

Article

Chiral Quaternary Ammoniums Derived from Dehydroabietylamine: Synthesis and Application to Alkynylation of Isatin Derivatives Catalyzed by Silver

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Abstract: Abietic acid and its derivatives have broadly been used in fine chemicals and are renewable resources. Its inherent chiral rigid tricyclic phenanthrene skeleton is unique. Its utilities in asymmetric catalysis remain to be explored. A series new amide-type chiral quaternary ammoniums bearing dehydroabietylamine were designed, and prepared by two convenient steps. Acylation of dehydroabietylamine with bromoacetyl chloride afforded amide holding bromoacetyl group in higher yields using triethyl amine as base. Subsequent quaternization reaction gave the desired amide-type chiral quaternary ammoniums. The new chiral quaternary ammoniums can be used as phase-transfer catalyst (PTC) for the transition metal-catalysed alkynylation of isatin derivatives.

Keywords: dehydroabietylamine; chiral quaternary ammoniums; alkynylation; isatin derivatives; phase-transfer catalyst (PTC)



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1. Introduction

Rosin can be abundantly obtained from pine trees as a kind of unique sustainable and renewable biomass resource. Abietic acid is an essential component of rosin, which has an inherent rigid tricyclic diterpene structure with favorable biocompatibility [1]. Abietic acid and its derivatives are therefore used as raw materials for the preparation of many kinds of fine chemicals due to their rigid hydrophobic structure (Figure 1), such as a monomer of polymer or cross-linking agent [2–14], surfactants [15–21], and bioactive compounds [22–27]. As one of the important commercially available derivatives of abietic acid, dehydroabietylamine has been broadly used in the preparation of antitumor therapies [28–31], epoxy resin [32], and quaternary ammonium surfactants [33–35]. However, its potential application has still not been well developed as an optical active amine with a rigid tricyclic phenanthrene skeleton. Chiral thioureas and thiuronium salts containing dehydroabietylamine group are prepared and used for the physical separation of racemic mixtures [36,37]. Wang's group developed a class of a chiral thioureas holding dehydroabietylamine group, which can be used as powerful chiral catalysts for many reactions [38–44], such as Michael addition, aza-Henry reaction, Mannich reaction, and Friedel–Crafts alkylation. A bifunctional squaramide catalyst was designed and utilized for efficient asymmetric Michael/cyclization cascade reaction [45].

Alkynes and their derivatives are important structural motifs in biologically significant pharmaceuticals and potential intermediates for many kinds of transformations. Alkynylation of aldehydes is one of the most efficient approaches for the preparation of optically active secondary propargylic alcohols [46–48]. In the early stages of this transformation,

stoichiometric amounts of metal reagents such as organolithium, organomagnesium, and diorganozinc compounds were needed to increase the nucleophilicity of the alkyne. An efficient method for the catalytic asymmetric alkynylation of aldehydes was developed by Carreira's pioneering work and carried forward by other groups [49–67]. Then, the formation of chiral tertiary alcohols was realized by enantioselective alkynylation of ketones, isatin derivatives and α -ketoesters [68–82]. Maruoka reported an interesting work on enantioselective alkynylation of isatin derivatives using a hybrid catalyst system consisting of chiral phase-transfer catalyst (PTC) and transition-metal catalyst [76]. Much great progress has been made in the counterion-mediated (chiral anion) enantioselective metal catalysis [83–96]. It should be noted that the example of transition metal catalysis on the condition of phase-transfer (chiral cation/ammonium) is very rare [97,98]. Following our interests to the addition of terminal alkyne and utility of chiral natural product [99,100], we had an interest to probe the possibility of quaternary ammonium containing dehydroabietylamine as chiral phase-transfer catalyst. Although the dehydroabietylamine has been broadly used for preparation of quaternary ammonium surfactants, the application of quaternary ammonium bearing dehydroabietylamine as chiral phase-transfer catalyst has been scarcely explored [33–35]. Herein, we report a practical synthesis of new chiral quaternary ammonium bearing dehydroabietylamine, using it as a phase-transfer catalyst for the transition-metal catalytic alkynylation of isatin derivatives.

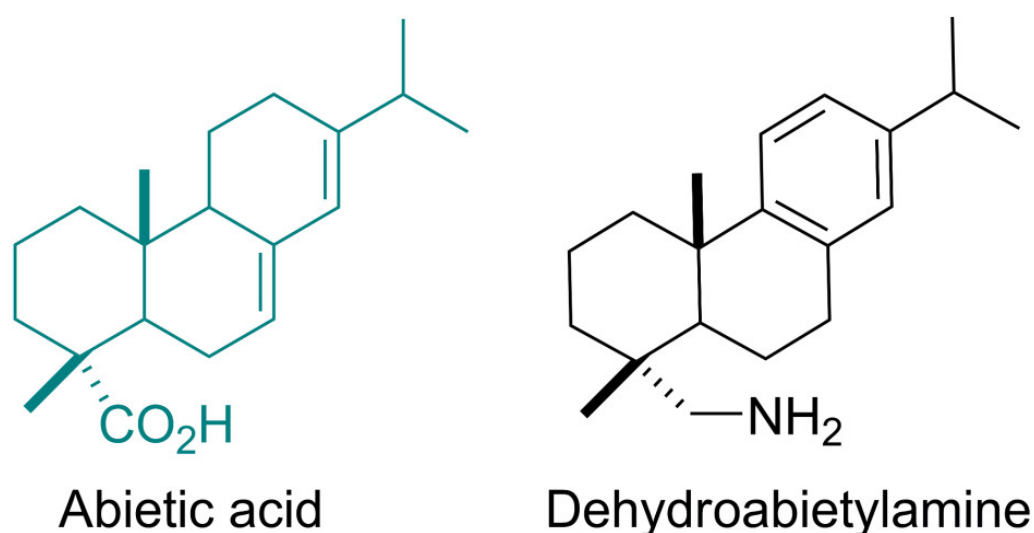


Figure 1. Structure of natural abietic acid and commercially available dehydroabietylamine.

2. Results and Discussion

2.1. Design and Synthesis of Chiral Dehydroabietylamine Quaternary Ammoniums

We envisaged that new chiral dehydroabietylamine quaternary ammonium derivatives should be conveniently prepared by short steps. Thus, five dehydroabietylamine quaternary ammoniums were derived from chain or cyclic tertiary amines (Figure 2).

The synthesis of dehydroabietylamine quaternary ammonium derivatives is shown in Scheme 1. Amidation reaction between bromoacetyl chloride **3** and commercially available dehydroabietylamine **2** produces bromide **4** in 85% yields using triethyl amine as base in CH_2Cl_2 . The quaternization reaction bromide **4** with triethyl amine, 1-methylpiperidine, 1-methylpyrrolidine, N,N,N',N' -tetramethyl-1,3-propanediamine, triethylene diamine (DABCO) gave the corresponding quaternary ammonium derivatives in high yields, respectively.

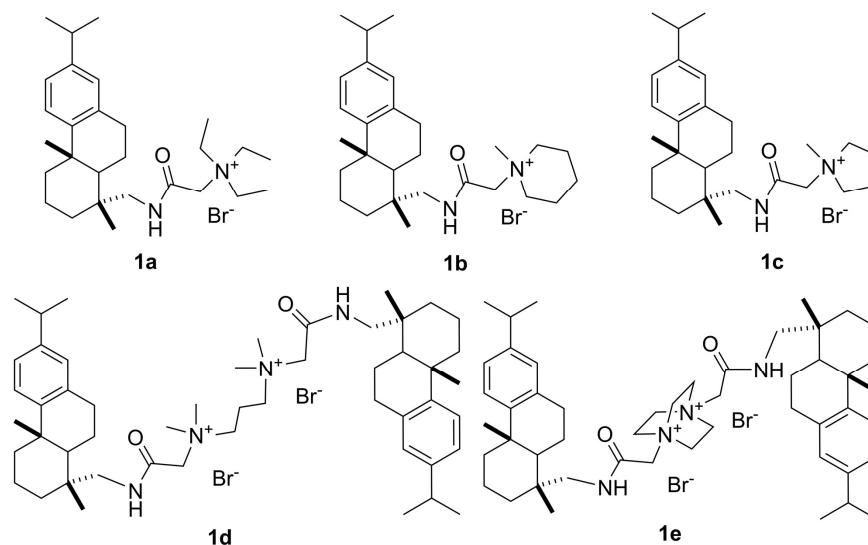
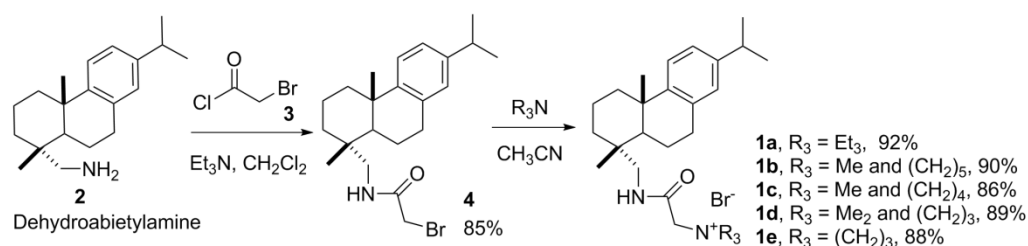


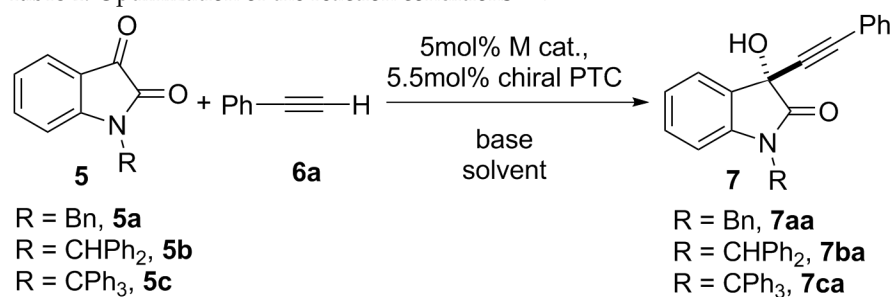
Figure 2. Structure of quaternary ammonium salt derived from commercially available dehydroabietylamine.



Scheme 1. Synthesis of chiral dehydroabietylamine quaternary ammonium derivatives.

2.2. Metal-Catalysed Alkynylation of Isatin Derivatives in the Presence of Chiral Quaternary Ammoniums

Our investigation began with the addition of phenylacetylene **6a** to isatin derivative **5a** (Table 1). Initially, the reaction was carried out by using 5 mol % of AgOAc and 5.5 mol % **1a** as catalyst and K₂CO₃ as base in THF. The desired product can be obtained in a 68% yield without enantioselectivity at 50 °C (Table 1, entry 1). Investigations into the effects of dehydroabietylamine quaternary ammonium derivatives suggested that marginal enantioselectivities were observed when **1d** and **1e** were used (Table 1, entries 2–5). The same enantioselectivity was obtained but the yield was slightly reduced when toluene was used as a solvent (Table 1, entry 6). Examination into the effects of metal catalyst precursors suggested that AgOAc was the best choice, although AgOTf, CuOTf and CuI were suitable catalysts for the present reaction (Table 1, entries 7–10). The reaction was very sluggish at room temperature (Table 1, entry 11). When **5b** was used as substrate, the enantioselectivity was increased to 6%ee (Table 1, entries 12–13). When **5c** was used as substrate, the screening of solvents suggested that the solvents have a distinct influence on catalytic activity (Table 1, entries 14–22). Mesitylene gave best result with respect to the enantioselectivity, whereas, THF, toluene, DMSO, and MeOH gave worse results (entries 14–16, 17–21). Investigations into the effects of bases suggested that all of the examined inorganic base carbonates were suitable bases for the present reaction (Table 1, entries 22–26). Finally, in the absence of AgOAc, no desired compound was observed, suggesting that metal catalyst played an important role in the transformation [101] (Table 1, entry 26).

Table 1. Optimization of the reaction conditions ^(a).

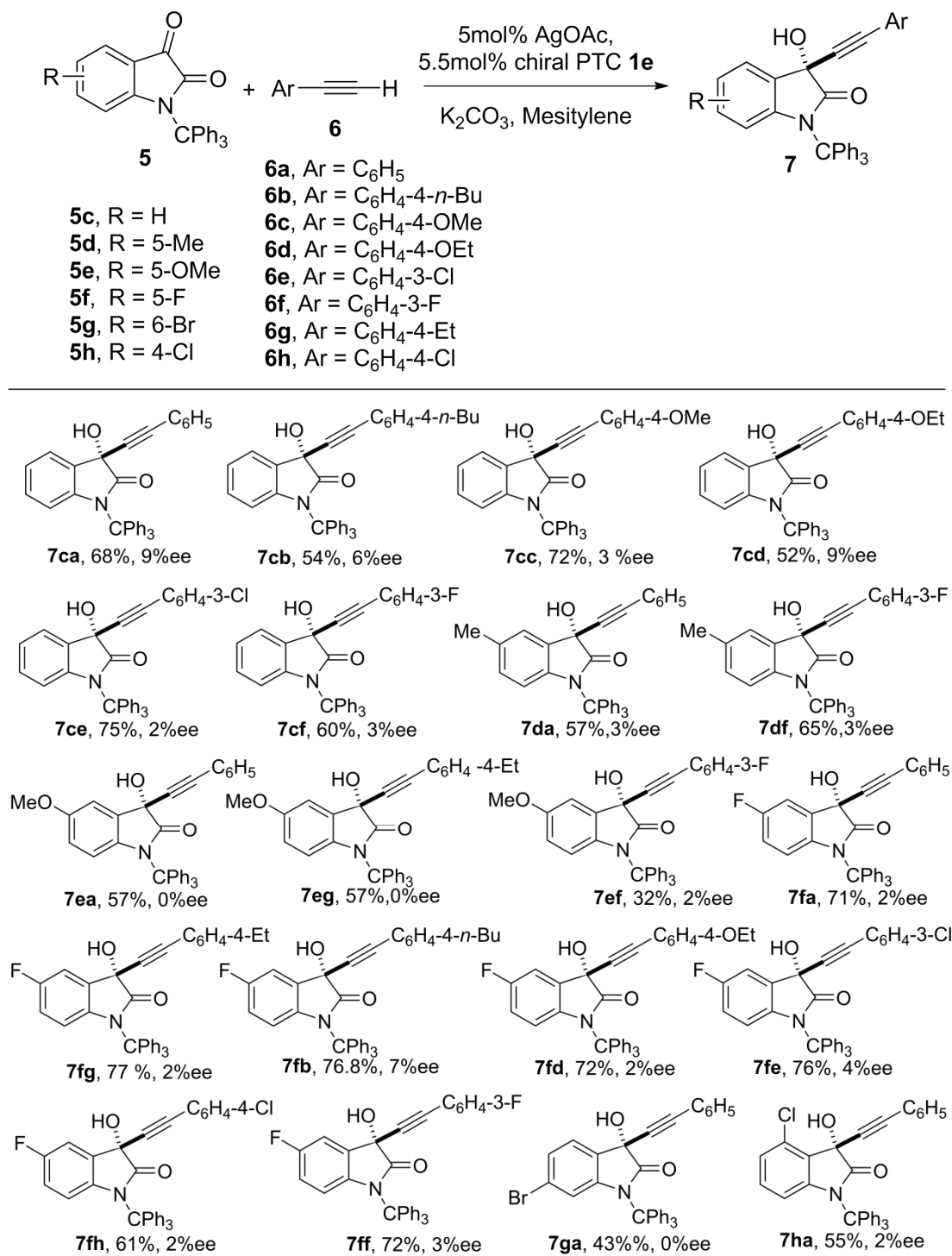
Entry	5	M Cat. (5 mol%)	PTC (5.5%)	Base	Solvent	Time (h)	T (°C)	Yield (%) ^(b)	Ee (%) ^(c)
1	5a	AgOAc	1a	K ₂ CO ₃	THF	12	50	68	0
2	5a	AgOAc	1b	K ₂ CO ₃	THF	12	50	62	0
3	5a	AgOAc	1c	K ₂ CO ₃	THF	12	50	48	0
4	5a	AgOAc	1d	K ₂ CO ₃	THF	12	50	73	2
5	5a	AgOAc	1e	K ₂ CO ₃	THF	12	50	79	3
6	5a	AgOAc	1e	K ₂ CO ₃	toluene	12	50	65	4
7	5a	AgTFA	1e	K ₂ CO ₃	THF	12	50	70	2
8	5a	AgOTf	1e	K ₂ CO ₃	THF	12	50	68	4
9	5a	CuOTf	1e	K ₂ CO ₃	THF	12	50	65	2
10	5a	CuI	1e	K ₂ CO ₃	THF	12	50	56	1
11	5a	AgOAc	1e	K ₂ CO ₃	THF	12	rt	trace	
12	5b	AgOAc	1e	K ₂ CO ₃	THF	12	50	71	2
13	5b	AgOAc	1e	K ₂ CO ₃	toluene	12	50	68	6
14	5c	AgOAc	1e	K ₂ CO ₃	THF	12	50	trace	
15	5c	AgOAc	1e	K ₂ CO ₃	toluene	12	50	trace	
16	5c	AgOAc	1e	K ₂ CO ₃	DMSO	12	50	trace	
17	5c	AgOAc	1e	K ₂ CO ₃	CH ₃ CN	12	50	70	5
18	5c	AgOAc	1e	K ₂ CO ₃	DMF	12	50	38	3
19	5c	AgOAc	1e	K ₂ CO ₃	CH ₂ Cl ₂	12	35	28	2
20	5c	AgOAc	1e	K ₂ CO ₃	dioxane	12	50	23	1
21	5c	AgOAc	1e	K ₂ CO ₃	MeOH	12	50	trace	
22	5c	AgOAc	1e	K ₂ CO ₃	Mesitylene	12	60	68	9
23	5c	AgOAc	1e	NEt ₃	Mesitylene	12	60	41	3
24	5c	AgOAc	1e	Na ₂ CO ₃	Mesitylene	12	60	65	8
25	5c	AgOAc	1e	Li ₂ CO ₃	Mesitylene	12	60	62	6
26	5c	AgOAc	1e	Cs ₂ CO ₃	Mesitylene	12	60	58	3
27	5c		1e	Cs ₂ CO ₃	Mesitylene	12	60	trace	

^(a) Reaction condition: Isatin 5 (0.2 mmol), phenylacetylene 6a (0.4 mmol), base (0.4 mmol), 5 mol % of metal catalyst, 5.5 mol% PTC, solvent (2 mL) at given temperature for 12 h. ^(b) Isolated yield. ^(c) The ee was determined by chiral HPLC analysis.

2.3. Scope for Addition of Alkynes to Isatin Derivatives

Next, studies on the expansion of the substrate scopes were then carried out using the relative optimal reaction conditions (Table 1, entry 21). As shown in Scheme 2, the different substituents and substitution patterns of the isatin and aryl acetylene were all tolerated. The 1-*n*-Butyl-4-ethynylbenzene was successfully added to 5c to give the corresponding product 7cb in a moderate yield and 6%ee. The reaction of 5c with 1-ethynyl-4-methoxybenzene and 1-ethynyl-4-ethoxybenzene, holding a strong electron-donating substituent, gave the desired products 7cc and 7cd in good yield with 3%ee and 9%ee, respectively. Aryl acetylene-bearing, electron-withdrawing substituents, including fluoro- and chloro-groups, were tested for the present reaction, and the desired products (7ce and 7cf) were obtained in good to high yields with 2%ee and 3%ee. The reaction of isatin derivative 5d holding methyl with phenylacetylene 6a and 1-ethynyl-3-fluorobenzene 6f gave the desired products, 7da and 7df, in good yields with 3%ee. The alkylation of isatin derivative 5e tolerating electron-donating substituents with phenylacetylene 6a, 1-ethyl-4-ethynylbenzene 6g, and

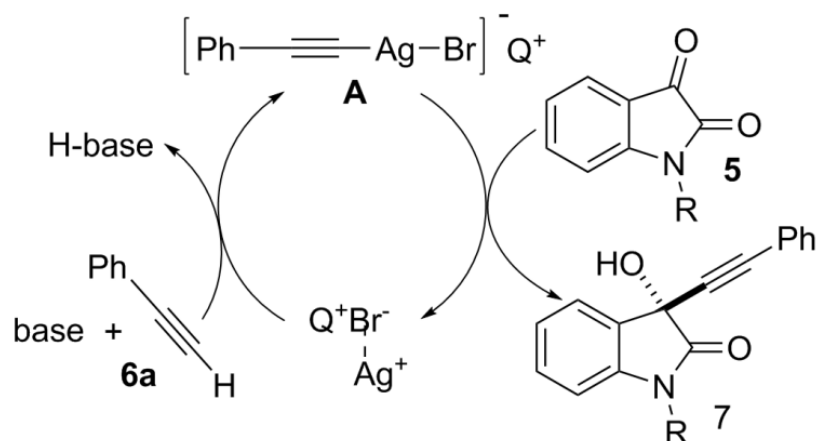
1-ethynyl-3-fluorobenzene **6f** gave the desired products, **7ea**, **7eg**, and **7df**, in moderate to good yields, respectively. Isatin derivatives (**5f**, **5g**, and **5h**) with electron-withdrawing substituents, including fluoro-, bromo-, and chloro-groups, smoothly reacted with aromatic alkynes containing a wide range of functionalities to give the corresponding products **7** in good to high yields. The results indicated that the electronic property and steric hindrance on the isatins or aromatic alkynes had a slight effect on the reaction.



Scheme 2. Substrate scope of the alkynylation reaction ^(a-c). (a) Reaction condition: Isatin **5** (0.2 mmol), arylacetylene **6** (0.4 mmol), base (0.4 mmol), 5 mol % of AgOAc, 5.5 mol% **1e**, solvent (2 mL) at given temperature for 12 h. (b) Isolated yield. (c) The ee was determined by chiral HPLC analysis.

2.4. Mechanism for Ag-Catalysed Alkynylation of Isatin Derivatives

On the basis of the experimental results as well as literature's working hypothesis [47,77], we propose the mechanism of the present Ag catalysed alkynylation of isatin derivatives, as shown in Scheme 3. We speculated that a silver alkynilide is formed by the coordination of terminal alkyne **6** with Ag(I) and deprotonation, which can produce a silver alkynilide ion pair intermediate **A** with chiral quaternary ammoniums catalyst (Q^+Br^-). The nucleophilic addition of the silver alkynilide intermediate **A** to isatin **5** affords the desired product **7**. Comparison with Maruoka's chiral quaternary ammoniums catalyst holding binaphthyl framework, a lower enantioselectivity was observed, which may be caused by the asymmetric center of the catalyst being far away from the nitrogen atom. The future focus will be to further modify the structure of the chiral quaternary ammonium containing dehydroabietylamine to improve the enantioselectivity.



Scheme 3. Proposed mechanism for Ag-catalysed alkynylation in the presence of chiral quaternary ammoniums.

3. Materials and Methods

3.1. General Information

The 1H and ^{13}C NMR data were acquired on a Bruker AV-400 and/or AV-600 MHz spectrometer (Billerica, MA, USA). HRMS data were obtained from Agilent 6520 Q-TOF LC/MS (Santa Clara, CA, USA). Commercial reagents were purchased and used without further purification. THF and toluene were distilled over benzophenone ketyl under nitrogen. DMF and MeOH were distilled over CaH_2 under nitrogen. Dioxane was distilled over $LiAlH_4$ under nitrogen.

3.2. General Procedure for the Synthesis of 2-Bromo-N-(((1*R*,4*a*S)-7-isopropyl-1,4*a*-dimethyl-1,2,3,4,4*a*,9,10,10*a*-octahydrophenanthren-1-yl) methyl) acetamide **4**

To a solution of dehydroabietylamine (2.850 g, 10.0 mmol) and triethylamine (1.525 g, 15.0 mmol) in dry dichloromethane (20 mL) at 0 °C under nitrogen atmosphere, was added dropwise a solution of bromoacetyl chloride (2.340 g, 15.0 mmol) in dry dichloromethane (10 mL). After the completion of addition, the reaction mixture was stirred at room temperature overnight and poured into saturated $NaHCO_3$ solution. The aqueous layer was extracted with dichloromethane (2×25 mL) and the combined organic phases were washed with brine solution, dried over anhydrous Na_2SO_4 and filtered. The solvent was removed under reduced pressure, and the residue was purified through silica gel column chromatography to give the product **4**, 3.440 g, 85%. 1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, $J = 8.0$ Hz, 1H), 7.00 (d, $J = 8.0$ Hz, 1H), 6.89 (s, 1H), 6.63–6.55 (s, amide rotomer, 1H), 4.05 (s, 1H), 3.89 (s, 1H), 3.26–3.20 (m, 1H), 3.17–3.15 (m, 1H), 2.92–2.89 (m, 1H), 2.85–2.81 (m, 2H), 2.30 (d, $J = 8.0$ Hz, 1H), 1.76–1.70 (m, 5H), 1.45–1.40 (m, 3H), 1.28–1.22 (m, 9H), 0.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 165.2, 146.9, 145.7, 134.7, 127.0, 124.2, 123.9, 50.7, 50.2, 45.7, 45.6, 42.9, 38.3, 37.53, 37.47, 36.2, 33.4, 30.4, 29.8, 25.4, 24.0, 23.97, 19.1, 18.63, 18.59,

18.57. HRMS-ESI (m/z): Calcd for $C_{22}H_{33}BrN_2O^+$ $[M+H]^+$: 406.1740, Found: 406.1728 (see the Supplementary Materials).

3.3. General Procedure for the Synthesis of Chiral Dehydroabietylamine Quaternary Ammoniums **1**

To a reaction tube were added above bromide **4** (445 mg, 1.1 mmol), CH_3CN (3 mL), and tertial amine (1 mmol **1a**, **1b**, **1c**; 0.5 mmol **1d**, **1e**). The mixture was stirred at 60 °C overnight. After being cooled to room temperature, AcOEt (10 mL) was added and the resulting solid was washed with AcOEt several times to give the quaternary ammonium salt.

3.3.1. N, N, N-Triethyl-2-(((1R,4aS)-7-Isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl) methyl) amino)-2-oxoethan-1-aminium bromide (**1a**)

A colorless powder, m.p. 217–219 °C. 1H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 7.15 (d, $J = 8.1$ Hz, 1H), 6.97 (d, $J = 8.1$ Hz, 1H), 6.86 (s, 1H), 4.63 (d, $J = 15.2$ Hz, 1H), 4.55 (d, $J = 15.2$ Hz, 1H), 3.54 (q, $J = 7.1$ Hz, 6H), 3.30 (dd, $J = 13.2$ and 7.1 Hz, 1H), 3.08 (dd, $J = 13.4$ and 5.5 Hz, 1H), 2.91–2.79 (m, 3H), 2.26 (d, $J = 12.7$ Hz, 1H), 1.97 (s, 3H), 1.93–1.91 (m, 1H), 1.74–1.69 (m, 3H), 1.55–1.41 (m, 4H), 1.37 (t, $J = 6.9$ Hz, 9H), 1.20 (d, $J = 6.9$ Hz, 6H), 0.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 147.4, 145.5, 134.8, 126.8, 124.1, 123.7, 27.2, 54.8, 50.4, 45.4, 38.3, 37.9, 37.4, 36.4, 35.4, 30.0, 25.3, 24.1, 19.1, 18.6, 18.5, and 8.2. HRMS-ESI (m/z): Calcd for $C_{28}H_{47}N_2O_3^+$ $[M-Br]^+$: 427.3683, Found: 427.3681.

3.3.2. 1-(2-(((1R,4aS)-7-Isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-2-oxoethyl)-1-methylpiperidin-1-ium bromide (**1b**)

A colorless powder, m.p. 278–280 °C. The 1H NMR (600 MHz, $CDCl_3$), δ 9.09 (s, 1H), 7.15 (d, $J = 8.2$ Hz, 1H), 6.97 (d, $J = 8.2$ Hz, 1H), 6.87 (s, 1H), 4.77 (d, $J = 13.5$ Hz, 1H), 4.70 (d, $J = 13.5$ Hz, 1H), 3.94–3.90 (m, 2H), 3.42–3.30 (m, 5H), 3.14–3.10 (m, 1H), 2.91–2.90 (m, 2H), 2.82–2.79 (m, 1H), 2.26 (d, $J = 12.6$ Hz, 1H), 1.96–1.90 (m, 3H), 1.93–1.91 (m, 1H), 1.84–1.65 (m, 10H), 1.58 (d, $J = 13.2$ Hz, 1H), 1.47–1.34 (m, 3H), 1.20 (d, $J = 6.9$ Hz, 6H), 0.97 (s, 3H). The ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.2, 147.3, 145.5, 134.8, 126.8, 124.1, 123.8, 62.7, 62.5, 50.5, 45.5, 38.3, 37.8, 37.4, 36.3, 33.4, 30.1, 25.3, 24.0, 20.9, 20.1, 19.1, 18.6, and 18.5. HRMS-ESI(m/z): Calcd for $C_{28}H_{45}N_2O_3^+$ $[M-Br]^+$: 425.3526, Found: 425.3536.

3.3.3. 1-(2-(((1R,4aS)-7-Isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-2-oxoethyl)-1-methylpyrrolidin-1-ium bromide (**1c**)

A colorless powder, m.p. 215–217 °C. The 1H NMR (600 MHz, $CDCl_3$), δ 8.95 (s, 1H), 7.15 (d, $J = 8.4$ Hz, 1H), 6.97 (d, $J = 8.4$ Hz, 1H), 6.87 (s, 1H), 4.77 (d, $J = 15.2$ Hz, 1H), 4.76 (d, $J = 15.2$ Hz, 1H), 3.99–3.94 (m, 2H), 3.67–3.66 (m, 1H), 3.56–3.54 (m, 1H), 3.30 (s, 3H), 3.26 (dd, $J = 12.6$ and 4.8 Hz, 1H), 3.17 (dd, $J = 13.2$ and 5.4 Hz, 1H), 2.91–2.90 (m, 2H), 2.81–2.79 (m, 1H), 2.29–2.26 (m, 3H), 2.13–2.09 (m, 2H), 1.85 (s, 3H), 1.64–1.61 (m, 3H), 1.55 (d, $J = 11.4$ Hz, 1H), 1.41–1.25 (m, 3H), 1.20 (d, $J = 7.2$ Hz, 6H), 0.97 (s, 3H). The ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 147.3, 145.5, 134.9, 126.8, 124.2, 123.8, 65.4, 63.5, 50.4, 49.9, 45.5, 38.3, 37.9, 37.4, 36.4, 33.4, 30.1, 25.4, 24.0, 21.5, 19.1, 18.6, and 18.5. HRMS-ESI(m/z): Calcd for $C_{27}H_{43}N_2O_3^+$ $[M-Br]^+$: 411.3370, Found: 411.3380.

3.3.4. N1,N3-Bis(2-(((1R,4aS)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-2-oxoethyl)-N1,N1,N3,N3-tetramethylpropane-1,3-diaminium bromide (**1d**)

A colorless powder, m.p. 299–301 °C. The 1H NMR (600 MHz, $CDCl_3$) δ 8.43 (s, 2H), 7.15 (d, $J = 7.8$ Hz, 2H), 6.99 (d, $J = 8.4$ Hz, 2H), 6.88 (s, 2H), 4.61 (d, $J = 14.4$ Hz, 2H), 4.31 (t, $J = 7.2$ Hz, 1H), 3.96–3.94 (m, 2H), 3.76–3.74 (m, 2H), 3.54–3.36 (m, 18H), 3.06–3.05 (m, 2H), 2.91–2.90 (m, 3H), 2.83–2.77 (m, 6H), 2.26 (d, $J = 12.3$ Hz, 2H), 2.04 (d, $J = 5.4$ Hz, 2H), 1.96–1.92 (m, 6H), 1.46–1.45 (m, 6H), 1.29–1.18 (m, 12H), 0.97–0.94 (m, 10H). The ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.7, 147.2, 145.8, 134.7, 131.0, 128.9, 127.0, 124.3, 124.1, 65.6, 62.8, 57.5, 53.5, 52.7, 50.5, 45.5, 38.3, 37.8, 37.5, 33.4, 30.5, 30.4, 29.7, 25.5, 24.1, 23.9, 19.1, 18.7, and 18.4. HRMS-ESI(m/z): Calcd for $C_{51}H_{82}N_4O_2^{2+}$ $[M-2Br]^{2+}$: 782.6427, Found: 782.6427

3.3.5. 1,4-Bis(2-(((1R,4aS)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-2-oxoethyl)-1,4-diazabicyclo[2.2.2]octane-1,4-dium bromide (**1e**)

A colorless powder, m.p. 327–329 °C. The ^1H NMR (400 MHz, DMSO- d_6) δ 8.51 (s, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 6.95 (d, $J = 8.0$ Hz, 2H), 6.85 (s, 2H), 4.44 (dd, $J = 24.4$ and 15.6 Hz, 4H), 4.14 (s, 12H), 3.20–3.16 (m, 2H), 2.98–2.93 (m, 2H), 2.80–2.75 (m, 6H), 2.27 (d, $J = 8.0$ Hz, 2H), 1.76–1.59 (m, 8H), 1.38–1.33 (m, 8H), 1.16–1.13 (m, 18H), 0.89 (s, 6H). The ^{13}C NMR (101 MHz, DMSO- d_6) δ 163.2, 147.4, 145.4, 134.9, 126.9, 124.6, 124.0, 62.2, 51.6, 49.3, 44.6, 38.3, 37.7, 37.5, 36.0, 33.4, 30.0, 25.7, 24.4, 19.2, 18.8, and 18.7. HRMS-ESI(m/z): Calcd for $\text{C}_{50}\text{H}_{76}\text{N}_4\text{O}_2^{2+}$ [M-2Br] $^{2+}$: 764.5957, Found: 764.5955.

3.4. General Procedure for Addition of Alkynes to Isatin Derivatives

Under an atmosphere of N_2 , a reaction tube was charged with isatin (0.20 mmol), AgOAc (0.01 mmol), quaternary ammonium salt (0.011 mmol), base (0.40 mmol). Then, mesitylene (2.0 mL) and alkyne (0.40 mmol) were added successively to the tube. The mixture was stirred at given temperature for 12 h. The mixture was directly purified through silica gel column chromatography to give the product **7**.

3.4.1. (S)-1-Benzyl-3-hydroxy-3-(phenylethynyl)indolin-2-one **7aa**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7aa** as a colorless solid, m.p. 179–181 °C. The ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 8.0$ Hz, 1H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.32–7.23 (m, 9H), 7.14 (d, $J = 8.0$ Hz, 1H), 6.73 (d, $J = 8.0$ Hz, 1H), 4.94 (s, 2H), 3.49 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 174.04, 142.20, 134.99, 132.11, 130.47, 129.10, 128.93, 128.77, 128.27, 127.84, 127.18, 124.82, 123.80, 121.57, 109.96, 86.62, 85.39, 69.62, and 44.12. HRMS-ESI(m/z): Calcd for $\text{C}_{23}\text{H}_{18}\text{NO}_2^+$ [M+H] $^+$: 340.1332, Found: 340.1373.

3.4.2. (S)-1-Benzhydryl-3-hydroxy-3-(phenylethynyl)indolin-2-one **7ba**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7ba** as a colorless solid, m.p. 189–191 °C. The ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, $J = 4.0$ Hz, 1H), 7.48 (d, $J = 8.0$ Hz, 2H), 7.37–7.28 (m, 13H), 7.11 (t, $J = 4.0$ Hz, 2H), 6.98 (s, 1H), 6.51 (d, $J = 4.0$ Hz, 1H), 3.09 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 174.32, 141.87, 137.10, 136.97, 132.14, 129.91, 129.02, 128.71, 128.67, 128.51, 128.36, 128.24, 127.97, 124.79, 123.50, 121.66, 112.03, 86.57, 86.51, 69.33, and 58.50. HRMS-ESI(m/z): Calcd for $\text{C}_{29}\text{H}_{21}\text{NNaO}_2^+$ [M+Na] $^+$: 438.1465, Found: 438.1469.

3.4.3. (S)-3-Hydroxy-3-(phenylethynyl)-1-tritylindolin-2-one **7ca**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7ca** as a yellow solid, m.p. 219–222 °C. The ^1H NMR (400 MHz, CDCl_3) δ 7.54 (d, $J = 4.0$ Hz, 1H), 7.48 (d, $J = 4.0$ Hz, 8H), 7.32–7.28 (m, 3H), 7.26 (t, $J = 8.0$ Hz, 6H), 7.20 (t, $J = 4.0$ Hz, 3H), 7.00 (d, $J = 8.0$ Hz, 1H), 6.98 (dd, $J = 4.0$ Hz and 16.0 Hz, 1H), 6.29 (d, $J = 4.0$ Hz, 1H), 3.61 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 174.57, 141.54, 140.52, 131.02, 128.14, 127.97, 127.95, 127.72, 127.27, 126.77, 126.02, 122.84, 122.05, 115.16, 85.13, 84.86, 73.27, and 68.68. HRMS-ESI(m/z): Calcd for $\text{C}_{35}\text{H}_{25}\text{NNaO}_2^+$ [M+Na] $^+$: 514.1778, Found: 514.1747.

3.4.4. (S)-3-((4-Butylphenyl)ethynyl)-3-hydroxy-1-tritylindolin-2-one **7cb**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7cb** as a yellow solid, m.p. 225–227 °C. The ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, $J = 4.0$ Hz, 1H), 7.51 (d, $J = 8.0$ Hz, 6H), 7.43 (d, $J = 8.0$ Hz, 2H), 7.31–7.22 (m, 12H), 7.18 (d, $J = 12.0$ Hz, 2H), 7.03 (t, $J = 4.0$ Hz, 1H), 6.32 (d, $J = 8.0$ Hz, 1H), 3.29 (s, 1H), 2.65 (t, $J = 8.0$ Hz, 3H), 1.62 (m, $J = 8.0$ Hz, 2H), 1.39 (q, $J = 8.0$ Hz, 2H), 0.96 (t, $J = 4.0$ Hz, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.64, 144.31, 144.58, 141.58, 132.00, 129.19, 129.00, 128.73, 128.45, 127.81, 127.06, 123.82, 123.07, 118.84, 116.19, 86.19, 85.44, 74.27, 69.73, 35.61, 33.34, 22.28, and 13.92. HRMS-ESI(m/z): Calcd for $\text{C}_{39}\text{H}_{33}\text{NNaO}_2^+$ [M+Na] $^+$: 570.2404, Found: 570.2428.

3.4.5. (S)-3-Hydroxy-3-((4-methoxyphenyl)ethynyl)-1-tritylindolin-2-one **7cc**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7cc** as a light yellow solid, m.p. 205–208 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.49 (d, $J = 4.0$ Hz, 2H), 7.47–7.27 (m, 8H), 7.26–7.21 (m, 12H), 7.01 (s, 1H), 6.86 (d, $J = 8.0$ Hz, 2H), 6.29 (d, $J = 8.0$ Hz, 1H), 3.82 (s, 3H), 3.26 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.01, 160.16, 142.59, 141.59, 133.64, 129.20, 128.71, 127.81, 127.07, 123.81, 123.06, 116.19, 113.95, 113.76, 86.05, 84.80, 74.28, 69.75, and 55.32. HRMS-ESI(m/z): Calcd for $\text{C}_{36}\text{H}_{27}\text{NNaO}_3^+$ [$\text{M}+\text{Na}$] $^+$: 544.1883, Found: 544.1875.

3.4.6. (S)-3-((4-Ethoxyphenyl)ethynyl)-3-hydroxy-1-tritylindolin-2-one **7cd**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7cd** as a yellow solid, m.p. 210–213 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.55–7.40 (m, 10H), 7.29–7.20 (m, 9H), 7.01 (q, $J = 4.0$ Hz, 2H), 6.84 (d, $J = 8.0$ Hz, 1H), 6.29 (d, $J = 8.0$ Hz, 1H), 4.05 (q, $J = 8.0$ Hz, 2H), 3.26 (s, 1H), 1.57 (t, $J = 5.2$ Hz, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 170.43, 154.33, 137.34, 136.36, 128.40, 123.97, 123.85, 123.46, 122.57, 121.83, 118.57, 117.82, 110.95, 109.19, 108.31, 80.91, 79.49, 69.04, 64.52, 58.30, and 9.46. HRMS-ESI(m/z): Calcd for $\text{C}_{37}\text{H}_{29}\text{NNaO}_3^+$ [$\text{M}+\text{Na}$] $^+$: 558.2040, Found: 558.2047.

3.4.7. (S)-3-((3-Chlorophenyl)ethynyl)-3-hydroxy-1-tritylindolin-2-one **7ce**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7ce** as a light yellow solid, m.p. 214–217 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.54 (d, $J = 8.0$ Hz, 1H), 7.47–7.45 (m, 7H), 7.35 (t, $J = 8.0$ Hz, 2H), 7.40–7.23 (m, 10H), 7.02 (t, $J = 8.0$ Hz, 1H), 6.96 (t, $J = 8.0$ Hz, 1H), 6.34 (d, $J = 8.0$ Hz, 1H), 3.33 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.39, 141.50, 134.21, 131.95, 130.19, 129.60, 129.38, 129.21, 128.98, 127.85, 127.15, 123.92, 123.21, 116.16, 90.47, 84.43, 74.48, and 69.65. HRMS-ESI(m/z): Calcd for $\text{C}_{35}\text{H}_{24}\text{ClNNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 548.1388, Found: 548.1381.

3.4.8. (S)-3-((3-Fluorophenyl)ethynyl)-3-hydroxy-1-tritylindolin-2-one **7cf**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7cf** as a light yellow solid, m.p. 212–214 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.55 (d, $J = 8.0$ Hz, 1H), 7.47 (d, $J = 4.0$ Hz, 6H), 7.29–7.17 (m, 12H), 7.07–6.96 (m, 3H), 6.31 (d, $J = 8.0$ Hz, 1H), 3.30 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.32, 142.67, 141.47, 129.95, 129.19, 128.96, 128.56, 127.98, 127.84, 127.14, 123.90, 123.19, 118.95, 118.80, 116.56, 116.41, 116.34, 86.98, 84.57, 74.43, and 69.63. HRMS-ESI(m/z): Calcd for $\text{C}_{35}\text{H}_{24}\text{FNNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 532.1683, Found: 532.1687.

3.4.9. (S)-3-Hydroxy-5-methyl-3-(phenylethynyl)-1-tritylindolin-2-one **7da**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7da** as a yellow solid, m.p. 213–215 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.48–7.46 (m, 7H), 7.37–7.33 (m, 3H), 7.28–7.24 (m, 8H), 7.23–7.20 (m, 3H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.16 (d, $J = 8.0$ Hz, 1H), 3.29 (s, 1H), 2.26 (s, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.55, 141.65, 140.17, 132.86, 132.10, 129.32, 129.23, 129.03, 128.80, 128.34, 127.81, 127.08, 124.51, 116.04, 86.28, 85.84, 74.29, 69.80, and 20.81. HRMS-ESI(m/z): Calcd for $\text{C}_{36}\text{H}_{27}\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 528.1734, Found: 528.1738.

3.4.10. (S)-3-((3-Fluorophenyl)ethynyl)-3-hydroxy-5-methyl-1-tritylindolin-2-one **7df**

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7df** as a yellow solid, m.p. 223–225 °C. ^1H NMR (400.0 MHz, CDCl_3), δ 7.46–7.43 (m, 7H), 7.28–7.10 (m, 12H), 7.07 (s, 1H), 6.76 (d, $J = 8.0$ Hz, 1H), 6.17 (d, $J = 8.0$ Hz, 1H), 3.30 (s, 1H), 2.26 (s, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.32, 141.57, 140.22, 129.47, 129.25, 129.22, 17.92, 127.82, 127.30, 127.12, 124.54, 118.97, 116.53, 116.14, 88.45, 87.17, 74.38, 69.71, and 20.79. HRMS-ESI(m/z): Calcd for $\text{C}_{36}\text{H}_{26}\text{FNNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 546.1840, Found: 546.1840.

3.4.11. (S)-3-Hydroxy-5-methoxy-3-(phenylethynyl)-1-tritylindolin-2-one 7ea

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7ea** as a light yellow solid, m.p. 223–225 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.50–7.45 (m, 8H), 7.35–7.28 (m, 3H), 7.28–7.20 (m, 9H), 7.14 (d, $J = 4.0$ Hz, 1H), 6.49 (d, $J = 8.0$ Hz, 1H), 6.18 (d, $J = 8.0$ Hz, 1H), 3.74 (s, 3H), 3.34 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 174.36, 157.81, 141.63, 135.72, 132.09, 131.46, 129.96, 129.24, 128.33, 127.81, 127.61, 127.09, 126.43, 109.72, 108.17, 88.57, 84.94, 69.97, 69.76, and 55.62. HRMS-ESI(m/z): Calcd for $\text{C}_{36}\text{H}_{27}\text{NNaO}_3^+$ [$\text{M}+\text{Na}$] $^+$: 544.1883, Found: 544.1879.

3.4.12. (S)-3-((4-Ethylphenyl)ethynyl)-3-hydroxy-5-methoxy-1-tritylindolin-2-one 7eg

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7eg** as a deep yellow solid, m.p. 198–200 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.47–7.45 (m, 6H), 7.41 (d, $J = 8.0$ Hz, 2H), 7.28–7.25 (m, 6H), 7.23–7.20 (m, 3H), 7.16 (d, $J = 8.0$ Hz, 2H), 7.13 (d, $J = 4.0$ Hz, 1H), 6.48 (dd, $J = 8.0$ Hz and 4.0 Hz, 1H), 6.17 (d, $J = 4.0$ Hz, 1H), 3.74 (s, 3H), 3.30 (s, 1H), 2.66 (q, $J = 4.0$ Hz, 2H), 1.25 (t, $J = 4.0$ Hz, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 179.45, 147.86, 141.65, 134.70, 132.11, 130.05, 129.23, 127.91, 127.80, 127.06, 116.98, 114.30, 109.67, 86.52, 83.97, 74.27, 69.99, 55.62, 28.86, and 15.30. HRMS-ESI(m/z): Calcd for $\text{C}_{38}\text{H}_{31}\text{NNaO}_3^+$ [$\text{M}+\text{Na}$] $^+$: 572.2196, Found: 572.2199.

3.4.13. (S)-3-((3-Fluorophenyl)ethynyl)-3-hydroxy-5-methoxy-1-tritylindolin-2-one 7ef

Silica gel column chromatography (hexane/AcOEt = 4/1) gave **7ef** as a yellow solid, m.p. 215–217 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.46 (d, $J = 4.0$ Hz, 7H), 7.31–7.07 (m, 18H), 6.51 (d, $J = 8.0$ Hz, 1H), 6.20 (d, $J = 8.0$ Hz, 1H), 3.74 (s, 3H), 3.36 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.11, 155.96, 141.54, 135.72, 129.97, 129.63, 129.22, 128.01, 127.84, 127.15, 118.97, 118.82, 117.15, 114.48, 109.73, 87.05, 74.41, 69.89, and 55.63. HRMS-ESI(m/z): Calcd for $\text{C}_{36}\text{H}_{26}\text{FNNaO}_3^+$ [$\text{M}+\text{Na}$] $^+$: 562.1789, Found: 562.1779.

3.4.14. (S)-5-Fluoro-3-hydroxy-3-(phenylethynyl)-1-tritylindolin-2-one 7fa

Silica gel column chromatography (hexane/AcOEt = 4/1) gave **7fa** as a yellow solid, m.p. 240–242 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.50–7.44 (m, 8H), 7.37–7.21 (m, 13H), 6.65 (d, $J = 8.0$ Hz, 1H), 6.23 (d, $J = 8.0$ Hz, 1H), 3.41 (s, 1H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.32, 142.67, 141.47, 129.95, 129.19, 128.96, 128.56, 127.98, 127.84, 127.14, 123.90, 123.19, 118.95, 118.80, 116.56, 116.41, 116.34, 86.98, 84.57, 74.43, and 69.63. HRMS-ESI(m/z): Calcd for $\text{C}_{35}\text{H}_{24}\text{FNNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 532.1683, Found: 532.1685.

3.4.15. (S)-3-((4-Ethylphenyl)ethynyl)-5-fluoro-3-hydroxy-1-tritylindolin-2-one 7fg

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7fg** as a deep yellow solid, m.p. 215–217 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.49–7.44 (m, 8H), 7.32–7.24 (m, 10H), 7.20 (d, $J = 8.0$ Hz, 2H), 6.70–6.66 (m, 1H), 6.23 (dd, $J = 8.0$ Hz and 4.0 Hz, 1H), 3.40 (s, 1H), 2.68 (q, $J = 4.0$ Hz, 2H), 1.24 (t, $J = 4.0$ Hz, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.43, 158.04, 145.80, 141.39, 138.40, 135.28, 132.13, 129.19, 127.97, 127.89, 127.21, 120.95, 118.67, 117.05, 111.58, 86.62, 84.93, 74.46, 69.71, 28.88, and 15.30. HRMS-ESI(m/z): Calcd for $\text{C}_{37}\text{H}_{28}\text{FNNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 560.1996, Found: 560.1992.

3.4.16. (S)-3-((4-Butylphenyl)ethynyl)-5-fluoro-3-hydroxy-1-tritylindolin-2-one 7fb

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7fb** as a deep yellow solid, m.p. 230–232 °C. The ^1H NMR (400 MHz, CDCl_3), δ 7.52 (d, $J = 8.0$ Hz, 6H), 7.46 (d, $J = 4.0$ Hz, 2H), 7.33–7.25 (m, 10H), 7.21 (d, $J = 8.0$ Hz, 2H), 6.70–6.67 (m, 1H), 6.28 (dd, $J = 8.0$ Hz and 4 Hz, 1H), 3.55 (s, 1H), 2.68 (t, $J = 4.0$ Hz, 2H), 1.68–1.61 (m, 2H), 1.42 (q, $J = 4.0$ Hz, 2H), 0.99 (t, $J = 4.0$ Hz, 3H). The ^{13}C NMR (101 MHz, CDCl_3) δ 175.48, 160.00, 158.06, 144.51, 141.43, 138.41, 132.09, 129.22, 128.52, 127.92, 127.22, 118.68, 117.07, 115.36, 115.18, 111.81, 111.61, 86.67, 85.01, 74.50, 69.75, 35.65, 33.36, 22.31, and 13.95. HRMS-ESI(m/z): Calcd for $\text{C}_{39}\text{H}_{32}\text{FNNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$: 588.2309, Found: 588.2316.

3.4.17. (S)-3-((4-Ethoxyphenyl)ethynyl)-5-fluoro-3-hydroxy-1-tritylindolin-2-one 7fd

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7fd** as a deep yellow solid, m.p. 200–202 °C. The ¹H NMR (400 MHz, CDCl₃), δ 7.45 (d, *J* = 4.0 Hz, 6H), 7.41 (d, *J* = 4.0 Hz, 2H), 7.28–7.20 (m, 10H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.66 (td, *J* = 8.0 Hz and 4.0 Hz, 1H), 6.20 (dd, *J* = 8.0 Hz and 4.0 Hz, 1H), 4.04 (q, *J* = 8.0 Hz, 2H), 3.37 (br, 1H), 1.42 (t, *J* = 8.0 Hz, 3H). The ¹³C NMR (101 MHz, CDCl₃) δ 175.48, 160.30, 159.81, 158.19, 141.37, 138.39, 133.70, 130.64, 129.19, 127.90, 127.21, 117.12, 117.07, 115.35, 115.19, 114.03, 113.50, 111.74, 115.35, 115.19, 114.03, 113.50, 111.74, 111.58, 86.51, 84.28, 74.44, 69.73, 63.58, and 14.72. HRMS-ESI(*m/z*): Calcd for C₃₇H₂₈FNNaO₃⁺ [M+H]⁺: 576.1945, Found: 576.1949.

3.4.18. (S)-3-((3-Chlorophenyl)ethynyl)-5-fluoro-3-hydroxy-1-tritylindolin-2-one 7fe

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7fe** as a yellow solid, m.p. 201–203 °C. The ¹H NMR (400 MHz, CDCl₃), δ 7.48(s, 1H), 7.44–7.35 (m, 6H), 7.36 (t, *J* = 4.0 Hz, 2H), 7.29–7.22 (m, 11H), 6.67 (t, *J* = 4.0 Hz, 1H), 6.24 (t, *J* = 4.0 Hz, 1H), 3.36 (s, 1H). The ¹³C NMR (101 MHz, CDCl₃) δ 141.25, 138.48, 130.22, 129.67, 129.57, 129.17, 127.93, 122.29, 122.11, 117.59, 117.26, 115.64, 115.49, 111.83, 111.66, 86.69, 84.83, 74.60, and 69.58. HRMS-ESI(*m/z*): Calcd for C₃₅H₂₃ClFNNaO₂⁺ [M+Na]⁺: 566.1294, Found: 566.1278.

3.4.19. (S)-3-((4-Chlorophenyl)ethynyl)-5-fluoro-3-hydroxy-1-tritylindolin-2-one 7fh

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7fh** as a yellow solid, m.p. 219–221 °C. The ¹H NMR (400 MHz, CDCl₃), δ 7.48–7.35 (m, 7H), 7.28 (t, *J* = 4.0 Hz, 2H), 7.26–7.21 (m, 11H), 6.68 (dd, *J* = 8.0 Hz and 4.0 Hz, 1H), 6.24 (dd, *J* = 4.0 Hz and 4.0 Hz, 1H), 3.40 (s, 1H). The ¹³C NMR (101 MHz, CDCl₃) δ 175.19, 159.83, 158.22, 141.27, 138.48, 135.42, 133.35, 130.18, 129.18, 128.80, 127.98, 127.28, 126.91, 119.96, 117.29, 115.60, 115.45, 111.83, 111.66, 86.48, 85.23, 74.59, and 69.63. HRMS-ESI(*m/z*): Calcd for C₃₅H₂₃ClFNNaO₂⁺ [M+Na]⁺: 566.1294, Found: 566.1283.

3.4.20. (S)-5-Fluoro-3-((3-fluorophenyl)ethynyl)-3-hydroxy-1-tritylindolin-2-one 7ff

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7ff** as a yellow solid, m.p. 211–213 °C. The ¹H NMR (400 MHz, CDCl₃), δ 7.45 (d, *J* = 8.0 Hz, 6H), 7.32–7.22 (m, 12H), 7.18 (d, *J* = 4.0 Hz, 1H), 7.09 (t, *J* = 4.0 Hz, 1H), 6.68 (t, *J* = 8.0 Hz, 1H), 6.24 (dd, *J* = 8.0 Hz and 4.0 Hz, 1H), 3.42 (s, 1H). The ¹³C NMR (101 MHz, CDCl₃) δ 175.14, 163.08, 161.44, 159.84, 158.22, 141.26, 138.48, 130.09, 130.03, 129.17, 128.03, 128.01, 127.93, 122.28, 119.00, 118.85, 117.30, 117.25, 116.76, 116.62, 115.63, 115.47, 111.84, 111.68, 86.42, 84.99, 74.59, and 69.59. HRMS-ESI(*m/z*): Calcd for C₃₅H₂₃F₂NNaO₂⁺ [M+H]⁺: 550.1589, Found: 550.1582.

3.4.21. (S)-6-Bromo-3-hydroxy-3-(phenylethynyl)-1-tritylindolin-2-one 7ga

Silica gel column chromatography (hexane/AcOEt = 3/1) gave **7ga** as a light yellow solid, m.p. 230–232 °C. The ¹H NMR (400 MHz, CDCl₃), δ 7.48–7.15 (m, 21H), 7.15 (dd, *J* = 8.0 and 1.4 Hz, 1H), 6.35 (d, *J* = 1.4 Hz, 1H), 3.38 (s, 1H). The ¹³C NMR (101 MHz, CDCl₃) δ 193.74, 159.54, 147.65, 143.86, 141.16, 132.08, 129.22, 129.14, 128.39, 127.96, 127.33, 126.09, 125.10, 122.57, 121.52, 119.30, 87.97, 85.51, 74.65, and 69.28. HRMS-ESI(*m/z*): Calcd for C₃₅H₂₄BrNNaO₂⁺ [M+H]⁺: 592.0883, Found: 592.0890.

3.4.22. (S)-4-Chloro-3-hydroxy-3-(phenylethynyl)-1-tritylindolin-2-one 7ha

Silica gel column chromatography (hexane/AcOEt = 5/1) gave **7ha** as a light yellow solid, m.p. 212–214 °C. The ¹H NMR (400 MHz, CDCl₃), δ 7.52 (dd, *J* = 8.0 Hz and 4.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 6H), 7.35–7.23 (m, 12H), 6.98 (t, *J* = 8.0 Hz, 1H), 6.89 (t, *J* = 8.0 Hz, 1H), 6.23 (d, *J* = 8.0 Hz, 1H), 3.37 (s, 1H). The ¹³C NMR (101 MHz, CDCl₃) δ 174.25, 144.35, 141.27, 132.29, 131.23, 129.56, 129.25, 129.19, 128.38, 127.94, 127.30, 125.69, 124.04, 121.73, 114.82, 86.18, 84.16, 74.81, and 69.63. HRMS-ESI(*m/z*): Calcd for C₃₅H₂₄ClNNaO₂⁺ [M+Na]⁺: 548.1388, Found: 548.1384.

4. Conclusions

In summary, a series of new amide-type chiral quaternary ammoniums bearing dehydroabietylamine were prepared by acylation of dehydroabietylamine with bromoacetyl chloride in higher yields using triethyl amine as base and subsequent quaternization reaction with tertial amines and/or tertial diamines. To some extent enantioselectivities were observed when using them as phase-transfer catalyst for the transition-metal catalytic alkynylation of isatin derivatives. Their chiral recognition ability or application in the others' asymmetric transformation will be examined.

Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/catal11121479/s1>, The ¹H NMR and ¹³C NMR of compounds 1, 4, 7; HPLC chart of compounds 7.

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