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Rh-Catalyzed Regioselective *ortho*-C−H Carbenoid Insertion of Diarylazines

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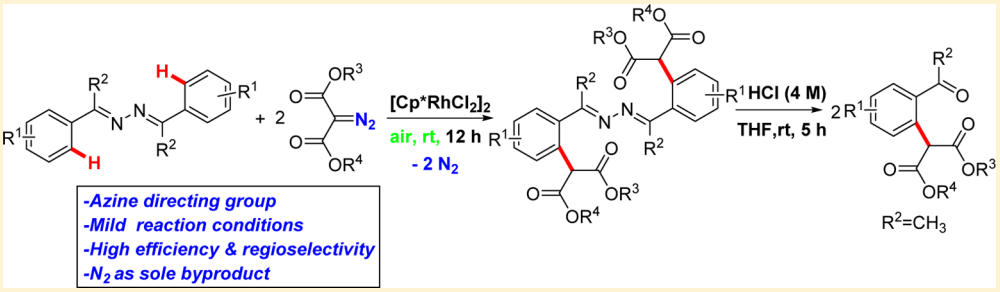
Supporting Information



ABSTRACT: The Rh-catalyzed *ortho*-C−H carbenoid insertion reaction of diarylazines with diazo compounds has been developed. A wide range of *ortho*-substituted diarylazines have been obtained in moderate to high yields with high regioselectivity at room temperature. The hydrolysis of the products could release ketones or aldehydes, giving access to aromatic 1,5-keto-diesters as valuable synthons for further chemical transformations.

INTRODUCTION

The transition-metal-catalyzed functionalization of C−H bonds has seen a tremendous development over the past decades.[1] In particular, great progress has been made in site-selective chemical transformations of less reactive C−H bonds.[2] The usage of directing groups is an efficient way to improve reactivity and selectivity.[3] Nitrogen-containing functional groups, such as pyridine,[4] pyrimidine,[5] imines,[6] oximes,[7] and hydrazones,[8] have been widely explored as directing groups because of their coordination ability with transition-metal atoms. Azines (Ar(R)-C═N—N═C(R)Ar), which possess valuable intrinsic physical and biological properties[9] and are useful organic synthetic intermediates,[10] have recently proved to be a viable directing group by Huang[11] and Zhu (Scheme 1a).[12] Nevertheless, the formation of difunctionalized products of these nitrogen-containing substructures is difficult to avoid.[13] Herein, the azine function is envisaged as a directing group for the Rh-catalyzed *ortho*-C−H carbenoid insertion reaction of diarylazines (Scheme 1b). In this protocol, the azine also acts as a bridging unit between two potentially reacting aromatic rings (Ar). Hereafter, two equivalent α-ketoaryl malonates could thus be obtained with diazomalonate in one step with a superior *ortho*-C−H site selectivity. The reaction could proceed smoothly at room temperature with broad functional group compatibility.

RESULTS AND DISCUSSION

Acetophenazine **1a** and dimethyl diazomalonate **2a** were first selected as model reactants to optimize the reaction conditions (Table 1). The expected C−H insertion product **3aa** was obtained in 89% isolated yield in the presence of $[Cp^*RhCl_2]_2$ (2.5 mol %), $AgSbF_6$ (10 mol %), and $PhCO_2H$ (25 mol %) in methanol at 25 °C in 12 h (entry 1). The structure of **3aa** was confirmed by a single crystal X-ray diffraction analysis (Supporting Information, Figure S1). No product was observed in the absence of the Rh(III) catalyst (entry 2). The absence of Ag(I) salt resulted in a lower yield of 69% (entry 3). Only 26% yield of the desired product was obtained in the absence of acid (entry 4). Next, the use of alternative solvents, such as water, 1,4-dioxane, or 2,2,2-trifluoroethanol (TFE), was shown to provide inferior results (entries 5−7). Other Ag(I) salts were then investigated. Slightly lower yields were obtained with $AgNO_3$ or $AgBF_4$. A yield of 88% was restored with AgOAc (Table 1, entries 8−10 vs 1). The cheaper AgOAc salt was chosen as an additive instead of $AgSbF_6$. No reaction was observed in the presence of strong acids, such as HCl or trifluoroacetic acid (TFA) (entries 11 and 12), but the addition of AcOH led to a 81% yield (entry 13). Next, we examined the effect of benzoic acid additives and found that the combination of both AgOAc and 2,4,6-trimethylbenzoic acid as additives increased the yield to 97% (entries 14 and 15).

With optimized conditions in hand, the scope of arylketazine substrates was investigated with dimethyl diazomalonate **2a** (Scheme 2). Aryl rings substituted with electron-donating groups were found to favor the carbenoid insertion of the

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Scheme 1. Azine-Directing-Group-Assisted *ortho*-C−H Functionalization

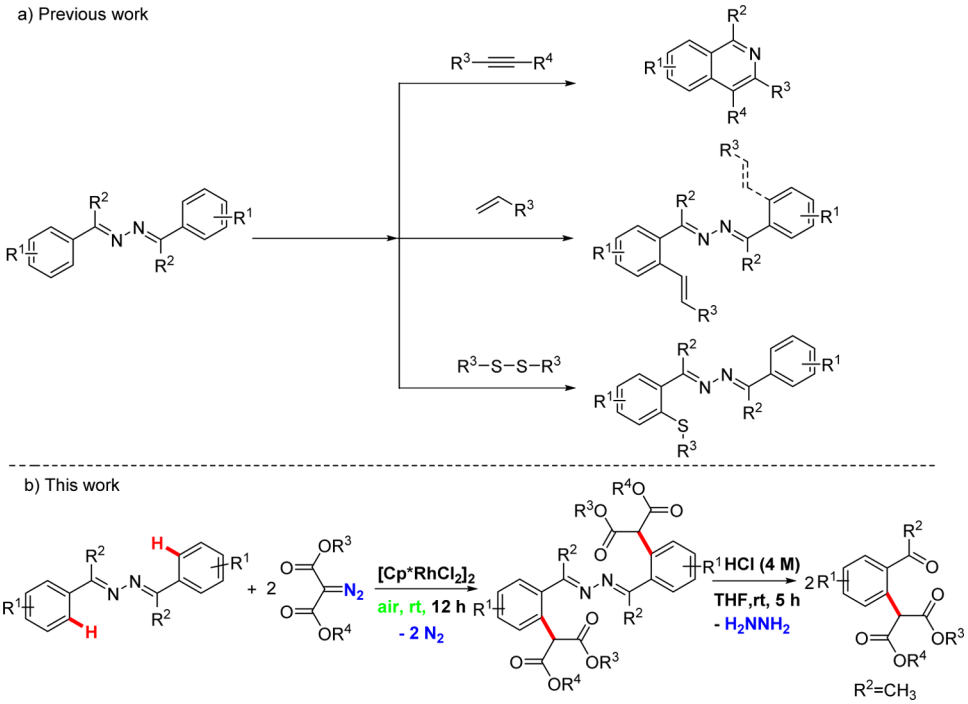
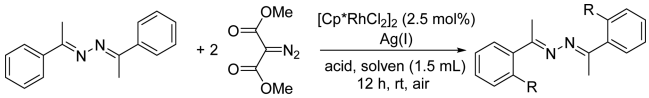


Table 1. Screening of Various Parameters for the Reaction of Acetophenazine with Dimethyl Diazomalonate[a]



1a 2a 3aa

entry	Ag(I)	acid	solvent	yield[b] (%)
1	$AgSbF_6$	PhCOOH	MeOH	89
2[c]	$AgSbF_6$	PhCOOH	MeOH	no
3	none	PhCOOH	MeOH	69
4	$AgSbF_6$	none	MeOH	26
5	$AgSbF_6$	PhCOOH	H_2O	19
6	$AgSbF_6$	PhCOOH	1,4-dioxane	trace
7	$AgSbF_6$	PhCOOH	TFE	no
8	$AgNO_3$	PhCOOH	MeOH	74
9	$AgBF_4$	PhCOOH	MeOH	81
10	AgOAc	PhCOOH	MeOH	88
11	AgOAc	HCl	MeOH	no
12	AgOAc	TFA	MeOH	no
13	AgOAc	AcOH	MeOH	81
14	AgOAc	*p*-nitrobenzoic acid	MeOH	87
15	AgOAc	2,4,6-trimethylbenzoic acid	MeOH	97

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), Ag(I) (10 mol %), acid (25 mol %), solvent (1.5 mL), 12 h, under air, rt. [b]Isolated yields. [c]Without $[Cp^*RhCl_2]_2$. TFE: 2,2,2-trifluoroethanol. TFA: trifluoroacetic acid.

ortho-C−H bond, providing the dimalonyl products in high yields (**3aa**−**3ga**). *para*-Substituted acetophenazines afforded the anticipated products (**3aa**−**3ea**) in substantial yields (74−93%). The *meta*-methyl acetophenazine **1f** gave the C-6-substituted product **3fa** at the less hindered position in 94% yield. However, when a methoxy group or fluoro was placed at the *meta* position in **1g** or **1h**, the major products were the hindered C-2-substituted products, isolated with 63% (**3ga**) and 68% yields (**3ga**), respectively, revealing an *ortho*-directing effect of the methoxy group and F atom. The reaction was found less efficient for ketazines substituted by electron-withdrawing groups (e.g., $-CF_3$, $-CN$, $-NO_2$) or halogens (Cl, Br, I). The meta-substitution with $-CF_3$, $-CN$, or $-NO_2$ did not afford the anticipated products, and the *para*-substitution by halogen atoms (Cl, Br) led to the monosubstituted product in low yields (<30%). When R^2 was ethyl, the targeted product (**3ia**) could be obtained in 85% yield. The other aryl-ketazine substrates, such as the α-tetralone azine (**3j**) and naphthyl methyl ketazine (**3k**), could give the corresponding products **3ja** and **3ka** both in 74% yields, albeit at 60 °C. Heating to 60 °C is also required for aldazine substrates, conceivably because of their lower coordinating ability as compared to that of ketazines. *o*-Methyl benzaldazine **1l** provided the dimalonyl product **3la** in 95% yield. *m*-Methyl benzaldazine **1m** led mainly to **3ma**, the dimalonylated product at the less hindered *ortho* position, in 75% yield (Scheme 2).

The scope of the diazo reactant was also examined (Scheme 3). Acetophenazine could react smoothly with various diazomalonates to afford the corresponding symmetrically substituted products in 86−94% yields. Either symmetrical or asymmetrical diazomalonates could be used as reactants, giving the symmetrical products **3ab**−**3ac** and asymmetrical products **3ad** in 86−94% yields. The aldazines **1l**−**m** were also found to give the anticipated products **3lb** (81%), **3mb** (60%), and **3me** (53%).

The aldehyde and ketone carbonyl groups could be recovered by treatment of the azine products **3** with concentrated aqueous HCl. This was illustrated for the *o*-malonyl-acetophenazine primary product **3aa**, which gave the corresponding tricarbonyl product **5aa** in 75% yield (Scheme 4). α-Arylmalonates are useful intermediates in organic synthesis. As a possible synthetic application, the intramolecular Claisen/Dieckmann condensation of **5aa** or analogues could lead to functional naphthalene derivatives with biological or pharmaceutical properties, such as selective inhibition of the human leukocyte elastase.[7b,14]

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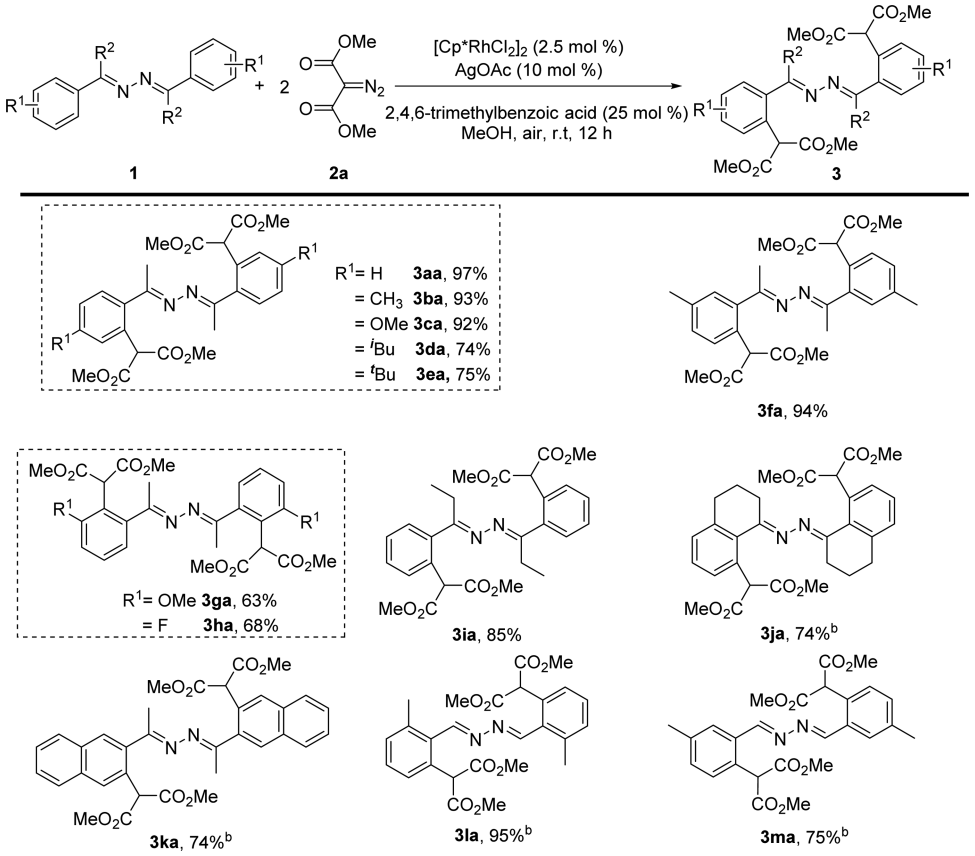
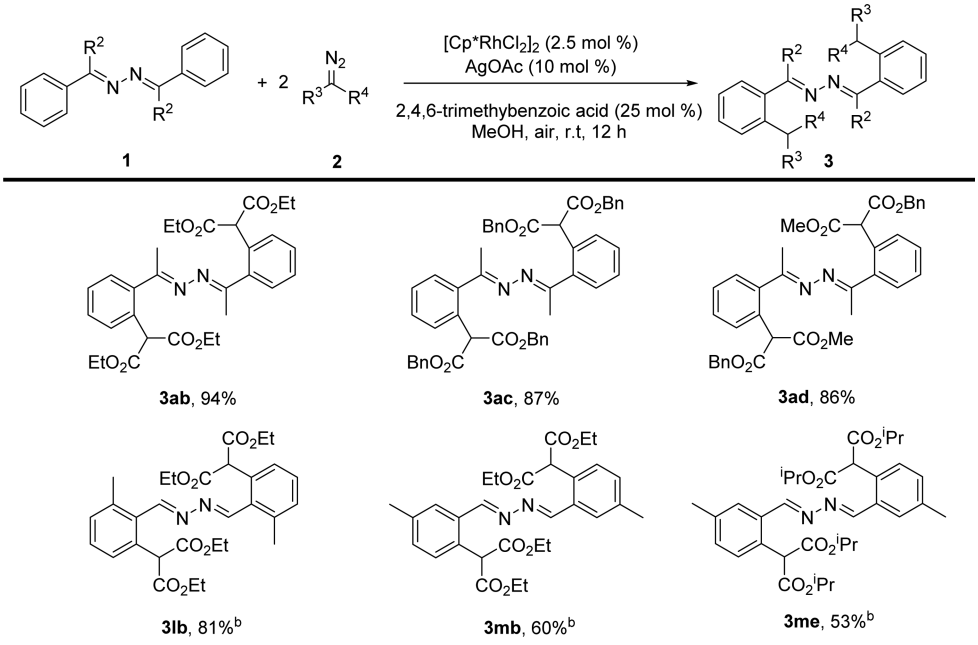
Scheme 2. Scope of the Azines[a]



[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), AgOAc (10 mol %), 2,4,6-trimethylbenzoic acid (25 mol %), MeOH (1.5 mL), 12 h, under air, rt. Isolated yields. [b]60 °C.

Scheme 3. Scope of the Diazomalonates[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), AgOAc (10 mol %), 2,4,6-trimethylbenzoic acid (25 mol %), MeOH (1.5 mL), 12 h, under air, rt. Isolated yields. [b]60 °C.

CONCLUSION

In conclusion, we developed an efficient procedure for the regioselective Rh-catalyzed *ortho*-C−H carbenoid insertion of α-diazomalonates with aryl-ketazine or -aldazine substrates. A wide range of *ortho*-substituted diarylazines were obtained in moderate to high yields at room temperature. The products

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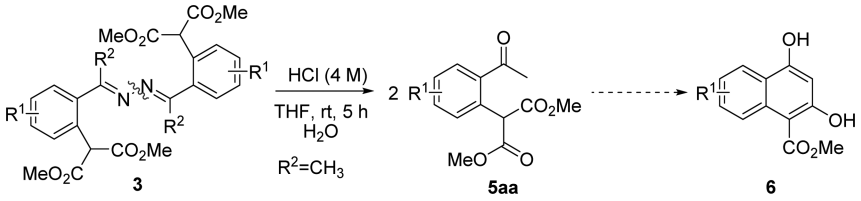
Scheme 4. Example of Synthetic Application of the Rh-Catalyzed C−C Coupling of diaryl Azines with Dimethyl Diazomalonate to Access *o*-Malonyl-acetophenones



could be regarded as versatile intermediates to build valuable molecular targets.

EXPERIMENTAL SECTION

General Methods. All reactions were conducted within a tube under an air atmosphere. Unless otherwise stated, all commercial materials and solvents were used directly without further purification. ^{1}H and ^{13}C NMR spectra were measured on a 400 MHz Bruker spectrometer (^{1}H 400 MHz, ^{13}C 100 MHz), using $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are reported in ppm referenced to the center of a triplet at 77.0 ppm of chloroform-*d*. High-resolution mass spectra (HRMS) were recorded using an Agilent 6450 spectrometer. High-resolution mass spectra (HRMS) were equipped with an ESI source and a TOF detector. Column chromatography was performed on silica gel (70−230 mesh ASTM) using the reported eluents. Thin-layer chromatography (TLC) was carried out on 4 cm × 15 cm plates with a layer thickness of 0.2 mm (silica gel 60 F254).

General Procedure for the Synthesis of Aromatic Ketazines 1 According to a Previously Reported Method.[15] Hydrazine hydrate (1.0 g, 16.6 mmol, 80%) was added to a solution of acetophenone (2.0 g, 16.6 mmol) and AcOH (119.0 mg, 1.7 mmol) in EtOH (15 mL), and then the mixture was heated to 100 °C with stirring and refluxed for 10 h. After cooling to room temperature, the mixture was filtered, washed with EtOH (40 mL × 4), and dried under vacuum. The corresponding bright yellow (1*E*,2*E*)-1,2-bis(1-phenylethylidene)hydrazine (**1a**) was obtained in 90% yield.

General Procedure for the Synthesis of Diazo Compounds 2 According to a Previously Reported Method.[16] To a solution of dimethyl malonate (10 mmol) and *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) (12 mmol) in anhydrous CH_3CN (20 mL) at 0 °C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (14 mmol) dropwise for 30 min. After stirring at room temperature overnight, the reaction mixture was concentrated under vacuum. Water (20 mL) was added. The resulting mixture was extracted with dichloromethane (2 × 20 mL). The combined organic layer was washed with brine (20 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate as the eluent to give the title diazo compounds.

Preparation of Products 3. Under an air atmosphere, a reaction tube (5 mL) equipped with a magnetic stirring bar was charged with arylazine **1** (0.2 mmol), diazomalonate **2** (0.45 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol %), AgOAc (0.02 mmol, 10 mol %), 2,4,6-trimethylbenzoic acid (0.05 mmol, 25 mol %), and MeOH (1.5 mL). The reaction mixture was stirred at room temperature for 12 h. The solvents were removed under reduced pressure, and the residue was purified by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 4:1) to give the desired product.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(2,1-phenylene))dimalonate (**3aa**).* Eluent: petroleum ether/ethyl acetate (4:1). White solid, 97% yield (96 mg), mp: 181−183 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.41 (m, 8H), 5.54 (s, 2H), 3.76 (s, 12H), 2.25 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 161.2, 138.8, 130.7, 129.8, 129.1, 128.4, 128.1, 54.6, 52.7, 18.3. HRMS (ESI) *m*/*z*: calcd for $C_{26}H_{29}N_2O_8^+$ (M + H$^+$), 497.1918; found, 497.1926.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(3-methyl-6,1-phenylene))dimalonate (**3ba**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 94% yield (99 mg), mp: 180−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.6 Hz, 2H), 7.29 (s, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.58 (s, 2H), 3.76 (s, 12H), 2.40 (s, 6H), 2.23 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 161.0, 139.2, 136.0, 130.6, 130.3, 128.9, 128.4, 54.6, 52.7, 21.4, 18.2. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{33}N_2O_8^+$ (M + H$^+$), 525.2231; found, 525.2235.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(3-methoxy-6,1-phenylene))dimalonate (**3ca**).* Eluent: petroleum ether/ethyl acetate (4:1). White solid, 92% yield (102 mg), mp: 177−178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 2.4 Hz, 2H), 6.93 (dd, *J* = 8.6, 2.5 Hz, 2H), 5.68 (s, 2H), 3.84 (s, 6H), 3.76 (s, 12H), 2.23 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 160.8, 159.8, 132.5, 131.5, 130.0, 115.6, 113.3, 55.4, 54.7, 52.6, 18.1. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{33}N_2O_{10}^+$ (M + H$^+$), 557.2130; found, 557.2136.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(3-isobutyl-6,1-phenylene))dimalonate (**3da**).* Eluent: petroleum ether/ethyl acetate (4:1). White solid, 74% yield (90 mg), mp: 140−141 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 1.2 Hz, 2H), 7.19 (dd, *J* = 8.0, 1.3 Hz, 2H), 5.59 (s, 2H), 3.75 (s, 12H), 2.52 (d, *J* = 6.8 Hz, 4H), 2.25 (s, 6H), 1.87 (m, 2H), 0.92 (d, *J* = 6.8 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 161.1, 142.7, 136.2, 130.7, 130.4, 128.8, 128.2, 54.6, 52.6, 45.0, 30.1, 22.2, 18.2. HRMS (ESI) *m*/*z*: calcd for $C_{34}H_{45}N_2O_8^+$ (M + H$^+$), 609.3170; found, 609.3178.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(3-(tert-butyl)-6,1-phenylene))dimalonate (**3ea**).* Eluent: petroleum ether/ethyl acetate (4:1). White solid, 75% yield (91 mg), mp: 148−150 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s, 2H), 7.42 (s, 4H), 5.61 (s, 2H), 3.76 (s, 12H), 2.24 (s, 6H), 1.34 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 161.0, 152.1, 136.0, 130.4, 128.2, 127.0, 125.0, 54.8, 52.6, 34.7, 31.1, 18.2. HRMS (ESI) *m*/*z*: calcd for $C_{34}H_{45}N_2O_8^+$ (M + H$^+$), 609.3170; found, 609.3179.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(4-methyl-2,1-phenylene))dimalonate (**3fa**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 94% yield (99 mg), mp: 189−191 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.6 Hz, 2H), 7.26 (s, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.47 (s, 2H), 3.75 (s, 12H), 2.39 (s, 6H), 2.24 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 161.2, 138.8, 137.9, 129.8, 129.6, 129.0, 127.7, 54.3, 52.6, 21.1, 18.3. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{33}N_2O_8^+$ (M + H$^+$), 525.2231; found, 525.2238.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(6-methoxy-2,1-phenylene))dimalonate (**3ga**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 63% yield (70 mg), mp: 173−175 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (t, *J* = 8.0 Hz, 2H), 7.11−7.05 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 5.32 (s, 2H), 3.84 (s, 6H), 3.73 (s, 12H), 2.21 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 161.8, 158.4, 140.3, 128.9, 121.4, 120.7, 112.6, 56.3, 52.3, 51.5, 18.3. HRMS (ESI) *m*/*z*: calcd for $C_{28}H_{33}N_2O_{10}^+$ (M + H$^+$), 557.2130; found, 557.2138.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(6-fluoro-2,1-phenylene))dimalonate (**3ha**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 68% yield (72 mg), mp: 126−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (m, 2H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.20−7.14 (m, 2H), 5.43 (s, 2H), 3.77 (s, 12H), 2.24 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 161.9 (d, *J* = 248.9 Hz),

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161.1 (d, J = 2.5 Hz), 140.6 (d, J = 3.7 Hz), 129.5 (d, J = 9.5 Hz), 124.0 (d, J = 2.9 Hz), 120.2 (d, J = 15.1 Hz), 116.6 (d, J = 23.2 Hz), 52.7, 51.1, 18.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ −110.4. HRMS (ESI) m/z: calcd for $C_{26}H_{27}F_2N_2O_8^+$ (M + H$^+$), 533.1730; found, 533.1734.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(propan-1-yl-1-ylidene))bis(2,1-phenylene))dimalonate (**3ia**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 85% yield (89 mg), mp: 153−154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 7.2 Hz, 2H), 7.46−7.39 (m, 6H), 5.43 (s, 2H), 3.75 (s, 12H), 2.74 (d, J = 7.6 Hz, 4H), 0.99 (t, J = 7.5 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 165.7, 138.0, 131.2, 129.9, 128.8, 127.9, 127.9, 54.2, 52.6, 24.9, 10.6. HRMS (ESI) m/z: calcd for $C_{28}H_{33}N_2O_8^+$ (M + H$^+$), 525.2231; found, 525.2238.

*Tetramethyl 2,2′-((8E,8′E)-Hydrazine-1,2-diylidenebis(5,6,7,8-tetrahydronaphthalene-1-yl-8-ylidene))dimalonate (**3ja**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 74% yield (81 mg), mp: 200−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (m, 4H), 7.19 (d, J = 7.2 Hz, 2H), 6.01 (s, 2H), 3.75 (s, 12H), 2.79−2.74 (m, 4H), 2.58 (t, J = 6.6 Hz, 4H), 1.86−1.78 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 169.7, 156.9, 142.6, 131.9, 131.4, 128.9, 128.5, 128.3, 56.1, 52.5, 31.1, 28.8, 21.4. HRMS (ESI) m/z: calcd for $C_{30}H_{33}N_2O_8^+$ (M + H$^+$), 549.2231; found, 549.2238.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(naphthalene-3,2-diyl))dimalonate (**3ka**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 74% yield (88 mg), mp: 229−230 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (s, 2H), 7.95 (s, 2H), 7.90−7.85 (m, 4H), 7.56−7.52 (m, 4H), 5.77 (s, 2H), 3.81 (s, 12H), 2.37 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 160.5, 136.2, 133.0, 132.3, 129.4, 128.7, 128.5, 128.0, 127.8, 127.2, 127.0, 55.1, 52.8, 18.2. HRMS (ESI) m/z: calcd for $C_{34}H_{33}N_2O_8^+$ (M + H$^+$), 597.2231; found, 597.2236.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(methanylylidene))bis(3-methyl-2,1-phenylene))dimalonate (**3la**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 95% yield (94 mg), mp: 230−232 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.97 (s, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.25 (d, J = 6.8 Hz, 4H), 5.71 (s, 2H), 3.78 (s, 12H), 2.50 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 161.7, 139.5, 132.6, 130.9, 130.7, 130.5, 127.7, 56.1, 52.7, 20.3. HRMS (ESI) m/z: calcd for $C_{26}H_{29}N_2O_8^+$ (M + H$^+$), 497.1918; found, 497.1926.

*Tetramethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(methanylylidene))bis(4-methyl-2,1-phenylene))dimalonate (**3ma**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 75% yield (74 mg), mp: 175−177 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 2H), 7.56 (s, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.80 (s, 2H), 3.78 (s, 12H), 2.40 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 162.7, 138.3, 132.3, 131.9, 131.8, 129.9, 129.8, 54.6, 52.8, 20.9. HRMS (ESI) m/z: calcd for $C_{26}H_{29}N_2O_8^+$ (M + H$^+$), 497.1918; found, 497.1925.

*Tetraethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(2,1-phenylene))dimalonate (**3ab**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 94% yield (104 mg), mp: 100−101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (dd, J = 6.9, 1.8 Hz, 2H), 7.48−7.37 (m, 6H), 5.48 (s, 2H), 4.29−4.17 (m, 8H), 2.26 (s, 6H), 1.26 (t, J = 7.1 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 160.9, 139.0, 130.9, 129.8, 128.9, 128.2, 127.9, 61.5, 54.8, 18.5, 14.0. HRMS (ESI) m/z: calcd for $C_{30}H_{37}N_2O_8^+$ (M + H$^+$), 553.2544; found, 553.2553.

*Tetrabenzyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene))bis(2,1-phenylene))dimalonate (**3ac**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow oil, 87% yield (139 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (dd, J = 5.2, 2.4 Hz, 2H), 7.34 (d, J = 2.0 Hz, 6H), 7.23 (s, 20H), 5.65 (s, 2H), 5.14 (d, J = 2.4 Hz, 8H), 2.07 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 160.9, 138.8, 135.3, 129.9, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 67.2, 54.8, 18.4. HRMS (ESI) m/z: calcd for $C_{50}H_{45}N_2O_8^+$ (M + H$^+$), 801.3170; found, 801.3175.

*1-Benzyl-3-methyl-2-(2-((E)-1-(((E)-1-(2-(1-(benzyloxy)-3-methoxy-1,3-dioxopropan-2-yl)phenyl)ethylidene)hydrazono)ethyl)-phenyl)malonate (**3ad**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow oil, 86% yield (111 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 2.8 Hz, 2H), 7.43−7.36 (m, 6H), 7.28 (s, 10H), 5.59 (d, J = 2.0 Hz, 2H), 5.19 (d, J = 5.2 Hz, 4H), 3.70 (d, J = 5.2 Hz, 6H), 2.16 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 168.5, 161.0, 138.8, 135.4, 130.6, 129.9, 129.0, 128.4, 128.3, 128.2, 128.0, 128.0, 67.2, 54.7, 52.6, 18.4. HRMS (ESI) m/z: calcd for $C_{38}H_{37}N_2O_8^+$ (M + H$^+$), 649.2544; found, 649.2549.

*Tetraethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(methanylylidene))bis(3-methyl-2,1-phenylene))dimalonate (**3 lb**).* Eluent: petroleum ether/ethyl acetate (4:1). White solid, 81% yield (89 mg), mp: 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.98 (s, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 7.24 (d, J = 7.6 Hz, 2H), 5.68 (s, 2H), 4.25 (m, 8H), 2.49 (s, 6H), 1.28 (t, J = 7.1 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 161.7, 139.4, 132.9, 131.0, 130.6, 130.3, 127.7, 61.6, 56.2, 20.4, 14.1. HRMS (ESI) m/z: calcd for $C_{30}H_{37}N_2O_8^+$ (M + H$^+$), 553.2544; found, 553.2538.

*Tetraethyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(methanylylidene))bis(4-methyl-2,1-phenylene))dimalonate (**3mb**).* Eluent: petroleum ether/ethyl acetate (4:1). White solid, 60% yield (66 mg), mp: 145−146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.77 (s, 2H), 7.58 (s, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 5.72 (s, 2H), 4.27−4.23 (m, 6H), 2.40 (s, 6H), 1.27 (t, J = 7.1 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 162.5, 138.1, 132.0, 131.7, 130.1, 129.9, 128.6, 61.7, 54.8, 20.9, 14.0. HRMS (ESI) m/z: calcd for $C_{30}H_{37}N_2O_8^+$ (M + H$^+$), 553.2544; found, 553.2540.

*Tetraisopropyl 2,2′-(((1E,1′E)-Hydrazine-1,2-diylidenebis(methanylylidene))bis(4-methyl-2,1-phenylene))dimalonate (**3me**).* Eluent: petroleum ether/ethyl acetate (4:1). Yellow solid, 53% yield (64 mg), mp: 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (s, 2H), 7.59 (s, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 9.2 Hz, 2H), 5.62 (s, 2H), 5.10 (m, 4H), 2.40 (s, 6H), 1.28 (d, J = 6.0 Hz, 12H), 1.25 (d, J = 6.4 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1, 162.3, 137.9, 132.0, 131.6, 130.4, 129.9, 128.6, 69.2, 55.0, 21.59, 21.58, 20.9. HRMS (ESI) m/z: calcd for $C_{34}H_{45}N_2O_8^+$ (M + H$^+$), 609.3170; found, 609.3171.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b01472.

Description of the X-ray structures and NMR spectra of the compounds (PDF)

Crystal data of the compounds (CIF)

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Notes

The authors declare no competing financial interest.

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