JOC The Journal of Organic Chemistry

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Boron Trifluoride Mediated Ring-Opening Reactions of *trans*-2-Aryl-3-nitro-cyclopropane-1,1-dicarboxylates. Synthesis of Aroylmethylidene Malonates as Potential Building Blocks for Heterocycles

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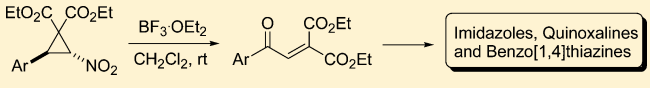
Supporting Information

ABSTRACT: *trans*-2-Aryl-3-nitro-cyclopropane-1,1-dicarboxylates, upon treatment with $BF_3{\cdot}OEt_2$, undergo ring-opening rearrangement and the Nef reaction to give aroylmethylidene malonates. The products are found to be potential precursors for heterocycles, such as imidazoles, quinoxalines, and benzo[1,4]thiazines.



Cyclopropanes having vicinal donor−acceptor (D−A) substituents are important building blocks in organic synthesis.[1] Because of the activation bestowed by the substituents, they readily undergo ring-opening upon treatment with Lewis acids to give 1,3-zwitterionic intermediates (also referred to as 1,3-dipoles) (Figure 1). These zwitterions

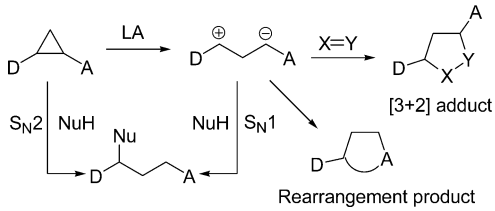


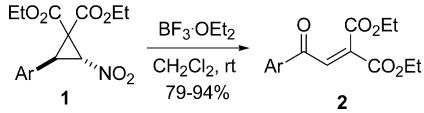
Figure 1. Common reactions of D−A cyclopropanes.

participate in many formal [3 + *n*] (*n* = 2, 3, 4) cycloaddition reactions with apt dipolarophiles to yield a variety of carbo- and heterocyclic compounds.[2] In addition, the zwitterions combine with nucleophiles in S_N1 fashion (or electrophiles) to give acyclic products[1b,3] or undergo ring-enlargement to give rearrangement products.[4] Sometimes, the D−A cyclopropanes are directly attacked by nucleophiles in stereodefined S_N2 fashion to give the corresponding ring-opened products.[5]

Within the class of D−A cyclopropanes, nitrosubstituted ones have received considerable attention owing to their unique chemical reactivity.[6] They mainly undergo nucleophilic ring-opening reactions[5] or isomerization to isooxazoline-*N*-oxides[4b−e] and seldom take part in formal cycloaddition reactions.[7] Among various nitrocyclopropanes, we are interested in *trans*-2-aryl-3-nitro-cyclopropane-1,1-dicarboxylates (**1**) because of their easy accessibility in both racemic and chiral forms. These D−A nitrocyclopropanes have been synthesized by Michael-initiated ring-closure (MIRC) methodology involving base-induced addition of malonates to bromo nitroolefins[8] or halomalonates to nitroolefins,[9] followed by ring closure or the oxidative cyclization of Michael adducts of nitroolefins with malonates.[10]

Even though the nitrocyclopropanes **1** were prepared as early as 1969,[8] their chemical properties have been scarcely explored. They were shown to undergo reactions with nucleophiles, such as sodiomalonate, sodium methoxide, and ammonia, to give ring-opened products with the loss of the nitro group.[11] A derivative of **1** (Ar = Ph and R = Et) has been reduced to the corresponding aminocyclopropane,[10] and in a recent report, a C−C bond of this derivative has been photochemically cleaved.[12] Except for these reactions, no other reactions of **1** have been reported to date. This prompted us to investigate the Lewis acid mediated reactions of **1**, and the study led to a facile access of aroylmethylidene malonates **2** (Scheme 1). Only dialkyl

Scheme 1. $BF_3{\cdot}OEt_2$-Mediated Ring-Opening Reactions of D−A Nitrocyclopropanes 1



benzoylmethylidene malonates are known in the series[13,14] and have been generally prepared by the Wittig reaction of the corresponding oxomalonates with benzoylmethylene triphenylphosphorane.[13] Nevertheless, these compounds have been frequently used as Michael acceptors in several synthetic studies.[13,15]

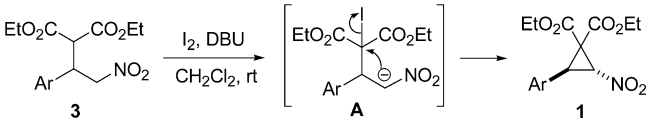
The requisite *trans*-2-aryl-3-nitro-cyclopropane-1,1-dicarboxylates (**1**) for the present study were prepared by an iodine/1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)-mediated direct cyclization of Michael adducts of nitrostyrenes with diethylmalonate (**3**). We had adopted this procedure earlier for the preparation of *trans*-2-aroyl-3-aryl-cyclopropane-1,1-dicarboxylates from the Michael adducts of chalcones with diethylmalonate.[16] An advantage of our procedure over Fan's procedure,[10] which uses

Received: December 23, 2013
Published: April 1, 2014

   dx.doi.org/10.1021/jo402848v | *J. Org. Chem.* 2014, 79, 3653−3658

iodobenzenediacetate and tetrabutylammonium iodide for the cyclization and affords mixtures of *trans*- and *cis*-cyclopropanes (dr 95:5), is the exclusive formation of *trans*-cyclopropanes. This may be due to DBU-induced isomerization of *cis*-cyclopropanes, if any formed, to more stable *trans*-diastereomers under the reaction conditions. We prepared an assortment of nitrocyclopropane dicarboxylates **1a**−**1l** in high yields simply by stirring the respective Michael adducts with iodine (2 equiv) and DBU (2 equiv) in dichloromethane (DCM) at room temperature for 10−25 min (Table 1, entries 1−12). The presence of

Table 1. Preparation of D−A Nitrocyclopropanes 1[a]



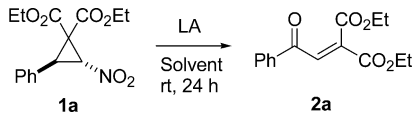
entry	Ar	time (min)	yield[b] (%)
1	Ph (**3a**)	15	94 (**1a**)
2	4-MeC_6H_4 (**3b**)	15	89 (**1b**)
3	4-$OMeC_6H_4$ (**3c**)	15	86 (**1c**)
4	4-ClC_6H_4 (**3d**)	10	96 (**1d**)
5	4-$NO_2C_6H_4$ (**3e**)	10	92 (**1e**)
6	3,4-$(OMe)_2C_6H_3$ (**3f**)	10	89 (**1f**)
7	3,4,5-$(OMe)_3C_6H_2$ (**3g**)	15	82 (**1g**)
8	2,6-$Cl_2C_6H_3$ (**3h**)	10	97 (**1h**)
9	2-*I*-4,5-$(OMe)_2C_6H_2$ (**3i**)	20	85 (**1i**)
10	1-naphthyl (**3j**)	15	98 (**1j**)
11	2-furyl (**3k**)	20	58 (**1k**)
12	2-thienyl (**3l**)	25	49 (**1l**)

[a]The reaction was conducted with **3** (1 mmol), iodine (2 mmol), and DBU (2 mmol) in CH_2Cl_2 (5 mL). [b]Isolated yield; all are single *trans*-diastereomers.

different mono- and polysubstituted phenyl (**1a**−**1i**), naphthyl (**1j**), and heteroaryl (**1k**−**1l**) rings are tolerated; however, the yield was low for cyclopropanes having heteroaryl rings. In fact, the cyclization did not work in the case of *N*-methylpyrrole or *N*-methylindole ring-containing Michael adduct. The reaction might proceed via formation of the iodinated-Michael adduct **A**, followed by base-promoted S_N2-type ring closure.

Next, we selected the nitrocyclopropane dicarboxylate **1a** as a model substrate and treated it with different Lewis acids to understand the mode of reactivity of this type of cyclopropane (Table 2). Since similar *trans*-2-aroyl-3-aryl-cyclopropane-1,1-dicarboxylates have been ring-opened with $AlCl_3$[17] and $SnCl_4$,[16] we first tested the suitability of these Lewis acids. When treated with $AlCl_3$ (1 equiv) in DCM at room temperature for 24 h, **1a** gave a mixture of diethyl benzoylmethylidene malonate (**2a**, 33%) and the corresponding saturated compound, diethyl phenacylmalonate (65%) (entry 1). On the other hand, $SnCl_4$ gave 53% of **2a** and a complicated mixture under the conditions (entry 2). When $BF_3{\cdot}OEt_2$ was employed as the Lewis acid, **1a** underwent smooth ring-opening and afforded **2a** in 81% isolated yield after 24 h (entry 3). Upon reducing the amount of Lewis acid to 50 mol %, the reaction did not go to completion and only 49% of **2a** was obtained after 24 h (entry 4). Increasing the amount of Lewis acid to 1.5 equiv gave **2a** in almost similar yield at a shorter reaction time of 20 h (entry 5). Change of solvent to 1,2-dichloroethane or toluene lowered the yield of **2a** (24 h), whereas, in tetrahydrofuran, **1a** remained inert even after 3 days (entries 6−8). We also screened a number of other Lewis acids. Of them, $FeCl_3$ and $ZnCl_2$ caused ring-opening in **1a** very slowly

Table 2. Optimization of Reaction Conditions for Ring-Opening of 1[a]



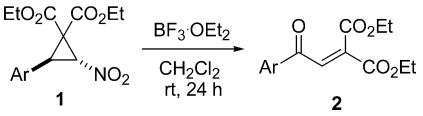
entry	Lewis acid (equiv)	solvent	yield (%)[b]
1	$AlCl_3$ (1.0)	DCM	33[c]
2	$SnCl_4$ (1.0)	DCM	53
3	$BF_3{\cdot}OEt_2$ (1.0)	DCM	81
4	$BF_3{\cdot}OEt_2$ (0.5)	DCM	49
5	$BF_3{\cdot}OEt_2$ (1.5)	DCM	80[d]
6	$BF_3{\cdot}OEt_2$ (1.0)	1,2-DCE	62
7	$BF_3{\cdot}OEt_2$ (1.0)	toluene	49
8	$BF_3{\cdot}OEt_2$ (1.0)	THF	NR[e]
9	$FeCl_3$ (1.0)	DCM	12
10	$ZnCl_2$ (1.0)	DCM	7

[a]The reaction was conducted with **1a** (1 mmol), Lewis acid (*x* mmol), and solvent (5 mL). [b]Isolated yield. [c]Diethyl phenacylmalonate is produced as a byproduct in 65% yield. [d]The reaction time was 20 h. [e]No reaction even after 3 days.

and thus formed **2a** in meager amounts in 24 h (entries 9 and 10). On the other hand, $TiCl_4$, $InCl_3$, MgI, and the metal triflates, AgOTf, $Cu(OTf)_2$, $In(OTf)_3$, $Sc(OTf)_3$, and $Yb(OTf)_3$, did not bring any change in **1a**. Thus, we selected $BF_3{\cdot}OEt_2$ (1 equiv) in DCM at room temperature for 24 h as optimal reaction conditions (entry 3) for the ring-opening reaction.

We then examined the scope of the ring-opening reaction for other D−A nitrocyclopropanes **1b**−**1l** under the optimized conditions (Table 3). The substrates **1b**−**1d**, which possess electron-donating and halogen substituents in the *p*-position of the phenyl ring, underwent facile ring-opening and gave the aroylmethylidene malonates **2b**−**2d** in good yields (entries 2−4). The reaction failed in the case of substrate **1e**, which bears an electron-withdrawing *p*-nitrophenyl ring, most likely due to the difficulty involved in the generation of a positive charge on the

Table 3. Ring-Opening Reactions of D−A Nitrocyclopropanes 1



entry	Ar	time (h)	yield (%)[a]
1	Ph (**1a**)	24	81 (**2a**)
2	4-MeC_6H_4 (**1b**)	12	86 (**2b**)
3	4-$OMeC_6H_4$ (**1c**)	12	86 (**2c**)
4	4-ClC_6H_4 (**1d**)	24	79 (**2d**)
5	4-$NO_2C_6H_4$ (**1e**)	24	NR[b]
6	3,4-$(OMe)_2C_6H_3$ (**1f**)	12	91 (**2f**)
7	3,4,5-$(OMe)_3C_6H_2$ (**1g**)	10	94 (**2g**)
8	2,6-$Cl_2C_6H_3$ (**1h**)	24	NR[b]
9	2-*I*-4,5-$(OMe)_2C_6H_2$ (**1i**)	24	85 (**2i**)
10	1-naphthyl (**1j**)	10	80 (**2j**)
11	2-furyl (**1k**)	–[c]	
12	2-thienyl (**1l**)	2[d]	27[e] (**2l**)

[a]Isolated yield. [b]No reaction. [c]The reaction produces a complicated mixture instantaneously even at −15 °C. [d]The reaction was carried out at −15 °C. [e]The yield was 33% when conducted using $FeCl_3$ (1 equiv) at −15 °C for 3 h.

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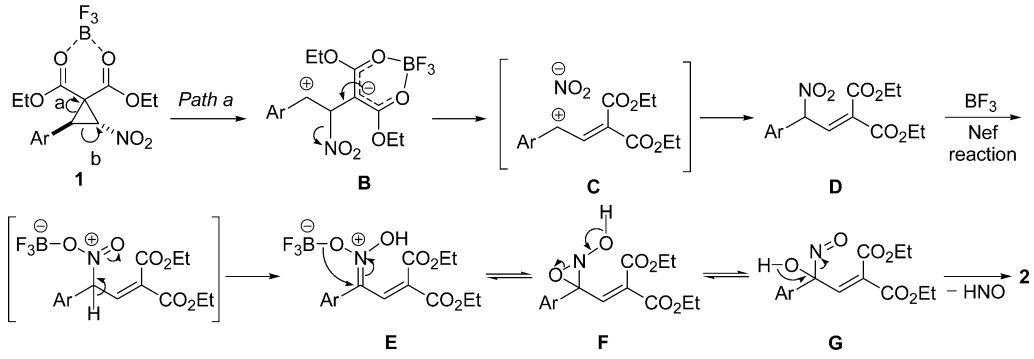
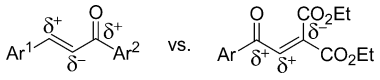
Scheme 2. Mechanism for the Formation of 2



Scheme 3. Comparison of Electrophilic Centers in Chalcones and Aroylmethylidene Malonates 2



Chalcones 2

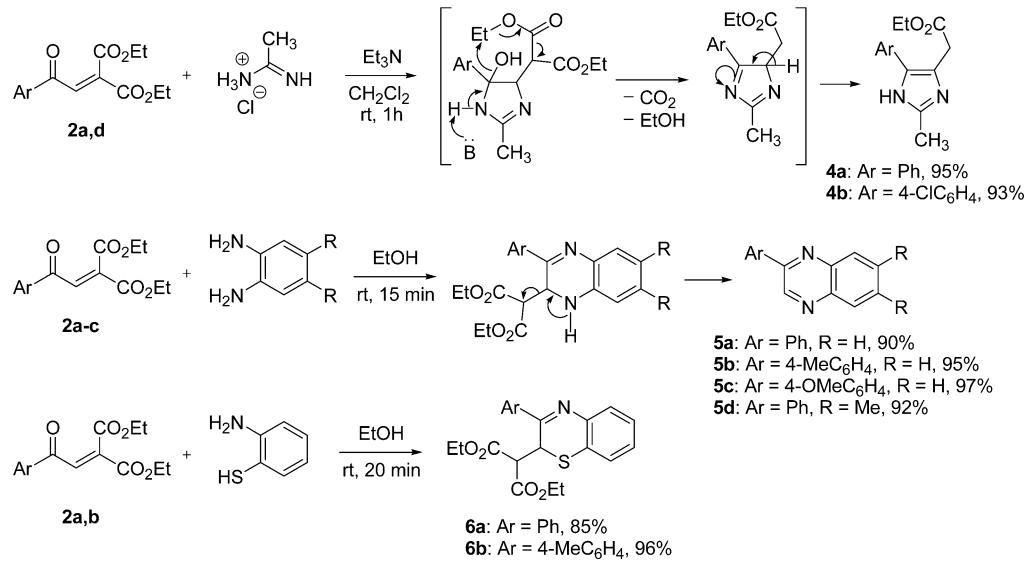
respective benzylic carbon in the zwitter ion intermediate (entry 5) (see mechanism). Among substrates **1f**–**1i**, which possess polysubstituted phenyl rings, except **1h**, all others gave the corresponding ring-opened products (entries 6–9); especially, trimethoxyphenyl-group-containing cyclopropane **1g** gave an excellent yield of 94% (entry 7). The reason for the failure of the reaction for **1h** (entry 8) may be attributed to the electron-withdrawing inductive effect of the *o*-chloro substituents. The ring-opening also works well for the naphthyl cyclopropane **1j** (entry 10). Unfortunately, the substrate **1k** having a furyl ring was incompatible for the reaction and gave a complicated mixture at room temperature as well as at −15 °C (entry 11). However, the thienyl cyclopropane **1l** furnished the corresponding ring-opened product **2l** at −15 °C, albeit in low yield (27%) (entry 12).

We propose the mechanism shown in Scheme 2 for the formation of aroylmethylidene malonates **2** from the nitrocyclopropanes **1**. There are two possible modes of ring-opening for this type of cyclopropanes (*paths a* and *b*) upon coordination of the Lewis acid to the malonyl and nitro moieties. However, only *path a* is followed due to more resonance stabilization offered to the carbanion by the malonyl unit. The zwitter ionic intermediate **B** so generated eliminates the nitro group to give the ion-pair **C**, which, upon recombination, yields the nitro compound **D**. The Nef reaction[18] of **D** in the presence of $BF_3 \cdot OEt_2$ furnishes the product **2**. Since there is no considerable amount of water in the reaction, we presume that the Nef reaction takes place via nitronic acid–BF_3 complex **E**, oxaziridine **F**, and hydroxynitroso intermediate **G** analogous to the mechanism reported by Ballini and co-workers.[19]

The product aroylmethylidene malonates could act as potential synthetic precursors like chalcones. Chalcones possess two electrophilic centers in 1,3-positions and undergo mainly Michael addition/cyclocondensation with nucleophiles (Scheme 3). Unlike chalcones, aroylmethylidene malonates possess two electrophilic centers in 1,2-positions and thus can exhibit a distinctive pattern of reactivity. Their use in asymmetric Michael addition and conjugate addition–cyclization has been documented.[13,15] However, other synthetic potentials of these compounds largely remain unexplored.

To demonstrate the utility of aroylmethylidene malonates in heterocyclic synthesis, we carried out a few reactions (Scheme 4). The cyclocondensation of **2a** and **2d** with acetamidine hydrochloride in the presence of triethylamine in DCM gave the imidazole derivatives **4a** and **4b** after monodecarbethox-

Scheme 4. Applications of Aroylmethylidene Malonates in Heterocycle Synthesis



dx.doi.org/10.1021/jo402848v | J. Org. Chem. 2014, 79, 3653–3658

ylation of the malonyl unit. When treated with *ortho*-phenylenediamines in ethanol, **2a**−**2c** afforded quinoxalines **5a**−**5d** in excellent yields with the loss of the malonyl unit. Similarly, the treatment of **2a** and **2b** with *o*-aminothiophenol furnished benzo[1,4]thiazine derivatives **6a** and **6b**. The heterocycles synthesized herein are present as substructures in many pharmaceutically relevant agents and natural products.[20] Particularly, quinoxaline **5d** was known to be an excellent inhibitor of platelet-derived growth factor receptor tyrosine kinase.[21]

In conclusion, we have developed a new iodine−DBU-mediated procedure for the preparation of 2-aryl-3-nitrocyclopropane-1,1-dicarboxylates as single *trans*-diastereomers. These nitrocyclopropanes, when treated with $BF_3{\cdot}OEt_2$, afforded synthetically useful aroylmethylidene malonates through ring-opening, rearrangement, and the Nef reaction. We have also proved the utility of the products in the synthesis of pharmaceutically important heterocycles, such as imidazoles, quinoxalines, and benzo[1,4]thiazines.

EXPERIMENTAL SECTION

General Remarks. Melting points were determined by the open capillary tube method and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer. High-resolution mass spectra (ESI) were recorded on a Q-TOF mass spectrometer. Low-resolution mass spectra (ESI) were recorded on an LC mass spectrometer. Elemental analyses were performed on a CHN analyzer. Thin-layer chromatography (TLC) was performed on precoated alumina sheets and detected under UV light. Silica gel (100−200 mesh) was used for column chromatography.

General Procedure for the Synthesis of Nitrocyclopropanes 1a−1l. To a mixture of Michael adduct **3** (1 mmol) and DBU (0.3 mL; 2 mmol) in dichloromethane (3 mL) was added iodine (508 mg; 2 mmol). The reaction mixture was stirred at ambient temperature for 15−25 min. After the reaction was complete, the reaction mixture was quenched with aq. $Na_2S_2O_3$ and extracted with dichloromethane. The organic layer was washed with water and dried (anhydrous Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using 5−10% ethyl acetate/hexane to give nitrocyclopropane **1**.

Diethyl 2-Nitro-3-phenyl-cyclopropane-1,1-dicarboxylate ***1a:***[10] Colorless oil; yield: 289 mg (94%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.30 (m, 5H), 5.41 (d, J = 6.0 Hz, 1H), 4.35−4.27 (m, 2H), 4.20 (d, J = 6.0 Hz, 1H), 4.03−3.96 (m, 2H), 1.31 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 163.2, 130.3, 128.7, 128.5, 128.3, 66.2, 63.0, 62.7, 46.2, 37.5, 13.9, 13.7 ppm.

Diethyl 2-(4-Methylphenyl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1b:***[10] Colorless oil; yield: 286 mg (89%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16−7.11 (m, 4H), 5.37 (d, J = 6.0 Hz, 1H), 4.37−4.24 (m, 2H), 4.15 (d, J = 6.0 Hz, 1H), 4.07−3.95 (m, 2H), 2.32 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.01 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 163.2, 138.4, 129.4, 128.2, 127.2, 66.3, 63.0, 62.6, 46.3, 37.4, 21.1, 13.9, 13.8 ppm.

Diethyl 2-(4-Methoxyphenyl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1c:***[10] Yellow oil; yield: 289 mg (86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 5.36 (d, J = 6.0 Hz, 1H), 4.31−4.28 (m, 2H), 4.13 (d, J = 6.0 Hz, 1H), 4.03−4.00 (m, 2H), 3.79 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.03 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 163.2, 159.7, 129.5, 122.1, 114.1, 66.5, 63.0, 62.6, 55.3, 46.4, 37.1, 13.9, 13.8 ppm.

Diethyl 2-(4-Chlorophenyl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1d:***[10] Yellow oil; yield: 330 mg (96%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.8 Hz, 2H), 5.37 (d, J = 6.0 Hz, 1H), 4.35−4.26 (m, 2H), 4.14 (d, J = 6.0 Hz, 1H), 4.08−3.99 (m, 2H), 1.31 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 163.2, 159.7, 129.5, 122.1, 114.1, 66.5, 63.0, 62.6, 55.3, 46.4, 37.1, 13.9, 13.8 ppm.

Diethyl 2-Nitro-3-(4-nitrophenyl)-cyclopropane-1,1-dicarboxylate ***1e:***[10] Yellow oil; yield: 324 mg (92%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.4 Hz, 2H), 5.44 (d, J = 6.0 Hz, 1H), 4.38−4.28 (m, 2H), 4.25 (d, J = 6.0 Hz, 1H), 4.10−4.01 (m, 2H), 1.32 (t, J = 7.0 Hz, 3H), 1.07 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 162.7, 148.0, 137.4, 129.6, 123.9, 65.9, 63.4, 63.2, 46.1, 36.6, 13.8 ppm.

Diethyl 2-(3,4-Dimethoxyphenyl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1f:*** Yellow semisolid; yield: 327 mg (89%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81 (s, 2H), 6.77 (s, 1H), 5.38 (d, J = 6.0 Hz, 1H), 4.33−4.29 (m, 2H), 4.15 (d, J = 6.0 Hz, 1H), 4.05−4.01 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.4, 163.2, 149.2, 149.1, 122.5, 120.6, 111.3, 111.0, 66.5, 63.0, 62.7, 56.0, 55.9, 46.4, 37.4, 13.87, 13.85 ppm; MS (ESI): m/z 390.05 [M + Na^+]. Anal. Calcd for $C_{17}H_{21}NO_8$: C 55.58, H 5.76, N 3.81; found: C 55.47, H 5.88, N 3.92.

Diethyl 2-Nitro-3-(3,4,5-trimethoxyphenyl)-cyclopropane-1,1-dicarboxylate ***1g:*** Yellow solid; yield: 326 mg (82%); m.p.: 122−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.45 (s, 2H), 5.38 (d, J = 5.6 Hz, 1H), 4.38−4.25 (m, 2H), 4.14 (d, J = 5.6 Hz, 1H), 4.11−3.91 (m, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.2, 163.1, 153.4, 138.2, 125.8, 105.4, 66.4, 63.0, 62.6, 60.8, 56.2, 46.3, 37.6, 13.8, 13.7 ppm; HRMS (ESI) calcd for $C_{18}H_{23}NO_9$: 420.1265 [M + Na^+], found: 420.1252.

Diethyl 2-(2,6-Dichlorophenyl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1h:*** White solid; yield: 365 mg (97%); m.p.: 76−78 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.32 (m, 2H), 7.23−7.19 (m, 1H), 5.31 (d, J = 6.4 Hz, 1H), 4.39−4.24 (m, 2H), 4.20−4.05 (m, 2H), 3.94 (d, J = 6.0 Hz, 1H), 1.31 (t, J = 7 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.2, 162.9, 136.5, 130.0, 128.7, 126.9, 69.4, 63.0, 62.8, 45.8, 34.5, 13.8, 13.6 ppm; MS (ESI): m/z 398.00 [M + Na^+]. Anal. Calcd for $C_{15}H_{15}Cl_2NO_6$: C 47.89, H 4.02, N 3.72; found: C 47.97, H 4.15, N 3.83.

Diethyl 2-(2-Iodo-4,5-dimethoxyphenyl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1i:*** Yellow semisolid; yield: 419 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (s, 1H), 6.59 (m, 1H), 5.30 (d, J = 6.0 Hz, 1H), 4.38−4.26 (m, 2H), 4.18−4.02 (m, 3H), 3.86 (s, 3H), 3.84 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H), 1.13 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5, 163.0, 149.6, 149.1, 125.8, 122.0, 112.3, 88.0, 68.2, 63.0, 62.9, 56.2, 56.1, 46.6, 41.8, 13.90, 13.87 ppm; HRMS (ESI) calcd for $C_{17}H_{20}INO_8$: 516.0126 [M + Na^+], found: 516.0121.

Diethyl 2-(Naphthalen-1-yl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1j:***[10] Crystalline white solid; yield: 350 mg (98%); m.p.: 82−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.86−7.81 (m, 2H), 7.63−7.59 (m, 1H), 7.54−7.51 (m, 1H), 7.45−7.40 (m, 2H), 5.57 (d, J = 6.0 Hz, 1H), 4.56 (d, J = 5.6 Hz, 1H), 4.42−4.37 (m, 2H), 3.79−3.66 (m, 2H), 1.36 (t, J = 7.0 Hz, 3H), 0.58 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7, 162.1, 133.6, 132.1, 129.3, 128.6, 127.0, 126.4, 126.3, 126.2, 124.9, 123.9, 66.3, 63.1, 62.4, 45.9, 36.7, 13.9, 13.2 ppm.

Diethyl 2-(Furan-2-yl)-3-nitro-cyclopropane-1,1-dicarboxylate ***1k:***[10] Brown oil; yield: 172 mg (58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (s, 1H), 6.35−6.31 (m, 2H), 5.35 (d, J = 6.0 Hz, 1H), 4.35−4.25 (m, 2H), 4.23−4.10 (m, 2H), 4.08 (d, J = 5.6 Hz, 1H), 1.29 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 162.7, 144.3, 142.9, 110.9, 109.8, 65.8, 63.1, 62.9, 45.4, 30.4, 13.80, 13.75 ppm.

Diethyl 2-Nitro-3-(thiophen-2-yl)-cyclopropane-1,1-dicarboxylate ***1l:***[10] Brown oil; yield: 153 mg (49%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.24 (m, 1H), 6.98−6.94 (m, 2H), 5.38 (d, J = 5.6 Hz, 1H), 4.35−4.27 (m, 2H), 4.21 (d, J = 7.2 Hz, 1H), 4.13−4.05 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.09 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.8, 162.7, 132.2, 127.6, 127.1, 126.3, 65.8, 63.1, 62.9, 46.8, 32.5, 13.9, 13.8 ppm.

General Procedure for Ring-Opening of Nitrocyclopropanes 2a−2l. To a solution of nitrocyclopropane **1** (1 mmol) in dichloromethane (5 mL) was added $BF_3{\cdot}OEt_2$ (0.13 mL; 1 mmol). The reaction mixture was stirred at room temperature for 24 h (12 h for **1b**, **1c**, and **1f**; 10 h for **1g** and **1j**; and 2 h at −15 °C for **1l**). The mixture was quenched with water, and the organic layer was separated. The layer was washed

dx.doi.org/10.1021/jo402848v | J. Org. Chem. 2014, 79, 3653−3658

with water and dried (anhydrous Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by wash column using 5−10% ethyl acetate/hexane.

Diethyl 2-(2-Oxo-2-phenyl-ethylidene)malonate ***2a:***[13] Yellow oil; yield: 224 mg (81%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.4 Hz, 2H), 7.85 (s, 1H), 7.65−7.61 (m, 1H), 7.53−7.49 (m, 2H), 4.38−4.27 (m, 4H), 1.36 (t, J = 7.0 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.2, 164.5, 162.9, 136.5, 136.1, 135.4, 134.2, 129.0, 128.8, 62.5, 62.0, 14.0, 13.7 ppm.

Diethyl 2-[2-(4-Methylphenyl)-2-oxo-ethylidene]malonate ***2b:*** Yellow oil; yield: 249 mg (86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.83 (m, 3H), 7.30 (d, J = 8.0 Hz, 2H), 4.37−4.26 (m, 4H), 2.43 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.7, 164.6, 163.0, 145.4, 136.2, 135.6, 133.7, 129.7, 129.0, 62.4, 61.9, 21.8, 14.0, 13.8 ppm; HRMS (ESI) calcd for $C_{16}H_{18}O_5$: 291.1227 [M + H$^+$], found: 291.1232.

Diethyl 2-[2-(4-Methoxyphenyl)-2-oxo-ethylidene]malonate ***2c:*** Yellow oil; yield: 263 mg (86%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.8 Hz, 2H), 7.84 (s, 1H), 6.97 (d, J = 8.8 Hz, 2H), 4.37−4.28 (m, 4H), 3.89 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.4, 164.7, 164.5, 163.0, 136.0, 135.5, 131.3, 129.3, 114.2, 62.4, 61.9, 55.6, 14.0, 13.8 ppm; HRMS (ESI) calcd for $C_{16}H_{18}O_6$: 307.1176 [M + H$^+$], found: 307.1181.

Diethyl 2-[2-(4-Chlorophenyl)-2-oxo-ethylidene]malonate ***2d:*** Yellow oil; yield: 246 mg (79%); H NMR (400 MHz, $CDCl_3$): δ 7.93−7.90 (m, 2H), 7.79 (s, 1H), 7.50−7.47 (m, 2H), 4.38−4.28 (m, 4H), 1.36 (t, J = 7.0 Hz, 3H), 1.27 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.0, 164.3, 162.8, 140.8, 136.9, 134.8, 134.4, 130.2, 129.3, 62.5, 62.0, 14.0, 13.8 ppm; HRMS (ESI) calcd for $C_{15}H_{15}ClO_5$: 311.0681 [M + H$^+$], found: 311.0687.

Diethyl 2-[2-(3,4-Dimethoxyphenyl)-2-oxo-ethylidene]malonate ***2f:*** Yellow oil; yield: 306 mg (91%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.60 (d, J = 10.4 Hz, 1H), 7.54 (s, 1H), 6.92 (d, J = 8.4 Hz, 1H), 4.37−4.29 (m, 4H), 3.97 (s, 3H), 3.94 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H), 1.28 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.3, 164.8, 163.0, 154.5, 149.6, 136.1, 135.2, 129.5, 124.3, 110.3, 110.1, 62.4, 61.9, 56.22, 56.11, 56.0, 14.0, 13.8 ppm; HRMS (ESI) calcd for $C_{17}H_{20}O_7$: 337.1282 [M + H$^+$], found: 337.1279.

Diethyl 2-[2-Oxo-2-(3,4,5-trimethoxyphenyl)-ethylidene]-malonate ***2g:*** Yellow oil; yield: 344 mg (94%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.21 (s, 2H), 4.38−4.27 (m, 4H), 3.94 (s, 3H), 3.92 (s, 6H), 1.36 (t, J = 7.2 Hz, 3H), 1.27 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.9, 164.6, 163.0, 153.3, 143.8, 136.4, 135.2, 131.2, 106.4, 62.5, 62.0, 61.0, 56.4, 14.0, 13.8 ppm; MS (ESI): m/z 388.98 [M + Na$^+$]; HRMS (ESI) calcd for $C_{18}H_{22}O_8$: 367.1387 [M + H$^+$], found: 367.1384. Anal. Calcd for $C_{18}H_{22}O_8$: C 59.01, H 6.05; found: C 59.25, H 6.17.

Diethyl 2-[2-(2-Iodo-4,5-dimethoxyphenyl)-2-oxo-ethylidene]-malonate ***2i:*** Yellow oil; yield: 393 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.34 (s, 1H), 7.13 (s, 1H), 4.36−4.27 (m, 4H), 3.93 (s, 3H), 3.89 (s, 3H), 1.33 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.4, 164.6, 162.9, 152.5, 149.1, 136.4, 135.1, 134.0, 123.0, 113.6, 83.6, 62.4, 62.0, 56.4, 56.2, 14.0, 13.9 ppm; HRMS (ESI) calcd for $C_{17}H_{19}IO_7$: 463.0248 [M + H$^+$], found: 463.0244.

Diethyl 2-(2-Naphthalen-1-yl-2-oxo-ethylidene)malonate ***2j:*** Yellow oil; yield: 261 mg (80%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.4 Hz, 1H), 7.96−7.89 (m, 2H), 7.80 (s, 1H), 7.66−7.62 (m, 1H), 7.59−7.51 (m, 2H), 4.35 (q, J = 7.2 Hz, 2H), 4.18 (q, J = 6.8 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.9, 164.5, 163.0, 138.4, 135.8, 134.5, 133.9, 133.4, 130.7, 130.4, 128.7, 128.6, 126.9, 125.7, 124.3, 62.4, 62.0, 14.1, 13.7 ppm; MS (ESI): m/z 349.02 [M + Na$^+$]. Anal. Calcd for $C_{19}H_{18}O_5$: C 69.93, H 5.56; found: C 70.18, H 5.73.

Diethyl 2-(2-Oxo-2-thiophen-2-yl-ethylidene)malonate ***2l:*** Yellow oil; yield: 76 mg (27%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 4.0 Hz, 1H), 7.77 (d, J = 4.8 Hz, 1H), 7.73 (s, 1H), 7.19 (t, J = 4.4 Hz, 1H), 4.40−4.32 (m, 4H), 1.35 (t, J = 7.2 Hz, 3H), 1.31 (t, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.3, 164.7, 162.8, 144.0, 137.2, 136.2, 133.8, 133.0, 128.7, 62.6, 62.1, 14.0, 13.9 ppm; HRMS (ESI) calcd for $C_{13}H_{14}O_5S$: 283.0635 [M + H$^+$], found: 283.0638.

General Procedure for the Synthesis of Imidazoles 4a and 4b. To a solution of aroylmethylidene malonate **2** (1 mmol) in dichloromethane (5 mL) were added acetamidine hydrochloride (95 mg; 1 mmol) and triethylamine (0.14 mL; 1 mmol). The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with water, and the organic layer was separated. The layer was washed with water and dried (anhydrous Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by wash column using 70−90% ethyl acetate/hexane.

Ethyl (2-Methyl-5-phenyl-1H-imidazol-4-yl)-acetate ***4a:*** Yellow semisolid; yield: 232 mg (95%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.46 (d, J = 7.2 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.27−7.22 (m, 1 H), 4.13 (q, J = 7.2 Hz, 2H), 3.71 (s, 2H), 2.29 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 144.2, 132.4, 131.8, 128.7, 127.11, 127.06, 123.9, 61.2, 32.3, 14.1, 13.4 ppm; HRMS (ESI) calcd for $C_{14}H_{16}N_2O_2$: 245.1285 [M + H$^+$], found 245.1283.

Ethyl [5-(4-Chlorophenyl)-2-methyl-1H-imidazol-4-yl]-acetate ***4b:*** Yellow semisolid; yield: 259 mg (93%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 6.80 (s, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.72 (s, 2H), 2.39 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 144.2, 133.0, 132.7, 130.6, 128.9, 128.3, 122.4, 61.5, 31.8, 14.1, 13.6 ppm; HRMS (ESI) calcd for $C_{14}H_{15}ClN_2O_2$: 279.0895 [M + H$^+$], found: 279.0895.

General Procedure for the Synthesis of Quinoxalines 5a−5d and Benzo[1,4]thiazines 6a and 6b. To a solution of aroylmethylidene malonate **2** (1 mmol) in ethanol (5 mL) was added *o*-phenylenediamine (108 mg, 1 mmol), 4,5-dimethyl-1,2-phenylenediamine (136 mg, 1 mmol), or *o*-aminothiophenol (0.11 mL; 1 mmol). The reaction mixture was stirred at room temperature for 15 min for **5a−5d** and 20 min for **6a** and **6b**. The reaction mixture was diluted with water, and the organic layer was separated. The layer was washed with water and dried (anhydrous Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by wash column using 5−10% ethyl acetate/hexane.

2-Phenyl-quinoxaline ***5a:***[22] White solid; yield: 185 mg (90%); m.p.: 74−76 °C [lit. 73−75 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.33 (s, 1H), 8.21−8.11 (m, 4H), 7.81−7.72 (m, 2H), 7.59−7.51 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.8, 142.3, 141.3, 140.6, 135.8, 129.3, 129.2, 128.6, 128.5, 128.12, 128.09, 126.5 ppm.

2-(4-Methylphenyl)-quinoxaline ***5b:***[23] White solid; yield: 209 mg (95%); m.p.: 88−90 °C [lit. 90−92 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.31 (s, 1H), 8.15−8.10 (m, 4H), 7.79−7.71 (m, 2H), 7.37 (d, J = 8.0 Hz, 2H), 2.45 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 143.3, 142.4, 141.5, 140.5, 134.0, 130.2, 129.9, 129.6, 129.3, 129.1, 127.5, 21.4 ppm.

2-(4-Methoxyphenyl)-quinoxaline ***5c:***[24] White solid; yield: 229 mg (97%); m.p.: 92−94 °C [lit. 92 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.29 (s, 1H), 8.19−8.08 (m, 4H), 7.78−7.69 (m, 2H), 7.08 (d, J = 8.4 Hz, 2H), 3.90 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 151.5, 143.1, 142.4, 141.3, 130.2, 129.41, 129.35, 129.1, 129.04, 128.99, 114.6, 55.4 ppm.

6,7-Dimethyl-2-phenylquinoxaline ***5d:***[21] White solid; yield: 215 mg (92%); m.p.: 124−126 °C [lit. 124 °C]; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.22 (s, 1H), 8.18−8.16 (m, 2H), 7.91 (s, 1H), 7.86 (s, 1H), 7.57−7.48 (m, 3H), 2.51 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.0, 142.4, 141.2, 140.8, 140.6, 140.1, 137.1, 129.8, 129.1, 128.7, 128.2, 127.4, 20.34, 20.31 ppm.

Diethyl 2-(3-Phenyl-2H-benzo[1,4]thiazin-2-yl)malonate ***6a:*** Yellow semisolid; yield: 326 mg (85%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11−8.08 (m, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.47−7.45 (m, 3H), 7.35−7.29 (m, 2H), 7.17 (t, J = 7.4 Hz, 1H), 4.93 (d, J = 10.8 Hz, 1H), 4.25−4.20 (m, 2H), 3.76−3.64 (m, 2H), 3.53 (d, J = 10.8 Hz, 1H), 1.26 (t, J = 7 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.5, 166.2, 155.4, 142.8, 137.1, 130.9, 128.6, 128.1, 128.0, 127.9, 127.1, 127.0, 119.4, 61.99, 61.95, 51.7, 32.8, 14.0, 13.4 ppm; HRMS (ESI) calcd for $C_{21}H_{21}NO_4S$: 384.1264 [M + H$^+$], found: 384.1262.

Diethyl 2-[3-(4-Methylphenyl)-2H-benzo[1,4]thiazin-2-yl]-malonate ***6b:*** Yellow semisolid; yield: 381 mg (96%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.0 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 1.2 Hz, 1H), 7.56−7.25 (m, 4H), 7.17−7.13 (m, 1H), 4.91 (d, J = 10.8 Hz, 1H), 4.22 (q, J =

dx.doi.org/10.1021/jo402848v | J. Org. Chem. 2014, 79, 3653−3658

7.2 Hz, 2H), 3.72 (q, J = 7.2 Hz, 2H), 3.53 (d, J = 11.2 Hz, 1H), 2.40 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H), 0.93 (t, J = 7.0 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 166.3, 155.3, 142.9, 141.4, 134.2, 129.3, 128.1, 128.0, 127.7, 127.0, 126.8, 119.3, 62.0, 61.9, 51.7, 32.7, 21.5, 14.0, 13.5 ppm; HRMS (ESI) calcd for $C_{22}H_{23}NO_4S$: 398.1421 [M + H$^+$], found: 398.1417.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors thank the Science and Engineering Research Board (SERB), India, for financial support and DST-FIST for the instrument facility at School of Chemistry, Bharathidasan University, India. T.S. thanks the Department of Science and Technology (DST) for an INSPIRE fellowship.

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