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Synthesis of Branched Tryptamines via the Domino Cloke–Stevens/Grandberg Rearrangement

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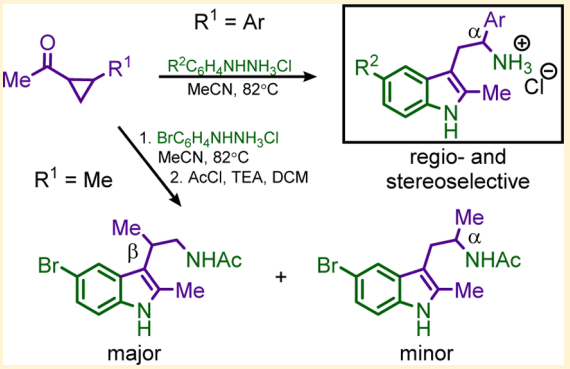
Supporting Information

ABSTRACT: The rearrangement of cyclopropylketone arylhydrazones generated *in situ* from arylhydrazine hydrochlorides and ketones leads to formation of tryptamine derivatives. The use of (2-arylcyclopropyl)ethanones in the reactions with model 4-bromophenylhydrazine hydrochloride gives branched tryptamines with aryl groups in the α-position to the amino group, while (2-methylcyclopropyl)ethanone gives a mixture of α- and β-substituted products in a ratio of 1:3. The method was found effective in the synthesis of enantiomerically pure tryptamine. Thus, (*R*,*R*)-(2-phenylcyclopropyl)ethanone gives the (*S*)-α-phenyltryptamine derivative with an enantiomeric excess over 99%.



Tryptamine derivatives possess high potential for the treatment of various diseases ranging from migraine[1] and obesity[2] to tumors.[3−5] Nevertheless, the application of many amines in pharmaceutics is limited to a large extent by their ready degradation in an organism by such enzymes as monoamine oxidase.[6] The chain branching in amines is known to be one of the methods to reduce the rate of drug metabolism.[7] The majority of known methods for the synthesis of branched tryptamines so far are based on modifications of indole derivatives.[8−17] There are scarce methods to construct a substituted aminoethylene fragment and an indole ring simultaneously. Thus, the tandem hydroformylation/Fischer indole synthesis starting from branched amino olefins and arylhydrazines gives branched tryptamines.[18] Tricyclic constrained tryptamine analogues are available via Fisher indolization of arylhydrazines and chiral bicyclic imines.[19]

Recently,[20] we have given a report on a new approach to tryptamines via Cloke–Stevens[21,22] and subsequent Grandberg[23] rearrangements of cyclopropylethanone arylhydrazones, wherein 4-bromophenylhydrazones demonstrated higher yields of tryptamines. With regard to our previous investigations on the cyclopropyliminium (Cloke–Stevens) rearrangement of cyclopropylazoles[24−26] including those[27] substituted at the cyclopropyl moiety, we assumed that cyclopropyl methyl ketone arylhydrazones substituted at the small cycle rearrange into branched tryptamines. The substituted ketones are easily available via the subsequent aldol condensation[28] and Corey–Chaykovsky[29] cyclopropanation.

In the previous studies, we have found that the rearrangement proceeds using cyclopropyl methyl ketone and either arylhydrazine hydrochloride or free arylhydrazine as starting material, the latter requiring addition of ammonium iodide, in either ethanol or acetonitrile.[5,20] The use of arylhydrazine and NH_4I gave lower yield of desired tryptamines and increased the yield of undesired tetrahydropyridazines. Although the reaction is slower in acetonitrile due to both the poor solubility of starting hydrochloride and its aprotic properties, this protocol is appealing since in most cases the product is separated by filtration.

The mechanism[20] that we suggested previously for the rearrangement of cyclopropylketone arylhydrazones formed *in situ* from the corresponding ketones and arylhydrazine hydrochlorides involves nucleophilic ring-opening of cyclopropane by chloride anion with subsequent ring-closure to give five- or six-membered cycles. Herein, when 2-substituted cyclopropylketones are introduced into the reaction (Table 1), the ring-opening can proceed via attack at two inequivalent carbon atoms in the cycle (paths **a** and **b**). However, the use of 2-arylcyclopropylethanones **1a**–**f** as starting material leads to ring-opening in intermediate **2** at the more substituted carbon

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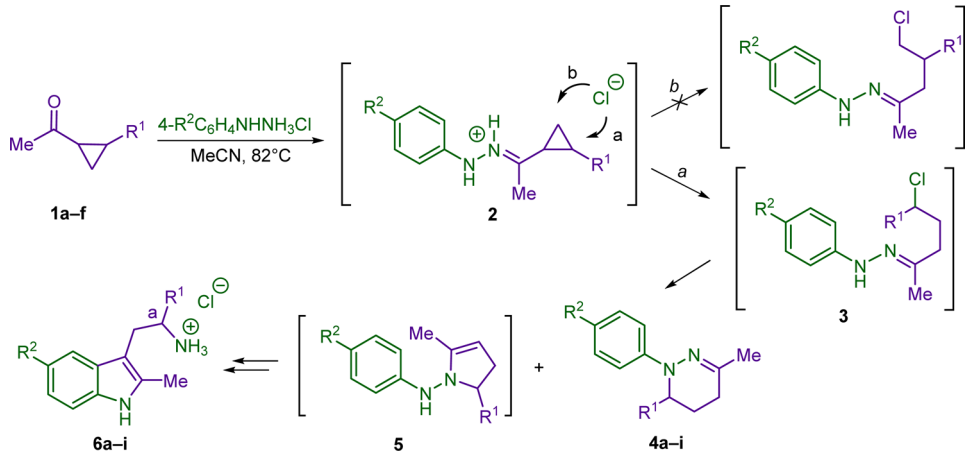
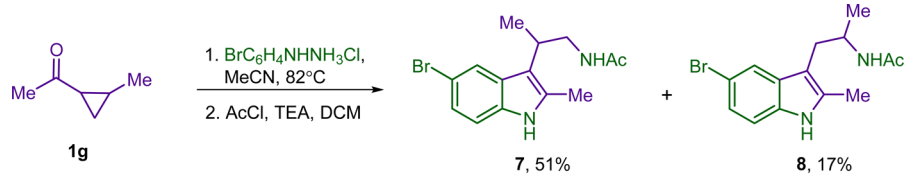
Table 1. Rearrangement of 2-Arylcyclopropylketone 4-Bromophenylhydrazones into Tryptamines and Tetrahydropyridazines



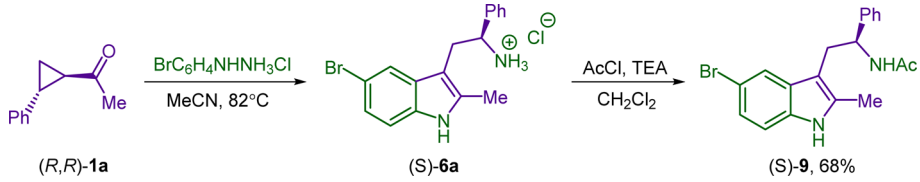
entry	ketone	R^1	R^2	products (yield, %)[a]	
1	**1a**	Ph	Br	**6a** (62)	**4a** (5)
2	**1b**	4-MeC_6H_4	Br	**6b** (68)	**4b** (9)
3	**1c**	4-$MeOC_6H_4$	Br	**6c** (51)	**4c** (12)
4	**1d**	4-FC_6H_4	Br	**6d** (50)	**4d** (19)
5	**1e**	4-ClC_6H_4	Br	**6e** (57)	**6e** (traces)
6	**1f**	2,4-$Cl_2C_6H_3$	Br	**6f** (66)	**6f** (traces)
7	**1a**	Ph	F	**6g** (49)	**4g** (11)
8	**1a**	Ph	H	**6h** (76)	**4h** (12)
9	**1a**	Ph	Me	**6i** (42)	**6i** (traces)

[a]Yields are given after purification by column chromatography.

Scheme 1. Rearrangement of (2-Methylcyclopropyl)ethanone 4-Bromophenylhydrazone into a Mixture of α- and β-Methylated Tryptamines 7 and 8



Scheme 2. Transformation of (*R*,*R*)-1a into (*S*)-α-Phenyltryptamine (*S*)-6a, and Further into (*S*)-9



atom (path **a**) to give γ-chloroketone arylhydrazones **3**, while path **b** is not realized. Subsequent cyclization gives tetrahydropyridazines **4a–i** as minor products and arylaminopyrrolines **5**, which in turn undergo a Fischer-type rearrangement into tryptamine derivative hydrochlorides **6a–i** as major products. It is worth noting that the formation of only trace amounts of tetrahydropyridazines **4e,f,i** is observed, while the yields of compounds **4a–d,g,h** are 5–19%, all products **4** tending to resinification.

Concerning the reaction scope, the method is most useful for the synthesis of 5-substituted tryptamines. However, an approach to other derivatives has been developed via regiocontrol in the Grandberg rearrangement by protection of an *o*-position in arylhydrazines with bromine.[30] It is also noteworthy that strong electron-withdrawing groups in the aromatic moiety reduce the cyclopropane ring-opening, as we have shown previously.[20]

In contrast to arylated derivatives, (2-methylcyclopropyl)-ethanone (**1g**) hydrazone rearranged with ring-opening proceeding preliminary at the less substituted carbon atom (path **b**) into β-substituted tryptamine and minor formation of α-substituted tryptamine. The products were converted into acylated derivatives **7** and **8** (Scheme 1), and the use of HPLC was required to separate the mixture. The introduction of methyl 2-acetylcyclopropanecarboxylate into the reaction did not give the desired tryptamine. It is worth mentioning that, besides NMR spectroscopy, the α- and β-substituted tryptamines are easily distinguished by mass spectrometry, namely, by the presence of a specific C_α–C_β fragmentation pattern.

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We have also applied this approach in the synthesis of an optically pure tryptamine derivative. The reaction of (*R*,*R*)-**1a** (ee > 99%) with 4-bromophenylhydrazine hydrochlorides and subsequent acylation of tryptamine hydrochloride (*S*)-**6a** obtained led to formation of acylated tryptamine (*S*)-**9** with an enantiomeric excess over 99% (Scheme 2). Direct acylation of the reaction mixture without separation of (*S*)-**6a** gave a higher yield (72%) of acylated tryptamine **9**, but with lower enantiomeric excess (92%) of (*S*)-**9**. It is worth noting that, in this case, double inversion of a carbon atom which is implied by the mechanism proposed changes configuration from (*R*) to (*S*) due to the CIP priority change. The absolute configuration was determined on the basis of single-crystal X-ray data.

Thus, we have developed a new method for the synthesis of α-arylated tryptamines based on the rearrangement of (2-arylcyclopropyl)ethanone arylhydrazones. The introduction of cyclopropyl ketone containing a methyl group into the reaction gave a mixture of isomers with predominant formation of the β-substituted derivative. We have also demonstrated the potential of our method in the synthesis of an optically pure α-phenyltryptamine derivative from a chiral ketone.

EXPERIMENTAL SECTION

General. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded at 300, 75, and 282 MHz, respectively, in $CDCl_3$ or DMSO-d_6 with tetramethylsilane as an internal reference standard. The NMR signal assignment was accomplished using DEPT, COSY, HSQC, HMBC spectra. High-resolution mass spectra (HRMS) were recorded using an ESI-TOF spectrometer. Column chromatography was performed with SiO_2 (230−400 mesh). Unless noted otherwise, all of the reagents were obtained from commercial suppliers and used without additional purification. DCM was preliminarily distilled over NaOH. 2-Arylcyclopropylethanones,[29] arylidenacetones,[28] 2-methylcyclopropylethanone,[31] and (*R*,*R*)-2-phenylcyclopropylethanone[32,33] were synthesized according to the literature procedures.

The X-ray crystal structure analysis of (*S*)-**9** was made on a diffractometer with a CCD detector (Mo Kα radiation, λ = 0.71073 Å, graphite monochromator, T = 120 K, 2θmax = 61.4°). The structure was solved in Olex2,[34,35] with the ShelXT[36] structure solution program using Direct Methods and refined with the ShelXL[36,37] refinement package using Least Squares minimization. Absorption correction was performed by the multiscan method implemented in SADABS.[38] The absolute configuration of the only stereocenter was determined to be S by anomalous dispersion (Flack parameter: 0.005(4)). Non-hydrogen atoms were refined anisotropically. Crystal data for (*S*)-**9**: $C_{19}H_{19}BrN_2O$ (M = 122.94 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 8.1146(11) Å, b = 19.140(3) Å, c = 11.5187(16) Å, β = 110.431(3), V = 1676.5(4) Å^3, Z = 4, T = 120 K, μ(Mo Kα) = 12.607 mm^{-1}, D_{calc} = 2.557 g/cm^3, 23 329 reflections measured (3.774 ≤ 2Θ ≤ 61.432), 10 315 unique (R_{int} = 0.0445, R_{sigma} = 0.0837), which were used in all calculations. The final R_1 was 0.0384 (I > 2σ(I)) and wR_2 was 0.0776 (all data). The crystal structure has been deposited with the Cambridge Crystallographic Data Center (CCDC reference number 1496493).

General Procedure for the Preparation of 2-Arylcyclopropylethanones 1. Potassium *tert*-butoxide (9.9 mmol) was added to a solution of Me_3SOI (9.1 mmol) in anhydrous DMSO (20 mL), and the mixture stirred for 0.5 h. Arylideneacetone (8.3 mmol) was added, and the mixture stirred for 3 h. The reaction mixture was treated with water and extracted with CH_2Cl_2. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and evaporated. Column chromatography on SiO_2 (chloroform−hexanes, 2:1) gave the desired product.

*1-(2-(4-Methoxyphenyl)cyclopropyl)ethanone (**1c**).* Colorless oil (0.91 g, 58%). IR (KBr) 3002, 2957, 2836, 1696, 1516, 1249 cm^{-1}. MS (m/z (rel intens, %)) 190 (38, M$^+$), 147 (100), 132 (9), 115 (12), 91 (18). HRMS: calcd for $C_{12}H_{15}O_2$ M + H, 191.1067, found: m/z 191.1067. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.10−6.96 (m, 2H, H(2,6)), 6.90−6.78 (m, 2H, H(3,5)), 3.79 (s, 3H, MeO), 2.50 (ddd, 1H, CHAr, J = 9.2, 6.7, 4.1 Hz), 2.30 (s, 3H, Me), 2.15 (ddd, 1H, CHAc, J = 8.2, 5.0, 4.1 Hz), 1.64 (ddd, 1H, CH_2, J = 9.2, 5.0, 4.3 Hz), 1.33 (ddd, 1H, CH_2, J = 8.2, 6.7, 4.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.0 (CO), 158.5 (C(4)), 132.4 (C(1)), 127.3 (C(2,6)), 114.1 (C(3,5)), 55.4 (MeO), 32.8 (CHAc), 30.8 (Me), 28.7 (CHAr), 18.9 (CH_2).

*1-(2-(4-Chlorophenyl)cyclopropyl)ethanone (**1e**).* Colorless oil (1.05 g, 65%). IR (KBr) 3005, 2923, 1699, 1496, 1393 cm^{-1}. MS (m/z (rel intens, %)) 194, 196 (63, M$^+$), 151, 153 (100), 144 (14), 116 (39), 115 (52). HRMS: calcd for $C_{11}H_{12}ClO$ M + H, 195.0571, found: m/z 195.0570. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27−7.22 (m, 2H, H(3, 5)), 7.05−6.99 (m, 2H, H(2, 6)), 2.50 (ddd, 1H, CHAr, J = 9.1, 6.6, 4.1 Hz), 2.30 (s, 3H, Me), 2.18 (ddd, 1H, CHAc, J = 8.3, 5.2, 4.1 Hz), 1.66 (ddd, 1H, CH_2, J = 9.4, 5.2, 4.4 Hz), 1.33 (ddd, 1H, CH_2, J = 8.3, 6.6, 4.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.5 (CO), 139.0 (C(4)), 132.3 (C(1)), 128.7 (C(3, 5)), 127.5 (C(2, 6)), 32.8 (CHAc), 30.9 (Me), 28.3 (CHAr), 19.1 (CH_2).

*1-(2-(2,4-Dichlorophenyl)cyclopropyl)ethanone (**1f**).* Colorless oil (1.18 g, 62%). IR (KBr) 3007, 2920, 1699, 1479, 1396 cm^{-1}. MS (m/z (rel intens, %)) 228, 230 (100, M$^+$), 185, 187 (85), 178, 180 (33), 150, 152 (57), 149, 151 (51), 115 (50). HRMS: calcd for $C_{11}H_{11}Cl_2O$ M + H, 229.0181, found: m/z 229.0184. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (d, 1H, H(3), J = 2.1 Hz), 7.17 (dd, 1H, H(5), J = 8.3, 2.1 Hz), 6.97 (d, 1H, H(6), J = 8.3 Hz), 2.63 (ddd, 1H, CHAr, J = 8.9, 7.0, 4.4 Hz), 2.34 (s, 3H, Me), 2.07−2.00 (m, 1H, CHAc), 1.71−1.64 (m, 1H, CH_2), 1.36 (ddd, 1H, CH_2, J = 7.9, 7.0, 4.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 206.5 (CO), 136.6 and 136.5 (C(1) and C(4)), 133.2 (C(2)), 129.3 (C(3)), 128.4 (C(6)), 127.2 (C(5)), 31.2 (CHAc), 30.8 (Me), 26.7 (CHAr), 16.9 (CH_2).

General Procedure for the Preparation of Tryptamines 6 and Tetrahydropyridazines 4. A mixture of arylhydrazine hydrochloride (1.2 mmol) and 2-arylcyclopropylethanone **1a−f** (1.56 mmol) in acetonitrile (10 mL) was heated at reflux for 16 h. Tryptamines **6a,b,d−g** precipitated and were filtered, while derivatives **6c,h−i** were extracted with water from the mixture diluted with chloroform. Tryptamines **6a−i** contaminated with NH_4Cl were additionally purified by flash column chromatography ($CHCl_3$−EtOH, 4:1). The organic phases (filtrates or extracts) were evaporated and subjected to column chromatography ($CHCl_3$−hexane, 2:1) to give tetrahydropyridazines **4a−d,g,h**.

*2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-phenylethan-1-aminium Chloride (**6a**).* Colorless crystals (0.27 g, 62%), mp: 151−153 °C. IR (KBr) 3459, 2958, 2911, 1608, 1502, 1465 cm^{-1}. MS (m/z (rel intens, %)) 223, 225 (21, $C_{10}H_{10}BrN^+$), 222, 224 (15, $C_{10}H_9BrN^+$), 143 (14, $C_{10}H_9N^+$), 106 (100, $CHPhNH_2^+$). HRMS: calcd for $C_{17}H_{18}BrN_2$ M − Cl, 329.0648, 331.0627, found m/z 329.0639, 331.0622. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.00 (s, 1H, NH), 8.84 (s, 3H, NH_3^+), 7.56 (d, 1H, H(4), J = 1.5 Hz), 7.24−7.38 (m, 5H, Ph), 7.16 (d, 1H, H(7), J = 8.5 Hz), 7.05 (dd, 1H, H(6), J = 8.5, 1.5 Hz), 4.20−4.33 (m, 1H, CH), 3.42 (dd, 1H, CH_2, J = 14.0, 4.1 Hz), 3.08 (dd, 1H, CH_2, J = 14.0, 10.4 Hz), 1.82 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 137.8 (*i*-Ph), 135.3 (C(2)), 133.7 (C(5)), 130.0 (C(7a)), 128.3, 127.4 (*o*-,*m*-Ph), 128.2 (*p*-Ph), 122.4 (C(6)), 119.6 (C(4)), 112.3 (C(7)), 111.0 (C(3a)), 104.3 (C(3)), 55.3 (CH), 30.3 (CH_2), 10.7 (Me).

*2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-(p-tolyl)ethan-1-aminium Chloride (**6b**).* Colorless crystals (0.31 g, 68%), mp: 169−171 °C. IR (KBr) 3417, 3346, 2921, 2887, 1627, 1518, 1470 cm^{-1}. MS (m/z (rel intens, %)) 223, 225 (7, $C_{10}H_{10}BrN^+$), 222, 224 (8, $C_{10}H_9BrN^+$), 143 (7, $C_{10}H_9N^+$), 120 (100, $CH(C_7H_7)NH_2^+$). HRMS: calcd for $C_{18}H_{20}BrN_2$ M − Cl, 343.0804, 345.0785, found m/z 343.0792, 345.0778. ^{1}H NMR (300 MHz, DMSO-d_6): δ 11.02 (s, 1H, NH), 8.80 (s, 3H, NH_3^+), 7.46 (d, 1H, 1H, H(4), J = 0.8 Hz), 7.19 (d, 2H, H(2′,6′), J = 7.8 Hz), 7.15 (d, 1H, H(7), J = 8.6 Hz), 7.10 (d, 2H, H(3′,5′), J = 7.8 Hz), 7.04 (dd, 1H, H(6), J = 8.6, 0.8 Hz), 4.21 (br.s, 1H, CH), 3.41 (m, 1H, H^a from CH_2), 3.06 (dd, 1H, H^b from CH_2, J = 13.1, 10.7 Hz), 2.27 (s, 3H, ArMe), 1.88 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 137.6 (C(1′)), 135.3 (C(2)), 134.8 (C(4′)), 133.7 (C(5)), 130.0 (C(7a)), 128.8 (C(3′, 5′)), 127.4 (C(2′,6′)),

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122.3 (C(6)), 119.6 (C(4)), 112.2 (C(7)), 111.0 (C(3a)), 104.4 (C(3)), 55.1 (CH), 30.3 (CH_2), 20.7 (ArMe), 10.8 (Me).

*2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-(4-methoxyphenyl)ethan-1-aminium Chloride (**6c**).* Colorless crystals (0.24 g, 51%), mp: 97−99 °C. IR (KBr) 3410, 2912, 1610, 1512, 1248 cm^{-1}. MS (*m*/*z* (rel intens, %)) 223, 225 (7, $C_{10}H_{10}BrN^+$), 222, 224 (16, $C_{10}H_9BrN^+$), 143 (6, $C_{10}H_9N^+$), 136 (100, $CH(MeOC_6H_4)NH_2^+$). HRMS: calcd for $C_{18}H_{20}BrN_2O$ M − Cl, 359.0754, 361.0734, found *m*/*z* 359.0758, 361.0740. ^1H NMR (300 MHz, DMSO-d_6): δ 11.02 (s, 1H, NH), 8.76 (s, 3H, NH_3^+), 7.50 (d, 1H, H(4), *J* = 1.5 Hz), 7.25 (d, 2H, H(2′,6′), *J* = 8.6 Hz), 7.15 (d, *J* = 8.5 Hz, 1H, H(7)), 7.04 (dd, *J* = 8.5, 1.5 Hz, 1H, H(6)), 6.86 (d, 2H, H(3′,5′), *J* = 8.6 Hz), 4.27−4.15 (m, 1H, CH), 3.72 (s, 3H, MeO), 3.39 (dd, 1H, H^a from CH_2, *J* = 13.7, 3.6 Hz), 3.06 (dd, 1H, H^b from CH_2, *J* = 13.7, 10.5 Hz), 1.90 (s, 3H, Me); ^{13}C NMR (75 MHz, DMSO-d_6): δ 159.3 (C(4′)), 135.3 (C(2)), 133.7 (C(5)), 130.0 (C(7a)), 129.7 (C(1′)), 128.8 (C(2′, 6′)), 122.3 (C(6)), 119.7 (C(4)), 113.7 (C(3′,5′)), 112.2 (C(7)) 111.0 (C(3a)), 104.5 (C(3)), 55.1 (MeO), 54.9 (CH), 30.3 (CH_2), 10.9 (Me).

*2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-(4-fluorophenyl)ethan-1-aminium Chloride (**6d**).* Colorless crystals (0.23 g, 50%), decomp. over 200 °C. IR (KBr) 3405, 2852, 1517, 1470, 1224 cm^{-1}. MS (*m*/*z* (rel intens, %)) 223, 225 (45, $C_{10}H_{10}BrN^+$), 222, 224 (46, $C_{10}H_9BrN^+$), 143 (20, $C_{10}H_9N^+$), 124 (100, $CH(FC_6H_4)NH_2^+$). HRMS: calcd for $C_{17}H_{17}BrFN_2$ M − Cl, 347.0554, 349.0533, found *m*/*z* 347.0560, 349.0536. ^1H NMR (300 MHz, DMSO-d_6): δ 11.02 (s, 1H, NH), 8.85 (s, 3H, NH_3^+), 7.50 (d, 1H, H(4), *J* = 1.7 Hz), 7.38 (dd, 2H, H(3′,5′), *J* = 8.6, 5.5 Hz), 7.16 (d, 1H, H(7), *J* = 8.4 Hz), 7.13 (d, 2H, H(2′,6′), *J* = 10.1 Hz), 7.05 (dd, 1H, H(6), *J* = 8.4, 1.7 Hz), 4.39−4.22 (m, 1H, CH), 3.42 (m, 1H, H^a from CH_2), 3.08 (dd, 1H, H^b from CH_2, *J* = 13.9, 10.4 Hz), 1.90 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 162.0 (d, C(4′), *J* = 244.5 Hz), 135.3 (C(2)), 134.1 (d, C(1′), *J* = 3.0 Hz), 129.9 (C(7a)), 129.7 (d, C(2′,6′), *J* = 8.3 Hz), 122.4 (C(6)), 119.6 (C(4)), 115.1 (d, C(3′,5′), *J* = 21.4 Hz), 112.3 (C(7)), 111.1 (C(3a)), 104.2 (C(3)), 54.7 (CH), 30.3 (CH_2), 10.8 (Me). ^{19}F NMR (282 MHz, DMSO-d_6): δ −113.8 (m).

*2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-(4-chlorophenyl)ethan-1-aminium Chloride (**6e**).* Colorless crystals (0.27 g, 57%), mp: 274−277 °C. IR (KBr) 3362, 2983, 2807, 1593, 1511, 1498 cm^{-1}. MS (*m*/*z* (rel intens, %)) 223, 225 (90, $C_{10}H_{10}BrN^+$), 222, 224 (86, $C_{10}H_9BrN^+$), 142 (33) and 140 (100, $CH(ClC_6H_4)NH_2^+$). HRMS: calcd for $C_{17}H_{17}BrClN_2$ M − Cl, 363.0258, 365.0237, 367.0209, found *m*/*z* 363.0244, 365.0234, 367.0209. ^1H NMR (300 MHz, DMSO-d_6): δ 11.04 (s, 1H, NH), 8.91 (s, 3H, NH_3^+), 7.49 (d, 1H, H(4), *J* = 1.8 Hz), 7.41−7.31 (m, 4H, C_6H_4), 7.16 (d, 1H, H(7), *J* = 8.5 Hz), 7.05 (dd, 1H, H(6), *J* = 8.5, 1.8 Hz), 4.31 (m, 1H, CH), 3.41 (dd, 1H, H^a from CH_2, *J* = 14.0, 4.2 Hz), 3.08 (dd, 1H, H^b from CH_2, *J* = 14.0, 10.4 Hz), 1.90 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 136.9 (C(4′)), 135.3 (C(2)), 133.7 (C(5)), 133.0 (C(1′)), 129.9 (C(7a)), 129.4 and 128.2 (C(2′,3′,5′,6′)), 122.4 (C(6)), 119.6 (C(4)), 112.3 (C(7)), 111.1 (C(3a)), 104.1 (C(3)), 54.6 (CH), 30.1 (CH_2), 10.8 (Me).

*2-(5-Bromo-2-methyl-1H-indol-3-yl)-1-(2,4-dichlorophenyl)-ethan-1-aminium Chloride (**6f**).* Colorless crystals (0.34 g, 66%), mp: 184−187 °C. IR (KBr) 3372, 2919, 2869, 1590, 1513, 1475 cm^{-1}. MS (*m*/*z* (rel intens, %)) 400 (3), 398 and 396 (6, M − Cl), 223, 225 (68, $C_{10}H_{10}BrN^+$), 222, 224 (66, $C_{10}H_9BrN^+$), 176 (63) and 174 (100, $CH(Cl_2C_6H_3)NH_2^+$), 143 (40, $C_{10}H_9N^+$), 147 (24) and 145 (41, $C_6H_3Cl_2^+$). HRMS: calcd for $C_{17}H_{16}BrCl_2N_2$ M − Cl, 396.9868, 398.9847, found: *m*/*z* 396.9853, 398.9835. ^1H NMR (300 MHz, DMSO-d_6): δ 11.04 (s, 1H, NH), 8.96 (s, 3H, NH_3^+), 8.07 (d, 1H, H(6′), *J* = 8.4 Hz), 7.58 (dd, 1H, H(5′), *J* = 8.4, 1.8 Hz), 7.46 (d, 1H, H(4), *J* = 1.7 Hz), 7.40 (d, 1H, H(3′), *J* = 1.8 Hz), 7.15 (d, 1H, H(7), *J* = 8.5 Hz), 7.03 (dd, 1H, H(6), *J* = 8.5, 1.7 Hz), 4.75 (dd, 1H, CH, *J* = 9.6, 4.5 Hz), 3.44 (dd, 1H, H^a from CH_2, *J* = 14.0, 4.5 Hz), 3.14 (dd, 1H, H^b from CH_2, *J* = 14.0, 9.6 Hz), 2.01 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 135.4 (C(2)), 134.9 (C(4′)), 133.9 (C(5)), 133.8 and 133.7 (C(1′) and C(2′)), 130.2 (C(7a)), 130.0 (C(6′)), 128.6 (C(3′)), 127.8 C(5′)), 122.4 (C(6)), 119.3 (C(4)), 112.2 (C(7)), 111.0 (C(3a)), 103.4 (C(3)), 50.8 (CH), 29.5 (CH_2), 10.9 (Me).

*2-(5-Fluoro-2-methyl-1H-indol-3-yl)-1-phenylethan-1-aminium Chloride (**6g**).* Colorless crystals (0.18 g, 49%), mp: 234−236 °C. IR (KBr) 3415, 3342, 3011, 2910, 1584, 1487 cm^{-1}. MS (*m*/*z* (rel intens, %)) 268 (2, M^+ − HCl) 163 (30, $C_{10}H_{10}FN^+$), 162 (43, $C_{10}H_9BrN^+$), 161 (16, $C_{10}H_8BrN^+$), 106 (100, $C_7H_8N^+$). HRMS: calcd for $C_{17}H_{18}FN_2$ M − Cl, 269.1449, found: *m*/*z* 269.1438. ^1H NMR (300 MHz, DMSO-d_6): δ 10.87 (s, 1H, NH), 8.53 (s, 3H, NH_3), 7.36−7.26 (m, 5H, Ph), 7.21 (dd, 1H, H(4), *J* = 10.3, 2.4 Hz), 7.17 (dd, 1H, H(6), *J* = 8.8, 4.6 Hz), 6.77 (m, 1H, H(6)), 4.26 (dd, 1H, CHPh, *J* = 9.9, 4.4 Hz), 3.40 (dd, 1H, H^a from CH_2, *J* = 13.9, 4.4 Hz), 3.07 (dd, 1H, H^b from CH_2, *J* = 13.8, 9.9 Hz), 1.84 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 156.7 (d, C(5), *J* = 230.3 Hz), 138.6 (*i*-Ph), 135.7 (C(2)), 131.7 (C(7a)), 128.51 (d, C(3a), *J* = 9.9 Hz), 128.2, 127.4 (*o*-,*m*-Ph), 128.0 (*p*-Ph), 111.1 (d, C(7), *J* = 9.8 Hz), 107.7 (d, C(6), *J* = 25.9 Hz), 105.0 (d, C(3), *J* = 4.4 Hz), 102.3 (d, C(4), *J* = 23.4 Hz), 55.4 (CH), 30.8 (CH_2), 10.8 (Me). ^{19}F NMR (282 MHz, DMSO-d_6): δ −126.5 (m).

*2-(2-Methyl-1H-indol-3-yl)-1-phenylethan-1-aminium Chloride (**6h**).* Colorless crystals (0.27 g, 76%), mp: 97−99 °C. IR (KBr) 3400, 3337, 3029, 2912, 1601, 1462 cm^{-1}. MS (*m*/*z* (rel intens, %)) 250 (4, M^+ − HCl) 145 (30, $C_{10}H_{11}N^+$), 144 (98, $C_{10}H_{10}N^+$), 143 (28, $C_{10}H_9N^+$), 106 (100, $C_7H_8N^+$). HRMS: calcd for $C_{18}H_{21}BrN_2$ M − Cl, 251.1543, found: *m*/*z* 251.1547. ^1H NMR (300 MHz, DMSO-d_6): δ 10.72 (s, 1H, NH), 7.46 (d, 1H, H(4), *J* = 7.5 Hz), 7.33−7.25 (m, 5H, Ph), 7.21 (d, 1H, H(7), *J* = 7.6 Hz), 6.97 (t, 1H, H(6), *J* = 7.6 Hz), 6.94−6.88 (m, 1H, H(5)), 6.22 (br.s, 3H, NH_3), 4.22 (dd, 1H, CH, *J* = 8.3, 5.7 Hz), 3.23 (dd, 1H, H^a from CH_2, *J* = 13.7, 5.7 Hz), 3.01 (dd, 1H, H^b from CH_2, *J* = 13.7, 8.3 Hz), 1.94 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 141.6 (*i*-Ph), 135.1 (C(7a)), 133.1 (C(2)), 128.3 (C(3a)), 128.1, 127.0 (*o*-,*m*-Ph), 127.4 (*p*-Ph), 119.9 (C(6)), 118.1 (C(5)), 117.4 (C(4)), 110.3 (C(7)), 105.6 (C(3)), 55.9 (CH), 32.5 (CH_2), 10.9 (Me).

*2-(2,5-Dimethyl-1H-indol-3-yl)-1-phenylethan-1-aminium Chloride (**6i**).* Colorless crystals (0.15 g, 42%)), mp: 154−157 °C. IR (KBr) 3397, 3249, 3008, 2912, 2858, 1591, 1457 cm^{-1}. MS (*m*/*z* (rel intens, %)) 280 (6, M^+ − HCl) 175 (62, $C_{11}H_{13}NO^+$), 174 (100, $C_{11}H_{12}NO^+$), 159 (17, $C_{10}H_9NO^+$), 106 (66, $C_7H_8N^+$). HRMS: calcd for $C_{18}H_{21}BrN_2$ M − Cl, 251.1543, found: *m*/*z* 251.1547. HRMS: calcd for $C_{18}H_{21}BrN_2$ M − Cl, 265.1699, found: *m*/*z* 265.1694. ^1H NMR (300 MHz, DMSO-d_6): δ 10.59 (s, 1H, NH), 7.36−7.27 (m, 5H, Ph), 7.21 (m, 1H, H(4)), 7.08 (d, 1H, H(7), *J* = 8.2 Hz), 6.78 (dd, 1H, H(6), *J* = 8.2, 1.6 Hz), 4.26 (dd, 1H, CHPh, *J* = 9.7, 4.7 Hz), 3.36 (dd, 1H, H^a from CH_2, *J* = 13.8, 4.7 Hz), 3.06 (dd, 1H, H^b from CH_2, *J* = 13.8, 9.7 Hz), 2.34 (s, 3H, Me), 1.85 (s, 3H, Me). ^{13}C NMR (75 MHz, DMSO-d_6): δ 139.1 (*i*-Ph), 133.4, 133.3 (C(2,3a)), 128.4 (C(7a)), 128.2, 127.3 (*o*-,*m*-Ph), 127.9 (*p*-Ph), 126.4 (C(5)), 121.4 (C(6)), 117.1 (C(4)), 110.0 (C(7)), 104.2 (C(3)), 55.5 (CH), 31.2 (CH_2), 21.3 (Me), 10.8 (Me).

*1-(4-Bromophenyl)-3-methyl-6-phenyl-1,4,5,6-tetrahydropyridazine (**4a**).* Colorless crystals (5%), mp: 124−128 °C. IR (KBr) 3444, 2928, 2906, 1584, 1486 cm^{-1}. MS (*m*/*z* (rel intens, %)) 328, 330 (100, M^+), 251, 253 (10), 183, 185 (28), 155, 157 (61). HRMS: calcd for $C_{17}H_{17}BrN_2$ M + H, 329.0648, 331.0628, found: *m*/*z* 329.0638, 331.0626. ^1H NMR (300 MHz, $CDCl_3$): δ 7.27−7.10 (m, 5H, Ar), 7.01 (d, 2H, *o*-Ph, *J* = 7.2 Hz), 6.91 (d, 2H, H(3′,5′), *J* = 8.9 Hz), 4.98 (br.s, 1H, CHPh), 2.21−2.04 (m, 2H, H(4)), 1.92 (s, 3H, Me), 1.95−1.85 (m, 1H, H(5)), 1.82−1.67 (m, 1H, H(5)). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.2 (CBr), 143.3 (C═N), 140.8 (*i*-Ph), 131.7 (C(2′,6′)), 128.9 (*m*-Ph), 127.3 (*p*-Ph), 126.2 (*o*-Ph), 114.6 (C(3′,5′)), 110.9 (C(1′)), 54.7 (C(6)), 25.2 (C(4)), 24.5 (Me), 21.7 (C(5)).

*1-(4-Bromophenyl)-3-methyl-6-(p-tolyl)-1,4,5,6-tetrahydropyridazine (**4b**).* Colorless crystals (9%), mp: 115−117 °C. IR (KBr) 3437, 2951, 2919, 1588, 1490 cm^{-1}. MS (*m*/*z* (rel intens, %)) 342, 344 (100, M^+), 183, 185 (23), 170, 172 (67), 155, 157 (48). HRMS: calcd for $C_{18}H_{19}BrN_2$ M + H, 343.0804, 345.0785, found: *m*/*z* 343.0804, 345.0814. ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (d, 2H, H(3′,5′), *J* = 9.0 Hz), 7.13 (d, 2H, H(3″,5″), *J* = 7.8 Hz), 7.02 (d, 2H, H(2′,6′), *J* = 9.0 Hz), 7.01 (d, 2H, H(2″,6″), *J* = 7.8 Hz), 5.05 (m, 1H, CH), 2.34 (s, 3H, ArMe), 2.28−2.10 (m, 2H, H(4)), 2.03 (s, 3H, Me),

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2.05−1.79 (m, 2H, H(5)). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.2 (C(4′)), 143.4 (C(3)), 137.7 and 136.8 (C(1′,4′)), 131.6 (C(3′,5′)), 129.6 (C(3″,5″)), 126.1 (C(2″,6″)), 114.6 (C(2′,6′)), 110.8 (C(1″)), 54.5 (C(6)), 25.2 (C(4)), 24.4 (Me), 21.7 (C(5)), 21.1 (ArMe).

*1-(4-Bromophenyl)-6-(4-methoxyphenyl)-3-methyl-1,4,5,6-tetrahydropyridazine (**4c**).* Colorless oil (12%). IR (KBr) 3436, 2930, 2906, 1586, 1505, 1489 cm^{-1}. MS (*m*/*z* (rel intens, %)) 358, 360 (100, M$^+$), 188 (36), 172 (89), 161 (39), 134 (64). HRMS: calcd for $C_{18}H_{19}BrN_2O$ M + H, 359.0754, 361.0734, found: *m*/*z* 359.0745, 359.0761. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30−7.22 (m, 2H, H(3′,5′)), 7.07−6.98 (m, 4H, H(2″,3″,5″,6″)), 6.88−6.81 (m, 2H, H(2′,6′)), 5.04 (m, 1H, CH), 3.79 (s, 3H, MeO), 2.29−2.06 (m, 2H, H(4)), 2.02 (s, 3H, Me), 2.04−1.79 (m, 2H, H(5)). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.9 (C(4″)), 146.2 (C(4′)), 143.4 (C(3)), 132.7 (C(1″)), 131.7 (C(3′,5′)), 127.4 (C(2″,6″)), 114.7 C(2′,6′)), 114.4 (C(3″,5″)), 110.9 (C(1′)), 55.5 (MeO), 54.2 (C(6)), 25.4 (C(5)), 24.5 (Me), 21.8 (C(4)).

*1-(4-Bromophenyl)-6-(4-fluorophenyl)-3-methyl-1,4,5,6-tetrahydropyridazine (**4d**).* Colorless crystals (19%), mp: 97−99 °C. IR (KBr) 2956, 2933, 1589, 1510, 1489 cm^{-1}. MS (*m*/*z* (rel intens, %)) 346, 348 (100, M$^+$), 155, 157 (60). HRMS: calcd for $C_{17}H_{16}BrFN_2$ M + H, 347.0554, 349.0533, found: *m*/*z* 347.0538, 349.0545. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17 (d, 2H, *J* = 7.5 Hz), 6.98 (dd, 2H, *J* = 8.2, 5.6 Hz), 6.92 (d, 2H, *J* = 6.0 Hz), 6.89 (d, 2H, *J* = 6.5 Hz), 4.97 (s, 1H, CHAr), 2.21−1.99 (m, 2H, H(4)), 1.93 (s, 3H, Me), 1.98−1.86 (m, 1H, H(5)), 1.79−1.64 (m, 1H, H(5)). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.14 (d, C(4″), *J* = 245.5 Hz), 146.0 (C(4′)), 143.4 (C(3)), 136.4 (C(1″)), 131.7 (C(2′,6′)), 127.91 (d, C(2″,6″), *J* = 8.0 Hz), 115.90 (d, C(3″,5″), *J* = 21.5 Hz), 114.6 (C(3′,5′), 111.1 (C(1′)), 54.1 (C(6)), 25.3 (C(5)), 24.4 (Me), 21.6 (C(4)). ^{19}F NMR (282 MHz, $CDCl_3$): δ −115.60 (m).

*1-(4-Fluorophenyl)-3-methyl-6-phenyl-1,4,5,6-tetrahydropyridazine (**4g**).* Colorless crystals (0.035 g, 11%), mp: 71−73 °C. IR (KBr) 3029, 2932, 1506, 1209, 824 cm^{-1}. MS (*m*/*z* (rel intens, %)) 268 (100, M$^+$), 191 (10), 156 (10), 123 (22), 95 (34). HRMS: calcd for $C_{17}H_{18}FN_2$ M + H, 269.1499, found: *m*/*z* 269.1499. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36−7.22 (m, 3H, H(3″,4″,5″)), 7.15 (d, 2H, H(2″,6″), *J* = 7.1 Hz), 7.11−6.98 (m, 2H, H(2′,6′)), 6.80−6.90 (m, 2H, H(3′,5′)), 5.01−5.08 (m, 1H, H(6)), 2.34−2.11 (m, 1H), 2.04 (s, 1H), 2.04−1.77 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6 (d, C(4′), *J* = 236.8 Hz), 143.6 (d, C(1′), *J* = 1.8 Hz), 142.4 (C(3)), 141.1 (C(1″)), 128.7 (C(3″,5″)), 127.0 (C(4″)), 126.1 (C(2″,6″)), 115.2 (d, C(3′,5′), *J* = 22.2 Hz), 114.0 (d, C(2′,6′), *J* = 7.4 Hz), 55.1 (C(6)), 25.2 (C(4)), 24.2 (Me), 21.6 (C(5)). ^{19}F NMR (282 MHz, $CDCl_3$): δ −127.8 (m).

*3-Methyl-1,6-diphenyl-1,4,5,6-tetrahydropyridazine (**4h**).* Colorless crystals (0.036 g, 12%), mp: 141−143 °C. IR (KBr) 3020, 2934, 1594, 1498, 1149, 750 cm^{-1}. MS (*m*/*z* (rel intens, %)) 250 (100, M$^+$), 180 (10), 173 (16), 156 (10), 117 (9), 77 (22). HRMS: calcd for $C_{17}H_{19}N_2$ M + H, 251.1543, found: *m*/*z* 251.1541. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38−7.13 (m, 9H, Ar), 6.79 (t, 1H, H(4′), *J* = 6.9 Hz), 5.13−5.18 (m, 1H, H(6)), 2.34−2.14 (m, 2H, H(4)), 2.05 (s, 1H), 2.09−1.77 (m, 2H, H(5)). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.1 (C(1′)), 142.5 (C(3)), 141.3 (C(1″)), 129.0 (C(3′,5′)), 128.8 (C(3″,5″)), 127.1 (C(4″)), 126.3 (C(2″,6″)), 118.8 (C(4′)), 113.1 (C(2′,6′)), 54.8 (C(6)), 25.2 (C(4)), 24.4 (Me), 21.9 (C(5)).

*(S)-N-(2-(5-bromo-2-methyl-1H-indol-3-yl)-1-phenylethyl)-acetamide (S)-**9**.* A mixture of 4-bromophenylhydrazine hydrochloride (0.22 g, 1 mmol) and (*R*,*R*)-2-phenylcyclopropylethanone (*R*,*R*)-**1a** (0.21 g, 1.2 mmol) in acetonitrile (20 mL) was heated at reflux for 16 h. The mixture was filtered and the residue was dried *in vacuo* to give crude (*S*)-**6a**, which was treated with dichloromethane (20 mL) and triethylamine (0.081 g, 0.8 mmol). A solution of acetyl chloride (0.058 g, 0.7 mmol) in CH_2Cl_2 (2 mL) was added dropwise in 5 min, and the mixture stirred for 1 h. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with a 1 M solution of K_2CO_3, brine, and the organic layer was dried over anhydrous Na_2SO_4, and evaporated. Column chromatography on silica gel (chloroform−AcOEt, 1:1) gave the desired product (*S*)-**9** (0.25 g, 68%, ee 99%). Colorless crystals, mp: 168−169 °C, $[\alpha]_D^{20}$ +66 (*c* 1, EtOAc). IR (KBr) 3425, 32.95, 2361, 1613 cm^{-1}. MS (*m*/*z* (rel intens, %)) 370, 371 (10, M$^+$), 311, 313 (27), 222, 224 (100), 148 (5), 143 (16), 106 (24). HRMS: calcd for $C_{19}H_{19}BrN_2O$ M + H, 371.0754, 373.0734, found: *m*/*z* 371.0754, 373.0743. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (s, 1H, H(1)), 7.46 (d, *J* = 1.8 Hz, 1H, H(4)), 7.33−7.21 (m, 3H, *m*-, *p*-Ph), 7.16 (dd, 1H, H(6), *J* = 8.5, 1.8 Hz), 7.12−7.03 (m, 3H, *o*-Ph, H(7)), 6.05 (d, 1H, NHAc, *J* = 7.9 Hz), 5.28 (dd, 1H, CH, *J* = 13.9, 6.2 Hz), 3.27−3.03 (m, 2H, CH_2), 1.97 (s, 3H, Ac), 1.87 (s, 3H, Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6 (Ac), 141.7 (*i*-Ph), 134.7 (C(2)), 133.9(C-(3a)), 131.1 (C(7a)), 128.6 (*m*-Ph), 127.5 (*p*-Ph), 126.7 (*o*-Ph), 123.8 (C(6)), 120.7 (C(4)), 112.8 (C(5)), 111.8 (C(7)), 106.5 (C(3)), 54.5 (CH), 31.9 (CH_2), 23.6(Ac), 11.3 (Me).

Racemic Tryptamine 9. A solution of AcCl (0.040 g, 0.5 mmol) in dichloromethane (2 mL) was added to the mixture of **6a** (0,10 g, 0.27 mmol) and TEA (0.08 g, 0.8 mmol) in CH_2Cl_2 (10 mL) dropwise in 5 min, and the mixture stirred for 1 h. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with a 1 M solution of K_2CO_3, brine, and the organic layer was dried over anhydrous Na_2SO_4 and evaporated. Column chromatography (chloroform−EtOH, 9:1) gave the desired product in a yield of 81% (0.081 g). Colorless crystals, mp: 167−169 °C; other physical properties correspond to those of (*S*)-**9**.

Rearrangement of 2-Methylcyclopropylethanone 4-Bromophenylhydrazone. A mixture of 4-bromophenylhydrazine hydrochloride (0.40 g, 1.8 mmol) and 2-methylcyclopropylethanone **7** (0.22 g, 2.2 mmol) in acetonitrile (20 mL) was refluxed for 18 h. The solvent was removed *in vacuo*, and the residue was treated with dichloromethane (20 mL) and triethylamine (0.40 g, 4.0 mmol). A solution of AcCl (0.17 g, 2.2 mmol) in CH_2Cl_2 (3 mL) was added dropwise in 5 min, and the mixture stirred for 1 h. The mixture was diluted with CH_2Cl_2 (20 mL) and washed with a 1 M solution of K_2CO_3, brine, and the organic layer was dried over anhydrous Na_2SO_4, and evaporated. Column chromatography on SiO_2 (chloroform−EtOH, 9:1) gave a mixture of tryptamines **7** and **8** in a yield of 68% (0.38 g, ratio 3:1). The major isomer **7** was purified using a preparative normal-phase HPLC column (21 × 250 mm, 5 μm), flow rate 12 mL min^{-1}, mobile phase: isocratic, isopropanol−hexane, 17% isopropanol; retention time 19.65 min. The minor isomer was analyzed in the mixture.

*N-(2-(5-Bromo-2-methyl-1H-indol-3-yl)propyl)acetamide **7**.* Colorless crystals, mp: 95−97 °C. IR (KBr) 3413, 3272, 2965, 2928, 1655 cm^{-1}. MS (*m*/*z* (rel intens, %)) 308, 310 (22, M$^+$), 249, 251 (20, M$^+$ − $AcNH_2$), 236, 238 (100, M$^+$ − CH_2NAc), 157 (27, M$^+$ − CH_2NHAc − Br), 106 (24, $PhCHNH_2^+$). HRMS: calcd for $C_{14}H_{17}BrN_2O$ M + H, 309.0597, 311.0577, found: *m*/*z* 309.0586, 311.0566. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (s, 1H, H(1)), 7.70 (d, 1H, H(4), *J* = 1.5 Hz), 7.21 (dd, 1H, H(6), *J* = 8.5, 1.5 Hz), 7.16 (d, 1H, H(7), *J* = 8.5 Hz), 5.42 (br.s, 1H, NH), 3.82 (ddd, 1H, H^a from CH_2, *J* = 12.9, 7.3, 5.7 Hz), 3.38−3.25 (m, 1H, H^b from CH_2), 3.26−3.16 (m, 1H, CH), 2.39 (s, 3H, Ac), 1.88 (s, 3H, Me), 1.41 (d, 3H, Me, *J* = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.2 (Ac), 134.3 (C(3a)), 133.2 (C(2)), 129.1 (C(7a)), 123.9, (C(6)), 121.5 (C(4)), 112.9 (C(3)), 112.6 (C(5)), 112.1 (C(7)), 45.1 (CH_2), 31.4 (CH), 23.4 (Ac), 18.4 and 12.2 (2 Me).

*N-(1-(5-Bromo-2-methyl-1H-indol-3-yl)propan-2-yl)acetamide **8**.* Colorless crystals. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (br.s, 1H, NH), 7.62 (d, 1H, H(4), *J* = 1.8 Hz), 7.18 (dd, 1H, H(6), *J* = 1.8, 8.3 Hz), 7.11 (d, 1H, H(7), *J* = 8.3 Hz), 5.50 (s, 1H, NHAc), 4.18−4.33 (m, 1H, CH), 2.73−2.90 (m, 2H, CH_2), 2.37 (s, 3H, Me), 1.93 (s, 3H, Ac), 1.09 (d, 3H, Me, *J* = 6.7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.7 (CO), 134.2 (C(2)), 134.0 (C(3a)), 131.3 (C(7a)), 123.8 (C(6)), 120.9 (C(4)), 112.3 (C(5)), 111.8 (C(7)), 107.7 (C(3)), 46.6 (CH), 30.7 (CH_2), 23.7 (Ac), 20.1 and 12.1 (2 Me).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02578.

Crystallographic data for compound (*S*)-**9** (CIF)

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^{1}H and ^{13}C NMR spectra for new compounds, a thermal ellipsoid plot, and chiral HPLC data (PDF)

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Notes

The authors declare no competing financial interest.

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