*)-2,5-bis{5′-[4-(diphenylamino)phenyl]-(2,2′-bithiophen)-5-yl}-3-hydroxypenta--2,4-dienamido]acetate (**33**; 8.6 mg, 8.3 μmol, 74%) as a red solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 14.8 (s, 1 H), 7.55 (d, J = 15.5 Hz, 1 H), 7.48 (d, J = 8.7 Hz, 2 H), 7.43 (d, J = 8.7 Hz, 2 H), 7.30–7.01 (m, 31 H), 6.95 (d, J = 3.4 Hz, 1 H), 6.37 (d, J = 15.5 Hz, 1 H), 6.13 (t, J = 5.3 Hz, 1 H), 3.98 (d, J = 5.3 Hz, 2 H), 1.45 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 168.4, 167.6, 147.5, 147.4, 147.3, 144.0, 143.5, 140.2, 139.7, 139.6, 137.8, 136.5, 135.3, 133.3, 131.7, 130.7, 129.9, 129.8, 129.3, 129.0, 128.2, 127.8, 126.4 (2×), 125.4, 125.3, 124.9, 124.6, 123.9, 123.6, 123.5, 123.4, 123.2, 122.9 (2×), 118.9, 97.2, 82.4, 42.0, 28.0 ppm. IR (neat): $\tilde{\nu}$ = 2929, 1739, 1616, 1592, 1490, 1455, 1328, 1281, 1155, 795, 754, 697 cm^{-1}. HRMS (ESI-TOF): calcd. for $C_{63}H_{52}N_3O_4S_4$ $[M + H]^+$ 1042.2841; found 1042.2810.

Supporting Information (see footnote on the first page of this article): Preparation of compounds **5**, **29**, and **31**, as well as ^{1}H and ^{13}C NMR spectra.

[1] K. Itami, J.-i. Yoshida, *Chem. Eur. J.* **2006**, *12*, 3966.
[2] G. T. Le, G. Abbenante, B. Becker, M. Grathwohl, J. Halliday, G. Tometzki, J. Zuegg, W. Meutermans, *Drug Discovery Today* **2003**, *8*, 701.
[3] P. H. Rasmussen, J. Rebek, *Tetrahedron Lett.* **1999**, *40*, 3511.
[4] B. A. Kulkarni, G. P. Roth, E. Lobkovsky, J. A. Porco, *J. Comb. Chem.* **2002**, *4*, 56.
[5] S. Yanagisawa, K. Ueda, H. Sekizawa, K. Itami, *J. Am. Chem. Soc.* **2009**, *131*, 14622.
[6] T. Doi, H. Inoue, M. Tokita, J. Watanabe, T. Takahashi, *J. Comb. Chem.* **2008**, *10*, 135.
[7] S. Fuse, S. Sugiyama, T. Takahashi, *Chem. Asian J.* **2010**, *5*, 2459.
[8] S. Sugiyama, S. Fuse, T. Takahashi, *Tetrahedron* **2011**, *67*, 6654.
[9] S. Fuse, H. Tago, M. M. Maitani, Y. Wada, T. Takahashi, *ACS Comb. Sci.* **2012**, *14*, 545.
[10] S. Fuse, S. Sugiyama, M. M. Maitani, Y. Wada, Y. Ogomi, S. Hayase, R. Katoh, T. Kaiho, T. Takahashi, *Chem. Eur. J.* **2014**, DOI: 10.1002/chem.201402093.
[11] J. J. Li, H. X. Wang, F. C. Qu, C. Musial, J. A. Tino, J. A. Robl, D. Slusarchyk, R. Golla, R. Seethala, K. Dickinson, L. Giupponi, G. Grover, P. Sleph, N. Flynn, B. J. Murphy, D. Gordon, M. Kung, R. Stoffel, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1799.
[12] G. Bertolini, M. Aquino, M. Biffi, G. d'Atri, F. Di Pierro, F. Ferrario, P. Mascagni, F. Somenzi, A. Zaliani, F. Leoni, *J. Med. Chem.* **1997**, *40*, 2011.
[13] F. C. Tucci, Y. F. Zhu, R. S. Struthers, Z. Q. Guo, T. D. Gross, M. W. Rowbottom, O. Acevedo, Y. H. Gao, J. Saunders, Q. Xie, G. J. Reinhart, X. J. Liu, N. Ling, A. K. L. Bonneville, T. K. Chen, H. Bozigian, C. Chen, *J. Med. Chem.* **2005**, *48*, 1169.
[14] 6-Benzyl-5-phenyl-1,3-oxazine-2,4(3*H*)-dione was used as a precursor of an anti-HIV compound: J. S. Larsen, M. T. A. Aal, E. B. Pedersen, C. Nielsen, *J. Heterocycl. Chem.* **2001**, *38*, 679.
[15] A. B. Shehata, M. A. Hassan, M. A. Nour, *J. Hazard. Mater.* **2003**, *102*, 121.
[16] M. F. Carroll, A. R. Bader, *J. Am. Chem. Soc.* **1953**, *75*, 5400.
[17] C. Kaneko, M. Sato, J.-I. Sakaki, Y. Abe, *J. Heterocycl. Chem.* **1990**, *27*, 25.
[18] K. P. Reber, S. D. Tilley, E. J. Sorensen, *Chem. Soc. Rev.* **2009**, *38*, 3022.
[19] U. Jahn, E. Dinca, *J. Org. Chem.* **2010**, *75*, 4480.
[20] H. Miyatake-Ondozabal, A. G. M. Barrett, *Org. Lett.* **2010**, *12*, 5573.
[21] T. Yoshinari, K. Ohmori, M. G. Schrems, A. Pfaltz, K. Suzuki, *Angew. Chem. Int. Ed.* **2010**, *49*, 881; *Angew. Chem.* **2010**, *122*, 893.
[22] K. Anderson, F. Calo, T. Pfaffeneder, A. J. P. White, A. G. M. Barrett, *Org. Lett.* **2011**, *13*, 5748.
[23] Y. Aoki, Y. Mochizuki, T. Yoshinari, K. Ohmori, K. Suzuki, *Chem. Lett.* **2011**, *40*, 1192.
[24] D. Petrović, R. Brückner, *Org. Lett.* **2011**, *13*, 6524.
[25] J. M. Tenenbaum, W. J. Morris, D. W. Custar, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2011**, *50*, 5892; *Angew. Chem.* **2011**, *123*, 6014.
[26] A. Odani, K. Ishihara, M. Ohtawa, H. Tomoda, S. Omura, T. Nagamitsu, *Tetrahedron* **2011**, *67*, 8195.
[27] J. Chen, J. Chen, Y. Xie, H. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 1024; *Angew. Chem.* **2012**, *124*, 1048.
[28] M. Fouché, L. Rooney, A. G. M. Barrett, *J. Org. Chem.* **2012**, *77*, 3060.
[29] A. Rentsch, M. Kalesse, *Angew. Chem. Int. Ed.* **2012**, *51*, 11381; *Angew. Chem.* **2012**, *124*, 11543.
[30] J. Xu, E. J. E. Caro-Diaz, A. Batova, S. D. E. Sullivan, E. A. Theodorakis, *Chem. Asian J.* **2012**, *7*, 1052.
[31] J. S. Yadav, S. Dhara, S. S. Hossain, D. K. Mohapatra, *J. Org. Chem.* **2012**, *77*, 9628.
[32] J. Cordes, A. G. M. Barrett, *Eur. J. Org. Chem.* **2013**, 1318.
[33] Q. Xiao, K. Young, A. Zakarian, *Org. Lett.* **2013**, *15*, 3314.
[34] T. Iwaoka, T. Murohashi, N. Katagiri, M. Sato, C. Kaneko, *J. Chem. Soc. Perkin Trans. 1* **1992**, 1393.
[35] T.-h. Fu, W. T. McElroy, M. Shamszad, R. W. Heidebrecht Jr., B. Gulledge, S. F. Martin, *Tetrahedron* **2013**, *69*, 5588.
[36] K. Gueogjian, F. V. Singh, J. M. Pena, M. Amaral, H. A. Stefani, *Synlett* **2010**, 427.
[37] A. S. Vieira, R. L. O. R. Cunha, C. F. Klitzke, J. Zukerman-Schpector, H. A. Stefani, *Tetrahedron* **2010**, *66*, 773.
[38] L. Capuano, G. Urhahn, A. Willmes, *Chem. Ber.* **1979**, *112*, 1012.
[39] Y. Chen, Y. Wang, Z. Sun, D. Ma, *Org. Lett.* **2008**, *10*, 625.
[40] A. Liguori, G. Sindona, N. Uccella, *J. Chem. Soc. Perkin Trans. 1* **1987**, 961.
[41] D. L. Smith, W. R. F. Goundry, H. W. Lam, *Chem. Commun.* **2012**, *48*, 1505.
[42] K. Takahashi, K. Yamada, H. Iida, *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3389.
[43] J. F. Wolfe, G. B. Trimitsis, *J. Org. Chem.* **1968**, *33*, 894.
[44] G. Jäger, J. Wenzelburger, *Justus Liebigs Ann. Chem. Ann. Chem.* **1976**, 1689.
[45] J. A. Hyatt, P. L. Feldman, R. J. Clemens, *J. Org. Chem.* **1984**, *49*, 5105.
[46] M. Sato, H. Ogasawara, T. Kato, *Chem. Pharm. Bull.* **1984**, *32*, 2602.
[47] J. A. Hyatt, P. W. Raynolds, "Ketene Cycloadditions" in *Organic Reactions*, John Wiley & Sons, Inc., Hoboken, New Jersey, **2004**.
[48] K. R. J. Thomas, Y.-C. Hsu, J. T. Lin, K.-M. Lee, K.-C. Ho, C.-H. Lai, Y.-M. Cheng, P.-T. Chou, *Chem. Mater.* **2008**, *20*, 1830.
[49] X.-H. Zhang, J. Ogawa, K. Sunahara, Y. Cui, Y. Uemura, T. Miyasaka, A. Furube, N. Koumura, K. Hara, S. Mori, *J. Phys. Chem. C* **2013**, *117*, 2024.

Received: April 24, 2014
Published Online: June 23, 2014

