Research Article

Journal of Labelled Compounds and Radiopharmaceuticals

Received 6 December 2007, Revised 7 January 2008, Accepted 10 January 2008 Published online 18 February 2008 in Wiley Interscience

(www.interscience.wiley.com) DOI: 10.1002/jlcr.1498

Synthesis of herbicidal ZJ0273 labeled with tritium and carbon-14

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ZJ0273, propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)benzylamino)benzoate, is a broad-spectrum herbicidal ingredient used for weed control in oilseed rape in China. Two mono-labeled ZJ0273, propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)[*phenyl*-3,4,5,6-$^{3}H_4$]benzylamino)benzoate (7) and propyl 4-(2-(4,6-dimethoxy[4,6-$^{14}C_2$]pyrimidin-2-yloxy)benzylamino)benzoate (12), were synthesized separately from [2,3,4,5,6-$^{3}H_5$]phenol in a four-step yield of 27% and from 4,6-dichloro-2-(methylthio)[4,6-$^{14}C_2$]pyrimidine in a three-step yield of 54%. In addition, two dual-labeled analogues of ZJ0273 were prepared by homogeneously mixing tritium-labeled ZJ0273 (7) in the benzyl ring separately with two carbon-14-labeled ZJ0273 (2, 12) in the benzoate ring and the pyrimidine ring. These labeled ZJ0273 could be used as radiotracers in the studies on the metabolism, mode of action, environmental behavior, and fate of ZJ0273.

Keywords: propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)benzylamino)benzoate; tritium; carbon-14; radiolabeled synthesis; herbicide

Introduction

ZJ0273 (**1**, Figure 1), propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)benzylamino)benzoate, is a broad-spectrum herbicidal ingredient, which was co-developed by the Shanghai Institute of Organic Chemistry and Zhejiang Institute of Chemical Industry, China.[1] It was formulated as herbicide under the trade name of Youli (EC) and Youli II (SC), which obtained temporary registration for weed control in oilseed rape in 2003.[2] The herbicides can provide effective pre- and post-emergence control of weed at the use rate ranging from 22.5 to 52.5 g active ingredient per hectare. ZJ0273 greatly inhibits acetolactate synthase (ALS) *in vivo* and it has little inhibitory effect on ALS *in vitro*, which differs from the typically commercial ALS inhibitors, such as sulfonylurea and pyrimidine salicylic acid herbicides.[3] However, insufficient data are available on the herbicidal toxicology of ZJ0273.[2] Radiolabeled ZJ0273 is, therefore, necessary to further elucidate the precise mechanism of action and to support the on-going studies on the environmental behavior and fate of ZJ0273.

In the previous study, we synthesized propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)benzylamino)[*phenyl*-U-$^{14}C_6$]benzoate (**2**, Figure 1) (A-Ring labeled with ^{14}C) from 4-amino[U-$^{14}C_6$]-benzoic acid.[4] The tracing experiments with (**2**) indicated that A-Ring can undergo metabolic degradation, limiting the usefulness of (**2**) for the toxicological study to some extent. Consequently, multi-position-labeled ZJ0273 with ^{3}H and ^{14}C in the other two aromatic rings were adopted to address this issue, thus assuring that metabolites from the radiotracers contained a ^{3}H or ^{14}C label. In this paper, we described our recent preparation of mono-labeled ZJ0273 and dual-labeled analogues of ZJ0273 with ^{14}C and ^{3}H, respectively (Figure 2).

Results and discussion

In optimized procedures,[5] the synthesis of two mono-labeled ZJ0273, propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)[*phenyl*-3,4,5,6-$^{3}H_4$]benzylamino)benzoate (**7**) (C-Ring labeled with ^{3}H) and propyl 4-(2-(4,6-dimethoxy[4,6-$^{14}C_2$]pyrimidin-2-yloxy)benzylamino)benzoate (**12**) (B-Ring labeled with ^{14}C), were accomplished from [2,3,4,5,6-$^{3}H_5$]phenol (**3**) in four steps (Scheme 1, (a) $MgCl_2$, Et_3N, CH_3CN, Ar; (b) HCOH, reflux; (c) propyl 4-aminobenzoate, MeOH, 15−20°C ; (d) $NaBH_4$, MeOH, 0−5°C; (e) 4,6-dimethoxy-2-(methylsulfonyl)pyrimidine, K_2CO_3, CH_3CN, 50−55°C) and from 4,6-dichloro-2-(methylthio)[4,6-$^{14}C_2$]pyrimidine (**8**) in three steps (Scheme 2, (f) MeONa, MeOH; (g) $Na_2WO_4 \cdot 2H_2O$, 30% H_2O_2, AcOH, 40−50°C; (h) K_2CO_3, CH_3CN, 50−55°C), respectively. The final products (**7**, **12**) were purified by silica gel flash chromatography and semipreparative HPLC in the overall yields of 27 and 54%. Their data from HPLC-MS (ESI), MS (EI), and ^{1}H NMR analysis consisted with those of the ZJ0273 standard sample, respectively. The chemical and radiochemical purities of the desired products (**7**, **12**) were found to be >98% and the specific activity of the products were found to be 4.896 and 1.024 mCi/mmol, determined by HPLC, Radio-TLC, and HPLC-LSC methods. Two dual-labeled analogues of ZJ0273 (**13**, **14**) were prepared by homogeneously mixing ^{3}H-labeled ZJ0273 (**7**) separately with two ^{14}C-labeled ZJ0273 (**2**, **12**) in solution. These labeled products (**7**, **12**, **13**, **14**) combining with the previously synthesized (**2**) labeled with ^{14}C could be effectively used as

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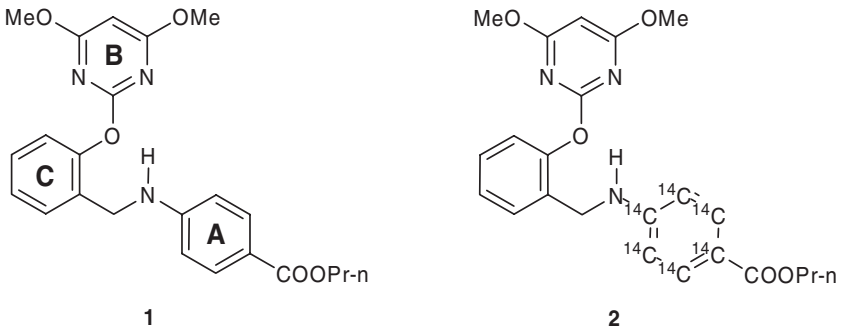


Figure 1. ZJ0273 (1) and propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)benzylamino)[*phenyl*-U-$^{14}C_6$]benzoate (2).

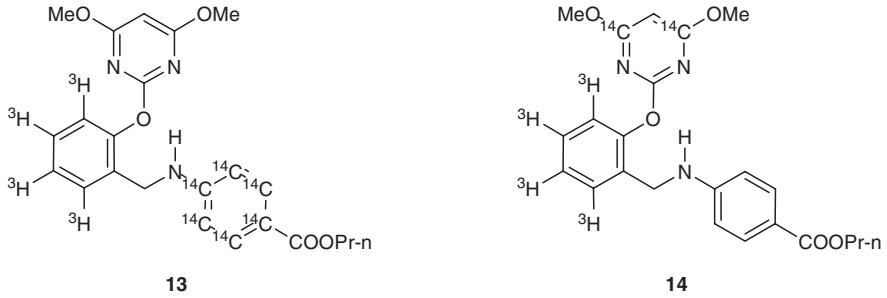
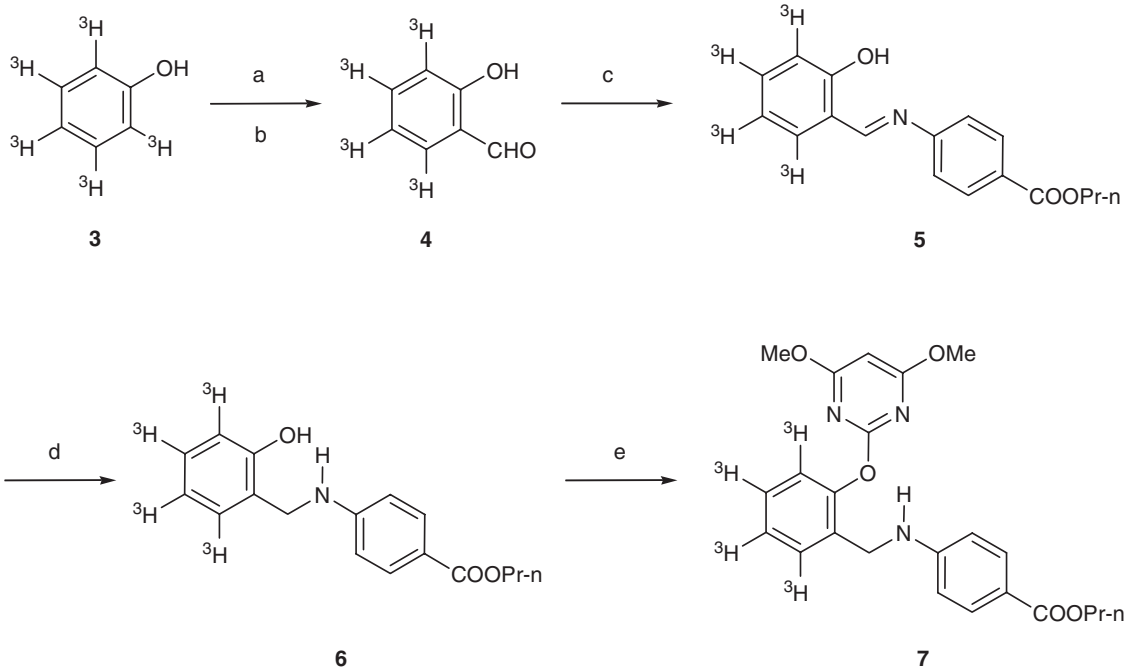


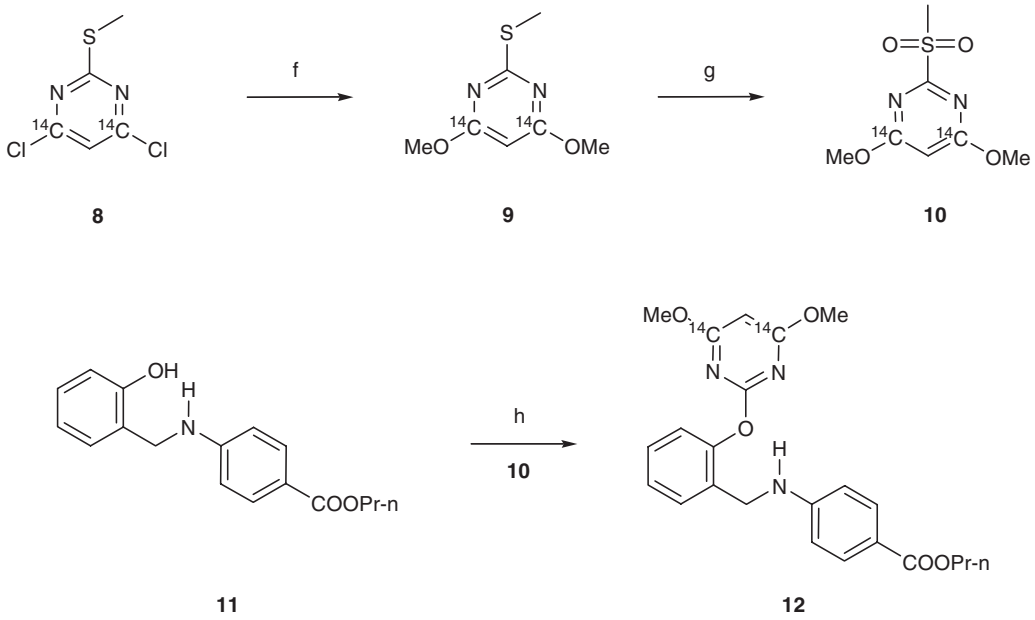
Figure 2. Two dual-labeled analogues of ZJ0273 (13, 14).



Scheme 1

radiotracers in the studies on the metabolism, mode of action, environmental behavior, and fate of ZJ0273.

In radiosynthesis, the labeling atoms must always be located in the skeleton or stable positions of the labeled molecules, so that the labeling atoms may not be lost in the subsequent tracing experiments. In the molecules of ZJ0273, there are three aromatic six-atom rings (A-Ring, B-Ring, and C-Ring). These three aromatic rings are attractive sites for radiolabeling because of their chemical and labeling stabilities. Therefore, the three aromatic rings in the molecules of ZJ0273 were labeled in the study. The C-Ring of ZJ0273 centrally links the A-Ring and B-Ring in the molecules of ZJ0273. It means that any behavior of the molecules must be related to C-Ring. Considering the three-ring characteristics of ZJ0273 and the previous synthesis of (**2**), ZJ0273 was labeled separately with ^{14}C in the pyrimidine ring (B-Ring) and with ^{3}H in the benzyl ring (C-Ring). With the aid of the mono-labeled products (**2**, **7**, and **12**), the trace of each aromatic ring could be revealed separately by parallel experiments so as



8 **9** **10** **11** **12**

Scheme 2

to fully track the fate of ZJ0273 in plant and soil. Two dual-labeled analogues of ZJ0273 (**13**, **14**) were prepared by homogeneously combining of ^{3}H-labeled (**7**) separately with ^{14}C-labeled (**2**) (radioactivity ratio 2:1) and ^{14}C-labeled (**12**) (radioactivity ratio 2:1). Each of dual-labeled analogues of ZJ0273 could demonstrate the fate of two corresponding aromatic rings in the molecules simultaneously, for the activity of ^{3}H and ^{14}C can be distinguished.

The synthesis of (**4**) is a key step in the four-step synthetic process (Scheme 1). Formylation of phenol is a classic reaction in organic chemistry and numerous traditional methods are available.[6] Most of the methods were abandoned for poor selectivity, low yield, high toxicity, or complicated workup. The reaction of phenol with paraformaldehyde in anhydrous magnesium dichloride-triethylamine system was preferred for the radiosynthesis due to its high selectivity, high yield, and simple workup.[7] The yield reached 93% in the optimized procedures in cold reactions.[5] Ethanol can quench the reaction;[7] hence, ethanol in the commercially available [2,3,4,5,6-$^{3}H_5$]phenol must be removed before reaction. To guarantee the chemical and radiochemical purities of the final labeled compounds, preparative HPLC was needed and the loss in the process was the main reason for the low overall yield of product (**7**). In addition, ZJ0273 can undergo O–N-type smiles rearrangement to a phenol derivative under acidic condition in a good yield at room temperature;[8] hence, it should be noted that all radiolabeled products (**2**, **7**, **12**, **13**, **14**) must not be kept in acidic solution.

Experimental

General

Radiochemicals [2,3,4,5,6-$^{3}H_5$]phenol (10.0 mCi, specific activity 5.00 mCi/mmol, radioactive concentration 1.00 mCi/mL, in ethanol) and 4,6-dichloro-2-(methylthio)[4,6-$^{14}C_2$]pyrimidine (2.5 mCi, specific activity 50.0 mCi/mmol, solid) were purchased from American Radiolabeled Chemicals, Inc., (Missouri, USA). Propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)benzylamino)[*phenyl*-U-$^{14}C_6$]benzoate (**2**) (specific activity 1.110 mCi/mmol, chemical and radiochemical purities $>$ 98%) was prepared in our radiochemical lab.[4] Anhydrous magnesium dichloride and 4,6-dichloro-2-(methylthio)pyrimidine were obtained from Sigma-Aldrich (USA). Paraformaldehyde, 2,5-diphenyloxazole (PPO, Scintillation Grade, 99%) and 1,4-bis(5-phenyloxazol-2-yl)benzene (POPOP, Scintillation Grade) were obtained from Acros Organics (Belgium). Methanol for HPLC was of chromatographic grade from SK Chemicals (Korea) and ultrapure water (18.2 MΩ/cm, 25°C) was prepared on Milli-Q academic instrument (Millipore, France). The standard of ZJ0273 and the related intermediates (purity exceeds 99%) were provided by the Shanghai Institute of Organic Chemistry, China. Scintillation cocktail was prepared as following prescription: PPO (7 g) and POPOP (0.5 g) dissolved in the mixture of xylene (650 mL) and 2-methoxyethanol (350 mL). All the other reagents were analytical grade and commercially available, unless otherwise stated. ^{1}H NMR spectra were measured on a Bruker DRX 300 spectrometer (Bruker, Switzerland) and MS were performed on Agilent 5973 instrument (Agilent Technologies, USA). GC-MS were recorded on Polaris Q instrument (Thermo Electron, USA) equipped with CP-Sil88 column (50 m $\times$ 0.32 mm $\times$ 0.25 μm, Chrompak Instrument Co., USA). HPLC-MS was conducted on Agilent 1100 LC/MSD instrument (Agilent Technologies). HPLC analysis and preparation were carried out on a Waters 996 series system (Waters Co., USA) consisting of automated gradient pump, photodiode array detector with Inertsil ODS-3 column (4.6 mm $\times$ 250 mm, GL Science Co., Japan), and Hypersil semi-preparative column (8 mm $\times$ 300 mm, Dalian Elite Co., China). TLC was run on GF_{254} plates and radio-TLC plates were scanned on Fujifilm BAS-1800II laser-based fluorescence and radioisotope imaging system (Fuji Co., Japan). Radioactivity was determined on WinSpectral-1414 liquid scintillation spectrometer (Wallac, Finland).

2-Hydroxy[*phenyl*-3,4,5,6-$^{3}H_4$]benzldehyde (4)

To silica gel (2 g, 100–200 mesh) was added the solution of [2,3,4,5,6-$^{3}H_5$]phenol in ethanol (10 mL, specific activity 5.00 mCi/mmol, radioactive concentration 1.00 mCi/mL) and mixed. Ethanol was removed *in vacuo* under argon. [2,3,4,5,6-$^{3}H_5$]phenol was eluted from silica gel with dry acetone, followed by evaporation of acetone and dryness over P_2O_5 to afford the starting material [2,3,4,5,6-$^{3}H_5$] phenol (**3**).

To a dried Schlenck tube was added (**3**) (188.0 mg, 2.00 mmol), anhydrous magnesium dichloride (285.6 mg, 3.00 mmol), anhydrous triethylamine (727.5 mg, 7.19 mmol), and anhydrous acetonitrile (4 mL, refluxed for 30 min with CaH_2), stirring under argon at room temperature for 10 min. Paraformaldehyde (405.0 mg, 13.49 mmol) was added to the tube. The mixture was refluxed for 4 h and allowed to cool to room temperature.[5,7] To the mixture was added 10% HCl (5 mL), followed by extraction with ethyl ether. The combined organic layers were washed with water and saturated brine, dried over anhydrous $MgCl_2$, and evaporated *in vacuo* to afford (**4**) (229.3 mg, 94%). GC-MS (EI, 70 eV) *m/z* (%): 122(M^+, 100). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 6.98–7.06(m, 2H, ArH), 7.51–7.58(m, 2H, ArH), 9.90(s, 1H, OH), 11.04(s, 1H, CHO).

Propyl 4-(2-hydroxy[*phenyl*-3,4,5,6-$^{3}H_4$]benzylideneamino)-benzoate (5)

To the stirred solution of propyl 4-aminobenzoate (336.9 mg, 1.88 mmol) in anhydrous methanol (2.5 mL) was added (**4**) (229.2 mg, 1.88 mmol) at 15–20°C and the stirring was continued for 1 h. The yellow precipitate formed immediately after ca. 30 min. The precipitate was filtered off under vacuum, washed with methanol (1.0 mL, 0–5°C), and then dried over P_2O_5 under vacuum to afford (**5**) (425.3 mg, 80%). MS (EI, 70 eV) *m/z* (%): 283(M^+, 100), 240(47), 224(48). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.05(t, J = 7.2 Hz, 3H, CH_3), 1.82(m, J = 7.2 Hz, J = 6.9 Hz, 2H, CH_2), 4.30(d, J = 6.9 Hz, 2H, OCH_2), 6.94–6.99(m, 2H, ArH), 7.30(d, J = 6.9 Hz, 2H, ArH), 7.39–7.43(m, 2H, ArH), 8.11(d, J = 6.9 Hz, 2H, ArH), 8.63(s, 1H, HC = N).

Propyl 4-(2-hydroxy[*phenyl*-3,4,5,6-$^{3}H_4$]benzylamino)benzoate (6)

Sodium borohydride (80 mg, 2.11 mmol) was added in portions to the vigorously stirred suspension of (**5**) (424.0 mg, 1.50 mmol) in anhydrous methanol (4 mL) at 0–5°C. The mixture was stirred for 30 min. To the resulting solution was added water (8 mL) then stirred for another 30 min. The solution was concentrated *in vacuo* to remove methanol and extracted with ethyl acetate. The combined organic layers were washed with saturated brine, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure to afford (**6**) (396.1 mg, 93%). HPLC-MS (ESI) *m/z*: 286($M+H^+$), 287($M+H^+$+1). MS (EI, 70 eV) *m/z* (%): 285(M^+, 46), 137(100), 179(36), 120(62), 107(55). ^{1}H NMR (CD_3SOCD_3, 300 MHz) δ: 0.93(t, J = 7.2 Hz, 3H, CH_3), 1.65(m, J = 7.2 Hz, J = 6.9 Hz, 2H, CH_2), 4.11(t, J = 6.9 Hz, 2H, OCH_2), 4.30(s, 2H, NCH), 6.65(t, J = 8.7 Hz, 2H, ArH), 6.66–7.18(m, 4H, ArH), 7.72(t, J = 8.7 Hz, 2H, ArH), 9.76(s, 1H, OH).

Propyl 4-(2-(4,6-dimethoxypyrimidin-2-yloxy)[*phenyl*-3,4,5,6-$^{3}H_4$]benzylamino) benzoate (7)

To the vigorously stirred solution of (**6**) (395.4 mg, 1.39 mmol) and 4,6-dimethoxy-2-(methylsulfonyl)pyrimidine (302.4 mg, 1.39 mmol) in anhydrous acetonitrile (5 mL) was added anhydrous potassium carbonate (670.3 mg, 4.85 mmol) at 50–55°C. The stirring was continued for 48 h.[5] The resulting mixture was filtered and concentrated under vacuum. The residue was subjected to silica gel flash chromatography (ethyl acetate/hexane 1:8–1:7) and semipreparative HPLC (inject volume 200 μL; methanol/water 75:25, by vol.; flow rate 3.00 mL/min; detection UV 254.0 nm; column temperature 30°C; the eluted liquid between 23.677–33.453 min were collected and concentrated) to afford (**7**) (230.3 mg, 39%). Radiochemical purity: 98.9%; chemical purity: 98.1%; specific activity: 4.896 mCi/mmol (determined by HPLC,[5] Radio-TLC, and HLPC-LSC methods[4]). HPLC-MS (ESI) *m/z*: 424.3($M+H^+$), 425.3($M+H^+$+1), 446.2($M+Na^+$). MS(EI, 70 eV) *m/z* (%): 245(100), 423(M^+, 62). ^{1}H NMR ($CDCl_3$, 300 MHz): 1.00(t, 3H, J = 7.2 Hz, CH_3), 1.74–1.75(m, 2H, J = 7.2 Hz, J = 6.9 Hz, CH_2), 3.79(s, 6H, OCH_3), 4.20(t, 2H, J = 6.9 Hz, OCH_2), 4.38(d, 2H, J = 5.6 Hz, NCH_2), 4.67(t, J = 5.4 Hz, 1H, NH), 5.77(s, 1H, CH), 6.49(d,2H, J = 8.8 Hz, ArH), 7.15–7.40(m, 4H, HAr), 7.80(d, 2H, J = 8.8 Hz, ArH). The data were consistent with those in reference.[9]

4,6-Dimethoxy-2-(methylthio)[4,6-$^{14}C_2$]pyrimidine (9)

To an accurately graduated flask (30.00 mL) equipped with a condenser was added sodium (1.250 g, 54.35 mmol) and anhydrous methanol (30 mL) at 0–5°C in an ice bath under argon. The mixture was stirred until it became clear, stirred for another 10 min, and allowed to cool to room temperature. The volume of the solution was increased to 30.00 mL by addition of anhydrous methanol to the reaction mixture to afford the solution of sodium methanolate (1.811 mmol/mL).

The resulting solution of sodium methanolate (2.76 mL, 5.0 mmol) was added dropwise to the stirred solution of 4,6-dichloro-2-(methylthio)[4,6-$^{14}C_2$]pyrimidine (**8**) (9.8 mg, 0.05 mmol, specific activity 50 mCi/mmol), 4,6-dichloro-2-(methylthio)pyrimidine (477.9 mg, 2.45 mmol) and anhydrous methanol (10 mL) in Schlenck tube over 10 min and refluxed for 5 h.[5,10] Water (10 mL) was added into the vigorously stirred reaction mixture, followed by extraction with ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated to afford (**9**) (437.6 mg, 94%). HPLC-MS (ESI) *m/z*: 187($M+H^+$), 188($M+H^+$+1). MS (EI, 70 eV) *m/z* (%): 186(M^+, 100), 171(20), 140(29), 125(26). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.53(s, 3H, SCH_3), 3.92(s, 6H, OCH_3), 5.71(s, 1H, CH).

4,6-Dimethoxy-2-(methylsulfonyl)[4,6-$^{14}C_2$]pyrimidine (10)

To a stirred solution of (**9**) (436.8 mg, 2.35 mmol) and sodium tungstate dihydrate (40.0 mg, 0.12 mmol) in acetic acid (2 mL) was added 30% hydrogen peroxide (0.50 mL, 4.90 mmol) at 40°C. The solution was stirred for 10 min, allowed to warm to 50°C, and stirred for 4 h.[5,10] The mixture was cooled to room temperature and evaporated acetic acid in vacuum. The residue was suspended in ethyl acetate (8 mL), washed with water, concentrated, and subjected to flash chromatograph (ethyl acetate/hexane 1:4) to afford (**10**) (429.9 mg, 84%). HPLC-MS (ESI) *m/z*: 219($M+H^+$), 220($M+H^+$+1). MS (EI, 70 eV) *m/z* (%): 218(M^+, 28), 139(100). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.32(s, 3H, SCH_3), 4.03(s, 6H, OCH_3), 6.18(s, 1H, CH).

Propyl 4-(2-(4,6-dimethoxy[4,6-$^{14}C_2$]pyrimidin-2-yloxy)benzylamino)benzoate (12)

A mixture of anhydrous potassium carbonate (812.7 mg, 5.88 mmol), propyl 4-(2-hydroxybenzylamino)benzoate (**11**)

(558.6 mg, 1.96 mmol) and (**10**) (428.1 mg, 1.96 mmol) in anhydrous acetonitrile (4 mL) was vigorously stirred at 50–55°C for 36 h.[5] The resulting mixture was worked up according to the same procedures described in the preparation of (**7**). The eluted liquid between 39.655–56.113 min in semipreparative HPLC (inject volume 200 μL; methanol/water 70:30; flow rate 3.00 mL/min; detection UV 254.0 nm; column temperature 30°C) was collected and evaporated under vacuum to afford (**12**) (574.4 mg, 69%). Radiochemical purity: 99.4%; chemical purity: 98.1%; specific activity: 1.024 mCi/mmol (determined by HPLC,[5] Radio-TLC, and HLPC-LSC methods[4]). HPLC-MS (ESI) *m/z*: 424($M+H^+$), 425($M+H^++1$), 446($M+Na^+$). MS (EI, 70 eV) *m/z* (%): 423(M^+, 24), 245(100). ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 0.99(t, $J=7.2$ Hz, 3H, CH_3), 1.74(m, $J=7.2$ Hz, $J=6.9$ Hz, 2H, CH_2), 3.81(s, 6H, OCH_3), 4.19(t, $J=6.9$ Hz, 2H, OCH_2) , 4.38(d, $J=5.4$ Hz, 2H, NCH_2), 4.67(t, $J=5.4$ Hz, 1H, NH), 5.78(s, 1H, CH), 6.49(d, $J=8.7$ Hz, 2H, ArH), 7.13–7.41(m, 4H, ArH), 7.81(d, $J=8.7$ Hz, 2H, ArH). The data were consistent with those in reference.[9]

Preparation of two dual-labeled analogues of ZJ0273 (13, 14)

The mixture of ^{14}C-labeled ZJ0273 (**2**) (100.0 mg, 1.110 mCi/mmol), ^{3}H-labeled ZJ0273 (**7**) (48.4 mg, 4.896 mCi/mmol), and ZJ0273 (**1**) (73.8 mg) was dissolved in acetone, followed by evaporation under vacuum to afford ^{3}H–^{14}C-labeled ZJ0273 (**13**) with the specific activities of 1.066 mCi/mmol for ^{3}H and 0.500 mCi/mmol for ^{14}C. Another ^{3}H–^{14}C-labeled ZJ0273 (**14**) with the specific activities of 1.066 mCi/mmol for ^{3}H and 0.484 mCi/mmol for ^{14}C was prepared with ^{3}H-labeled ZJ0273 (**7**) (100.0 mg, 4.896 mCi/mmol), ^{14}C-labeled ZJ0273 (**12**) (44.6 mg, 1.024 mCi/mmol), and ZJ0273 (**1**) (60.2 mg) as the above procedures.

Acknowledgements

The authors gratefully acknowledge the financial support from Key Program of National Natural Science Foundation of China (20632070) and Knowledge Innovation Program of the Chinese Academy of Science (KGCX3-SYW-203).

REFERENCES

[1] L. Lu, J. Chen, J. Wu, W. Ling, L. S. Mao, M. Z. Li, X. Cai, L. W. Peng, Y. Wu, S. G. Wu, H. J. Wang, G. C. Wang, H. Cui, S. D. Han, W. L. Qiu, Y. H. Wang, US patent 6800590B2, 5 October 2004.
[2] Q. H. Tang, J. Chen, L. Lu, *Chinese J. Pestic.* **2005**, *44*, 496–502.
[3] J. Chen, J. Yuan, J. D. Liu, Q. M. Fu, J. Wu, *Acta Phytophyl. Sin.* **2005**, *32*, 48–52.
[4] Z. M. Yang, Q. F. Ye, Q. H. Tang, L. Lu, Z. Y. Chen, *Acta Chim. Sin.* **2005**, *63*, 1999–2003.
[5] Z. M. Yang, Q. F. Ye, Q. H. Tang, L. Lu, *J. Nucl. Agri. Sci.* **2006**, *20*, 423–428.
[6] A. Robert, J. Robert, L. Daniel, N. James, *J. Chem. Soc. Perkin Trans. 1* **1994**, *13*, 1823–1831.
[7] N. U. Hofslϕkken, L. Skattebϕl, *Acta Chem. Scand.* **1999**, *53*, 258–262.
[8] H. Y. Wang, Y. X. Liao, Y. L. Guo, Q. H. Tang, L. Lu, *Synlett* **2005**, *8*, 1239–1242.
[9] J. Wu, P. Z. Zhang, L. Lu, Q. S. Yu, X. R. Hu, J. M. Gu, *Chinese J. Struct. Chem.* **2003**, *22*, 613–616.
[10] Y. Nezu, M. Miyazaki, K. Sugiyama, N. Wada, I. Kajiwarab, T. Miyazawa, *Pestic. Sci.* **1996**, *47*, 115–124.