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A simple synthesis of dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl]fumarates: potential intermediates in the synthesis of polysubstituted five- and six-membered heterocycles

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Abstract: In this communication, a simple synthesis of dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl] fumarates is described. Methyl ketones were transformed by treatment with *N*,*N*-dimethylacetamide dimethyl acetal (DMADMA) into 3-dimethylamino-1-(substituted)but-2-en-1-ones, followed by treatment with ammonium acetate into (*Z*)-3-amino-1-(substituted)but-2-en-1-ones and addition to dimethyl acetylenedicarboxylate. These novel polysubstituted butadienes are potential intermediates for the metal-free preparation of polysubstituted five- and six-membered heterocycles.

Keywords: enaminones; methyl ketones; polysubstituted butadienes; (*Z*)-3-amino-1-(substituted)but-2-en-1-ones; 2-[(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl] fumarates.

1 Introduction

3-Dimethylaminopropenoates and related enaminones have been demonstrated to exhibit a broad applicability in heterocyclic synthesis [1–5], including the preparation of natural products and their analogues, such as aplysinopsins [6, 7], meridianines [8, 9], and dipodazines [10–12]. Recently, polysubstituted butadienes have been prepared by microwave-assisted [2+2] cycloadditions of enaminones to electron-poor acetylenes [13, 14].

Polysubstituted aminobutadienes prepared by this procedure are suitable for the preparation of polysubstituted pyridine derivatives. They also represent a group of isomeric intermediates in regard to the aminobutadienes prepared *via* Michael addition in the Bohlmann-Rahtz synthesis of pyridine derivatives [15, 16]. On this basis, a simple metal-free synthesis of 2-alkyl-, 2-cycloalkyl-, 2-aryl-, and 2-heteroaryl-substituted pyridine-3,4-dicarboxylates and their *N*-oxides has been developed [17].

The electron-poor propyne iminium triflates, prepared from 3-trifloxypropene iminium triflates by elimination of triflic acid, underwent [2+2] and [2+4] cycloadditions with enamines [18]. Their reactivity toward imines has been also reported [19, 20]. Recently, we reported on a simple one-pot metal-free synthesis of 2,4,5-trisubstituted pyridine derivatives and their *N*-oxides by [2+2] cycloaddition of propyne iminium salts as electron-poor acetylenes to enaminones as an extension of the research recently developed in our laboratory [21]. We also recently reported on a simple, metal-free synthesis of polysubstituted benzene derivatives, where *N*,*N*-dimethylacetamide dimethyl acetal (DMADMA) served as the reagent and building block for generating aromatic final products [22].

We have reported on another application of the enaminone system in the synthesis of heterocyclic compounds. We have expanded the DMADMA methodology on aryl- and (hetero)aryl-enaminone systems, as well as on aromatic and heteroaromatic carboxamides, to prepare *N*,*N*,6-trimethyl-4-(substituted)pyridin-2-amines and N^2,N^2,N^4,N^4-tetramethyl-6-(substituted) pyridine-2,4-diamines as the final products [23].

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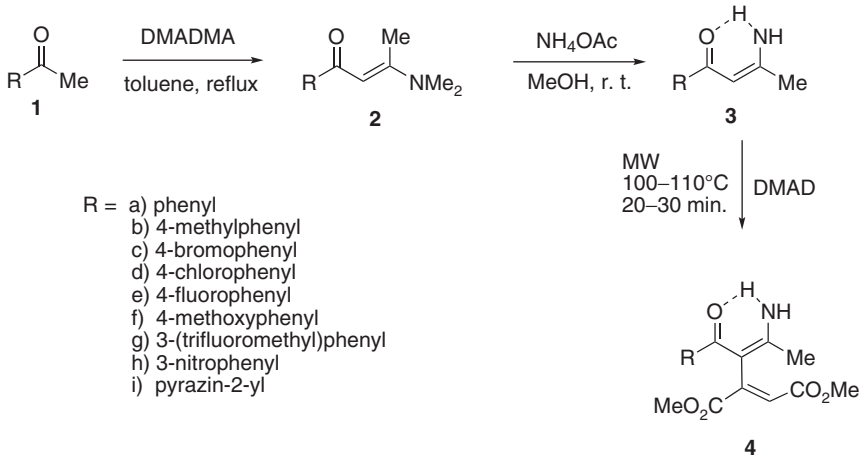
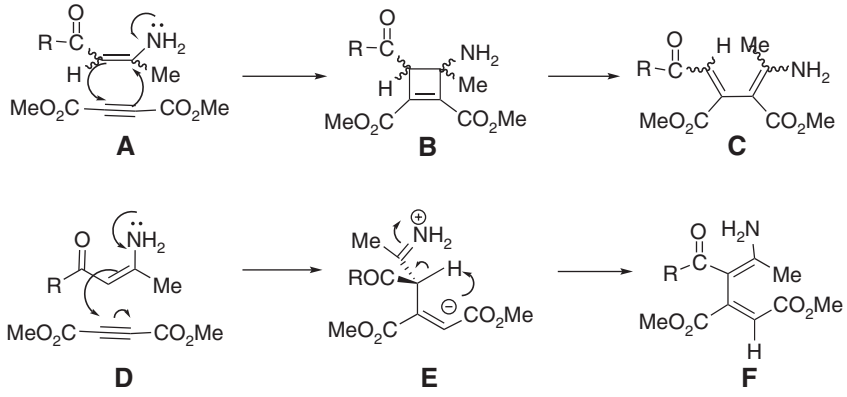
2 Results and discussion

It has been reported that enaminones **2**, which are easily prepared from methyl ketones **1** using amide acetals, such as *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA), undergo self-condensation in the presence of ammonium acetate affording 2,5-disubstituted pyridine derivatives [24, 25]. Meanwhile, when using DMADMA, the enaminone products of the condensation reaction do not undergo self-condensation in acidic media. Therefore, the dimethylamino group can be readily replaced with the amino group, using ammonium acetate as an active form of ammonia [26]. It is known that the methyl group attached to the enaminone system is acidic and is capable of participating in condensation reactions [22, 27].

Ketones **1a–i** were transformed with DMADMA into enaminones **2a–i**, which were treated with ammonium acetate to substitute the *N*,*N*-dimethylamino group with an amino group to give (*Z*)-3-amino-1-(substituted)but-2-en-1-ones **3a–i** as was reported earlier [23]. Enaminones **2a–i** did not react in [2+2] cycloaddition reaction with acetylenedicarboxylate either under normal thermal conditions or under microwave irradiation. The enaminones **3a–i** reacted with dimethyl acetylenedicarboxylate by heating in acetonitrile at reflux temperature for 2.5–4.5 h or by microwave irradiation for 20–30 min. The [2-(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2yl]fumarates **4a–i,** a new type of polysubstituted butadienes, were formed in 30%–65% yields (Scheme 1). The formation of these polysubstituted butadienes is not a result of [2+2]cycloaddition according to the sequence **A** → **B** → **C** as shown on Scheme 2 reported earlier for a series of enaminones without a methyl group at position 3 [28]. They are formed according to the reaction sequence **D** → **E** → **F**.



Scheme 1: Formation of [2-(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl]fumarates **4a–i**.



Scheme 2: Proposed mechanism for the formation of **4a–i**.

2.1 Structure determination

The structures of new compounds were determined on the basis of ^{1}H and ^{13}C NMR, IR, HRMS spectra, and microanalyses for C, H, and N. The structures of compounds **4a** and **4e** were confirmed by X-ray crystal structure determinations (Figs. 1 and 2).

3 Conclusion

In conclusion, we have described a simple synthesis of dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl] fumarates from methyl ketones *via* 3-dimethylamino-1-(substituted)but-2-en-1-ones and (*Z*)-3-amino-1-(substituted) but-2-en-1-ones. This novel polysubstituted butadienes are potential intermediates for the metal-free preparation of polysubstituted five- and six-membered heterocycles.

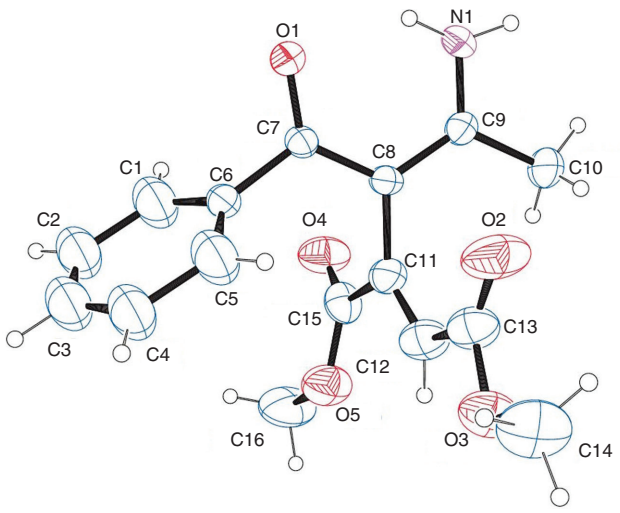


Fig. 1: ORTEP representation of **4a**. Displacement ellipsoids drawn at the 30% probability level, H atoms as spheres with arbitrary radii

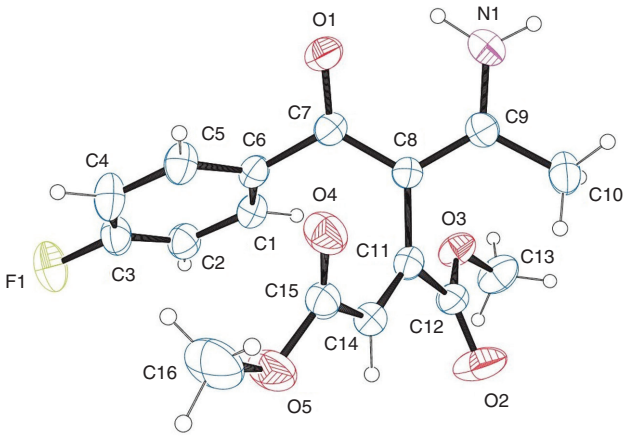


Fig. 2: ORTEP representation of **4e**. Displacement ellipsoids drawn at the 30% probability level, H atoms as spheres with arbitrary radii.

4 Experimental section

Melting points were determined on a Stanford Research Systems MPA100 OptiMelt automated melting point system. The NMR spectra were obtained on a Bruker Avance DPX 300 at 300 MHz for ^{1}H and 75.5 MHz for ^{13}C and on a Bruker Avance III UltraShield 500 plus at 500 MHz for ^{1}H and 126 MHz for ^{13}C, using $CDCl_3$ and $[D_6]DMSO$ with Me_4Si as the internal standard, as solvents. Mass spectra were recorded on an Agilent 6224 Accurate Mass TOF LC/MS spectrometer, IR spectra on a Perkin Elmer Spectrum BX FTIR spectrophotometer. Microanalyses were performed on a Perkin-Elmer CHN Analyzer 2400 II. Column chromatography (CC) was performed on silica gel (silica gel 60, particle size 35–70 μm; Fluka). Compounds **2z–i** and **3a–i** were prepared according to the procedure described in the literature [23].

4.1 General procedure for the preparation of dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl]fumarates 4a–i

A solution of 3-amino-1-(substituted)but-2-en-1-ones (**3a–i**, 1 mmol) and dimethyl acetylenedicarboxylate (2 mmol) in acetonitrile (2 mL) was placed in a microwave tube equipped with a magnetic stirring bar. The reaction mixture was then heated *via* microwave irradiation (300 W) in a closed vessel at an automatically controlled constant temperature (CEM Corporation Discover microwave unit). The reaction temperatures were between 100°C and 110°C, and the reaction times were 20–30 min. After the completion of the reaction, the volatile components were evaporated *in vacuo* and the product was washed with diethyl ether or purified by column chromatography ethyl acetate/petroleum ether 1:2.

The following compounds were prepared in this manner.

4.1.1 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-phenylbut-2-en-2-yl]fumarate (4a)

Prepared from **3a** (330 mg, 2 mmol) and DMAD (568 mg, 4 mmol). Yield: 392 mg (65%) of a yellow crystalline solid; m.p. 147°C–149°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.91

(3H, s, Me), 3.62 (3H, s, COOMe), 3.69 (3H, s, COOMe), 5.55 (1H, br. s, NH_2), 6.70 (1H, s, CH), 7.23–7.32 (5H, m, Ph), 10.95 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.9, 52.0, 52.9, 101.5, 127.2, 127.7, 129.2, 129.4, 142.4, 144.0, 163.1, 165.8, 168.2, 193.3 ppm. – IR (KBr): ν = 3271, 3130, 1715, 1602, 1471, 1433, 1376, 1300, 1283, 1247, 1215, 1168, 1146, 1054, 1025, 990, 942, 900, 863, 779, 743, 706 cm^{-1}. – HRMS: *m/z* = 304.1180 (calcd. 304.1179 for $C_{16}H_{18}NO_5$, $[M+H]^+$). – $C_{16}H_{17}NO_5$ (303.1): calcd. C 63.36, H 5.65, N 4.62; found C 63.24, H 5.63, N 4.61.

4.1.2 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(*p*-tolyl)but-2-en-2-yl]fumarate (4b)

Prepared from **3b** (87 mg, 0.5 mmol) and DMAD (142 mg, 1 mmol). Yield: 90 mg (57%) of a yellow solid; m.p. 137°C–139°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.90 (3H, s, Me), 2.30 (3H, s, Me), 3.62 (3H, s, COOMe), 3.69 (3H, s, COOMe), 5.53 (1H, br. s, NH_2), 6.70 (1H, s, CH), 7.03–7.06 (2H, m, Ph), 7.19–7.22 (2H, m, Ph), 10.92 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.5, 21.9, 52.0; 52.8, 101.5, 127.3, 128.4, 128.9, 139.5, 139.7, 144.2, 162.9, 165.8, 168.3, 193.4 ppm. – IR (KBr): ν = 3263, 3117, 2945, 1718, 1637, 1582, 1562, 1466, 1430, 1375, 1245, 1169, 1140, 1055, 1027, 868, 829, 787, 767, 712 cm^{-1}. – HRMS: *m/z* = 318.1331 (calcd. 318.1336 for $C_{17}H_{20}NO_5$, $[M+H]^+$). – $C_{17}H_{19}NO_5$ (317.1): calcd. C 64.34, H 6.04, N 4.41; found C 64.20, H 6.07, N 4.40.

4.1.3 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(4-bromophenyl) but-2-en-2-yl]fumarate (4c)

Prepared from **3c** (239 mg, 1 mmol) and DMAD (284 mg, 2 mmol). Yield: 200 mg (52%) of a yellow solid; m.p. 154°C–157°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.89 (3H, s, Me), 3.66 (3H, s, COOMe), 3.67 (3H, s, COOMe), 5.73 (1H, br. s, NH_2), 6.70 (1H, s, CH), 7.17–7.21 (2H, m, Ph), 7.36–7.39 (2H, m, Ph), 10.90 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.9, 52.0, 53.0, 101.0, 123.7, 128.9, 129.6, 130.9, 141.2, 143.7, 163.6, 165.7, 168.1, 191.9 ppm. – IR (KBr): ν = 3257, 3116, 2945, 1717, 1638, 1583, 1467, 1431, 1390, 1246, 1193, 1170, 1139, 1067, 1028, 1010, 906, 880, 867, 831, 770, 708 cm^{-1}. – HRMS: *m/z* = 382.0280 (calcd. 382.0285 for $C_{16}H_{17}BrNO_5$, $[M+H]^+$). – $C_{16}H_{16}BrNO_5$ (381.0): calcd. C 50.28, H 4.22, N 3.66; found C 50.14, H 4.21, N 3.69.

4.1.4 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(4-chlorophenyl) but-2-en-2-yl]fumarate (4d)

Prepared from **3d** (700 mg, 3.60 mmol) and DMAD (1022 mg, 7.20 mmol). Yield: 674 mg, (55%) of a yellow solid; m.p. 158°C–160°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.93 (3H, s, Me), 3.69 (3H, s, COOMe), 3.71 (3H, s, COOMe), 5.65 (1H, br. s, NH_2), 6.74 (1H, s, CH), 7.23–7.26 (2H, m, Ph), 7.28–7.30 (2H, m, Ph), 10.94 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.9, 52.0, 53.0, 101.1, 128.0, 128.7, 129.6, 135.4, 140.8, 143.8, 163.4, 165.7 168.1; 191.9 ppm. – IR (KBr): ν = 3257, 2946, 1718, 1639, 1583, 1469, 1431, 1246, 1194, 1170, 1140, 1086, 1055, 1029, 1014, 906, 868, 835, 771, 709 cm^{-1}. – HRMS: *m/z* = 338.0788 (calcd. 338.0790 for $C_{16}H_{17}NO_5$, $[M+H]^+$). – $C_{16}H_{16}ClNO_5$ (337.1): calcd. C 56.90, H 4.78, N 4.15; found C 57.00, H 4.77, N 4.23.

4.1.5 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(4-fluorophenyl) but-2-en-2-yl]fumarate (4e)

Prepared from **3e** (90 mg, 0.5 mmol) and DMAD (142 mg, 1.0 mmol). Yield: 84 mg (52%) of a yellow precipitate; m.p. 142–144°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.92 (3H, s, Me), 3.66 (3H, s, COOMe), 3.69 (3H, s, COOMe), 5.53 (1H, br. s., NH_2), 6.71 (1H, s, CH), 6.91–6.96 (2H, m, C_6H_4), 7.32–7.36 (2H, m, C_6H_4), 10.92 (1H, br. s., NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.9, 52.0, 52.9, 101.2, 114.7 (d, *J* = 21.6 Hz), 129.3, 129.4 (d, *J* = 8.8 Hz), 138.6 (d, *J* = 3.2 Hz), 144.0, 163.3, 163.3 (d, *J* = 249 Hz), 165.8, 168.2, 192.0 ppm. – IR(KBr): ν = 3391, 2947, 1718, 1698, 1595, 1478, 1435, 1377, 1257, 1216, 1174, 1135, 1093, 1037, 1019, 908, 881, 866, 848, 787, 762, 718 cm^{-1}. – HRMS: *m/z* = 322.1088 (calc. 322.1085 for $C_{16}H_{17}FNO_5$, $[M+H]^+$). – $C_{16}H_{16}FNO_5$ (321.1): calc. C 59.81, H 5.02, N 4.36; found C 59.53, H 5.11, N 4.21.

4.1.6 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(4-methoxyphenyl)but-2-en-2-yl]fumarate (4f)

Prepared from **3f** (600 mg, 3.14 mmol) and DMAD (1022 mg, 7.20 mmol). Yield: 778 mg (74%) of a yellow precipitate; m.p. 136°C–138°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.91 (3H, s, Me), 3.63 (3H, s, COOMe), 3.69 (3H, s, COOMe), 3.79 (3H, s, OMe), 5.52 (1H, br. s, NH_2), 6.72 (1H, s, CH), 6.75–6.78 (2H, m, Ph), 7.30–7.34 (2H, m, Ph), 10.88 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.9, 51.9, 52.9, 101.5, 113.0, 128.6, 129.2, 135.1, 144.4, 160.6, 162.7, 165.9, 168.4, 192.8 ppm. – IR (KBr): ν = 3415, 2943, 1723, 1702, 1591,

1567, 1475, 1433, 1243, 1169, 1023, 914, 881, 862, 790 cm^{-1}. – $C_{17}H_{19}NO_6$ (333.1): calcd. C 61.25, H 5.75, N 4.20; found C 61.08, H 5.77, N 4.17.

4.1.7 Dimethyl 2-{(*Z*)-3-amino-1-oxo-1-[3-(trifluoromethyl) phenyl]but-2-en-2-yl}fumarate (4g)

Prepared from **3g** (573 mg, 2.5 mmol) and DMAD (710 mg, 5.0 mmol). Yield: 277 mg (30%) of a yellow precipitate; m.p. 130°C–132°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.93 (3H, s, CH_3), 3.67 (3H, s, COOMe), 3.69 (3H, s, COOMe), 5.63 (1H, br. s, NH_2), 6.70 (1H, s, CH), 7.36–7.39 (1H, m, Ph), 7.48–7.49 (1H, m, Ph), 7.54–7.55 (1H, m, Ph), 10.92 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 22.0, 52.0, 53.0, 101.0, 124.0 (q, J = 27.0 Hz), 124.2 (q, J = 3.9 Hz), 125.9 (q, J = 3.6 Hz), 128.3, 130.1 (q, J = 32.5 Hz), 130.2, 143.0, 143.5, 163.7, 165.6, 168.0, 191.5 ppm. – IR (KBr): ν = 3343, 2956, 1717, 1613, 1582, 1467, 1431, 1386, 1332, 1278, 1248, 1157, 1124, 1069, 1049, 1021, 939, 908, 876, 815, 788, 772, 702 cm^{-1}. – HRMS: m/z = 372.1050 (calcd. 372.1053 for $C_{17}H_{17}F_3NO_5$, $[M+H]^+$). – $C_{17}H_{16}F_3NO_5$ (371.1): calcd. C 54.99, H 4.34, N 3.77; found C 54.89, H 4.35, N 3.75.

4.1.8 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(3-nitrophenyl) but-2-en-2-yl]fumarate (4h)

Prepared from **3h** (103 mg, 0.5 mmol) and DMAD (142 mg, 1.0 mmol). Yield: 66 mg (38%) of a yellow precipitate; m.p. 140°C–142°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.94 (3H, s, Me), 3.68 (3H, s, COOMe), 3.75 (3H, s, COOMe), 5.73 (1H, br. s, NH_2), 6.72 (1H, s, CH), 7.43–7.46 (1H, t, J = 5 Hz, Ph), 7.65–7.68 (1H, m, Ph), 8.13–8.20 (2H, m, Ph), 10.89 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 22.0, 52.2, 53.2, 100.6, 122.2, 124.0, 129.0, 130.7, 133.1, 143.2, 143.8, 147.6, 164.1, 165.5, 167.9, 190.1 ppm. – IR (KBr): ν = 3398, 2949, 1726, 1709, 1607, 1529, 1476, 1435, 1349, 1299, 1246, 1214, 1175, 1146, 1092, 1077, 1042, 1017, 903, 877, 840, 810, 791, 773, 745, 714 cm^{-1}. – HRMS: m/z = 349.1032 (calcd. 349.1030 for $C_{16}H_{17}N_2O_7$, $[M+H]^+$). – $C_{16}H_{16}N_2O_7$ (348.1): calcd. C 55.17, H 4.63, N 8.04; found C 55.25, H 4.60, N 7.96.

4.1.9 Dimethyl 2-[(*Z*)-3-amino-1-oxo-1-(1-pyrazin-2-yl) but-2-en-2-yl]fumarate (4i)

Prepared from **3i** (89 mg, 0.55 mmol) and DMAD (120 mg, 0825 mmol). Yield: 104 mg (62%) of a brown precipitate; m.p. 113°C–115°C. – ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.97 (3H, s, Me), 3.62 (3H, s, COOMe), 3.81 (3H, s, COOMe), 5.97 (1H, br. s, NH_2), 6.78 (1H, s, CH), 8.32–8.34 (1H, m, Ar), 8.50–8.51 (1H, m, Ar), 9.06 (1H, m, Ar), 11.17 (1H, br. s, NH_2) ppm. – ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 22.0, 51.9, 52.9, 100.3, 128.0, 141.2, 144.0, 144.9, 145.1, 152.0, 165.2, 165.9, 168.0, 185.4 ppm. – IR (KBr): ν = 3355, 2950, 1732, 1702, 1592, 1560, 1471, 1433, 1301, 1256, 1138, 1201, 861, 772 cm^{-1}. – HRMS: m/z = 306.1086 (calcd. 306.1084 for $C_{14}H_{16}N_3O_5$, $[M+H]^+$). – $C_{14}H_{15}N_3O_5$ (305.1): calcd. C 55.08, H 4.95, N 13.76; found C 54.03, H 4.84, N 12.96.

4.2 Crystal structure determinations

Single crystal X-ray diffraction data of compounds **4a** and **4e** were collected at room temperature on an Agilent SuperNova diffractometer (Dual, Cu at zero, Atlas) using MoK_α (λ = 0.71073 Å) radiation at ambient temperature. Data reduction and integration were performed with the software package Crysalis Pro [29]. Both structures were solved by direct methods with the program Sir97 [30, 31]. Full-matrix least-squares refinement on F^2 with anisotropic displacement parameters for all non-hydrogen atoms using Shelxl2013 [32, 33] was employed. All hydrogen atoms were initially located in the difference Fourier maps. Carbon-attached hydrogens were subsequently treated as riding atoms in geometrically idealized positions with bond lengths C–H of 0.96 Å for methyl and 0.93 Å for aromatic C–H bonds. The corresponding displacement parameters U_{iso}(H) were 1.5 times higher than those of the carrier methyl carbons and 1.2 times higher than aromatic carbon atoms. The hydrogen atoms of the amino group were refined isotropically and without any restraints in **4e,** whereas in **4a**, both N–H bonds were restrained to 0.87(2) Å. In **4a**, due to a more pronounced disorder of the terminal groups the phenyl carbon atoms (with exceptions of C6 attached to the rest of molecule) were restrained during refinement (EADP restraints). Similarly, EADP restraints were also used for C12 and C13. Figures depicting the structures were prepared with Ortep [34, 35].

4.2.1 Crystallographic data

For **4a**: $C_{16}H_{17}NO_5$, M_r = 303.30, orange prisms, 0.15 × 0.25 × 0.30 mm^3, orthorhombic, space group $P2_12_12_1$ (no. 19), a = 16.7212(8) Å, b = 10.6319(7) Å, c = 9.2340(5) Å, V = 1641.60(16) $Å^3$, Z = 4, D_x = 1.227 Mg m^{-3}, F(000) = 640 e, μ = 0.09 mm^{-1}, T = 293(2) K, MoK_α radiation, λ = 0.71073 Å, ω scans, θ range 2.92–30.36°; hkl range: –17 < h < 23, –14 < k < 14, –10 < l < 12; 10242 measured, 4335 independent and 2340 observed reflections, R_{int} = 0.0681, multi-scan

absorption correction, refinement on F^2, $R(F)$ [$F^2 > 2\,\sigma(F^2)$] = 0.0990, $wR(F^2)$ (all data) = 0.2917, 4335 contributing reflections, 175 parameters, 2 restraints, SHELXL2013 weighting scheme, absolute structure could not be determined reliably (x(Flack) = 2.2(10)), $\Delta\rho_{max}$ = 0.53 e Å^{-3}, $\Delta\rho_{min}$ = −0.30 e Å^{-3}.

For **4e**: $C_{16}H_{16}FNO_5$, M_r = 321.30, yellow prisms, 0.30 × 0.30 × 0.45 mm^3, triclinic, space group $P\bar{1}$ (no. 2), a = 8.0223(8) Å, b = 9.5519(11) Å, c = 11.1434(9) Å, α = 69.294(9)°, β = 87.285(7)°, γ = 83.598(9)°, V = 793.73(14) Å^3, Z = 2, D_x = 1.344 Mg m^{-3}, $F(000)$ = 336 e, μ = 0.11 mm^{-1}, T = 293(2) K, MoK_α radiation, λ = 0.71073 Å, ω scans, θ range 3.20–30.44°; hkl range: –11 < h < 10, –12 < k < 11, –15 < l < 10; 6919 measured, 4134 independent and 2377 observed reflections, R_{int} = 0.0450, multi-scan absorption correction, refinement on F^2, $R(F)$ [$F^2 > 2\,\sigma(F^2)$] = 0.0676, $wR(F^2)$ (all data) = 0.2169, 4134 contributing reflections, 219 parameters, 0 restraints, SHELXL2013 weighting scheme, $\Delta\rho_{max}$ = 0.24 e Å^{-3}, $\Delta\rho_{min}$ = −0.23 e Å^{-3}.

CCDC 1446156 and 1446157 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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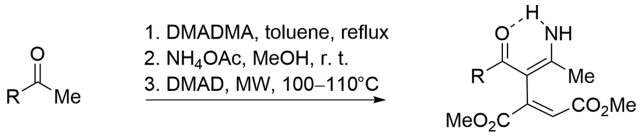
Graphical synopsis

Rok Šinkovec, Uroš Grošelj, Benjamin Prek, Marta Počkaj, Sebastijan Ričko, Jurij Svete and Branko Stanovnik

A simple synthesis of dimethyl 2-[(Z)-3-amino-1-oxo-1-(substituted)but-2-en-2-yl]fumarates: potential intermediates in the synthesis of polysubstituted five- and six-membered heterocycles



R = phenyl, 4-methylphenyl, 4-bromophenyl, 4-chlorophenyl, 4-fluorophenyl, 4-methoxyphenyl, 3-(trifluoromethyl)phenyl, 3-nitrophenyl, pyrazin-2-yl

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