Kobe University Repository : Kernel

PDF issue: 2025-12-05

Preparation of Fluorescent Materials from Biomass-Derived Furfural and Natural Amino Acid Cysteine through Cross-Coupling Reactions for Extended π-Conjugation

Tanaka, Shota
Ashida, Kana
Tatsuta, Go
Mori, Atsunori

(Citation)
Synlett,26(11):1496-1500

(Issue Date)
2015-07

(Resource Type)
journal article

(Version)
Accepted Manuscript

(Rights)
©Georg Thieme Verlag Stuttgart · New York

(URL)
https://hdl.handle.net/20.500.14094/90003952

Preparation of Fluorescent Materials from Biomass-derived Furfural and Natural Amino Acid Cysteine through Cross-coupling Reactions for Extended π-Conjugation

Shota Tanaka, Kana Ashida, Go Tatsuta, and Atsunori Mori*

Department of Chemical Science and Engineering, Kobe University, 1-1 Rokkodai, Nada, Kobe 657-8501, Japan

Fax: +81 788036181

E-mail: amori@kobe-u.ac.jp

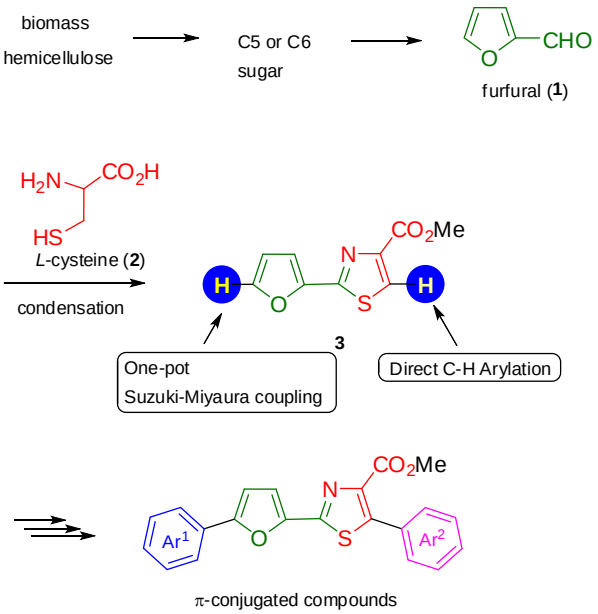
Received: The date will be inserted once the manuscript is accepted.

Dedication - To Professor Peter Vollhardt for his great contribution to Synlett

Abstract: Preparation of 2-furylthiazole-4-carboxylic acid methyl ester is achieved in four steps from biomass derived heteroaromatic compound furfural and a natural amino acid *L*-cysteine. One-pot bromination and following Pd-catalyzed arylation with arylboronates of the thus obtained furylthiazole at the furan ring gives arylated furylthiazole in excellent yields. Further arylation at the C-H bond of the thiazole ring (5-position) in the presence of AgF as an additive leads to diarylated furylthiazoles, which show strong photoluminescence. Homocoupling at the C-H bond of thiazole is also carried out with AgF to afford the corresponding further conjugated product composed of eight (hetero)aromatic rings.

Key words: Furfural, *L*-cysteine, cross coupling, π-conjugation, photoluminescence

Extended π-conjugated molecules consisted of heteroaromatic compounds have attracted much attention as advanced organic materials, which are potentially applied for the preparation of organic electronic materials such as organic semiconductors, light emitting diodes, and liquid crystalline materials.[1] Transition metal-catalyzed coupling reactions forming C-C bond is a powerful tool for further extension of π-conjugation and a variety of cross coupling strategies with organic halides and main group organometallic compounds have been effectively employed to synthesize such conjugated molecules.[2] Coupling reactions at the C-H bond of heteroaromatic compounds, which involve superior atom and step efficiencies without using prepared organometallic species, have also been employed recently.[3] We have been engaged in the development of C-C bond and C-N bond formation reactions of heteroaromatic compounds with transition metal-catalyzed C-H functionalization reactions of thiophenes, thiazoles, furans, etc.[4] Accordingly, a wide range of conjugated organic molecules are successfully prepared with these coupling reactions. In conjunction with the resources for the component of extended π-conjugated molecules, (hetero)aromatic compounds derived from fossil oil are mainly employed so far, whereas utilization of biomass-derived molecules for advanced optoelectronic materials with extended π-conjugation has less been remarked. If heteroaromatic component can be replaced with molecules derived from biomass resources and, indeed, lead to the advanced organic compound, constitution of sustainable fabrication

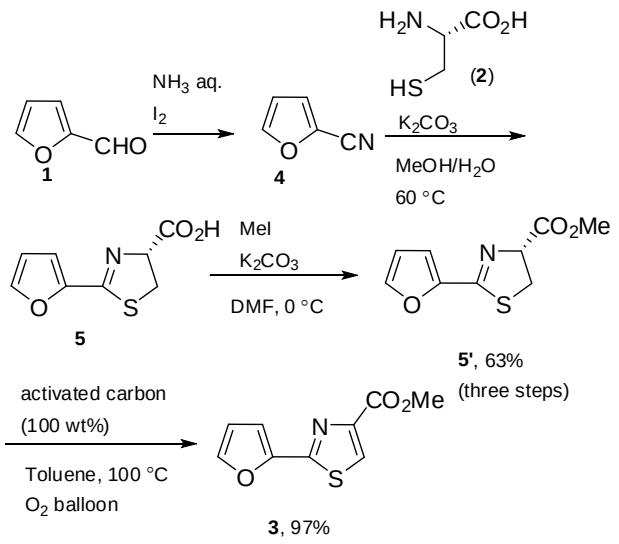


Scheme 1. Synthetic approach of extended π-conjugated

process would be achieved. Furfural (**1**) and hydroxymethylfurfural (HMF) are well-known as a key intermediate transformable to various chemicals and these are prepared by conversion of hemicellulose or cellulose through C5 or C6 sugar.[5] Therefore, development of the practical pathway to furan derivatives from biomass has recently been major concern[6] and transformation of furfural or HMF as a carbon resource to various chemicals such as fuels, pesticides, or plastics have been reported.[7] Although furan-containing conjugated polymers or organic molecules are expected to be applied for organic electronic materials,[8] such synthetic approach with furfural has little been studied. We focused on the use of amino acid derivative *L*-cysteine (**2**) by condensation of the formyl group of **1**, which form another heteroaromatic ring to extend π-conjugation leading to furylated thiazole **3**. The obtained product can also be subjected to cross-coupling reactions on the furan and thiazole rings to extend further π-conjugation. Herein, we report synthesis of highly π-conjugated (hetero)aromatic organic molecules bearing a furylthiazole moiety by the reaction of furfural and *L*-cysteine and further transformation into

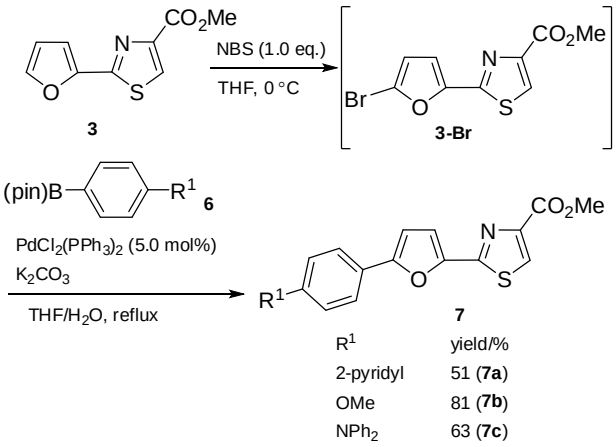
more conjugated materials that are potentially applicable as organic electronic materials.

Synthesis of 2-furylthiazole-4-carboxylic acid methyl ester (**3**) was carried out from furfural and *L*-cysteine based on the protocol to afford thiazoline by condensation followed by oxidative aromatization into thiazole.[9] Furfural **1** was converted to 2-cyanofuran **4** with iodine and aqueous ammonia. Condensation reaction of **4** with *L*-cysteine (**2**) occurred under weakly-basic conditions in methanol and water at 60 ºC to give 4-carboxy-2-furylthiazoline **5**. Esterification of the obtained thiazoline **5** was performed with methyl iodide and potassium carbonate in DMF to give furylthiazoline **5'**. These three steps were performed without isolation of the intermediate to result in 63% overall yield. Aromatization of the thiazoline ring of **5'** with 100 wt% of activated carbon under oxygen atmosphere in toluene at 100 ºC proceeded to give 2-furylthiazole **3** in 97% yield.[10] Since C-H bonds of furan and thiazole rings have been shown to undergo a variety of functionalization reactions in the presence of a transition metal catalyst, the obtained **3** can be utilized for further coupling reactions to extend π-conjugation.



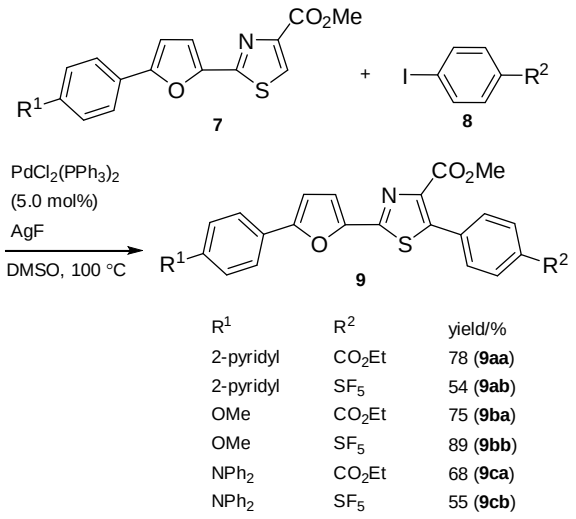
Scheme 2. Synthesis of 2-furylated thiazole **3** from furfural (**1**) and cysteine (**2**)

We next carried out the introduction of aryl group into 2-furylthiazole **3** via halogenation of the furan ring and palladium-catalyzed cross coupling reaction with aryl boronate ester **6**. The reaction of 2-furylthiazole **3** with *N*-bromosuccinimide (NBS) in THF at 0 °C exclusively occurred to give the brominated product at the α-position of the furan ring in 89% yield. The obtained bromide **3-Br** reacted with **6** in the presence of palladium catalyst to afford arylated product in excellent yield. It was found to be necessary to use bromide **3-Br** for the next reaction as shown in Scheme 3 without isolation.[11] The reaction with **6a** (R^1 = 2-pyridyl) was found to proceed successfully to give arylation product **7a** in 51% yield. The one-pot reaction of **3** with 4-methoxyphenyl boronate esters **6b** also occurred to afford arylated products **7b** in 81% yield and the coupling reaction with triphenylamine-4-boronate **6c** afforded the corresponding coupling product **7c** in 63% yield.



Scheme 3. One-pot arylation of 2-furylazole with Suzuki-Miyaura cross coupling

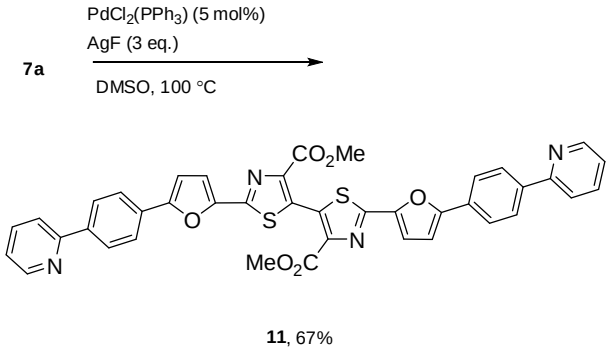
With the obtained (hetero)aromatic compound composed of three-ring system **7,** we then carried out palladium-catalyzed direct C-H arylation of **7** at the C-H bond of thiazole with aryl iodide **8**.[4a-d] These results are summarized in Scheme 4. The reaction of **7a** with ethyl 4-iodobenzoate (**8a**) in the presence of 5.0 mol% of palladium catalyst and silver fluoride as an additive in DMSO at 100 ºC took place to afford 2,5-diarylated furylthiazole **9aa** in 78% yield. The reaction with 4-iodophenylsulfur pentafluoride (**8b**), which possessed a strong electron-withdrawing group,[12] also proceeded to give **9ab** in 54% yield. When the reaction of 4-methoxyphenyl substituted furylthiazole **7b** with **8a** and **8b** were carried out, **9ba** and **9bb** were obtained in 75% and 89% yields, respectively. The reaction of **7c** bearing *N*,*N*-diphenylamino group as a substituent proceeded with **8a** and **8b** to afford **9ca** and **9cb** (68% and 55%, respectively).



R^1	R^2	yield/%
2-pyridyl	CO_2Et	78 (**9aa**)
2-pyridyl	SF_5	54 (**9ab**)
OMe	CO_2Et	75 (**9ba**)
OMe	SF_5	89 (**9bb**)
NPh_2	CO_2Et	68 (**9ca**)
NPh_2	SF_5	55 (**9cb**)

Scheme 4. Direct C-H arylation of 2-furylthiazole at the C-H bond of thiazole ring

Further extension of π-conjugation was also achieved by dehydrogenative homocoupling reaction at the C-H bond of thiazole **7**.[13] As shown in Scheme 5, the reaction was performed in the presence of palladium catalyst and silver fluoride in DMSO at 100 °C to give highly conjugated **11** composed of the 8 ring system in 67% yield.



Scheme 5 Palladium-catalyzed homo-coupling reaction of thiazole **7a**

Table 1 summarizes UV-vis absorption and photoluminescent properties of thus obtained furylthiazole derivatives. Absorption and emission maxima of furylthiazole **3** exhibited 305 nm and 357 nm, respectively, with a low quantum yield (Φ = 0.028). It was found that monoarylated products **7a-c** showed absorption and emission at higher wavelengths than those of **3**. In particular, λ_{em} of **7c** bearing triphenylamine as a donor group reached to 472 nm. Diarylated furylthiazoles bearing a 2-pyridyl substituent, **9aa** and **9ab**, showed strong blue fluorescence, whereas methoxy-substituted **9ba** and **9bb** indicated smaller quantum yields. Remarkable shifts of both absorption and emission maxima to longer wavelengths were observed in the compounds bearing 4-(*N*,*N*-diphenylamino)-phenyl group, **9ca** and **9cb**, which showed yellow fluorescence. Absorption and emission maxima of **11**, which has longest conjugation with 8 ring system, was observed in slightly longer wavelength than that of **7a** although the quantum yield was decreased (Φ = 0.03).

Table 1. UV-vis absorption and photoluminescent properties of thiazole derivatives

compound	log ε	λ_{abs},nm [a]	λ_{em} ,nm[b]	Φ [c]
9aa	4.46	373	462	0.40
9ab	4.45	373	460	0.43
9ba	4.30	376	493	0.16
9bb	4.27	375	484	0.17
9ca	4.36	408	539	0.18
9cb	4.34	391	537	0.20
11	4.60	368	531	0.03
7a	4.51	356	418	0.32
7b	4.11	361	418	0.66
7c	4.43	391	472	0.61
3	4.32	305	357	0.03

[a] Measurements of absorption spectra were carried out as a chloroform solution (1.0×10^{-5} M). [b] Measured as a chloroform solution (1.0×10^{-6} M). [c] The quantum yield Φ was estimated based on **7**-diethylamino-4-methylcoumarin as 0.01 mM solution of ethyl acetate (Φ=0.99).

In conclusion, biomass based π-conjugated heteroaromatic compounds were synthesized using furfural (**1**) and *L*-cysteine (**2**) as resources. The obtained 2-furylthiazole-4-carboxylic acid methyl ester (**3**) formed from furfural in four steps was found to be transformable by the transition-metal-catalyzed coupling reaction at the C-H bonds of furan and thiazole rings. One-pot arylation of **3** occurred to afford arylated furylthiazole **7** by bromination and following Suzuki-Miyaura coupling sequence. Palladium-catalyzed direct C-H arylation of **7** took place to give 2,5-diarylthiazole **9**, which was found to show strong photoluminescence. Because of structural and synthetic diversities to introduce various substituent at the C-H bonds of both furan and thiazole rings, further molecular design would extend utilities of biomass-based organic electronic materials.[14]

Supporting Information for this article including experimental details, spectroscopic characteristics, and copies of NMR spectra is available online at http://www.thieme-

connect.com/products/ejournals/journal/10.1055/s-00000083.

Acknowledgment

This work was supported financially by Special Coordination Funds for Promoting Science and Technology, Creation of Innovation Centers for Advanced Interdisciplinary Research Areas (Innovative Bioproduction Kobe) and Kakenhi (Challenging Exploratory Research # 26620146, 2014-2016) by MEXT, Japan. ST thanks JSPS for the Research Fellowship for Young Scientists.

References

(1) (a) Takimiya, K.; Osaka, I.; Mori, T.; Nakano, M. *Acc. Chem. Res*. **2014**, *47*, 1493. (b) Murphy, A. R.; Fréchet, J. M. J. *Chem. Rev.* **2007,** *107*, 1066. (c) Allard, S.; Forster, M.; Souharce, B.; Thiem, H.; Scherf, U. *Angew. Chem. Int. Ed.* **2008**, *47*, 4070. (d) Mishra, A.; Ma, C.-Q.; Bäuerle, P. *Chem. Rev.* **2009,** *109*, 1141. (e) Li, C.; Liu, M.; Pschirer, N. G.; Baumgarten, M.; Müllen, K. *Chem. Rev.* **2010,** *110*, 6817. (f) Nielsen, C. B.; McCulloch, I. *Progress in Polymer Science*, **2013**, *38*, 2053.

(2) Diederich, F.; Stang, P. J.; Eds. *Metal-Catalyzed Cross-Coupling Reaction*, Wiley-VCH: Weinheim, 1998.

(3) Reviews on C–H coupling of heteroaromatic compounds: (a) Campeau, L.-C.; Fagnou, K. *Chem. Commun*. **2006**, 1253. (b) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem. Int. Ed*. **2009**, *48*, 9792. (c) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev.* **2009**, *38*, 2447. (d) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev*. **2007**, *107*, 174. (e) Seregin, I. V.; Gevorgyan. V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (f) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (g) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (h) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200. (i) Sugie, A.; Mori, A. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 548. (j) Ackermann, L. *Chem. Rev*. **2011**, *111*, 1315. (k) Yamaguchi, J.; Muto, K.; Itami, K. *Eur. J. Org. Chem.* **2013**, 19. (l) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem* **2010**, *2*, 20.

(4) (a) Mori, A.; Sekiguchi, A.; Masui, K.; Shimada, T.; Horie, M.; Osakada, K.; Kawamoto, M.; Ikeda, T. *J. Am. Chem. Soc.* **2003**, *125*, 1700. (b) Masui, K.; Ikegami, H.; Mori, A. *J. Am. Chem. Soc.* **2004**, *126*, 5074. (c) Masui, K.; Mori, A.; Okano, K.; Takamura, K.; Kinoshita, M.; Ikeda, T. *Org. Lett.* **2004**, *6*, 2011. (d) Kobayashi, K.; Sugie, A.; Takahashi, M.; Masui, K.; Mori, A. *Org. Lett.* **2005**, *7*, 5083. (e) Monguchi, D.; Fujiwara, T.; Furukawa, H.; Mori, A. *Org. Lett.* **2009**, *11*, 1607. (f) Masuda, N.; Tanba, S.; Sugie, A.; Monguchi, D.; Koumura, N.; Hara, K.; Mori, A. *Org. Lett.* **2009**, *11*, 2297. (g) Tamba, S.; Okubo, Y.; Tanaka, S.; Monguchi, D.; Mori, A. *J. Org. Chem.* **2010**, *75*, 6998. (h) Tanaka, S.; Tanaka, D.; Tatsuta, G.; Murakami, K.; Tamba, S.; Sugie, A.; Mori, A. *Chem. Eur. J.* 2013, **19**, 1658. (i) Tanaka, S.; Tanaka, D.; Sugie, A.; Mori, A. *Tetrahedron Lett* **2012**, *53*, 1173. (j) Tanaka, S.; Tamba, S.; Tanaka, D.; Sugie, A.; Mori, A. *J. Am. Chem. Soc.* **2011**, *133*, 16734.

(5) (a) Karinen, R.; Vilonen, K.; Niemelä, M. *ChemSusChem* **2011**, *4*, 1002. (b) Lange, J.-P. ; van der Heide, E.; van Buijtenen, J.; Price, R. *ChemSusChem* **2012**, *5*, 150. (c) Binder, J. B.; Raines, R. T. *J. Am. Chem. Soc*. **2009**, *131*, 1979.

(6) (a) Gürbüz, E. I.; Gallo, J. M. R.; Alonso, D. M.; Wettstein, S. G.; Lim, W. Y.; Dumesic, J. A. *Angew. Chem. Int. Ed*. **2013**, *52*, 1270. (b) Román-Leshkov, Y.; Chheda, J. N.; Dumesic, J. A. *Science* **2006**, *312*, 1933.

(7) (a) Chheda, J. N.; Huber, G. W.; Dumesic, J. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 7164. (b) Lichtenthaler, F. W. *Acc. Chem. Res.* **2002**, *35*, 728. (c) Tachibana, Y.; Masuda, T.; Funabashi, M.; Kunioka, M. *Biomacromolecules*, **2010**, *11*, 2760. (d) Wegenhart, B. L.; Liu, S.; Thom, M.; Stanley, D.; Abu-Omar, M. M. *ACS Catal*. **2012**, *2*, 2524. (e) Sutton, A. D.; Waldie, F. D.; Wu, R.; Schlaf, M.; Pete Silks III, L. A.; Gordon, J. C. *Nat. Chem*., **2013**, *5*, 428. (f) Chang, F.; Dutta, S.; Becnel, J. J.; Estep, A. S.; Mascal, M. *J. Agric. Food Chem.* **2014**, *62*, 476.

(8) (a) Tsuji, H.; Ilies, L.; Nakamura, E. *Synlett*, **2014**, *25*, 2099. (b) Yiu, A. T.; Beaujuge, P. M.; Lee, O. P.; Woo, C. H.; Toney, M. F.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2012**, *134*, 2180. (c) He, J.; Guo, F.; Li, X.; Wu, W.; Yang, J.; Hua, J. *Chem. Eur. J.* **2012**, *18*, 7903. (d) Warnan, J.; Labban, A. E.; Cabanetos, C.; Hoke, E. T.; Shukla, P. K.; Risko, C.; Brédas, J.-L.; McGehee, M. D.; Beaujuge, P. M.; *Chem. Mater*. **2014**, *26*, 2299.

(9) Maltsev, O. V.; Walter, V.; Brandl, M. J.; Hintermann, L. *Synthesis*, **2013**, *45*, 2763.

(10) (a) Hayashi, M. *Chem. Rec.*, **2008**, *8*, 252. (b) Dhayalan, V.; Hayashi, M. *Synthesis*, **2012**, *44*, 2209.

(11) Mo, F.; Yan, J. M.; Qiu, D.; Li, F.; Zhang, Y.; Wang, J. *Angew. Chem. Int. Ed.* **2010**, *49*, 2028.

(12) Sheppard, W. A. *J. Am. Chem. Soc*. **1962**, *84*, 3072.

(13) AgF is shown to sever as an oxidant for homocoupling reaction in the absence of aryl halide. See ref 4b.

(14) **Preparation of 2-furylthiazole-4-carboxylic acid methyl ester (3):** To a solution of 2-cyanofuran (**4**) in 2:1 methanol/water (43 mL) were added *L*-cysteine (1.82 g, 15 mmol) and potassium carbonate (2.07 g, 15 mmol). The solution warmed to 60 °C and stirred for 21.5 h under nitrogen atmosphere. After cooling to room temperature, the reaction mixture was diluted with methanol and the solution was concentrated under reduced pressure to leave a crude solid, which was purified by short column chromatography on silica gel (methyl acetate) to afford furylthiazoline carboxylic acid **5** as orange crude solid.
To a solution of the crude solid of **5** in *N*,*N*-dimethylformamide (100 mL) were added potassium carbonate (4.14 g, 30 mmol) at room temperature under an nitrogen atmosphere. After cooling to 0 °C, methyl iodide (1.87 mL, 30 mmol) was added dropwise. After stirring for 1.5 h at 0 °C, the mixture was quenched by water and the solution was poured into the mixture of diethyl ether/water to result in separation into two phases. Aqueous was extracted with diethyl ether repeatedly and the combined organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to leave a crude oil, which was purified by column chromatography on silica gel (hexane/MeOAc = 3/1) to afford 1.33 g of furyl-thiazoline carboxylic acid methyl ester **5'** (63%).
To a 20 mL Schlenk tube equipped with a magnetic stirring bar were added **5'** (105.6 mg, 0.5 mmol) and toluene (1.5 mL). To the solution was added activated carbon (105.6 mg, 100 wt%) and stirring was continued at 100 °C for 22.5 h under oxygen atmosphere. After cooling to room temperature, the mixture was diluted with chloroform and passed through a Celite pad, which was washed with chloroform repeatedly. The

filtrate was concentrated under reduced pressure to leave the crude solid, which was purified by column chromatography on silica gel to afford 98.3 mg of **3** as a yellow solid (94 %). The reaction was also performed in a larger scale under similar conditions with **5'** (2.58 g, 12.2 mmol) and activated carbon (12.2 g, 100 wt%) in 40 mL of toluene to afford 1.51g **3** (59% yield). M.p. 88.6-89.5 °C; ^{1}H NMR (300 Hz, DMSO-d_6) δ 3.97 (s, 3H), 6.56 (dd, J = 1.8, 3.5 Hz, 1H), 7.17 (dd, J = 0.7, 3.5 Hz, 1H), 7.53 (dd, J = 0.7, 1.8 Hz, 1H), 8.14 (s, 1H); ^{13}C NMR (125 Hz, DMSO-d_6) δ 53.1, 111.3, 113.8, 129.3, 146.4, 147.5, 148.4, 158.6, 162.0; IR (ATR) 3143, 3117, 3103, 1729, 1623, 1594, 1505, 1482, 1463, 1436, 1345, 1258, 1231, 1212, 1159, 1103, 1026, 1006, 978, 879, 859, 840, 775, 751, 619 cm^{-1}; HRMS (ESI+) Calcd for $C_9H_7NO_3SNa$ $[M+Na]^+$: 232.0044; found: m/z 232.0045.