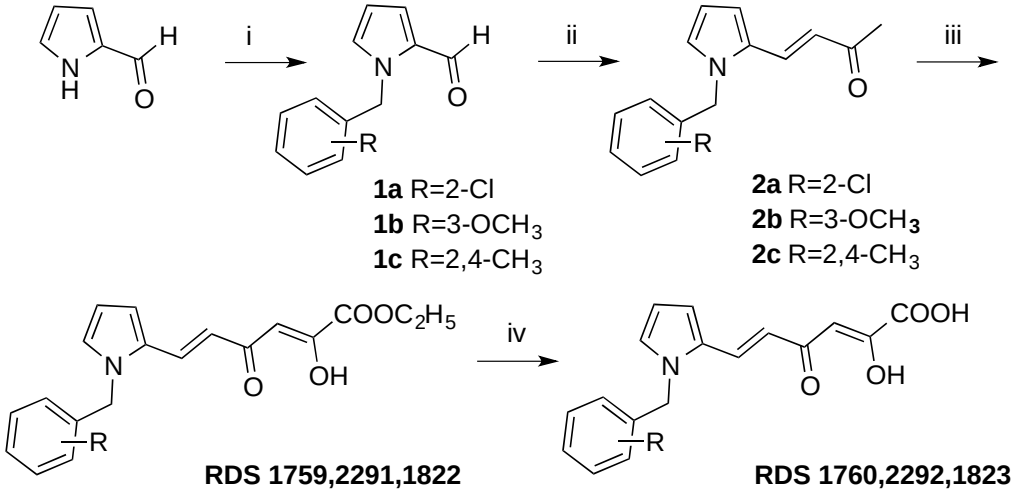
SUPPORTING INFORMATIONS

S1. Chemistry. The synthesis of derivatives RDS 1759, 2291, 1822 and RDS 1760, 2292, 1823 is reported in Scheme 1. The mono- and di-substituted-N-benzyl-pyrrolyl diketohexenoic acids were synthesized in a four-step parallel procedure (Scheme 1) using a Büchi SynCor reactor. Pyrrole-2-carboxaldehyde was alkylated with the appropriate benzyl bromide in the presence of NaH to afford the N-substituted-pyrrole-2-carboxaldehydes 1a-c, which were converted to the corresponding 3-buten-2-ones 2a-c by condensation with acetone using NaOH as a base. Compounds 2a-c were then reacted with diethyl oxalate in the presence of NaOEt as a base to obtain hexenoic esters RDS 1759, 2291, 1822, that were finally hydrolyzed in basic medium to give the corresponding acids RDS 1760, 2292, 1823.

The synthesic patway to obtain derivative RDS 1712 and RDS 2401 is outlined in Scheme 2. The common intermediates 7a-b were obtained starting from 4 and 6, respectively. The commercially available 2-formylpyrrole was alkylated in alkaline medium (K_2CO_3) to reach 3, which was subjected to the shift of the formyl chain from 2- to 3- position of the pyrrole ring to achieve derivative 4. Afterwards, derivative 4 underwent to a condensation reaction in presence of acetone affording 7a. Conversely, derivative 6 was synthesized building the pyrrole ring via TosMIC reaction, starting from (3E,5E)-6-phenylhexa-3,5-dien-2-one (1). Compound 6 was then converted into the alkylated intermediate 7b by alkylation in alkaline medium (K_2CO_3) in presence of 4-fluorobenzylbromide. The common intermediates 7a-b were converted in to the desired products RDS 1759, 2291, 1822 and RDS 1760, 2292, 1823 with the same procedure described above.

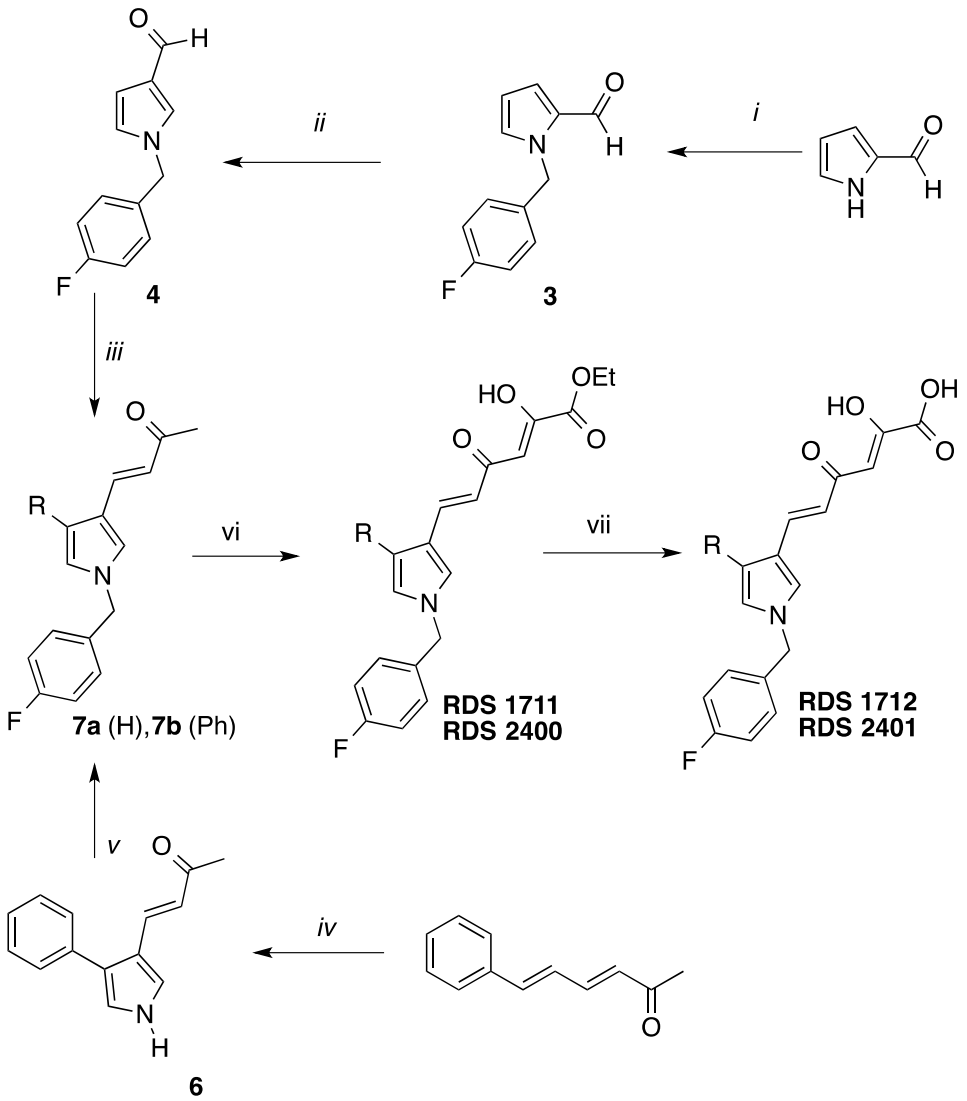
The compounds RDS1643 and RDS 1644 were synthesized as described previously (2).

Scheme 1. [a] Synthesis of derivatives RDS 1759, 2291, 1822 and RDS 1760, 2292, 1823.



[a] Reagents and conditions: i: substituted benzyl bromide, NaH, room temp; ii: acetone, 5 N NaOH, 50 °C; iii: diethyl oxalate, sodium ethoxide, THF_a, room temp; iv: 1 N NaOH, 1:1 THF-methanol, room temp.

Scheme 2. Synthesis of DKA derivatives RDS 1711, 2400 and RDS 1712, 2401



[a] Reagents and conditions: (i) 4-fluorobenzyl bromide, K_2CO_3, DMF, 100 °C, 24 h; (ii) Trifluoroacetic acid, 80 °C, 24 h; (iii) acetone, 4 N NaOH, room temp, 24 h; (iv) Et_2O/DMSO, NaH, TosMIC, inert atm, room temp, 1 h; (v) 4-fluorobenzyl bromide, K_2CO_3, DMF, 100 °C, 24 h; (vi) diethyl oxalate, C_2H_5ONa, THF, room temp, 2 h; (vii) 1 N NaOH, THF/CH_3OH, room temp, 5 min.

Chemistry. General.

Melting points were determined with a Buchi 530 capillary apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer Spectrum-One spectrophotometer. 1H NMR spectra were recorded on a bruker AC 400 spectrometer. Merck silica gel 60 F254 plates were used for analytical TLC. Developed plates were visualized by UV light. Column chromatography was performed on silica gel (Merck; 70−230 mesh). Compounds purity were always >95% determined by highpressure liquid chromatography (HPLC). HPLC analysis was carried out using Shimadzu LC-10AD VP and CTO-10AC VP. Column used was generally Suplex pKb-100 (250 mm x 4.6 mm, 5 μm). Buchi SynCor was used for parallel synthesis using 50 mL test tubes. Solvents were reagent grade and, when necessary, purified and dried by standard methods. Organic solutions were dried over anhydrous sodium sulfate (Merck). Concentration of solution after reactions and extractions involved the use of a rotary evaporator operating at reduced pressure of approximately 20 Torr. Analytical results agreed to within ±0.40% of the theoretical values. Dimethylsulfoxide-d_6 99.9% (code 44,139-2) and deuterochloroform 98.8% (code 41,675-4) of isotopic purity (Aldrich) were used.

General procedure for the synthesis of N-[(phenyl)metyl]pyrrole-2-carboxaldehyde. The tubes (25 mL each one) were charged with a solution of pyrrole-2-carboxaldehyde (0.016 mol) in 30 mL of dry DMF treated with NaH (0.018 mol) and placed in the Büchi SynCor reactor. Than the appropriate benzyl halide (0.011 mol) were added and the reaction mixtures were stirred with bascular stirring in Büchi Syncore at room temperature at 250 rpm overnight. The solution was diluted with water and extracted with ethyl acetate. The collected organic extract was washed with brine (three times), and dried, and the solvent was evaporated under reduced pressure to obtain crude 1a-c, that were purify by column chromatography.

General procedure for the synthesis of 4-(pyrrol-3-yl)but-3-en-2-one. The tubes (25 mL each one) were charged with a solution of the appropriate aldehyde 1a-c (0.0068 mol) in 14 mL of acetone were treated with 9.8 mL of NaOH 5 N and stirred at 50 °C with bascular stirring in Büchi Syncore at room temperature at 250 rpm overnight, and then treated with water. The reaction mixture was extracted with ethyl acetate. The collected organic extract was washed with brine (three times), and dried, and the solvent was evaporated under reduced pressure to obtain crude derivatives 2a-c, that were purify by column chromatography.

General procedure for the synthesis of Diketo Esters. The tubes (25 mL each one) were charged with a solution of the appropriated acetyl derivative 2a-c (0.077 mol) and diethyl oxalate (0.077 mol) dissolved in 8 mL of dry THF and placed in the Büchi SynCor reactor. The reaction mixtures were treated, under argon stream, with NaOEt obtained by the dissolution of Na (0.0155 mol) in 17 mL of absolute ethanol. The mixture was stirred with bascular stirring in Büchi Syncore at room temperature at 250 rpm for 1 h 30 min, then was poured into n-hexane (60 mL). The collected precipitate was vigorously stirred for 30 min in 1 N HCl (60 mL). The solid that formed was filtered, washed with water and light petroleum ether and dried under IR lamp to efford the pure diketo ester RDS 1759, 1822, 2291. Yield (%), melting point (°C), recrystallization solvent, IR, ^{1}H NMR, and analytical data are reported for each of the following compounds.

6-[1-(2-Chlorophenyl)methyl-1H-pyrrol-2-yl]-2,4-dioxo-5-hexenoic acid ethyl ester (RDS 1759). 100%; 98-99 °C; ligroina; IR ν 3400 (OH), 1720 (C=O ester), 1600 (C=O ketone) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.36 (t, 3H, CH_2CH_3), 4.38 (q, 2H, CH_2CH_3), 5.33 (s, 2H, CH_2), 6.33-6.40 (m, 3H, pyrrole β, hexanoate C3-H and hexanoate C5-H), 6.64 (m, 1H, pyrrole β), 6.85-6.92 (m, 2H, benzene H and pyrrole α), 7.13-7.27 (m, 2H, benzene H), 7.46 (m, 1H, benzene H), 7.58 (d, 1H, J_t = 15.0 Hz, hexanoate C6-H), 12-16 (sb, 1H, OH). Anal. ($C_{19}H_{18}ClNO_4$) C, H, N, Cl.

6-[1-(3-Methoxyphenyl)methyl-1H-pyrrol-2-yl]-2,4-dioxo-5-hexenoic acid ethyl ester (RDS 1822). 100%; 80-82 °C; ligroina; IR ν 3400 (OH), 1729 (C=O ester), 1585 (C=O ketone) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (t, 3H, CH_2CH_3), 3.76 (s, 3H, CH_3), 4.33 (q, 2H, CH_2CH_3), 5.20 (s, 2H, CH_2), 6.30 (s, 1H, pyrrole β), 6.34-6.37 (m, 2H, hexanoate C3-H and hexanoate C5-H), 6.56-6.68 (m, 2H, benzene H), 6.80-6.85 (m, 2H, benzene H and pyrrole β), 6.92 (s, 1H, pyrrole α), 7.25 (m, 1H, benzene H), 7.63 (d, 1H, J_t = 15.3 Hz, hexanoate C6-H), 12-16 (sb, 1H, OH). Anal. ($C_{20}H_{21}NO_5$) C, H, N.

6-[1-(2,4-Dimethylphenyl)methyl-1H-pyrrol-2-yl]-2,4-dioxo-5-hexenoic acid ethyl ester (RDS 2291). 98%; 102-104 °C; benzene/cyclohexane; IR ν 3400 (OH), 1747 (C=O ester), 1711 (C=O ketone) cm^{-1}; ^1H NMR (DMF-d_7) δ 1.44 (t, 3H, CH_2CH_3), 2.33 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 4.40 (q, 2H, CH_2CH_3), 5.21 (s, 2H, CH_2), 6.33 (m, 1H, pyrrole β), 6.40-6.44 (m, 2H, J_t = 15.3 Hz, hexanoate C5-H and hexanoate C3-H), 6.66 (d, 1H, benzene H), 6.81 (m, 1H, pyrrole β), 6.92 (m, 1H, pyrrole α), 7.00 (d, 1H, benzene H), 7.09 (s, 1H, benzene H), 7.70 (d, 1H, J_t = 15.3 Hz, hexanoate C6-H,), 12-16 (sb, 1H, OH). Anal. ($C_{21}H_{23}NO_4$) C, H, N.

General procedure for the synthesis of Diketo Acids. The Tubes (25 mL each one) were charged with a mixture of 1 N NaOH (9.48 mL) and the appropriated ester RDS 1759, 1822, 2291 (0.0028 mol) in 1:1 THF-Methanol (12 mL) was stirred with bascular stirring in Büchi Syncore at room temperature at 250 rpm for 1 h 30 min, and then poured into crushed ice. The aqueous mixture was treated with 1 N HCl until pH 3 was reached, and extracted with ethyl acetate (three times). The collected organic extract was washed with brine (three times), and dried, and the solvent was evaporated under reduced pressure to give the pure diketo acids RDS 1760, 1823, 2292. Yield (%), melting point (°C), recrystallization solvent, IR, ^1H NMR, and analytical data are reported for each of the following compounds.

6-[1-(2-Chlorophenyl)methyl-1H-pyrrol-2-yl]-2,4-dioxo-5-hexenoic acid (RDS 1760). 61%; 157-159 °C; toluene; IR ν 3400 (OH), 1688 (C=O acid), 1588 (C=O ketone) cm^{-1}; ^1H NMR (DMSO-d_6) δ 5.47 (s, 2H, CH_2), 6.31 (m, 1H, pyrrole β), 6.43 (s, 1H, hexanoate C3-H), 6.54 (m, 1H, pyrrole β), 6.67 (d, 1H, J_t = 15.5 Hz, hexanoate C5-H), 7.02 (s, 1H, pyrrole α), 7.25-7.32 (m, 3H, benzene H), 7.48-7.58 (m, 2H, J_t = 15.5 Hz, benzene H and hexanoate C6-H), 12-18 (sb, 2H, OH acid and OH enole). Anal. ($C_{17}H_{14}ClNO_4$) C, H, N, Cl.

6-[1-(3-Methoxyphenyl)methyl-1H-pyrrol-2-yl]-2,4-dioxo-5-hexenoic acid (RDS 1823). 100%; 145-147 °C; toluene; IR ν 3400 (OH), 1713 (C=O acid), 1614 (C=O ketone) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.70 (s, 3H, CH_3), 5.36 (s, 2H, CH_2), 6.27 (m, 1H, pyrrole β), 6.43 (s, 1H, hexanoate C3-H), 6.60-6.64 (m, 3H, benzene H and hexanoate C5-H), 6.82 (m, 1H, benzene H), 6.97 (m, 1H, pyrrole β), 7.22 (m, 1H, benzene H), 7.29 (m, 1H, pyrrole α), 7.64 (d, 1H, J_t = 15.4 Hz, hexanoate C6-H), 12-18 (sb, 2H, OH acid and OH enole). Anal. ($C_{18}H_{17}NO_5$) C, H, N.

6-[1-(2,4-Dimethylphenyl)methyl-1H-pyrrol-2-yl]-2,4-dioxo-5-hexenoic acid (RDS 2292). 59%; 151-153°C; toluene; IR ν 3400 (OH), 1747 (C=O acid), 1711 (C=O ketone) cm^{-1}; ^1H NMR (DMF) δ 2.47 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 5.68 (s, 2H, CH_2), 6.56 (m, 1H, pyrrole β), 6.69-6.73 (m, 2H, benzene H and hexanoate C3-H), 6.95 (d, 1H, J_t = 15.7 Hz, hexanoate C5-H), 7.17 (d, 1H, benzene H), 7.28 (s, 1H, benzene H), 7.33 (s, 1H, pyrrole β), 7.42 (s, 1H pyrrole α), 7.94 (d, 1H, J_t = 15.7 Hz, hexanoate C6-H), 12-18 (sb, 2H, OH acid and OH enole). Anal. ($C_{19}H_{11}NO_4$) C, H, N.

Synthesis of pyrrole nucleus. To a solution of □,□-unsaturated ketone (5.42 mmol) and toluene-4-sulfonylmethylisocyanide (1.16 g, 5.96 mmol, 1.1 eq) in a mixture of anhydrous dimethyl sulfoxide / ethyl ether (14:30 mL) was added dropwise into a well-stirred suspension of sodium hydride (60% in paraffine oil; 0.48 g, 11.93 mmol, 2.2 eq) in dry ethyl ether (30 mL) under argon atmosphere. After the addition, the mixture was stirred at room temperature for 1 hour. The reaction was treated with water and extracted with ethyl acetate. The organic layer was washed with brine, dried over

anhydrous sodium sulfate and concentrated under vacuum. The crude product, was purified by chromatography on aluminum oxide (using chloroform as eluent), to afford the pure product. Yield (%), melting point (°C), recrystallization solvent, IR, ^{1}H NMR are reported for each compounds.

Alkylation of the pyrrolic nitrogen. A mixture of opportune pyrrole (1.1 mmol), alkylating agent (3.3 mmol), and anhydrous K_2CO_3 (210 mg, 1.5 mmol) in dry DMF (10 mL) was stirred at 100 °C for 2 h. After the mixture was cooled, Treated with water (40 mL), extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous sodium sulfate and concentrated under vacuum. The crude product, was purified by chromatography on silica gel to afford the pure product. Chromatographic eluent, yield (%), melting point (°C), recrystallization solvent, IR, ^{1}H NMR are reported for the compound.

Condensation of pyrrole carboxaldehyde with acetone. The opportune pyrrole carboxaldehyde (0.075 mol) was dissolved in 250 mL of acetone. To this mixture was added NaOH 4N (110 mL) and the reaction was stirred at room temperature for 24 h. After this period water (300 mL) and ethyl acetate (250 mL) were added. The organic layer was separated, washed with water (2 x 100 mL), dried over sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified with column chromatography on silica gel, to obtain pure products. Chromatographic eluent, yield (%), melting point (°C), recrystallization solvent, IR, ^{1}H NMR are reported for each compounds.

Shift from α to β of the acetyl group. A mixture of opportune alpha acetyl-substituted pyrrole (1.23 mmol) in trifluoroacetic acid (5 mL), was heated at 80 °C for 20 h. After this period the reaction was quenched with water (30 mL) and extracted with ethyl acetate (2 x 50 mL). The organic layers were collected, dried over sodium sulfate, filtered and evaporated under vacuum. The crude product was purified with chromatography on silica gel (chloroform as eluent) to afford pure product as a brown oils. Yield (%), melting point (°C), recrystallization solvent, IR, ^{1}H NMR are reported for each compounds.

Synthesis of Diketo Esters. Freshly prepared sodium ethoxide (390 mg, 5.5 mmol) was added into a well-stirred mixture of the appropriate acetyl derivative (2.7 mmol) and diethyl oxalate (790 mg, 5.4 mmol) in anhydrous THF (2.7 mL) under nitrogen atmosphere. The mixture was stirred at room temperature for 2 h, and then was poured into n-hexane (50 mL). The collected precipitate was vigorously stirred for 30 min in 1 N HCl (50 mL). The yellow solid that formed was filtered, washed with water, and dried under IR lamp to afford the pure diketo esters. Yield (%), melting point (°C), IR, ^{1}H NMR are reported for each compounds.

Synthesis of diketo acids. A mixture of 1 N NaOH (6.5 mL) and the appropriate ester (1.3 mmol) in 1:1 THF/methanol (12 mL) was stirred at room temperature for 40 min and then poured onto crushed ice. The aqueous layer was treated with 1 N HCl until pH 3 was reached, and the solid that formed was collected by filtration, then washed with water and desiccated under a warming lamp to afford pure acids. Yield (%), melting point (°C), IR, ^{1}H NMR are reported for each compounds.

1-(4-Fluorobenzyl)-1H-pyrrole-2-carboxaldehyde (3). Compound 3 was prepared from commercially available pyrrole-2-carboxaldehyde by means GP-B, using 4-fluorobenzyl bromide as alkylating agent. Chloroform; 80% as brown oil; IR □ 1640 (C=O) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.54 (s, 2H, CH_2), 6.30 (t, 1H, J = 4 Hz, pyrrole C4-H), 6.9-7.0 (m, 4H, benzene H), 7.15 (d, 1H, J = 4 Hz, pyrrole C3-H), 7.17 (d, 1H, J = 4 Hz, pyrrole C5-H), 9.57 (s, 1H, CHO). Anal. (C12H10FNO) C, H, N, F.

1-(4-Fluorobenzyl)-1H-pyrrole-3-carboxaldehyde (4). Compound 4 was prepared from 3 by means GP-D. 55% as brown oil; IR □ 1640 (C=O aldehyde) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 2H, CH_2), 6.6 (s, 1H, pyrrole C4-H), 6.7 (s, 1H, pyrrole C-2H), 7.0-7.2 (m, 4H, benzene H), 7.31 (s, 1H, pyrrole C2-H), 9.75 (s, 1H, CHO). Anal. (C12H10FNO) C, H, N, F.

4-(4-Phenyl-1H-pyrrol-3-yl)but-3-en-2-one (6). Compound 6 was prepared from (3E,5E)-6-phenylhexa-3,5-dien-2-one by means GP-A. 56% as brown solid. M.P; toluene; IR □1640 (C=O ketone) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 2.47 (s, 3H, CH_3), 6.88 (s, 1H, J = 16.5 Hz, butenone C3-H), 7.10-

7.55 (M, 7H, pyrrole C2-H, pyrrole C5-H and benzene H), 7.81 (s, 1H, J = 16.5 Hz, butenone C4-H), 9.0 (sb, 1H, NH). Anal. (C14H13NO) C, H, N.

4-(1-(4-Fluorobenzyl)-1H-pyrrol-3-yl)but-3-en-2-one (7a). Compound 7a was prepared from 4 by means GP-C. 70% as brown oil; IR 1655 (C=O ketone) cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.34 (s, 3H, CH_3), 5.07 (s, 2H, CH_2), 6.43-6.48 (m, 2H, pyrrole C4-H and butenone C3-H), 6.71 (s, 1H, pyrrole C2-H), 7.0 (s, 1H, pyrrole C5-H), 7.06-7.12 (m, 2H, benzene H), 7.15-7.18 (m, 2H, benzene H), 7.49 (d, 1H, butenone C4-H, J = 16 Hz). Anal. (C15H14FNO) C, H, N, F.

4-(1-(4-Fluorobenzyl)-4-phenyl-1H-pyrrol-3-yl)but-3-en-2-one (7b). Compound 7b was prepared from 6 by means GP-B, using 4-fluorobenzyl bromide as alkylating agent. Chloroform; 63% as brown oil; IR 1640 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$) δ 2.44 (s, 3H, CH_3), 5.07 (s, 2H, CH_2), 6.82 (s, 1H, J = 16.3 Hz, butenone C3-H), 6.90 (s, 1H,), 6.99-7.54 (m, 11H, pyrrole C2-H, pyrrole C5-H, benzene H and benzyl H), 7.80 (s, 1H, J = 16.3 Hz, butenone C4-H). Anal. (C21H18FNO) C, H, N, F.

Ethyl 6-(1-(4-fluorobenzyl)-4-phenyl-1H-pyrrol-3-yl)-2-hydroxy-4-oxohexa-2,5-dienoate (RDS 1711). Compound RDS 1711 was prepared from 7a by means GP-F. 56% as yellow solid; 121-122°C; cyclohexane; IR 2900 (OH enole), 1720 (C=O ester), 1620 (C=O ketone) cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.43 (t, 3H, CH_3CH_2), 4.40 (q, 2H, CH_2CH_3), 5.09 (s, 2H, CH_2), 6.73 (s, 1H, hexanoate C3-H) 6.87 (d, 1H, J = 16.6 Hz, hexanoate C5-H), 7.01 (s, 1H, pyrrole C5-H), 7.08-7.54 (m, 10H, pyrrole C2-H, benzene H and benzyl H), 7.74 (d, 1H, hexanoate C6-H), 15 (bs, 1H, enole). Anal. (C25H21FNO4) C, H, N, F.

Ester 6-(1-(4-fluorobenzyl)-1H-pyrrol-3-yl)-2-hydroxy-4-oxohexa-2,5-dienoate (RDS 2400). Compound RDS 2400 was prepared from 7b by means GP-F. 41% as yellow solid; 88-90 °C; ligroine; IR 3400 (OH enole), 1725 (C=O ester), 1625 (C=O ketone) cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.44 (t, 3H, J = 7 Hz, CH_3CH_2), 4.41 (q, 2H, J = 7 Hz, CH_2CH_3), 5.08 (s, 2H, CH_2), 6.39 (s, 1H, J = 16 Hz, hexanoate C5-H), 6.5-6.6 (m, 2H, pyrrole C4-H and hexanoate C3-H), 6.7 (t, 1H, pyrrole C5-

H), 7.0 (t, 1H, pyrrole C2-H), 7.08-7.20 (m, 4H, benzene H), 7.75 (s, 1H, J = 16 Hz, hexanoate C6-H), 14 (br s, 1H, enole). Anal. ($C_{19}H_{18}FNO_4$) C, H, N, F.

6-(1-(4-Fluorobenzyl)-1H-pyrrol-3-yl)-2-hydroxy-4-oxohexa-2,5-dienoic acid (RDS 2401). Compound RDS 2401 was prepared from RDS 2400 by means GP-G. 92% as yellow solid; >300 °C; DMF/H_2O; IR 3500-2500 (OH acid and enole), 1720 (C=O acid), 1630 (C=O ketone) cm^{-1}. ^1H NMR (DMF d_7) δ 5.34 (s, 2H, benzyl), 6.39 (s, 1H, hexanoate C3-H), 6.54 (d, 1H, hexanoate C5-H), 6.7 (bs, 1H, pyrrole C4-H), 7.38-7.67 (m, 7H, pyrrole C2-H, pyrrole C5-H, benzene H and hexanoate C6-H), 14 (br s, 2H, OH enole and acid). Anal. ($C_{17}H_{16}FNO_4$) C, H, N, F.

6-(1-(4-Fluorobenzyl)-4-phenyl-1H-pyrrol-3-yl)-2-hydroxy-4-oxohexa-2,5-dienoic acid (RDS 1712). Compound RDS 1712 was prepared from RDS1711 by means GP-G. 75% as yellow solid; 128-129°C; benzene; IR 3500-2500 (OH acid and enole), 1700 (C=O acid), 1600 (C=O ketone) cm^{-1}. ^1H NMR ($CDCl_3$) δ 5.20 (s, 2H, CH_2), 6.75 (bs, 1H, hexanoate C3-H), 6.80 (d, 1H, hexanoate C5-H), 7.1-7.6 (m, 12H, pyrrole C2-H, pyrrole C5-H, benzene H, benzyl H and hexanoate C6-H), 14 (br s, 2H, enole and acid). Anal. ($C_{23}H_{17}FNO_4$) C, H, N, F.

1. Nongkhlaw, R. L.; Nongrum, R.; Myrboh B.(2001) Synthesis of substituted hexa-3,5-dienoic acid methyl esters from conjugated dienones J. Chem. Soc., Perkin Trans. 1: 1300-1303.
2. Costi R et al. (2013) 6-(1-Benzyl-1H-pyrrol-2-yl)-2,4-dioxo-5-hexenoic Acids as Dual Inhibitors of recombinant HIV-1 Integrase and Ribonuclease H, Synthesized by a Parallel Synthesis Approach. J Med Chem.56: 8588-98.

Analyses

Compd	Elemental Analyses Calculated/ Found				
	C	H	N	Cl	F
RDS 1759	63.41	5.04	3.89	9.86	
	63.21	4.87	4.01	9.80	
RDS 1822	67.58	5.96	3.94		
	67.59	5.98	3.98		
RDS 2291	71.36	6.56	3.97		
	71.32	5.47	3.64		
RDS 1760	61.53	4.26	4.22	10.69	
	61.59	4.36	4.37	10.71	
RDS 1823	66.03	5.24	4.28		
	65.98	5.23	4.33		
RDS 2292	70.13	5.89	4.31		
	70.10	5.90	4.29		
RDS 1711	71.59	5.29	3.34		4.53
	71.53	5.34	3.31		4.66
RDS 2400	66.46	5.28	4.08		5.53
	66.50	5.20	3.99		5.61

RDS 2401	64.76	4.48	4.44	6.03
	64.70	4.51	4.49	6.15
RDS1712	70.58	4.64	5.58	4.85
	70.40	4.57	5.51	4.76

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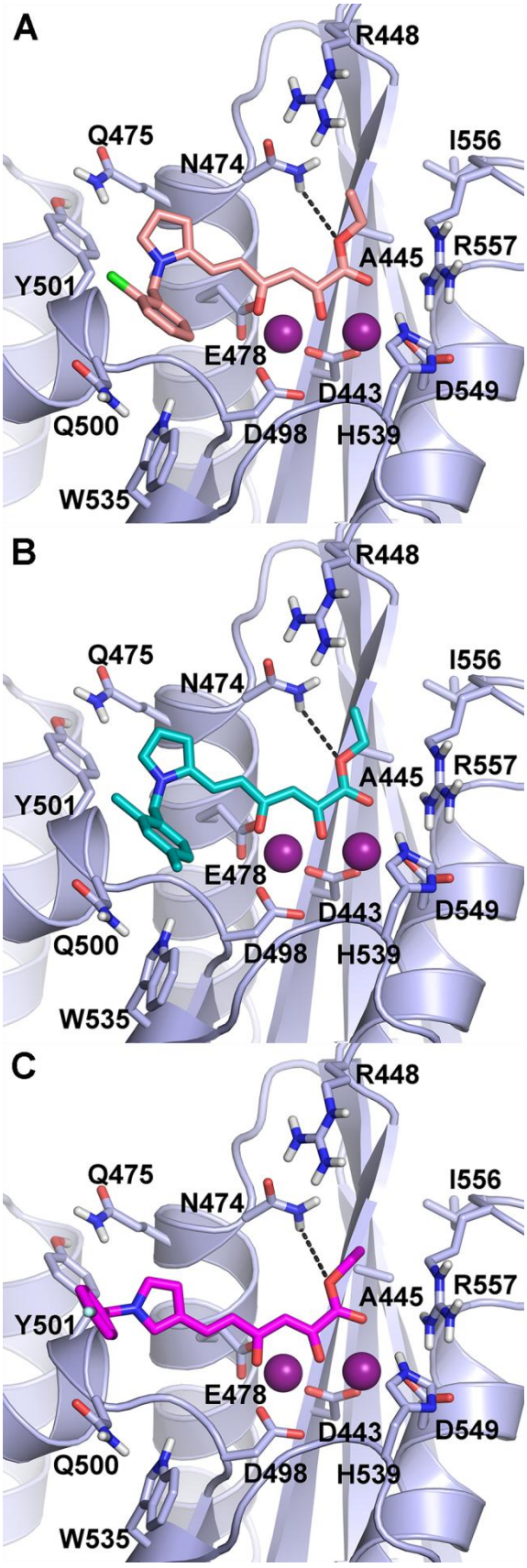
Figure S2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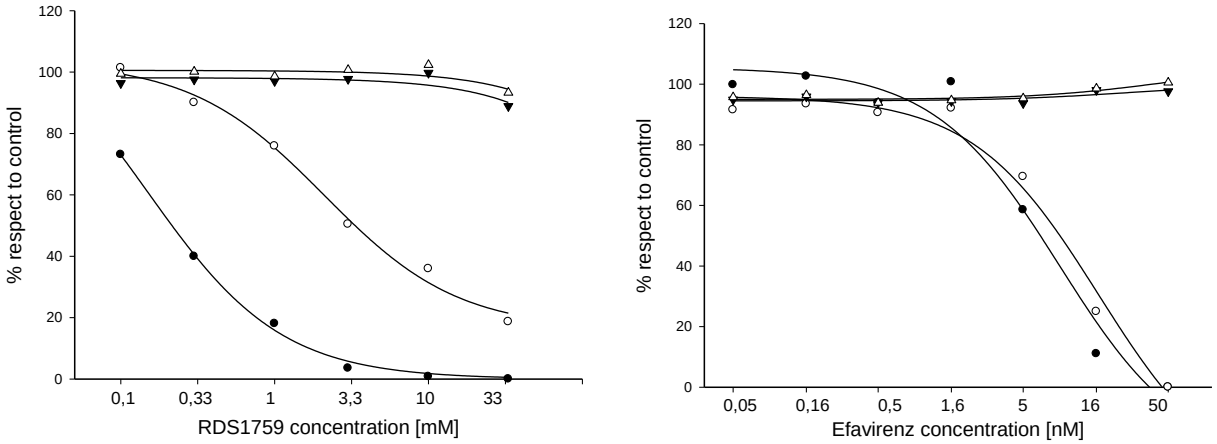
Q500
D498
H539
W535

Figure S2. Binding modes of compounds RDS1759, RDS2291 and RDS2400 at the HIV-1 RNase H active site. RDS1759 (A), RDS2291 (B) and RDS2400 (C) are represented as pink, cyan, and magenta sticks, respectively. The receptor is shown as purple cartoons. Amino acids involved in ligand binding are highlighted as sticks. The active site ions Mg^{2+} ions are represented as magenta spheres.

Figure S2. Time-dependent viral replication inhibition by RDS1759.



HIV-1 infected MT4 cells were treated with increasing concentrations of RDS1759 (Panel A) and EFV (Panel B). Percentage of GFP emitting cells was measured at 24 hours p.i. (●) and 48 hours p.i. (○). MT4 cell viability was also evaluated at 24 hours p.i. (▼) and 48 hours (Δ).