A Facile and Efficient Approach to the Synthesis of Novel Chiral Molecular Tweezers Based on Deoxycholic Acid under Microwave Irradiation

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Abstract: A rapid, safe and efficient method for the synthesis of novel molecular tweezers with one chiral arm based on deoxycholic acid was reported. Ten new molecular tweezers have been synthesized in good yields. The structures of these new molecular tweezers were characterized by ^{1}H NMR, IR, MS spectra and elemental analysis. These chiral molecular tweezers showed good enantioselectivity for *D*-amino acid methyl esters.

Keywords: Molecular tweezer, deoxycholic acid, synthesis, microwave irradiation, molecular recognition.

1. INTRODUCTION

As an essential feature of biochemical systems, molecular recognition plays pivotal role in life processes. The design and synthesis of model receptor to recognize substrates of biochemical significance to mimic biological events are of keen interest in molecular recognition research [1, 2]. In recent years, many interesting receptors have been developed. Among the various types of artificial receptors designed so far, a special class of receptors called molecular tweezers, which are particularly effective in regard to complementarities with substrates since functional groups attached to the interior of the tweezer converge on substrates held inside [3] has attracted more and more attention in molecular recognition, mimic enzyme catalysis, self-assembly of molecular structure, the resolution of race mates as well as molecular devices [4-6].

Moreover, the recent development in so called "green chemistry" shows that alternative methods of carrying out chemical transformation can minimize the environmental harmfulness of classical reactions. One of the most popular and interesting approach in this field is the application of microwave techniques for organic synthesis. This technology can enhance the selectivity and reactivity, improve product yields along with several eco-friendly advantages in green chemistry [7-9]. For this reason, the application of microwave irradiation for activation of reaction, in general and under solvent-free conditions in particular, has gained popularity over the usual homogeneous and heterogeneous reactions.

The natural rigid concave structure and inherent asymmetry of cholic acid pose it as ideal building blocks for the construction of molecular tweezers. With our continuous investigation on the methodology of microwave-assisted green synthesis of molecular tweezers [10-13], herein, we report a simple, green, safe and rapid method to obtain new deoxycholic acid molecular tweezer artificial receptors containing naphthoyloxy arm, which are expected to form π-π stacking interaction with substrates in molecular recognition. The synthetic route is shown in Scheme **1**.

2. RESULTS AND DISCUSSION

In order to make a quantitative comparison in synthesis molecular tweezers **5a-5j** between microwave irradiation and conventional heating, a series of experiments were carried out. As indicated in Table **1**, the reaction times were considerably shorter, only 18-21 minutes, however, the synthesis of these molecular tweezers in conventional heating required 35-39 h in dichloromethane and yields of reaction increased (38%-71%) relative to (84%-92%).

In searching for the best reaction results of this reaction, we took the synthesis of **5a** for example and carried out several experimental works in different conditions: such as microwave irradiation power, time and solvent (as shown in Table **2**). From Table **2**, we found that 19 min was the optimum reaction time when the yield was the highest under the same power (200 W). However, more byproducts could be afforded when lengthening the reaction time; In addition, we irradiated the reaction using different powers under the same reaction time (19 min). As a result, 200 W was the optimum power; Finally, dichloromethane, chloroform and tetrahydrofuran were compared to evaluate the solvent effect on the reaction. Different solvents were employed under the similar reaction conditions, but the results were much different as shown in Table **2**.

Considering dichloromethane is less toxic than chloroform and easily removed than the other two solvents, we conclude that dichloromethane is the best solvent in this reaction. For comparison purpose, the best yield (up to 89%) is obtained in the condition of irradiating 19 min at 200W using dichloromethane as solvent.

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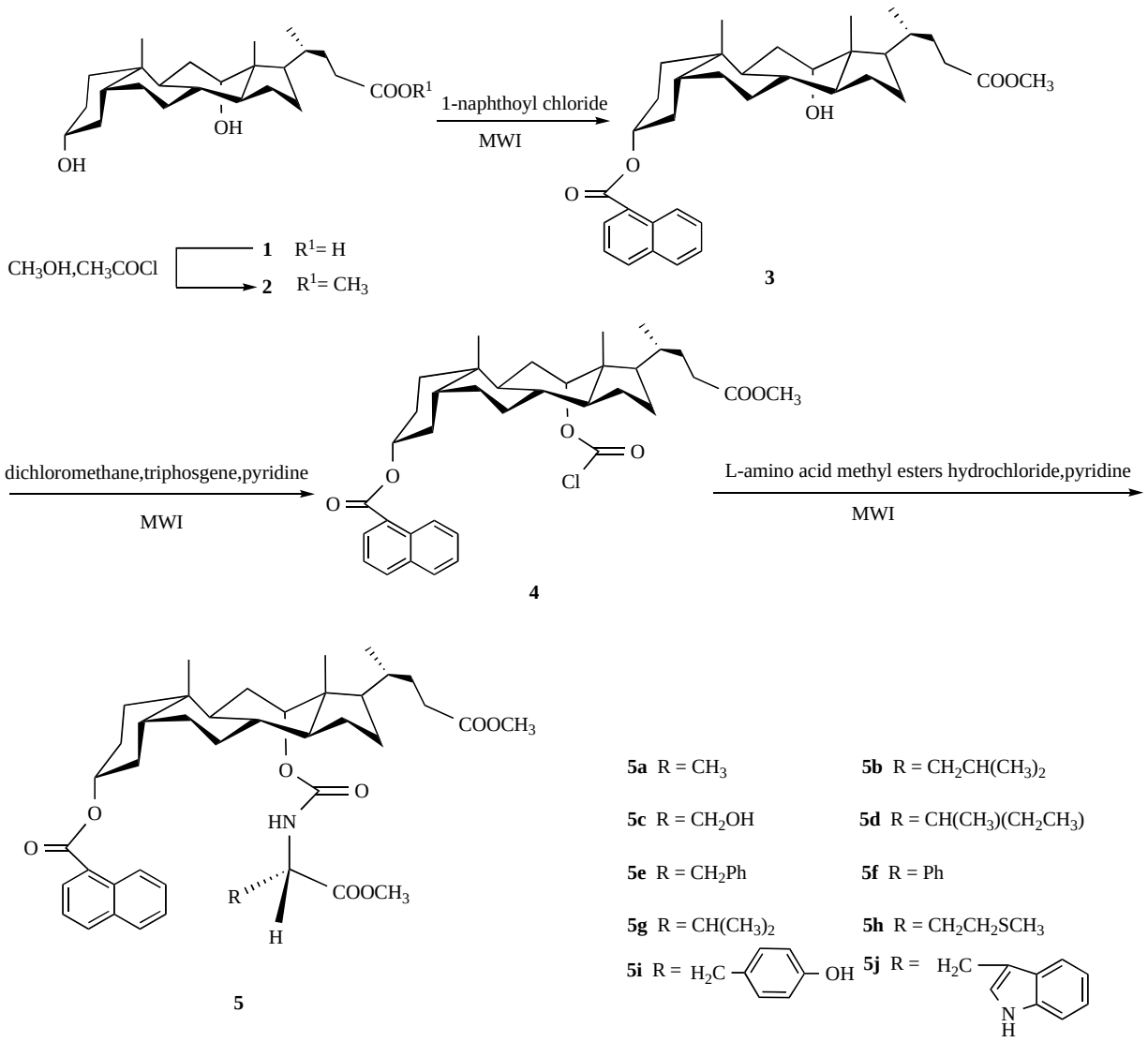

Scheme 1. Synthesis of chiral molecular tweezers **5a-5j**.

Table 1. Synthetic Comparison of Molecular Tweezers 5a-5j Between Microwave Irradiation and Conventional Heating

Compd	Conventional method			Microwave method		
5a	**Solvent(mL)**	**T/min**	**Yield/%**	**Solvent(mL)**	**T/min**	**Yield/%**
5a	20	2160	67	10	19	89
5b	20	2160	60	10	19	88
5c	20	2340	52	10	21	87
5d	20	2160	64	10	19	90
5e	20	2280	71	10	21	92
5f	20	2220	43	10	18	85
5g	20	2340	40	10	21	86
5h	20	2100	62	10	19	90
5i	20	2280	50	10	20	88
5j	20	2100	38	10	21	84

Table 2. Synthetic Comparison of Molecular Tweezers 5a in Different Conditions

Material	Solvent	T/min	Product	Power/W	Yield/%
intermediate **3**	CH_2Cl_2	12	**5a**	200	50
intermediate **3**	CH_2Cl_2	19	**5a**	200	89
intermediate **3**	CH_2Cl_2	20	**5a**	200	84
intermediate **3**	CH_2Cl_2	25	**5a**	200	82
intermediate **3**	CH_2Cl_2	19	**5a**	50	45
intermediate **3**	CH_2Cl_2	19	**5a**	150	80
intermediate **3**	CH_2Cl_2	19	**5a**	250	79
intermediate **3**	THF	19	**5a**	200	70
intermediate **3**	THF	25	**5a**	200	73
intermediate **3**	$CHCl_3$	19	**5a**	200	84
intermediate **3**	$CHCl_3$	25	**5a**	200	81

It is important to note that in the process of obtaining product **5a-5j** from intermediate **3**. Triphosgene was added to a solution of intermediate **3** in dry dichloromethane at room temperature. After irradiating the reaction mixture for 9 min at 200 W, intermediate **4** was formed, then *L*-amino acid methyl esters hydrochloride and dry pyridine were added directly to the mixture bypassing the separation of acyl chloride (intermediate **4**). Our methodology has shown that under microwave irradiation novel chiral molecular tweezers receptors can be synthesized in one-pot.

The enantioselective recognition of molecular tweezers **5e**, **5f** for some amino acid methyl esters have been investigated by UV-Visible spectra titration in chloroform at 25℃. The titration data were analyzed by using the Hildebrand-Benesi equation [14]. The preliminary results, as expected, showed that all these molecular tweezers posses the ability to complex with amino acid methyl esters examined. The association constants (K_a) and Gibbs free energy changes ($-\triangle G^0$) for inclusion complexation of molecular tweezers **5e**, **5f** with all *D*–amino acid methyl esters are higher than with all *L*–amino acid methyl esters. The enantioselectivity K_D/K_L for **5e**, for example, is 5.3 for Phe-OMe. It shows fairly good enantioselective recognition which could be obtained practical application in chiral resolution. The details of complexing experiments are under further studies.

3. EXPERIMENTAL

3.1. General

Melting points were determined on a micro-melting point apparatus and the thermometer was uncorrected. Infrared spectra were obtained on 1700 Perkin-Elmer FTIR using KBr disks. ^{1}H NMR spectra were recorded on a Varian INOVA 400 MHz spectrometer using $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were determined on Finnigan LCQ^{DECA} instrument. Elemental analysis was performed on a Carlo-Erba-1106 autoanalyzer. Microwave irradiation was carried out with a MCL-3 microwave oven (very safe, reliable) at full power (700 W), which was modified from domestic microwave oven and tested to conform to the performance index before use. Optical rotation was measured on a Wzz-2B polarimeter. Solvents were dried and distilled according to established procedures. Reactions were monitored by thin layer chromatography (TLC), Column chromatography purifications were carried out using silica gel. All reagents were purchased from commercial corporations. Deoxycholic acid was converted to methyl *3α, 12α*-dihydroxy-7-deoxy-*5β* -cholan-*24*-oate (**2**) following a reported procedure [15]. Intermediate (**3**) was prepared by known procedures [16]. All the *L*-amino acid methyl esters hydrochloride were obtained from the esterification of corresponding *L* -amino acids and methanol in the presence of thionyl chloride.

3.2. General Procedure for the Synthesis of Molecular Tweezers 5a-5j under Microwave Irradiation

Triphosgene (0.2 mmol) was added to a solution of compound **3** (0.5 mmol) in 10 mL dry dichloromethane and 0.1 mL dry pyridine at room temperature. After irradiating the reaction mixture for 9 min at 200 W, compound **4** was formed, then *L*-amino acid methyl esters hydrochloride (1 mmol) and 0.2 mL dry pyridine were added directly to the mixture, irradiated continually for 9-12 min at the same power. The solvent was removed and the residue was diluted with 20 mL ethyl acetate and washed with 10% $NaHCO_3$ (10 mL×3), brine (10 mL×3), and finally dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel H with dichloromethane/ethyl acetate as eluant.

3.2.1. Molecular Tweezer 5a

Prepared according to the general procedure to afford the product **5a** as a white crystals; yield 89%; Mp: 41–42℃. $[\alpha]_D^{20}$ = +62.17°(*c* 0.15, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (s, 3H, 18-CH_3), 0.86 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.96 (s, 3H, 19-CH_3), 3.56 (s, 3H, $COOCH_3$), 3.66 (s, 3H, $COOCH_3$), 4.34-4.41 (m, 1H, 3*β*-H), 4.97 (s, 1H, 12*β*-H), 5.05-5.11 (m, 1H, NCH), 5.30 (d, 1H, *J* = 8.4 Hz, CONH), 7.47-7.62 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz,

ArH), 8.01 (d, 1H, *J* = 8.0 Hz, ArH), 8.21 (d, 1H, *J* = 7.2 Hz, ArH), 8.87 (d, 1H, *J* = 8.4 Hz, ArH); IR (KBr, cm^{-1}): 3432, 2942, 2869, 1719, 1654, 1515, 1449, 1247; ESI–MS *m/z* (%): 712.7 $[(M+23)^+$, 100]; Elemental analysis: Found (%): C, 71.56; H, 8.02; N, 2.04 Calcd. For $C_{41}H_{55}NO_8$: C, 71.38; H, 8.04; N, 2.03.

3.2.2. Molecular Tweezer 5b

Prepared according to the general procedure to afford the product **5b** as a white crystals; yield 88%; Mp: 57–58℃. $[\alpha]_D^{20}$ = +35.72° (*c* 0.092, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73 (s, 3H, 18-CH_3), 0.94 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.96 (s, 3H, 19-CH_3), 3.52 (s, 3H, $COOCH_3$), 3.66 (s, 3H, $COOCH_3$), 4.35-4.41 (m, 1H, 3β-H), 4.97 (s, 1H, 12β-H), 5.05-5.08 (m, 1H, NCH), 5.14 (d, 1H, *J* = 9.2 Hz, CONH), 7.47-7.62 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.00 (d, 1H, *J* = 8.0 Hz, ArH), 8.22 (d, 1H, *J* = 7.2 Hz, ArH), 8.88 (d, 1H, *J* = 8.8 Hz, ArH); IR (KBr, cm^{-1}): 3400, 2949, 2868, 1713, 1450, 1384, 1246, 1199; ESI–MS *m/z* (%): 1485.7 $[(2M+23)^+$, 100]; Elemental analysis: Found (%): C, 72.09; H, 8.38; N, 1.89 Calcd. For $C_{44}H_{61}NO_8$: C, 72.20; H, 8.40; N, 1.91.

3.2.3. Molecular Tweezer 5c

Prepared according to the general procedure to afford the product **5c** as a yellow crystals; yield 87%; Mp: 77–78℃. $[\alpha]_D^{20}$ = +61.32° (*c* 0.082, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (s, 3H, 18-CH_3), 0.87 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.96 (s, 3H, 19-CH_3), 3.59 (s, 3H, $COOCH_3$), 3.65 (s, 3H, $COOCH_3$), 3.75-3.99 (m, 3H, OH+OCH_2), 4.44-4.46 (m, 1H, 3β-H), 5.04-5.12 (m, 1H, NCH), 4.99 (s, 1H, 12β-H), 5.70 (d, 1H, *J* = 8.0 Hz, CONH), 7.47-7.63 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.00 (d, 1H, *J* = 8.0 Hz, ArH), 8.20 (d, 1H, *J* = 7.2 Hz, ArH), 8.87 (d, 1H, *J* = 8.8 Hz, ArH); IR (KBr, cm^{-1}): 3438, 2946, 2869, 1715, 1511, 1449, 1244, 1201; ESI–MS *m/z* (%): 706.6 $[(M+1)^+$, 100]; Elemental analysis: Found (%): C, 69.80; H, 7.89; N, 2.01 Calcd. For $C_{41}H_{55}NO_9$: C, 69.76; H, 7.85; N, 1.98.

3.2.4. Molecular Tweezer 5d

Prepared according to the general procedure to afford the product **5d** as a colorless crystals; yield 90%; Mp: 62–63℃. $[\alpha]_D^{20}$ = +34.63° (*c* 0.14, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (s, 3H, 18-CH_3), 0.92 (d, 3H, *J* = 6.8 Hz, 21-CH_3), 0.96 (s, 3H, 19-CH_3), 3.49 (s, 3H, $COOCH_3$), 3.66 (s, 3H, $COOCH_3$), 4.31-4.35 (m, 1H, 3β-H), 4.98 (s, 1H, 12β-H), 5.03-5.10 (m, 1H, NCH), 5.27 (d, 1H, *J* = 9.6 Hz, CONH), 7.47-7.62 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.00 (d, 1H, *J* = 8.0 Hz, ArH), 8.23 (d, 1H, *J* = 7.2 Hz, ArH), 8.88 (d, 1H, *J* = 9.2 Hz, ArH); IR (KBr, cm^{-1}): 3377, 2950, 2870, 1716, 1510, 1450, 1246, 1200; ESI–MS *m/z* (%): 753.2 $[(M+23)^+$, 100]; Elemental analysis: Found (%): C, 72.24; H, 8.38; N, 1.89 Calcd. For $C_{44}H_{61}NO_8$: C, 72.20; H, 8.40; N, 1.91.

3.2.5. Molecular Tweezer 5e

Prepared according to the general procedure to afford the product **5e** as a white crystals; yield 92%; Mp: 59–61℃. $[\alpha]_D^{20}$ = +32.77° (*c* 0.10, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 (s, 3H, 18-CH_3), 0.79 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.95 (s, 3H, 19-CH_3), 3.00-3.17 (m, 2H, $PhCH_2$), 3.49 (s, 3H, $COOCH_3$), 3.68 (s, 3H, $COOCH_3$), 4.64-4.70 (m, 1H, 3β-H), 4.94 (s, 1H, 12β-H), 5.03-5.09 (m, 1H, NCH), 5.22 (d, 1H, *J* = 8.4 Hz, CONH), 7.06-7.29 (m, 5H, ArH), 7.46-7.61 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.00 (d, 1H, *J* = 8.0 Hz, ArH), 8.18 (d, 1H, *J* = 7.2 Hz, ArH), 8.87 (d, 1H, *J* = 8.8 Hz, ArH); IR (KBr, cm^{-1}): 3430, 2943, 2868, 1716, 1509, 1447, 1246, 1201; ESI–MS *m/z* (%): 788.6 $[(M+23)^+$, 100]; Elemental analysis: Found (%): C, 73.68; H, 7.70; N, 1.81 Calcd. For $C_{47}H_{59}NO_8$: C, 73.70; H, 7.76; N, 1.83.

3.2.6. Molecular Tweezer 5f

Prepared according to the general procedure to afford the product **5f** as a white crystals; yield 85%; Mp: 113–114℃. $[\alpha]_D^{20}$ = +44.04° (*c* 0.14, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.70 (s, 3H, 18-CH_3), 0.97 (s, 3H, 19-CH_3), 3.58 (s, 3H, $COOCH_3$), 3.66 (s, 3H, $COOCH_3$), 4.95 (s, 1H, 12β-H), 5.07-5.12 (m, 1H, 3β-H), 5.36 (d, 1H, *J* = 8.0 Hz, NCH), 5.84 (d, 1H, *J* = 8.0 Hz, CONH), 7.00-7.35 (m, 5H, ArH), 7.48-7.63 (m, 3H, ArH), 7.89 (d, 1H, *J* = 8.0 Hz, ArH), 8.02 (d, 1H, *J* = 7.6 Hz, ArH), 8.24 (d, 1H, *J* = 7.2 Hz, ArH), 8.90 (d, 1H, *J* = 8.8 Hz, ArH); IR (KBr, cm^{-1}): 3432, 2946, 2869, 1717, 1501, 1447, 1382, 1200; ESI–MS *m/z* (%): 774.8 $[(M+23)^+$, 100]; Elemental analysis: Found (%): C, 73.50; H, 7.59; N, 1.84 Calcd. For $C_{46}H_{57}NO_8$: C, 73.47; H, 7.64; N, 1.86.

3.2.7. Molecular Tweezer 5g

Prepared according to the general procedure to afford the product **5g** as a yellow crystals; yield 86%; Mp: 64–65℃. $[\alpha]_D^{20}$ = +38.46° (*c* 0.16, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (s, 3H, 18-CH_3), 0.87 (d, 3H, *J* = 6.8 Hz, 21-CH_3), 0.96 (s, 3H, 19-CH_3), 3.49 (s, 3H, $COOCH_3$), 3.65 (s, 3H, $COOCH_3$), 4.28-4.31 (m, 1H, 3β-H), 4.98 (s, 1H, 12β-H), 5.03-5.11 (m, 1H, NCH), 5.27 (d, 1H, *J* = 9.6 Hz, CONH), 7.47-7.62 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.4 Hz, ArH), 8.00 (d, 1H, *J* = 8.0 Hz, ArH), 8.24 (d, 1H, *J* = 7.2 Hz, ArH), 8.89 (d, 1H, *J* = 8.8 Hz, ArH); IR (KBr, cm^{-1}): 3435, 2948, 2870, 1717, 1629, 1450, 1385, 1199; ESI–MS *m/z* (%): 740.8 $[(M+23)^+$, 100]; Elemental analysis: Found (%): C, 71.53; H, 8.30; N, 1.98 Calcd. For $C_{43}H_{59}NO_8$: C, 71.94; H, 8.28; N, 1.95.

3.2.8. Molecular Tweezer 5h

Prepared according to the general procedure to afford the product **5h** as a yellow crystals; yield 90%; Mp:72–73℃. $[\alpha]_D^{20}$ = +57.91° (*c* 0.11, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (s, 3H, 18-CH_3), 0.86 (d, 3H, *J* = 6.4 Hz, 21-CH_3), 0.96 (s, 3H, 19-CH_3), 3.54 (s, 3H, $COOCH_3$), 3.66 (s, 3H, $COOCH_3$), 4.45-4.50 (m, 1H, 3β-H), 4.98 (s, 1H, 12β-H), 5.03-5.10 (m, 1H, NCH), 5.37 (d, 1H, *J* = 8.4 Hz, CONH), 7.48-7.62 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.01 (d, 1H, *J* = 8.4 Hz, ArH), 8.21 (d, 1H, *J* = 7.2 Hz, ArH), 8.87 (d, 1H, *J* = 8.4 Hz, ArH); IR (KBr, cm^{-1}): 3397, 2923, 2863, 1715, 1516, 1446, 1383, 1198; ESI–MS *m/z* (%): 1521.5 $[(2M+23)^+$, 100]; Elemental analysis: Found (%): C, 68.90; H, 7.89; N, 1.85 Calcd. For $C_{43}H_{59}NO_8S$: C, 68.86; H, 7.93; N, 1.87.

3.2.9. Molecular Tweezer 5i

Prepared according to the general procedure to afford the product **5i** as a yellow crystals; yield 88%; Mp: 86–87℃. $[\alpha]_D^{20}$ = +37.87° (*c* 0.068, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.61 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.68 (s, 3H, 18-CH_3), 0.93 (s, 3H, 19-CH_3), 2.32-2.40 (m, 1H, OH), 2.69-3.23 (m, 2H, $PhCH_2$), 3.52 (s, 3H, $COOCH_3$), 3.71 (s, 3H, $COOCH_3$), 4.58-4.64 (m, 1H, 3β-H), 4.87 (s, 1H, 12β-H), 5.03-5.09 (m, 1H, NCH), 5.14 (d, 1H, *J* = 9.2 Hz, CONH), 6.77 (d, 2H, *J* = 8.4 Hz, ArH), 6.99 (d, 2H, *J* = 8.4 Hz, ArH), 7.48-7.62 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.01 (d, 1H, *J* = 8.4 Hz, ArH), 8.21 (d, 1H, *J* = 8.4 Hz, ArH), 8.87 (d, 1H, *J* = 8.8 Hz, ArH); IR (KBr, cm^{-1}): 3432, 2943, 2868, 1712, 1515, 1445, 1247, 1201; ESI–MS *m/z* (%): 1586.7 $[(2M+23)^+$, 100]; Elemental analysis: Found (%): C, 72.23; H, 7.57; N, 1.81 Calcd. For $C_{47}H_{59}NO_9$: C, 72.19; H, 7.60; N, 1.79.

3.2.10. Molecular Tweezer 5j

Prepared according to the general procedure to afford the product **5j** as a yellow crystals; yield 84%; Mp: 104–105℃. $[\alpha]_D^{20}$ = +55.18° (*c* 0.16, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.71 (s, 3H, 18-CH_3), 0.77 (d, 3H, *J* = 6.0 Hz, 21-CH_3), 0.94 (s, 3H, 19-CH_3), 3.20-3.36 (m, 2H, $PhCH_2$), 3.47 (s, 3H, $COOCH_3$), 3.72 (s, 3H, $COOCH_3$), 4.70-4.75 (m, 1H, 3β-H), 4.94 (s, 1H, 12β-H), 5.03-5.09 (m, 1H, NCH), 5.29 (d, 1H, *J* = 10.0 Hz, CONH), 7.00-7.29 (m, 5H, ArH+indole-CH), 7.42-7.61 (m, 3H, ArH), 7.88 (d, 1H, *J* = 8.0 Hz, ArH), 8.00 (d, 1H, *J* = 8.4 Hz, ArH), 8.16 (d, 1H, *J* = 7.2 Hz, ArH), 8.60 (s, 1H, indole-NH), 8.85 (d, 1H, *J* = 8.4 Hz, ArH); IR (KBr, cm^{-1}): 3397, 2944, 2867, 1714, 1508, 1447, 1245, 1015; ESI–MS *m/z* (%): 827.7 $[(M+23)^+$, 100]; Elemental analysis: Found (%): C, 73.07; H, 7.48; N, 3.50 Calcd. For $C_{49}H_{60}N_2O_8$: C, 73.11; H, 7.51; N, 3.48.

3.3. General Procedure for the Synthesis of Molecular Tweezers 5a-5j Under Conventional Heating Method

Triphosgene (0.2 mmol) was added to a solution of compound **3** (0.5 mmol) in 20 mL dry dichloromethane and 0.1 mL dry pyridine at room temperature. The solution was refluxing for 18 h, and compound **4** was formed, then *L*-amino acid methyl esters hydrochloride (1 mmol) and 0.2 mL dry pyridine were added directly to the mixture which was further refluxed for 17-21 h. The solvent was removed and the residue was diluted with 20 mL ethyl acetate and washed with 10% $NaHCO_3$ (10 mL×3), brine (10 mL×3), and finally dried over anhydrous Na_2SO_4. The crude product was purified by column chromatography on silica gel H with dichloromethane/ethyl acetate as eluant, in 38~71% yields.

CONCLUSION

In summary, we developed a successful synthetic route to prepare a novel class of chiral molecular tweezers based on deoxycholic acid under microwave irradiation in one-pot. The present method has many advantages comparing to the conventional method, such as shorter reaction times, good product yields and finally agreement with the green chemistry protocols. In addition, avoiding the use of toxic phosgene, triphosgene was used in the synthetic process of these tweezers, which provided a convenient and safe procedure for the synthesis of molecular tweezers.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Web site along with the published article.

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