temperature, the solution was neutralized with solid Na_2CO_3 (0.5 g). After filtering and removal of the solvent, pentane was added to the residue. Upon cooling, 258 mg (86%) of (*Z*)-2-(4-methoxyphenyl)-2-methoxy-1-phenylvinyl trifluoromethanesulfonate (**14**) were obtained; mp 52–53 °C; IR (KBr) 1666 (m), 1617 (m), 1522 (s), 1422 (s), 1315/1306 (m), 1267, 1248, 1228, 1211 (all vs), 1182, 1144, 1103, 1013, 967 (all s) cm^{-1}; UV (cyclohexane) λ_{max} (log ϵ) 234 nm (4.21), 289 nm (4.07); ^1H NMR ($CDCl_3$) δ 3.52 (s, 3 H), 3.79 (s, 3 H), 6.83 and 7.18 (AA'BB'), 7.20 (s, 5 H); ^{19}F NMR ($CDCl_3$) δ 87.7. Anal. Calcd for $C_{17}H_{15}F_3O_5S$ (388.4): C, 52.58; H, 3.89. Found: C, 52.6; H, 3.95.

X-ray Analysis of 7. Crystal data: monoclinic space group $C2/c$; a = 20.175 (5) Å, b = 9.475 (7) Å, c = 18.279 (4) Å, β = 101.78 (2)°; 4 molecules per unit cell, calculated density D_x = 1.419 g cm^{-3}. **Data collection**: CAD4 automated diffractometer, monochromatized Mo Kα radiation, crystal size 0.70 × 0.25 × 0.23 mm. Two asymmetric units were measured in the range $2 \leq \theta \leq 22°$, which after averaging gave 2907 unique reflections. Scan width (0.70 + 0.35 tan θ)°, scan speed 1.33–4.0 deg min^{-1}. The average intensity loss of three monitoring reflections was 1.6% which was corrected linearly. No absorption correction was applied. **Structure solution and refinement**: The phase problem was solved with MULTAN82. Missing heavy atoms and hydrogen atoms were located in ΔF maps. The heavy atoms were refined anisotropically, the H atoms isotropically with the fixed B value of their bond neighbors. Full matrix refinement (2326 reflections with $I > 2(I)$, unit weights) converged at R = 0.045, R_W = 0.041. The largest shift/error ratio was 0.30 for heavy atoms and 0.68 for H atoms at this point. Final coordinates, temperature factors, and bond geometry tables are found in the supplementary material. All calculations were done with the Enraf Nonius SDP package on a PDP 11/23 plus computer.

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Registry No. 2b, 3493-18-3; **2c**, 3580-75-4; (*Z*)-**4a**, 89849-96-7; (*E*)-**4a**, 89849-97-8; (*E*)-**4b**, 89849-98-9; (*Z*)-**4b**, 89849-99-0; (*E*)-**4c**, 89850-00-0; (*Z*)-**4c**, 89850-01-1; **5a**, 134-81-6; **5b**, 22711-23-5; **5c**, 22711-21-3; **6**, 4254-17-5; **7**, 89850-02-2; **8**, 7509-44-6; **9**, 89850-04-4; **14**, 89850-05-5; PhC≡CPh, 501-65-5; *p*-ClC_6H_4C≡CPh, 5172-02-1; azibenzil, 3469-17-8; triflic anhydride, 358-23-6; benzoin methyl ether, 3524-62-7.

Supplementary Material Available: Tables of postional and thermal parameters of **7**, bond distances and angles, and observed and calculated structure factors (18 pages). Ordering information is given on any current masthead page.

Notes

Activated Alkynes as Partners in Pictet–Spengler Condensations

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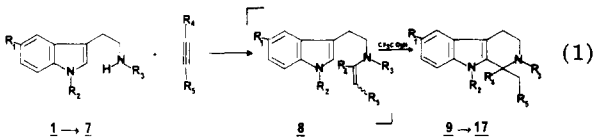
One of the most useful syntheses of tetrahydro-β-carbolines is the Pictet–Spengler condensation of tryptamines with ketones or aldehydes.[2] Its generally accepted mechanism involves a cationic cyclization of an iminium ion on the indole nucleus and, in principle, any enamine preparation ought to be applicable to a tetrahydro-β-carboline synthesis. The purpose of this paper is to propose an alternative to the Pictet–Spengler reaction on the basis of the condensation of tryptamines with suitable alkynes.

Reaction of tryptamines **1** → **7** with dimethyl acetylenedicarboxylate (DMAD) and of **7** with methyl propiolate or butynone yields enamines **8** as shown by ^1H NMR of the crude reaction mixtures. Protonation of these enamines brought about by an excess of trifluoroacetic acid leads directly to 1,2,3,4-tetrahydro-β-carbolines **9** → **17** (eq 1, Table I) in yields ranging from 76% to 99.5%. The overall sequence can be accomplished in ca. 30 min.



(1)

Starting materials are either commercially available (**1**, **5**) or prepared according to the literature (**2**,[4] **3**,[5] **4**,[6] **7**[7]). Methyl *N*-(2-(3-indolyl)ethyl)glycinate (**6**) is prepared by reductive condensation of tryptamine with methyl glyoxylate after thermal depolymerization of the reagent.[8]

The structure of compounds **9** → **17** are supported by their spectral properties as well as by combustion analysis or by high-resolution mass spectroscopy. Usual preparations of the corresponding monoester compounds involve the tedious use of the mono ethyl ester of oxaloacetic acid;[9] the diethyl ester corresponding to **9** has previously been prepared from tryptamine and diethyl oxaloacetate.[9] It is worth noting that, in our hands, Pictet–Spengler reactions between N_a-methyltryptamines **3** and **4** and carbonyl partners gave poor and irreproducible yields.

Experimental Section

General Procedures. All melting points were determined on a Koffler apparatus and are corrected; IR spectra were recorded on a Beckmann Acculab 2 spectrometer and UV spectra on a LERES-SPILA S28 photometer; ^1H NMR spectra were measured on a Perkin-Elmer R12B spectrometer (60 MHz) or on a IEF 400 instrument, a prototype built at the University of Orsay (401 MHz). Mass spectra were recorded on a JEOL D300 spectrometer. Elemental analysis were performed by the Microanalysis Department of the Faculty of Sciences of Reims.

Typical Procedure for Pictet–Spengler Reactions. Preparation of 15. To a solution of N_b-benzyltryptamine (**7**;

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(6) Made by reductive alkylation[7] of **3**.
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(8) We thank the "Société Française, Hoechst" for a generous gift of methyl glyoxylate.
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Table I. Pictet-Spengler Reactions

compd no.	tryptamine R_1	tryptamine R_2	tryptamine R_3	alkyne R_4	alkyne R_5	tetrahydro-β-carboline	% yield	mp, °C (solvent of cryst)
1	H	H	H	CO_2CH_3	CO_2CH_3	9	83	127 (ether–methanol, 1:1)
2	H	H	C_2H_5	CO_2CH_3	CO_2CH_3	10	89.5	112 (ether–methanol, 1:4)
3	H	CH_3	H	CO_2CH_3	CO_2CH_3	11	74.5	
4	H	CH_3	$CH_2C_6H_5$	CO_2CH_3	CO_2CH_3	12	92	
5	OCH_3	H	H	CO_2CH_3	CO_2CH_3	13	72.5	148
6	H	H	$CH_2CO_2CH_3$	CO_2CH_3	CO_2CH_3	14	91.5	
7	H	H	$CH_2C_6H_5$	CO_2CH_3	CO_2CH_3	15	99.5	148 (ethanol)
7	H	H	$CH_2C_6H_5$	H	CO_2CH_3	16	85	
7	H	H	$CH_2C_6H_5$	H	$COCH_3$	17	76	189 (ether)

10 g, 40 mmol), in 100 mL of $CHCl_3$, one adds in sequence dimethyl acetylenedicarboxylate (5.68 g, 40 mmol, 1 equiv) and trifluoroacetic acid (3.6 mL and then 3.5 mL, 2.4 equiv) at 5-min intervals with continuous stirring at room temperature. After 10 min, the reaction mixture is poured into 100 mL of water and made alkaline by an excess of aqueous 6 N NaOH. The organic layer is separated, washed with water, dried over Na_2SO_4, filtered, and evaporated in vacuo to afford 15.6 g of a white foam, homogeneous on TLC. An analytical sample is obtained by crystallization from ethanol (mp 148 °C): UV λ_{max}^{MeOH} 229 nm, 277, 281, 288; IR ν 3400, 1720, 1205 cm^{-1}; MS, m/e 392 ($M^{+\cdot}$, 1.5), 333 (100), 319 (7), 91 (65); ^1H NMR (401 MHz, $CDCl_3$) δ 9.3 (1 H, s), 4.15 and 3.50 (2 H, AB system, J = 14 Hz), 3.78 and 3.73 (2 × 3 H, s), 3.47 and 3.0 (2 H, AB system, J = 17 Hz). Anal. Calcd for $C_{23}H_{24}N_2O_4$: C, 70.4; H, 6.1; N, 7.1. Found: 70.5; H, 6.1; N, 7.2.

Spectral Data for New Compounds. Data for 9: UV λ_{max}^{MeOH} 226 nm, 275, 282, 291; IR (Nujol) 3360, 1725, 1710, 1700 cm^{-1}; MS, m/e 302 ($M^{+\cdot}$, 12, $C_{16}H_{18}N_2O_4$), 244 (15), 243 (100), 229 (14), 211 (8), 144 (7); ^1H NMR (401 MHz, $CDCl_3$) 8.37 (1 H, s), 3.83 and 3.72 (2 × 3 H, s), 3.35 and 2.94 (2 H, AB system, J = 17 Hz).

Data for 10: UV λ_{max}^{MeOH} 227 nm, 276, 281, 288; IR ν 3400, 1730, 1720 cm^{-1}; MS, m/e 330 ($M^{+\cdot}$, 2), 271 (100), 257 (8); ^1H NMR (401 MHz, $CDCl_3$) δ 9.22 (1 H, s), 3.71 and 3.7 (2 × 3 H, s), 3.32 and 2.85 (2 H, AB system, J = 17 Hz), 1.15 (3 H, t, J = 7 Hz). Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.4; H, 6.7; N, 8.5. Found: C, 65.4; H, 6.7; N, 8.6.

Data for 11: UV λ_{max}^{MeOH} 229 nm, 279, 289, 297; IR ν 3340, 1730, 1200 cm^{-1}; MS, m/e 316 ($M^{+\cdot}$, 11, $C_{17}H_{20}N_2O_4$), 257 (100), 243 (8), 225 (12), 158 (15), 144 (7); ^1H NMR (60 MHz, $CDCl_3$) 3.75 (6 H, s), 3.6 (3 H, s), 3.45 and 2.95 (2 H, AB system, J = 17 Hz).

Data for 12: UV λ_{max}^{MeOH} 231 nm, 278 (sh), 287, 295 (sh); IR ν 1725, 1690, 1220, 730 cm^{-1}; MS, m/e 406 ($M^{+\cdot}$, 4, $C_{24}H_{26}N_2O_4$), 347 (100), 333 (11), 271 (16), 157 (13), 91 (83); ^1H NMR (60 MHz, $CDCl_3$) δ 4.05 (1 H, d, J = 14 Hz), 3.8 (3 H, s), 3.65 (3 H, s), 3.35 (3 H, s).

Data for 13: UV λ_{max}^{MeOH} 230 nm, 280, 300 (sh), 310; IR (Nujol) ν 3360, 1725, 1700 cm^{-1}; MS, m/e 332 ($M^{+\cdot}$, 9, $C_{17}H_{20}N_2O_5$), 273 (100), 259 (19), 174 (10); ^1H NMR (60 MHz, $CDCl_3$) δ 9.1 (1 H, s), 3.9 (3 H, s), 1.7 (3 H, s).

Data for 14: UV λ_{max}^{MeOH} 227 nm, 278, 282, 288; IR ν 3400, 1745, 1730, 1715, 1200 cm^{-1}; MS, m/e 374 ($M^{+\cdot}$, 2.5, $C_{19}H_{22}N_2O_6$), 315 (100), 301 (10), 283 (17); ^1H NMR (60 MHz, $CDCl_3$) δ 9.45 (1 H, s), 3.85 (6 H, s), 3.8 (3 H, s), 3.65 (2 H, s).

Data for 16: UV λ_{max}^{MeOH} 232 nm, 273, 282, 290; IR ν 3400, 1730 cm^{-1}; MS, m/e 334 ($M^{+\cdot}$, 18, $C_{21}H_{22}N_2O_2$), 261 (100), 169 (35), 154 (15), 91 (100); ^1H NMR (401 MHz, $CDCl_3$) δ 8.47 (1 H, s), 4.21 (1 H, dd, J = 4.5, 9.5 Hz), 3.82 (2 H, s), 3.73 (3 H, s), 2.98 (1 H, dd, J = 4.5, 16 Hz), 2.86 (1 H, dd, J = 9.5, 16 Hz).

Data for 18: UV_{max}^{MeOH} 228 nm, 281, 289; IR (Nujol) ν 3320, 1690, 1625 cm^{-1}; MS, m/e 318 ($M^{+\cdot}$, 14, $C_{21}H_{22}N_2O$), 261 (100), 199 (22), 169 (15), 156 (22), 91 (88); ^1H NMR (60 MHz, $CDCl_3$) δ 8.9 (1 H, s), 4.85 (1 H, d, J = 8 Hz), 4.2 (2 H, s), 2.15 (3 H, s).

Preparation of Methyl *N*-(2-(3-Indolyl)ethyl)glycinate (6). A solution of methyl glyoxylate (1 g, 11.3 mmol, polymerized form) in 20 mL of benzene is heated at 80 °C for 15 min. Tryptamine (1; 2 g, 12.5 mmol) is then added and stirring is continued for 5 min at 80 °C. In vacuo evaporation leaves a foamy residue (3.1 g) whose NMR properties are consistent with an imine structure (1 H, s at 7.65 ppm; 3 H, s at 3.85 ppm). This residue is dissolved in 25 mL of MeOH, and $NaBH_4$ (1.2 g) is added portionwise over 45 min. Usual workup gives 2.16 g of a thick oil, homogeneous on TLC: ^1H NMR (60 MHz, $CDCl_3$) δ 8.65 (1 H, s), 6.9 (1 H, d, J = 3 Hz), 3.7 (3 H, s), 3.45 (2 H, s), 3.0 (4 H, s), 2.35 (1 H, s).

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Registry No. 1, 61-54-1; 2, 61-53-0; 3, 7518-21-0; 4, 56999-36-1; 5, 608-07-1; 6, 89827-47-4; 7, 15741-79-4; 9, 89827-48-5; 10, 89848-03-3; 11, 89827-49-6; 12, 89827-50-9; 13, 89827-51-0; 14, 89827-52-1; 15, 89827-53-2; 16, 89827-54-3; 17, 89827-55-4; DMAD, 762-42-5; methyl propiolate, 922-67-8; butynone, 1423-60-5; methyl glyoxylate, 922-68-9.

A Convenient Synthesis of Bis(*N*-methylpiperazinyl)aluminum Hydride: A Reagent for the Reduction of Carboxylic Acids to Aldehydes

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The central nature of the carbonyl group in organic synthesis spurs interest in transformations between various types of carbonyl compounds. One such transformation that remains somewhat problematic is the reduction of carboxylic acids to the corresponding aldehydes. A number of procedures are known for this transformation, including reduction with thexylborane,[1] lithium aluminum hydride reduction to the primary alcohol followed by reoxidation to the aldehyde, and preparation of various acid derivatives (e.g., acid chlorides or esters) followed by reduction.[2-4] These methods suffer various disadvantages; most are two-step procedures, workups may require chromatography, and selectivity is not always high, especially if conjugate reduction is possible.

Some years ago, bis(*N*-methylpiperazinyl)aluminum hydride (BMPA) was first prepared[5] from the reaction of aluminum hydride with *N*-methylpiperazine and shown to reduce aliphatic and aromatic acids to aldehydes in good yields. However, apart from this set of papers by Mu-

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