Periselectivity Switch of Acylketenes in Cycloadditions with 1-Azadienes: Microwave-Assisted Diastereoselective Three-Component Synthesis of α-Spiro-δ-lactams

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Supporting Information

Content:
General experimental information and Procedures (p. S2)
Full characterization data for compounds 4a-q (p. S3)
Full characterization data for compounds 10a-e (p. S9)
Copies of $^1$H and $^{13}$C NMR (including DEPT 135) spectra for all compounds (p. S11)
General experimental information:
All reactions under microwave irradiation were performed in a CEM Discover 1-300W system equipped with a build-in pressure measurement sensor and a vertically focused IR temperature sensor (mode Discover Standard), or in a Anton-Paar Monowave 300 system equipped with a build-in pressure measurement sensor and IR and optic fibre temperature sensors following the general procedures below. The reactions were monitored by TLC visualized with p-anisaldehyde and H₂SO₄ in EtOH. Flash chromatography was performed on 40-63 µm silica gel eluted with EtOAc or Et₂O or CH₂Cl₂ in petroleum ether (bp 40-60 °C). NMR data were recorded at 300 MHz in CDCl₃ using as internal standards the residual CHCl₃ signal for ¹H NMR (δ = 7.26) and the deuterated solvent signal for ¹³C NMR (δ = 77.0). Coupling constants are in Hertz (Hz) and the classical abbreviations are used to describe the signal multiplicities. High resolution mass spectra were obtained at the Spectropole (http://www.spectropole.u-3mrs.fr/). All commercially available reagents were used as received. Anhydrous toluene was obtained from a solvent purification system.

Cyclic 2-diazo-1,3-diketones 1 were obtained by treatment of the corresponding 1,3-diketones with p-toluenesulfonyl azide according to the reported procedure in similar yields and purities.¹

Azido compounds 9 were obtained from the corresponding anilines by treatment with sodium nitrite followed by treatment with sodium azide according to the reported procedure in similar yields and purities.²

General procedure A: Multicomponent reaction (MC)
A solution of diazo compound 1, amine 2 (1 equiv) and aldehyde 3 (1 equiv) in 2-3 mL of anhydrous toluene (ca. 0.4 M) under an argon atmosphere in a microwave dedicated sealed tube containing a Teflon coated magnetic stirring bar was irradiated at 140 °C for 15 minutes after a ramp up time of 2 minutes, cooled down to 50 °C by airflow, concentrated, and directly purified by flash chromatography.

General procedure B: One-pot reaction (SW)
A solution of amine 2 (1 equiv) and aldehyde 3 (1 equiv) in 2-3 mL of anhydrous toluene (ca. 0.4 M) under an argon atmosphere in a microwave dedicated sealed tube containing a Teflon coated magnetic stirring bar was irradiated at 140 °C for 15 minutes (ramp up time = 2 min), cooled down to 50 °C by airflow, and concentrated directly in the reaction vessel. To the resulting material placed under an argon atmosphere was added diazo compound 1 and anhydrous toluene (2-3 mL, ca. 0.4M), the reaction vessel was sealed, and this mixture was irradiated at 140 °C after a ramp up time of 2 minutes (160 °C for compounds 4j, 4o and 4p; 200 °C for compounds 4f and 4q) for 15 minutes (45 minutes for compound 4f). The resulting reaction mixture was cooled down to 50 °C by airflow, concentrated, and directly purified by flash chromatography.

General procedure C: Consecutive reaction
To a solution of azido compound 9 in 1.5-2.5 mL of anhydrous toluene (ca. 0.5 M) under an argon atmosphere in a microwave dedicated tube containing a Teflon coated magnetic stirring bar was added trimethylphosphine (1 equiv) in toluene (0.5-1 mL) via a syringe, and the mixture was stirred 30 minutes at room temperature. To the resulting solution was added benzalacetone or cinnamaldehyde (1 equiv), the tube was sealed, and the resulting mixture was irradiated at 140 °C for 15 minutes after a ramp up time of 2 minutes. The resulting mixture was cooled down to 50 °C by airflow, and the diazo compound 1 (1 equiv) was added to the mixture. The reaction vessel was sealed again, the mixture was irradiated at 140 °C for 15 minutes after a ramp up time of 2 minutes, cooled down to 50 °C by airflow, concentrated, and directly purified by flash chromatography.

Compound 4a:

Following the general procedure A (MC), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (126 mg, 0.76 mmol), cinnamaldehyde (95 µL, 0.76 mmol) and benzylamine (83 µL, 0.76 mmol) afforded compound 4a as a colorless oil (203 mg, 74%).

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (132 mg, 0.79 mmol), cinnamaldehyde (100 µL, 0.79 mmol) and benzylamine (87 µL, 0.79 mmol) afforded compound 4a as a colorless oil (238 mg, 99%).

RF (EtO/PE : 1/9) = 0.32


13C NMR (75 MHz, δ ppm/CDCl3) : 212.7 (C), 167.8 (C), 139.1 (C), 136.7 (C), 129.5 (CH), 129.5 (CH), 128.6 (CH), 128.6 (CH), 128.4 (CH), 128.4 (CH), 127.7 (CH), 127.5 (CH), 127.5 (CH), 127.4 (CH), 108.3 (CH), 60.8 (C), 55.0 (CH2), 50.1 (CH2), 49.7 (CH), 45.0 (CH2), 32.3 (C), 29.7 (CH3), 29.4 (CH3).

1H NMR (300 MHz, δ ppm/CDCl3) : 7.37-7.36 (m, 4H), 7.32-7.28 (m, 4H), 7.22-7.19 (m, 2H), 6.25 (dd, J = 2.8, 8.0 Hz, 1H), 5.15 (dd, J = 2.7, 8.0 Hz, 1H), 4.87 (d, J = 15.1 Hz, 1H), 4.75 (d, J = 15.1 Hz, 1H), 3.77 (dd, J = 2.8 Hz, 1H), 2.74 (dd, J = 1.1, 13.7 Hz, 1H), 2.02 (d, J = 13.7 Hz, 1H), 1.88 (dd, J = 1.4, 16.8 Hz, 1H), 1.25 (d, J = 16.8 Hz, 1H), 1.07 (s, 3H), 0.80 (s, 3H).

Compound 4b:

Following the general procedure A (MC), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (115 mg, 0.69 mmol), cinnamaldehyde (87 µL, 0.69 mmol) and furfurylamine (61 µL, 0.69 mmol) afforded compound 4b as a colorless sticky oil (169 mg, 70%).

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (158 mg, 0.95 mmol), cinnamaldehyde (120 µL, 0.95 mmol) and furfurylamine (84 µL, 0.95 mmol) afforded compound 4b as a colorless sticky oil (233 mg, 70%).

RF (EtO/PE : 2/8) = 0.25

HRMS (ESI+) : [M+H]+ calcld for C22H23NO3 350.1751, found 350.1751.

13C NMR (75 MHz, δ ppm/CDCl3) : 212.4 (C), 167.7 (C), 150.2 (C), 142.3 (CH), 139.0 (C), 129.5 (CH), 129.5 (CH), 128.2 (CH), 128.4 (CH), 127.4 (CH), 127.7 (CH), 110.4 (CH), 108.3 (CH), 108.2 (CH), 60.7 (C), 54.9 (CH2), 49.6 (CH), 45.1 (CH2), 43.3 (CH2), 32.3 (C), 29.8 (CH3), 29.3 (CH3).

1H NMR (300 MHz, δ ppm/CDCl3) : 7.37-7.15 (m, 6H), 6.36-6.31 (m, 3H), 5.14 (dd, J = 2.8, 8.0 Hz, 1H), 4.85 (d, J = 15.5 Hz, 1H), 4.65 (d, J = 15.5 Hz, 1H), 3.72 (dd, J = 2.8, 2.8 Hz, 1H), 2.67 (dd, J = 1.6, 13.7 Hz, 1H), 1.97 (d, J = 13.7 Hz, 1H), 1.84 (dd, J = 1.5, 16.8 Hz, 1H), 1.23 (d, J = 16.8 Hz, 1H), 1.04 (s, 3H), 0.78 (s, 3H).

Compound 4c:

Following the general procedure A (MC), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (155 mg, 0.93 mmol), cinnamaldehyde (117 µL, 0.93 mmol) and allylamine (70 µL, 0.93 mmol) afforded compound 4c as a colorless oil (156 mg, 54%).

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (158 mg, 0.95 mmol), cinnamaldehyde (120 µL, 0.95 mmol) and allylamine (71 µL, 0.95 mmol) afforded compound 4c as a colorless oil (190 mg, 64%).

RF (EtO/PE : 2/8) = 0.37

HRMS (ESI+) : [M+H]+ calcld for C20H23NO2 310.1802, found 310.1801.

13C NMR (75 MHz, δ ppm/CDCl3) : 212.7 (C), 167.5 (C), 139.2 (C), 132.4 (CH), 129.6 (CH), 129.6 (CH), 129.4 (CH), 128.4 (CH), 128.4 (CH), 127.7 (CH), 117.2 (CH2), 108.0 (CH), 60.8 (C), 55.0 (CH2), 49.6 (CH), 49.1 (CH2), 44.9 (CH2), 32.2 (C), 29.7 (CH2), 29.3 (CH3).

1H NMR (300 MHz, δ ppm/CDCl3) : 7.30-7.26 (m, 3H), 7.21-7.18 (m, 2H), 6.20 (dd, J = 3.0, 7.9 Hz, 1H), 5.82 (dd, J = 5.4, 10.2, 17.2 Hz, 1H), 5.33-5.17 (m, 2H), 5.13 (dd, J = 3.0, 7.9 Hz, 1H), 4.26-4.10 (m, 2H), 3.74 (dd, J = 2.8, 2.8 Hz, 1H), 2.67 (dd, J = 1.6, 13.6 Hz, 1H), 1.96 (d, J = 13.6 Hz, 1H), 1.80 (dd, J = 1.6, 16.8 Hz, 1H), 1.17 (d, J = 16.8 Hz, 1H), 1.01 (s, 3H), 0.75 (s, 3H).
Compound 4d:

Following the general procedure B (SW), reaction between 5-methyl-2-diazo-1,3-cyclohexandione 1b (121 mg, 0.79 mmol), cinnamaldehyde (100 µL, 0.79 mmol) and allylamine (60 µL, 0.79 mmol) afforded compound 4d as a yellow oil (185 mg, 79%, d.r. = 1.2 : 1).

Major diastereomer:
RF (Et₂O/PE : 2/8) = 0.19
HRMS (ESI⁺): [M+H]⁺ calcld for C₁₉H₂₂NO₂ 296.1645, found 296.1648.
¹³C NMR (75 MHz, δ ppm/CDCl₃) : 213.9 (C), 167.5 (C), 139.4 (C), 132.4 (CH), 129.0 (CH), 128.7 (CH), 128.7 (CH), 128.6 (CH), 128.6 (CH), 127.6 (CH), 117.2 (CH₂), 108.5 (CH), 61.3 (C), 49.3 (CH), 48.9 (CH₂), 47.6 (CH₂), 41.1 (CH₃), 26.7 (CH), 20.4 (CH₃).

¹H NMR (300 MHz, δ ppm/CDCl₃) : 7.28-7.16 (m, 5H), 6.19 (dd, J = 2.8, 7.9 Hz, 1H), 5.81 (tdd, J = 5.4, 10.2, 17.2 Hz, 1H), 5.32-5.17 (m, 2H), 5.13 (dd, J = 3.1, 7.9 Hz, 1H), 4.27-4.08 (m, 2H), 3.79 (dd, J = 2.8, 2.8 Hz, 1H), 2.65 (dd, J = 10.8, 13.5 Hz, 1H), 2.74 (ddd, J = 2.0, 7.1, 13.4 Hz, 1H), 2.03-1.93 (m, 1H), 1.73 (dd, J = 10.8, 18.6 Hz, 1H), 1.31-1.17 (m, 1H), 0.92 (d, J = 6.4 Hz, 3H).

Minor diastereomer:
RF (Et₂O/PE : 2/8) = 0.23
HRMS (ESI⁺): [M+H]⁺ calcld for C₁₉H₂₂NO₂ 296.1645, found 296.1648.
¹³C NMR (75 MHz, δ ppm/CDCl₃) : 213.4 (C), 167.4 (C), 139.2 (C), 132.4 (CH), 129.7 (CH), 129.7 (CH), 128.9 (CH), 128.4 (CH), 128.4 (CH), 127.5 (CH), 117.3 (CH₂), 108.4 (CH), 60.6 (C), 48.7 (CH₂), 48.5 (CH₂), 48.4 (CH), 40.7 (CH₂), 28.7 (CH), 20.1 (CH₃).

¹H NMR (300 MHz, δ ppm/CDCl₃) : 7.30-7.17 (m, 5H), 6.17 (dd, J = 3.1, 7.9 Hz, 1H), 5.81 (tdd, J = 5.4, 10.2, 17.2 Hz, 1H), 5.32-5.18 (m, 2H), 5.17-5.13 (m, 1H), 4.28-4.03 (m, 2H), 3.75 (dd, J = 2.9, 2.9 Hz, 1H), 2.73-2.65 (m, 1H), 2.41-2.27 (m, 1H), 2.10 (ddd, J = 2.0, 6.8, 16.9 Hz, 1H), 1.59 (dd, J = 11.1, 13.0 Hz, 1H), 1.01-0.91 (m, 1H), 0.87 (d, J = 6.4 Hz, 3H).

Compound 4e:

Following the general procedure B (SW), reaction between 2-diazo-1,3-cyclohexandione 1c (110 mg, 0.79 mmol), cinnamaldehyde (100 µL, 0.79 mmol) and allylamine (60 µL, 0.79 mmol) afforded compound 4e as a yellow oil (163 mg, 73%).

RF (Et₂O/PE : 3/7) = 0.26
¹³C NMR (75 MHz, δ ppm/CDCl₃) : 214.5 (C), 167.6 (C), 139.4 (C), 132.5 (CH), 129.2 (CH), 129.2 (CH), 129.0 (CH), 128.6 (CH), 128.6 (CH), 127.6 (CH), 117.3 (CH₂), 108.6 (CH), 59.1 (C), 48.9 (CH), 48.9 (CH), 39.8 (CH₂), 32.6 (CH₂), 19.4 (CH₃).

¹H NMR (300 MHz, δ ppm/CDCl₃) : 7.30-7.27 (m, 3H), 7.22-7.19 (m, 2H), 6.19 (dd, J = 3.0, 8.0 Hz, 1H), 5.82 (tdd, J = 5.4, 10.2, 17.2 Hz, 1H), 5.34-5.19 (m, 2H), 5.15 (dd, J = 3.0, 8.0 Hz, 1H), 4.29-4.08 (m, 2H), 3.81 (dd, J = 3.0, 3.0 Hz, 1H), 2.88 (td, J = 7.4, 13.4 Hz, 1H), 2.14-1.98 (m, 2H), 1.88-1.74 (m, 1H), 1.62 (ddd, J = 7.8, 8.9, 17.8 Hz, 1H), 1.29-1.14 (m, 1H).

Compound 4f:

Following the general procedure B (SW), reaction between 2-diazo-1,3-cycloheptandione 1d (152 mg, 1.0 mmol), cinnamaldehyde (126 µL, 1.0 mmol) and benzylamine (109 µL, 1.0 mmol) afforded compound 4f as a yellow oil (183 mg, 53%).

RF (AcOEt/PE : 2/8) = 0.29
¹³C NMR (75 MHz, δ ppm/CDCl₃) : 206.7 (C), 169.0 (C), 140.1 (C), 136.6 (C), 128.6 (CH), 128.6 (CH), 128.2 (CH), 128.2 (CH), 127.9 (CH), 127.9 (CH), 127.6 (CH), 127.8 (CH), 127.6 (CH), 126.9 (CH), 126.8 (CH), 109.8 (CH), 59.6 (C), 49.6 (CH₂), 47.4 (CH), 41.8 (CH₂), 36.2 (CH₂), 26.6 (CH₂), 21.1 (CH₂).

¹H NMR (300 MHz, δ ppm/CDCl₃) : 7.37-7.30 (m, 5H), 7.20-7.18 (m, 3H), 7.12-7.09 (m, 2H), 6.09 (d, J = 7.7 Hz, 1H), 5.30 (dd, J = 5.6, 7.7 Hz, 1H), 4.86 (d, J = 14.7 Hz, 1H), 4.70 (d, J = 14.7 Hz, 1H), 3.65 (d, J = 5.7 Hz, 1H), 2.88 (ddd, J = 5.4, 8.5, 14.4 Hz, 1H), 2.55-2.49 (m, 1H), 2.22-2.14 (m, 1H), 1.98-1.88 (m, 3H), 1.77-1.70 (m, 2H).
Compound 4g:

Following the general procedure A (MC), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (173 mg, 1.04 mmol), cinnamaldehyde (131 µL, 1.04 mmol) and i-propylamine (89 µL, 1.04 mmol) afforded compound 4g as a colorless oil (200 mg, 62%).

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (158 mg, 0.95 mmol), cinnamaldehyde (120 µL, 0.95 mmol) and i-propylamine (81 µL, 0.95 mmol) afforded compound 4g as a colorless oil (188 mg, 63%).

RF (EtO/PE : 2/8) = 0.34

HRMS (ESI+) : [M+H]^+ calcld for C_{20}H_{25}NO_2 312.1958, found 312.1956.

$^1$H NMR (300 MHz, δ ppm/CDCl$_3$) : 7.28-7.23 (m, 3H), 7.18-7.15 (m, 2H), 6.29 (dd, J = 2.7, 8.1 Hz, 1H), 5.15 (dd, J = 2.9, 8.1 Hz, 1H), 4.82 (hept, J = 7.0 Hz, 1H), 3.66 (dd, J = 2.8, 2.8 Hz, 1H), 2.61 (dd, J = 1.4, 13.7 Hz, 1H), 1.95 (d, J = 13.7 Hz, 1H), 1.23 (d, J = 16.6 Hz, 1H), 1.23 (d, J = 7.0 Hz, 3H), 1.18 (d, J = 7 Hz, 3H), 1.01 (s, 3H), 0.76 (s, 3H).

Compound 4h:

Following the general procedure A (MC), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (162 mg, 0.97 mmol), cinnamaldehyde (123 µL, 0.97 mmol) and n-propylamine (80 µL, 0.97 mmol) afforded compound 4h as a colorless oil (151 mg, 50%).

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (158 mg, 0.95 mmol), cinnamaldehyde (120 µL, 0.95 mmol) and n-propylamine (78 µL, 0.95 mmol) afforded compound 4h as a colorless oil (257 mg, 87%).

RF (EtO/PE : 2/8) = 0.37

HRMS (ESI+) : [M+H]^+ calcld for C_{20}H_{25}NO_2 312.1958, found 312.1959.

$^1$H NMR (300 MHz, δ ppm/CDCl$_3$) : 7.29-7.24 (m, 3H), 7.20-7.16 (m, 2H), 6.20 (dd, J = 2.9, 7.9 Hz, 1H), 5.08 (dd, J = 2.8, 7.9 Hz, 1H), 3.70 (dd, J = 2.9, 2.9 Hz, 1H), 3.40 (dd, J = 6.8, 5.7 Hz, 2H), 2.64 (dd, J = 1.6, 13.7 Hz, 1H), 1.94 (d, J = 13.7 Hz, 1H), 1.79 (dd, J = 1.3, 16.8 Hz, 1H), 1.62 (tq, J = 7.5, 5.7 Hz, 2H), 1.18 (d, J = 16.8 Hz, 1H), 1.01 (s, 3H), 0.92 (t, J = 7.5 Hz, 3H), 0.74 (s, 3H).

Compound 4i:

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (132 mg, 0.79 mmol), cinnamaldehyde (100 µL, 0.79 mmol) and (S)-(-)-α-methylbenzylamine (101 µL, 0.79 mmol) afforded compound 4i as a yellow oil (281 mg, 95%, d.r. = 1.5 : 1).

RF (EtO/PE : 1/9) = 0.25 & 0.19

HRMS (ESI+) : [M+H]^+ calcld for C_{25}H_{27}NO_2 374.2115, found 374.2124.

$^1$H NMR (300 MHz, δ ppm/CDCl$_3$) : 7.48-7.19 (m, 22H), 6.17-6.01 (m, 2H), 5.12-5.08 (m, 2H), 3.77 (dd, J = 3.0, 3.0 Hz, 1H), 3.69 (dd, J = 3.0, 3.0 Hz, 1H), 2.80-2.68 (m, 2H), 2.05-1.84 (m, 4H), 1.67 (d, J = 7.3 Hz, 3H), 1.61 (d, J = 7.1 Hz, 3H), 1.35-1.18 (m, 2H), 1.10 (s, 3H), 1.09 (s, 3H), 0.83 (s, 3H), 0.82 (s, 3H).
Compound 4j:

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (166 mg, 1.0 mmol), α-methylcinnamaldehyde (140 µL, 1.0 mmol) and benzylamine (109 µL, 1.0 mmol) afforded compound 4j as a colorless oil (275 mg, 74%).

Rf (Et2O/PE : 4/6) = 0.39


13C NMR (75 MHz, δ ppm/CDCl3) : 212.3 (C), 168.7 (C), 137.2 (C), 136.8 (C), 128.9 (CH), 128.7 (CH), 128.7 (CH), 128.2 (CH), 128.2 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 123.8 (CH), 117.1 (C), 60.1 (C), 55.7 (CH), 54.9 (CH2), 50.0 (CH2), 49.5 (CH2), 33.3 (C), 30.4 (CH3), 29.6 (CH3), 19.0 (CH3).

1H NMR (300 MHz, δ ppm/CDCl3) : 3.3 Hz, 1H), 5.08 (dd, 1H), 4.78 (d, J = 13.9 Hz, 1H), 2.1 (d, J = 17.1 Hz, 1H), 2.02 (d, J = 17.1 Hz, 1H), 1.57 (d, J = 1.7 Hz, 3H), 1.16 (s, 3H), 1.09 (s, 3H).

Compound 4k:

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (193 mg, 1.60 mmol), furfural (142 mg, 1.60 mmol) and furfurylamine (103 µL, 1.60 mmol) afforded compound 4k as an orange oil (284 mg, 52%).

Rf (AcOEt/PE : 2/8) = 0.44


13C NMR (75 MHz, δ ppm/CDCl3) : 211.52 (C), 167.7 (C), 152.2 (C), 150.1 (C), 142.3 (CH), 141.9 (CH), 129.6 (CH), 110.7 (CH), 110.4 (CH), 108.5 (CH), 108.3 (CH), 105.2 (CH), 59.5 (C), 53.6 (CH2), 45.7 (CH2), 43.2 (CH2), 32.5 (C), 29.8 (CH3), 29.2 (CH3).

1H NMR (300 MHz, δ ppm/CDCl3) : 3.78-7.33 (m, 2H), 6.32-6.27 (m, 4H), 6.15 (d, J = 3.3 Hz, 1H), 5.08 (dd, J = 3.3, 7.8 Hz, 1H), 4.81 (d, J = 15.6 Hz, 1H), 4.61 (d, J = 15.6 Hz, 1H), 3.86 (dd, J = 2.7, 2.7 Hz, 1H), 2.65 (dd, J = 1.4, 13.7 Hz, 1H), 2.06 (d, J = 13.7 Hz, 1H), 1.93 (d, J = 16.7 Hz, 1H), 1.42 (d, J = 16.7 Hz, 1H), 1.06 (s, 3H), 0.95 (s, 3H).

Compound 4l:

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (156 mg, 0.94 mmol), 2-methoxycinnamaldehyde (152 mg, 0.94 mmol) and allylamine (70 µL, 0.94 mmol) afforded compound 4l as a colorless oil (242 mg, 76%).

Rf (Et2O/PE : 2/8) = 0.17


13C NMR (75 MHz, δ ppm/CDCl3) : 212.4 (C), 168.1 (C), 156.6 (C), 132.4 (CH), 129.2 (CH), 129.0 (CH), 128.3 (CH), 125.6 (CH), 120.5 (CH), 117.2 (CH2), 110.3 (CH), 108.3 (CH), 60.6 (C), 54.8 (CH3), 54.6 (CH2), 48.4 (CH2), 46.4 (CH2), 40.2 (CH), 32.4 (C), 29.7 (CH3), 29.4 (CH3).

1H NMR (300 MHz, δ ppm/CDCl3) : 7.22-7.10 (m, 2H), 6.88-6.82 (m, 2H), 6.2 (dd, J = 2.0, 7.8 Hz, 1H), 5.80 (tdd, J = 5.6, 10.2, 17.2 Hz, 1H), 5.30-5.16 (m, 2H), 5.08-5.04 (m, 1H), 4.39-4.38 (m, 1H), 4.14-4.12 (m, 2H), 3.74 (s, 3H), 2.39 (d, J = 13.9 Hz, 1H), 2.14 (d, J = 13.9 Hz, 1H), 1.99 (d, J = 16.8 Hz, 1H), 1.71 (d, J = 16.8 Hz, 1H), 1.05 (s, 3H), 0.93 (s, 3H).
Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (189 mg, 1.14 mmol) and furfurylamine (181 µL, 0.92 mmol) afforded compound 4o as a yellow oil (108 mg, 24%).

**RF** (AcOEt/PE : 4:6) = 0.59

**HRMS** (ESI+) : [M+H]+ calcd for C_{22}H_{22}N_{2}O_{5} 394.4205, found 394.4204.

**13C NMR** (75 MHz, δ ppm/CDCl3) : 212.6 (C), 169.3 (C), 149.8 (C), 148.9 (C), 142.6 (CH), 133.5 (C), 133.2 (CH), 130.1 (CH), 129.7 (CH), 128.1 (CH), 124.6 (CH), 110.6 (CH), 109.3 (CH), 107.8 (CH), 59.8 (C), 54.4 (CH2), 51.7 (CH3), 43.6 (CH), 42.5 (CH2), 33.7 (C), 30.9 (CH3), 29.5 (CH3).

**1H NMR** (300 MHz, δ ppm/CDCl3) : 7.84-7.80 (m, 1H), 7.42 (dd, J = 1.2, 1.2 Hz, 1H), 7.37-7.32 (m, 2H), 7.08-7.05 (m, 1H), 6.43-6.38 (m, 3H), 5.23 (dd, J = 6.1, 7.7 Hz, 1H), 4.88 (d, J = 15.3 Hz, 1H), 4.60 (d, J = 15.3 Hz, 1H), 4.33 (d, J = 6.1 Hz, 1H), 2.35-2.04 (m, 4H), 1.17 (s, 3H), 1.13 (s, 3H).

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Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (153 mg, 0.92 mmol), 4-methoxycinnamaldehyde (149 mg, 0.92 mmol) and furfurylamine (81 µL, 0.92 mmol) afforded compound 4n as an orange oil (161 mg, 50%).

**RF** (AcOEt/PE : 2:8) = 0.44

**HRMS** (ESI+) : [M+H]+ calcd for C_{26}H_{30}N_{2}O_{2} 403.2380, found 403.2381.

**13C NMR** (75 MHz, δ ppm/CDCl3) : 213.3 (C), 168.2 (C), 150.0 (C), 136.9 (C), 130.2 (CH), 130.2 (CH), 129.2 (CH), 128.6 (CH), 128.6 (CH), 127.5 (CH), 127.5 (CH), 127.4 (CH), 126.3 (C), 112.3 (CH), 112.3 (CH), 109.2 (CH), 61.1 (C), 55.1 (CH2), 50.2 (CH2), 49.0 (CH), 45.0 (CH2), 40.4 (CH2), 32.5 (C), 29.9 (CH3), 29.4 (CH3).

**1H NMR** (300 MHz, δ ppm/CDCl3) : 7.36-7.35 (m, 1H), 7.07 (d, J = 8.6 Hz, 2H), 6.82 (d, J = 8.6 Hz, 2H), 6.35-6.28 (m, 3H), 5.10 (dd, J = 2.9, 8.1 Hz, 1H), 4.83 (d, J = 15.5 Hz, 1H), 4.63 (d, J = 15.5 Hz, 1H), 3.76 (s, 3H), 3.67 (dd, J = 2.8, 2.8 Hz, 1H), 2.65 (dd, J = 1.5, 13.6 Hz, 1H), 1.95 (d, J = 13.6 Hz, 1H), 1.84 (dd, J = 1.4, 16.7 Hz, 1H), 1.27 (d, J = 16.7 Hz, 1H), 1.03 (s, 3H), 0.81 (s, 3H).

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Following the general procedure A (MC), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (137 mg, 0.82 mmol), 4-(dimethylamino)cinnamaldehyde (144 mg, 0.82 mmol) and benzylamine (90 µL, 0.82 mmol) afforded compound 4m as a yellow oil (161 mg, 50%).

**RF** (AcOEt/PE : 2:8) = 0.34

**HRMS** (ESI+) : [M+H]+ calcd for C_{23}H_{25}NO_{4} 380.1856, found 380.1867.

**13C NMR** (75 MHz, δ ppm/CDCl3) : 212.6 (C), 167.7 (C), 159.0 (C), 150.2 (C), 142.3 (CH), 130.9 (C), 130.5 (CH), 130.5 (CH), 129.1 (CH), 113.7 (CH), 113.7 (CH), 110.4 (CH), 108.6 (CH), 108.3 (CH), 60.8 (C), 55.1 (CH2), 55.0 (CH2), 48.8 (CH), 45.2 (CH2), 43.2 (CH2), 32.4 (C), 29.9 (CH3), 29.3 (CH3).

**1H NMR** (300 MHz, δ ppm/CDCl3) : 7.38-7.37 (m, 4H), 7.08 (m, 2H), 7.05 (m, 1H), 6.38 (m, 3H), 2.72 (dd, J = 6.1, 7.7 Hz, 1H), 1.95 (d, J = 13.6 Hz, 1H), 1.84 (dd, J = 1.4, 16.7 Hz, 1H), 1.27 (d, J = 16.7 Hz, 1H), 1.03 (s, 3H), 0.81 (s, 3H).
Compound 4p:

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (166 mg, 1.0 mmol), trans-trans-hexadienal (110 µL, 1.0 mmol) and allylamine (75 µL, 1.0 mmol) afforded compound 4p as a yellow oil (83 mg, 30%).

\[ \text{Rf} (\text{Et}_2\text{O/PE : 2/8}) = 0.28 \]

**HRMS** (ESI+): [M+H]⁺ calcd for C₁₇H₂₃NO₂ 274.1802, found 274.1803.

**¹³C NMR** (75 MHz, δ ppm/CDCl₃): 212.8 (C), 168.3 (C), 132.5 (CH), 129.2 (CH), 128.3 (CH), 128.3 (CH), 117.1 (CH₂), 107.3 (CH), 59.9 (C), 55.1 (CH₂), 48.7 (CH₂), 46.9 (CH), 46.4 (CH₂), 33.2 (C), 30.3 (CH₃), 29.6 (CH₃), 17.8 (CH₃).

**¹H NMR** (300 MHz, δ ppm/CDCl₃): 6.01 (dd, \( J \) = 2.3, 7.8 Hz, 1H), 5.75 (tdd, \( J \) = 5.4, 10.2, 17.2 Hz, 1H), 5.56 (qd, \( J \) = 6.3, 15.2 Hz, 1H), 5.34 (qdd, \( J \) = 1.6, 9.1, 15.2 Hz, 1H), 5.23-5.13 (m, 2H), 4.93 (dd, \( J \) = 3.6, 7.8 Hz, 1H), 4.10-4.07 (m, 2H), 3.01 (ddd, \( J \) = 2.3, 3.1, 9.1 Hz, 1H), 2.46 (d, \( J \) = 13.6 Hz, 1H), 2.20-2.15 (m, 2H), 1.86 (d, \( J \) = 13.6 Hz, 1H), 1.69 (dd, \( J \) = 1.6, 6.3 Hz, 3H), 1.11 (s, 3H), 1.10 (s, 3H).

MW = 273,3700

Compound 4q:

Following the general procedure B (SW), reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (166 mg, 1.0 mmol), L(-)-perillaldehyde (155 µL, 1.0 mmol) and allylamine (75 µL, 1.0 mmol) afforded compound 4q as a yellow oil (154 mg, 47%, d.r. = 4 : 1).

\[ \text{Rf} (\text{Et}_2\text{O/PE : 2/8}) = 0.27 & 0.28 \]

**HRMS** (ESI+): [M+H]⁺ calcd for C₂₁H₂₉NO₂ 328.2271, found 328.2270.

**¹³C NMR** (75 MHz, δ ppm/CDCl₃): 214.0 (C), 213.8 (C), 167.2 (C), 167.2 (C), 148.9 (C), 146.1 (C), 132.6 (CH), 132.6 (CH), 121.4 (CH), 121.1 (CH), 117.6 (C), 117.0 (CH₂), 116.9 (CH₂), 116.5 (C), 110.8 (CH₂), 109.1 (CH₂), 60.6 (C), 60.2 (C), 55.4 (CH₂), 55.4 (CH₂), 48.9 (CH₂), 48.8 (CH₂), 48.1 (CH₂), 47.5 (CH₂), 44.9 (CH), 44.6 (CH), 39.8 (CH), 38.1 (CH), 33.5 (CH₂), 32.8 (C), 32.7 (C), 31.4 (CH₂), 30.7 (CH₃), 30.6 (CH₃), 30.1 (CH₂), 29.7 (CH₃), 29.7 (CH₃), 29.0 (CH₂), 27.3 (CH₂), 25.6 (CH₂), 22.0 (CH₃), 20.6 (CH₃).

**¹H NMR** (300 MHz, δ ppm/CDCl₃): 5.77-5.64 (m, 4H), 5.21-5.07 (m, 4H), 4.84-4.63 (m, 4H), 4.11-3.93 (m, 4H), 2.67-2.61 (m, 2H), 2.56-2.34 (m, 2H), 2.27-2.03 (m, 7H), 1.87-1.40 (m, 14H), 1.20-1.07 (m, 16H), 0.85-0.79 (m, 1H).

MW = 327,46
Compound 10a:

Following the general procedure C, reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (129 mg, 0.78 mmol), trans-benzalacetone (114 mg, 0.78 mmol) and 4-azidoanisole (116 mg, 0.78 mmol) afforded compound 10a as a yellow solid (202 mg, 69%).

RF (AcOEt/PE : 2/8) = 0.34

HRMS (ESI+) : [M+H]+ calcd for C_{25}H_{27}NO_{3} 390.2064, found 390.2068.

^{13}C NMR (75 MHz, δ ppm/CDCl_{3}) : 212.5 (C), 169.4 (C), 158.8 (C), 139.9 (C), 136.8 (C), 131.6 (C), 129.5 (CH), 129.5 (CH), 128.3 (CH), 128.3 (CH), 128.3 (CH), 128.5 (CH), 128.5 (CH), 127.5 (CH), 114.2 (CH), 114.2 (CH), 105.5 (CH), 60.6 (C), 55.2 (CH), 55.2 (CH_{2}), 48.9 (CH), 44.4 (CH_{2}), 32.2 (C), 29.7 (CH_{3}), 29.3 (CH_{3}), 20.4 (CH_{3}).

^{1}H NMR (300 MHz, δ ppm/CDCl_{3}) : 7.37-6.91 (m, 9H), 5.04-5.03 (m, 1H), 3.82 (dd, J = 2.4, 2.4 Hz, 1H), 3.80 (s, 3H), 2.69 (dd, J = 1.6, 13.7 Hz, 1H), 1.99 (d, J = 13.7 Hz, 1H), 1.85 (d, J = 16.6 Hz, 1H), 1.68-1.67 (m, 3H), 1.28 (d, J = 16.6 Hz, 1H), 0.99 (s, 3H), 0.76 (s, 3H).

MW = 389,4868

Compound 10b:

Following the general procedure C, reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (117 mg, 0.70 mmol), cinnamaldehyde (89 µL, 0.70 mmol) and 4-azidoanisole (105 mg, 0.70 mmol) afforded compound 10b as a white solid (199 mg, 75%).

RF (AcOEt/PE : 2/8) = 0.34

HRMS (ESI+) : [M+H]+ calcd for C_{24}H_{25}NO_{3} 376.1907, found 376.1911.

^{13}C NMR (75 MHz, δ ppm/CDCl_{3}) : 212.6 (C), 168.1 (C), 158.5 (C), 139.2 (C), 143.0 (C), 131.3 (CH), 129.6 (CH), 129.6 (CH), 128.5 (CH), 128.5 (CH), 127.8 (CH), 127.5 (CH), 127.5 (CH), 114.3 (CH), 114.3 (CH), 107.5 (CH), 61.1 (C), 55.4 (CH_{3}), 55.1 (CH_{3}), 49.6 (CH), 44.7 (CH_{2}), 32.3 (C), 29.8 (CH_{3}), 29.4 (CH_{3}).

^{1}H NMR (300 MHz, δ ppm/CDCl_{3}) : 7.36-7.22 (m, 7H), 6.93 (d, J = 8.6 Hz, 2H), 6.42 (dd, J = 3.0, 8.0 Hz, 1H), 5.19 (dd, J = 2.7, 8.0 Hz, 1H), 3.90 (dd, J = 2.7, 2.7 Hz, 1H), 3.80 (s, 3H), 2.75 (d, J = 13.7 Hz, 1H), 2.03 (d, J = 13.7 Hz, 1H), 1.87 (d, J = 16.7 Hz, 1H), 1.24 (d, J = 16.7 Hz, 1H), 1.03 (s, 3H), 0.79 (s, 3H).

MW = 375,4602

Compound 10c:

Following the general procedure C, reaction between 5,5-dimethyl-2-diazo-1,3-cyclohexandione 1a (105 mg, 0.63 mmol), cinnamaldehyde (80 µL, 0.63 mmol) and 4-azido-1-nitrobenzene (104 mg, 0.63 mmol) afforded compound 10c as a yellow solid (87 mg, 35%), recrystallization of which from Et_{2}O provided monocrystalline needles suitable for X-ray diffraction structural analysis. These data have been deposited with the Cambridge Crystallographic Data Center under the CCDC number 773144.

RF (AcOEt/PE : 2/8) = 0.37

^{13}C NMR (75 MHz, δ ppm/CDCl_{3}) : 212.1 (C), 167.9 (C), 146.4 (C), 145.9 (C), 138.6 (C), 129.7 (CH), 129.6 (CH), 129.6 (CH), 128.7 (CH), 128.7 (CH), 128.1 (CH), 126.5 (CH), 126.5 (CH), 124.4 (CH), 124.4 (CH), 109.9 (CH), 61.3 (C), 55.2 (CH_{2}), 49.4 (CH), 44.3 (CH_{3}), 32.4 (C), 29.7 (CH_{3}), 29.4 (CH_{3}).

^{1}H NMR (300 MHz, δ ppm/CDCl_{3}) : 8.27 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.8 Hz, 2H), 7.38-7.24 (m, 5H), 6.52 (dd, J = 3.1, 8.0 Hz, 1H), 5.36 (dd, J = 2.7, 8.0 Hz, 1H), 3.92 (dd, J = 2.7, 2.7 Hz, 1H), 2.74 (d, J = 13.8 Hz, 1H), 2.05 (d, J = 13.8 Hz, 1H), 1.87 (dd, J = 1.4, 16.5 Hz, 1H), 1.23 (d, J = 16.5 Hz, 1H), 1.02 (s, 3H), 0.81 (s, 3H).

MW = 390,4318
**Compound 10d:**

Following the general procedure C, reaction between 2-diazo-1,3-cyclohexandione 1c (88 mg, 0.64 mmol), *trans*-benzalacetone (93 mg, 0.64 mmol) and 4-bromo-1-azidobenzene (126 mg, 0.64 mmol) afforded compound 10d as a white solid (189 mg, 72%).

Rf (AcOEt/PE : 2/8) = 0.35

HRMS (ESI+) : [M+H]+ calcd for C_{22}H_{21}BrNO_{2} 410.0750, found 410.0755.

$^{13}$C NMR (75 MHz, δ ppm/CDCl$_3$) : 214.2 (C), 169.1 (C), 139.9 (C), 137.9 (C), 135.8 (C), 132.3 (CH), 132.3 (CH), 129.1 (CH), 129.1 (CH), 129.1 (CH), 128.7 (CH), 128.7 (CH), 128.7 (CH), 127.7 (CH), 121.8 (C), 107.0 (CH), 59.1 (C), 48.4 (CH), 40.0 (CH$_2$), 31.9 (CH$_2$), 20.4 (CH), 19.1 (CH$_2$).

$^1$H NMR (300 MHz, δ ppm/CDCl$_3$) : 7.55 (d, J = 8.7 Hz, 2H), 7.34-7.24 (m, 5H), 7.08 (d, J = 8.1 Hz, 2H), 5.07 (dd, J = 1.6, 2.7 Hz, 1H), 3.89 (dd, J = 2.7 Hz, 1H), 2.95-2.85 (m, 1H), 2.14-1.96 (m, 2H), 1.80-1.60 (m, 2H), 1.67 (dd, J = 1.6, 2.7 Hz, 3H), 1.13-1.03 (m, 1H).

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**Compound 10e:**

Following the general procedure C, reaction between 2-diazo-1,3-cyclohexandione 1c (72 mg, 0.52 mmol), *trans*-benzalacetone (76 mg, 0.52 mmol) and 2-iodo-1-azidobenzene (127 mg, 0.52 mmol) afforded compound 10e as a white solid (50 mg, 21%).

Rf (AcOEt/PE : 2/8) = 0.24

HRMS (ESI+) : [M+H]+ calcd for C_{22}H_{21}INO_{2} 458.0611, 458.0614.

$^{13}$C NMR (75 MHz, δ ppm/CDCl$_3$) : 214.2 (C), 168.4 (C), 141.5 (C), 140.0 (C), 139.3 (CH), 135.0 (C), 130.5 (CH), 129.8 (CH), 129.3 (CH), 129.1 (CH), 128.6 (CH), 128.6 (CH), 127.6 (CH), 107.2 (CH), 100.0 (C), 59.1 (C), 48.4 (CH), 40.0 (CH$_2$), 32.1 (CH$_2$), 20.1 (CH$_3$), 19.1 (CH$_3$).

$^1$H NMR (300 MHz, δ ppm/CDCl$_3$) : 7.91 (dd, J = 1.3, 7.7 Hz, 1H), 7.43 (dd, J = 1.2, 7.7 Hz, 1H), 7.36-7.25 (m, 6H), 7.09 (ddd, J = 1.8, 7.7, 7.7 Hz, 1H), 5.14 (dd, J = 1.2, 2.5 Hz, 1H), 3.94 (dd, J = 2.7, 2.7 Hz, 1H), 2.95 (td, J = 7.4, 13.2 Hz, 1H), 2.19-2.00 (m, 2H), 1.84-1.67 (m, 2H), 1.61 (dd, J = 1.2, 2.5 Hz, 3H), 1.21-1.08 (m, 1H).
• Compound 4a:

(75 MHz / CDCl₃)

(300 MHz / CDCl₃)
- Compound 4b:
• Compound 4c:
• Compound 4d (major diastereomer):
• Compound 4d (minor diastereomer):
• Compound 4e:
Compound 4f:
• Compound 4g:
• Compound 4h:
• Compound 4i:

(d.r. = 1.5 : 1)

(70 MHz / CDCl₃)

(d.r. = 1.5 : 1)

(300 MHz / CDCl₃)
• Compound 4j:
• Compound 4k:

(75 MHz / CDCl₃)

(300 MHz / CDCl₃)
- Compound 4l:
• Compound 4m:
• Compound 4n:
• Compound 4o:
• Compound 4p:
• Compound 4q:
• Compound 10a:
• Compound 10b:
• Compound 10c:
• Compound 10d:
Compound 10e: