A Platinum Open Access Journal for Organic Chemistry

Paper

Free to Authors and Readers | DOAJ Seal | *Arkivoc* **2024** (2) 202312080

Formal allene insertion into amides. Reaction of propargyl magnesium bromide with morpholine amides

Amir M. Al Mufti,[a,b] Marina V. Molchanova,[a,c] Ivan N. Myasnyanko,[a,d] Mikhail S. Baranov,[a,d] Viktoria A. Ikonnikova,[a,b] Andrey A. Mikhaylov[a,*]

[a] *Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences, 16/10 Miklukho-Maklaya St., Moscow, 117997, Russia*

[b] *D.I. Mendeleev University of Chemical Technology of Russia, 9 Miusskaya sq., 125047 Moscow, Russia*

[c] *Lomonosov Moscow State University, Leninskie Gory 1 (3), Moscow, 119991, Russia*

[d] *Pirogov Russian National Research Medical University, 1 Ostrovityanova St., Moscow 117997, Russia*

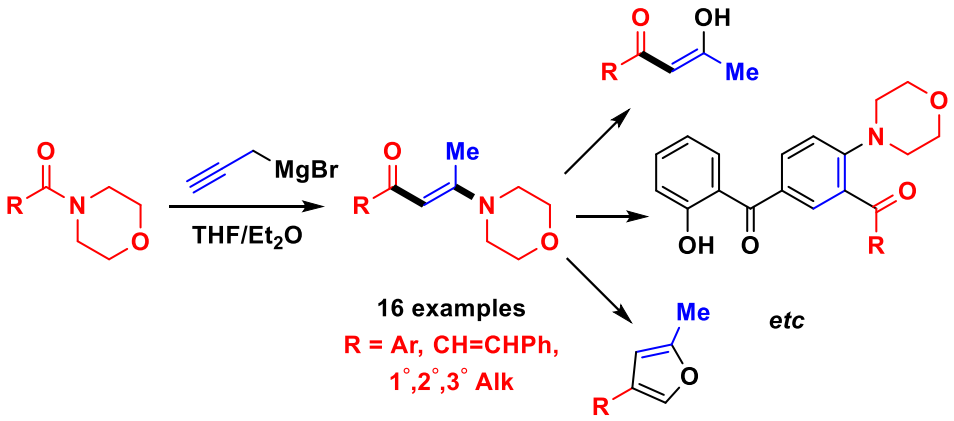
Email: mikhaylov_andrey@yahoo.com

Dedicated to Professor Samir Zard, the best teacher one can imagine

Received 09-12-2023 **Accepted Manuscript** 10-24-2023 **Published on line** 11-08-2023

Abstract

Propargyl magnesium bromide rapidly undergoes addition to morpholine amides forming push-pull enaminones – products of allene formal insertion. The scope of the reaction and functional group tolerance are demonstrated on 16 examples, giving rise either to enaminones or 1,3-diketones after instant hydrolysis on silica. Further approaches for direct utilization of crude enaminones are also demonstrated.



Keywords: Grignard addition, morpholine amides, enamines, 1,3-diketones, allenes

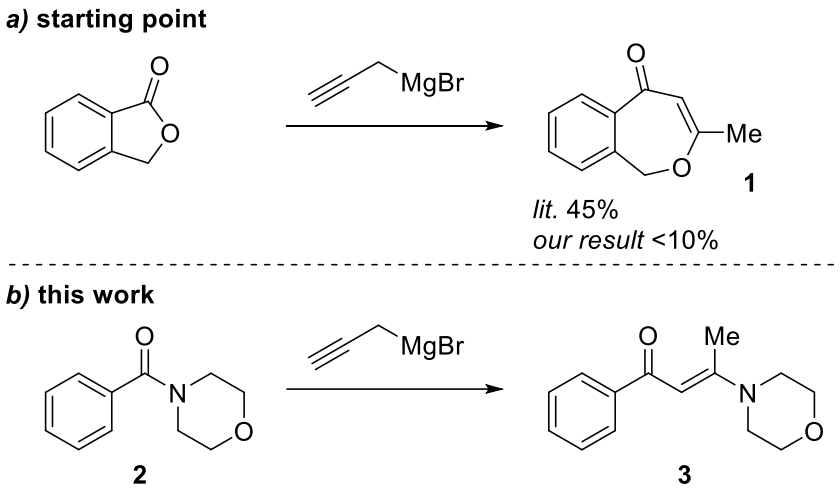
Cite as *Arkivoc* **2024** (2) 202312080

DOI: https://doi.org/10.24820/ark.5550190.p012.080

Introduction

Recently we have become interested in synthesis of 3-methylbenzo[*c*]oxepin-5(1*H*)-ones **1**, which we considered as promising building blocks for total synthesis of the rearranged angucyclinone derivatives.[1,2] The only description in literature approach to such heterocycles employs addition of propargyl magnesium bromide to phthalides and the following acidic work-up.[3] This reaction has intrigued us, because it is a rare example of Grignard mono addition to an ester.

Attempts to reproduce this literature precedent on unsubstituted phthalide however have failed (mostly di-addition product was formed), which have prompted us to search for alternative pathways (Scheme 1). During such studies we attempted addition of the same Grignard reagent to morpholine amides **2**, which are known to undergo selective monoaddition providing access to ketone derivatives.[4]



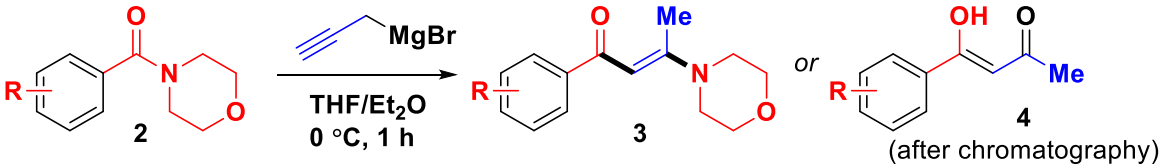
Scheme 1. *a)* Literature precedent and our attempts to reproduce it; *b)* reaction, developed in this work.

It was discovered that the product of the above reaction was not the expected allenyl ketone[5,6] but enaminone **3** as predominant product. Although its formation could be predicted based on the related literature precedents,[7,8] it was previously undescribed. Extreme ease of such transformation and availability of the starting materials prompted us to study its synthetic potential. Thus, this reaction opens the opportunity to prepare regioselectively enaminones in a single step from cheap morpholine amides and could be regarded as a preparative method.

Synthesis of enaminones is generally performed directly by amine action on 1,3-diketones,[9,10] which are in hand prepared by Claisen condensation of ketone and ester.[11] However, in recent years several new methods for synthesis of both 1,3-diketones and enaminones have emerged: reaction of amides (instead of esters) in Claisen condensation;[12,13] addition of organometallic nucleophiles to borylated ketoesters;[14] sulfur extrusion in the Eschenmoser contraction reaction;[15,16] condensation of azaenolate, derived from LDA, to methyl esters;[17] amine addition to ynones;[18,19] as well as some others.[20] In comparison to already developed methods, the current protocol is using the more powerful nucleophile and is rather fast, although allows synthesis of enaminones with methyl group only. However, this reaction provides an alternative to aldol-type reactions of acetone, which are known to be problematic.[21]

Results and Discussion

Optimization of the reaction conditions was performed on unsubstituted phenyl derivative **2a**. There were two key factors found, responsible for reproducibility and feasibility of results: 1) proper stoichiometry of reagents to achieve full conversion of the initial amide as well as to mitigate undesired side-processes (which however occur only in use of great excess of Grignard reagent) and 2) proper quenching and work-up of the reaction mixture. Neither reaction temperature (-78 °C or 0 °C), nor solvent (THF or Et_2O) or concentration had much impact on the reaction course. Therefor, the optimal conditions were the use of 1.2 equiv. of propargyl magnesium bromide (titrated with menthol/phenanthroline)[22] at 0 °C in THF, followed by slow quench with water. Enaminone **3a** was formed in ca. 70% yield based on ^{1}H NMR but its isolation was complicated with rapid hydrolysis into corresponding diketone **4a** (existing mostly in tautomeric enol form in solution according to NMR analysis), which occurs quantitively during silica gel chromatography. Use of the alternative sorbents was also inefficient. The primary product **3a** could be isolated by precipitation from acetone with pentane, although with significant material losses. Thus, further scope determination was performed with isolation of 1,3-diketones **4**, while enaminones **3** were characterized only in selected cases.

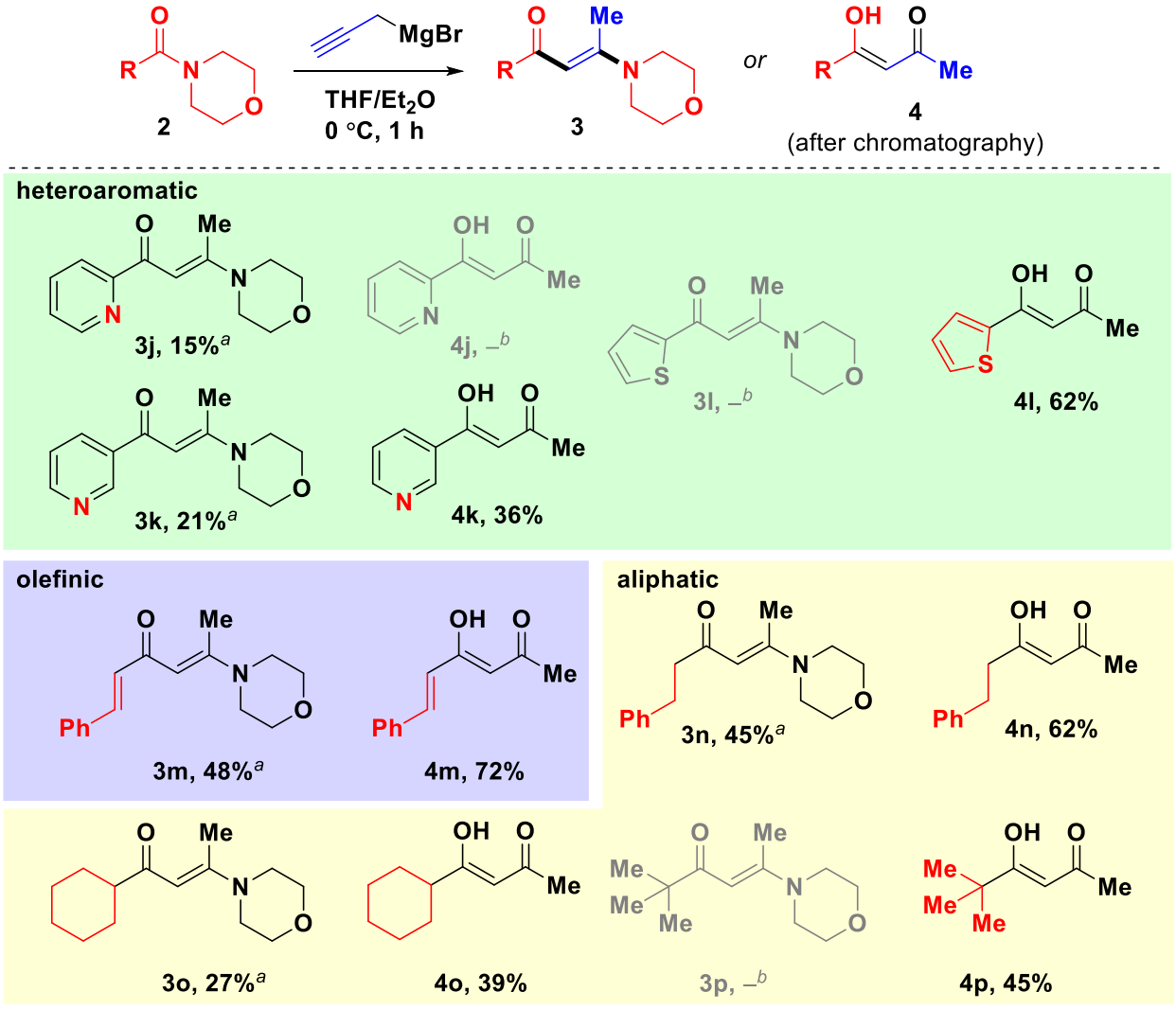


a, R = H,	**3a, 38%**[a]	**4a, 76%**[c]
b, R = 4-Cl,	**3b, 41%**[a]	**4b, 72%**[c]
c, R = 4-Br,	**3c, 21%**[a]	**4c, 56%**[c]
d, R = 4-F,	**3d, 45%**[a]	**4d, 82%**[c]
e, R = 4-Me,	3e, –[b]	**4e, 67%**[c]
f, R = 4-OMe,	**3f, 37%**[a]	**4f, 64%**[c]
g, R = 4-NO_2,	3g, 0%	4g, 0%
h, R = 3-OMe,	3h, –[b]	**4h, 75%**[c]
i, R = 2-OMe,	3i, –[b]	**4i, 68%**[c]

[a] - recrystallized; [b] - not isolated; [c] - isolated yield after hydrolisys on silica.

Scheme 2. Substrate scope for the preparation of the aromatic enaminones **3** and diketones **4.**

The scope of the reaction was established on differently substituted amides **2** (Scheme 2). The efficiency of the addition to 4-substituted aromatic amides **2b-f** was relatively the same. Diketones **4b-f** were obtained in 56-82% yields. In most cases, enaminones **3** were also isolated in 21-45% yields after recrystallization. The only exception was nitro derivative **4g**, which we were unable to prepare due to the reaction of the nitro group with organometallic reagent. Both *m*- and *o*-methoxy derivatives **2h** and **2i** were participating in the reaction giving rise to 1,3-diketones **4h** and **4i** in 75% and 68% yield, respectively, meaning that the reaction is, at least in part, tolerant to steric hindrance.

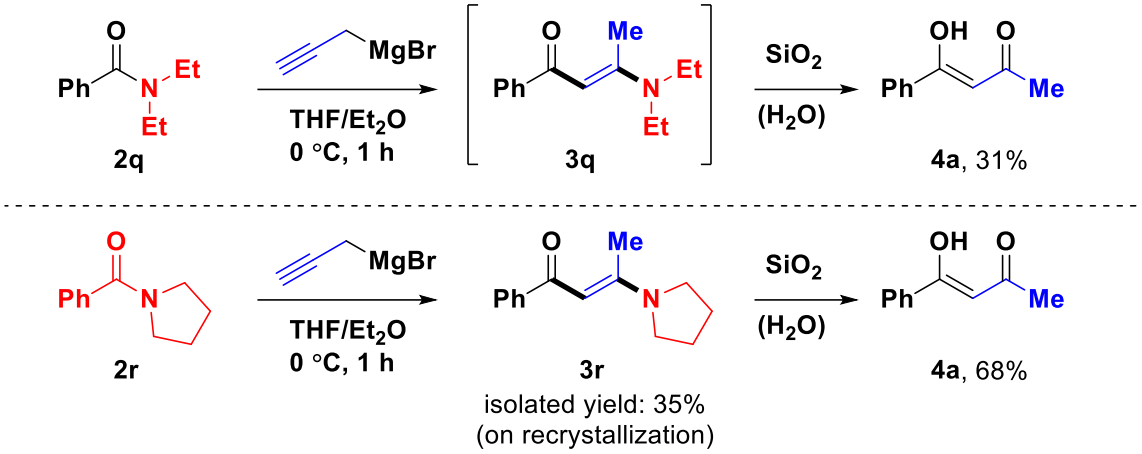


[a] - recrystallized; [b] - not isolated; [c] - isolated yield after hydrolisys on silica.

Scheme 3. Substrate scope for the preparation of the heteroaromatic, olefinic and aliphatic enaminones **3** and diketones **4.**

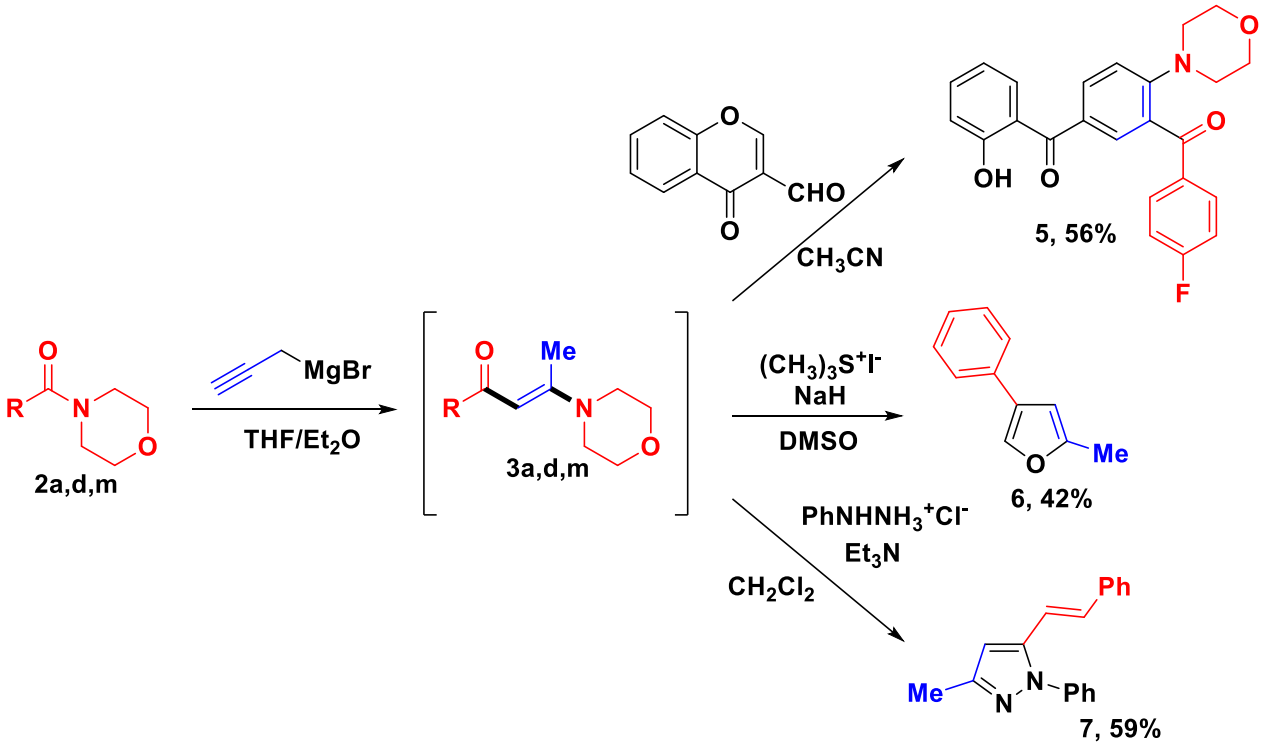
Later, we studied heteroaromatic derivatives (Scheme 3). Both 2-pyridinyl and 3-pyridinyl amides **2j** and **2k** participated in the reaction, although we observed some complications during aqueous work-up due to high polarity and water solubility of the products. No matter, both enamines **3j,k** and diketone **4k** were isolated in pure form, although the yields were low. There was no such problem with thiophene derivative **2l** - product **4l** was obtained in 62% yield.

Then, amides **2m-p** with olefin and alkyl substituent were examined (Scheme 3). Cinnamyl derivatives **3m** and **4m** were obtained with the same effectiveness as aryl derivatives. Amides **2n-p** with all the primary, secondary and tertiary alkyl groups were able to participate in the reaction, although the yield of secondary and tertiary diketones **4o,p** dropped down to ca. 40%, probably due to steric hindrance.



Scheme 4. Reaction of alternative amide derivatives **2q,r**.

We further briefly examined reactivity of other substituted amides, namely diethyl benzamide **2q** and pyrrolidine benzamide **2r** (Scheme 4). In both cases, the formation of enaminone product **3** was observed. Based on NMR analysis of the reaction mixture, the yield of diethylamino derivative **3q** was low. A number of by-products, as well as unreacted starting material were observed. After chromatography 31% of diketone **4a** was isolated. In contrast, enaminone **3r** was obtained in high yield, which allowed its isolation by recrystallization (35% isolated yield). Overall yield of the Grignard addition in this case could be estimated as 68%, based on isolated 1,3-diketone **4a**. Such results are in accordance with literature data on the amides reactivity.[4,7]



Scheme 5. Chemical transformations of crude enaminones **3**, prepared *via* the discovered reaction.

Taken into account, that we experienced some problems upon isolation of the primary formed enaminones **3** and that they are often used directly after preparation, their utilization in the next step without purification was envisioned (Scheme 5). It was demonstrated on three conceptually different reactions: 1) condensation to form aromatic ring,[23] 2) recently discovered Corey-Chaykovsky reaction-based furan synthesis[19] and 3) reaction with bisnucleophile such as phenyl hydrazine. Amide **2d** was converted *via* the reaction of crude enaminone with 4-oxo-4*H*-chromene-3-carbaldehyde into the trisubstituted benzene derivative **5** in 56% on 2 steps. Reaction of the crude enaminone **3a** with dimethylsulfonium ylide resulted in isolation of 2-methyl-4-phenylfuran **6** in 42% yield, based on **2a**. Cinnamyl morpholine amide **2m** was converted into pyrazole derivative **7** in 59% on 2 steps.

Conclusions

In summary, we have serendipitously discovered original interaction pathway of Grignard reagents with amides. Differently substituted morpholine amides react with propargyl magnesium bromide giving rise to β-enaminones – products of formal allene insertion. The discovered reaction provides preparative access to various 1,3-diketones, which are obtained after spontaneous hydrolysis, or, if enaminone is used crude as it is, to various valuable heterocyclic or aromatic compounds. This approach is operationally simple and cheap alternative to already known methods.

Experimental Section

General. All reactions were performed in round-bottom flasks fitted with rubber septa. Reactions sensitive to air and/or moisture were performed under a positive pressure of argon. Air- and moisture-sensitive liquids were transferred by syringe. Analytical thin-layer chromatography (TLC) was performed using aluminum plates pre-coated with silica gel (silica gel 60 F_{254}, Sorbfil). TLC plates were visualized by exposure to 254 nm ultraviolet light (UV) or were stained by submersion in acidic ethanolic solution of vanillin followed by brief heating (vanillin) or submersion in aqueous potassium permanganate solution followed by extensive washing with water ($KMnO_4$). Flash-column chromatography was carried out on silica gel (60 Å, 230–400 mesh, Merck). All solvents for chromatography and extractions were technical grade and distilled prior use.
All reagents were obtained from commercial suppliers and were used without further purification. Et_2O and THF were stored over sodium benzophenone ketyl and were distilled directly prior use.
Nuclear magnetic resonance spectra were recorded using Bruker Fourier 300, Bruker Avance 800 instruments at indicated temperature. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances), coupling constant (*J*) in Hertz, integration. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvents ($CHCl_3$, δ 7.26 ppm). Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonances of the NMR solvents ($CDCl_3$, δ 77.16 ppm).
High-resolution mass spectra were recorded on a Bruker micrOTOF-Q II mass spectrometer using electrospray ionization (ESI–TOF). Melting points were determined on Kofler melting point apparatus and are uncorrected.

Preparation of propargylmagnesium bromide: An oven-dried 50 mL two-necked round-bottomed flask is charged with the magnesium turnings (288 mg, 12.0 mmol, 1.2 equiv.) and mercury dichloride (100 mg, 0.38

mmol, 0.04 eq) and equipped with a Teflon-coated magnetic stir bar (oval shaped, 3.0 x 1.0 cm). The side neck of the flask is fitted with a rubber septum, the central neck is equipped with water-cooled condenser (20.0 cm height) which is fitted with rubber septum connected to argon balloon. Anhydrous Et_2O (10 mL) is added *via* syringe and the reaction mixture is heated to a gentle reflux. Part (ca. 1/10, 0.2 mL) of propargyl bromide (1.12 ml, 10 mmol, 1 equiv., 80% solution in toluene) solution in Et_2O (2 mL) was added *via* syringe to the reaction mixture. It usually took 5-15 min of reflux to initiate Grignard reagent formation. Then the Grignard reaction was initiated (intense exothermic effect, adhesion of magnesium turnings) heating plate was removed and the residual propargyl bromide was added dropwise at such rate to keep the solution reflux (generally, 1 drop per 3 sec). After the addition was completed, the reaction mixture was allowed to cool down during 10 minutes. The resulting propargylmagnesium bromide was titrated with menthol (20 mg) in THF solution (1 ml) using phenanthroline as indicator (typical molarity observed 0.5-0.7 M)[22] and then used in the next step within 30 minutes after the Grignard reagent preparation.

General procedure: An oven-dried Schlenk flask (25 ml) with a magnetic stirrer and amide **2** (3 mmol, 1 equiv.) was purged with argon. THF (3 mL) was added *via* syringe through a septum to dissolve the starting material. The flask was cooled to 0 °C in an ice water bath. Then, propargylmagnesium bromide (3.6 mmol, 1.2 eq.) was added. After one hour at 0 °C, distilled water (0.5 mL) was added dropwise and the mixture was transferred to a separating funnel with Et_2O (40 mL) and water (40 mL). Organic layer was separated and the aqueous one was extracted with Et_2O (40 mL), the combined organic phase was washed with brine and dried over sodium sulfate. Solvents were removed in vacuo. The resulting enamine **3** was isolated in a pure form by recrystallization from acetone/pentane or converted to the 1,3-diketone **4** by column chromatography on silica gel (eluent hexane/EtOAc).

1-Phenyl-3-morpholinobut-2-en-1-one (3a)[24]

Yield 265 mg (1.1 mmol, 38%), yellow solid, mp = 142−145 °C

^{1}H NMR (300 MHz, 300K, $CDCl_3$) δ = 7.83 (dd, J = 7.9, 1.8 Hz, 2H), 7.48–7.34 (m, 3H), 5.88 (s, 1H), 3.76 (t, *J* = 4.9 Hz, 4H), 3.42 (t, *J* = 4.9 Hz, 4H), 2.61 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 189.6, 162.9, 142.6, 130.8, 128.2 (2×*C*), 127.5 (2×*C*), 94.8, 66.5 (2×*C*), 46.5 (2×*C*), 16.3.

1-Phenylbutane-1,3-dione (4a)[25]

Yield 370 mg (2.3 mmol, 76%), white solid, mp 54−56 °C, R_f = 0.47 (hexane/EtOAc, 3/1); *92:8 enol/keto forms*

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.15 (br s, 1H), 7.87 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.51 (tt, *J* = 7.2, 1.5 Hz, 2H), 7.43 (t, *J* = 7.7 Hz, 2H), 6.17 (s, 1H), 2.19 (s, 3H); δ (*keto form, selected signals*) = 4.09 (s, 2H), 2.29 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 193.9, 183.5, 135.0, 132.4, 128.7 (2×*C*), 127.1 (2×*C*), 96.8, 25.9.

1-(4-Chlorophenyl)-3-morpholinobut-2-en-1-one (3b)

Yield 330 mg (1.2 mmol, 41%), orange solid, mp = 83−85 °C

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 7.77 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 5.80 (s, 1H), 3.81–3.70 (m, 4H), 3.47–3.28 (m, 4H), 2.60 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$) δ = 188.0, 163.4, 141.0, 136.8, 128.9 (2×*C*), 128.4 (2×*C*), 94.1, 66.4 (2×*C*), 46.5 (2×*C*), 16.3.

HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{17}Cl^{35}NO_2$ 266.0942; Found 266.0939.

1-(4-Chlorophenyl)butane-1,3-dione (4b)[26]

Yield 425 mg (2.2 mmol, 72%), beige solid, mp= 85−87 °C, R_f = 0.42 (hexane/EtOAc, 3/1); *95:5 enol/keto forms*

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.08 (br s, 1H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 6.13 (s, 1H), 2.20 (s, 3H); δ (*keto form*) = 7.87 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 4.07 (s, 2H), 2.30 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 193.8, 182.4, 138.7, 133.5, 129.1 (2×*C*), 128.5 (2×*C*), 96.8, 25.9.

1-(4-Bromophenyl)-3-morpholinobut-2-en-1-one (3c)

Yield 195 mg (0.6 mmol, 21%), brown solid, mp = 122−124 °C

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 7.70 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 5.80 (s, 1H), 3.80–3.74 (m, 4H), 3.46–3.40 (m, 4H), 2.61 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 188.2, 163.5, 141.4, 131.4 (2×*C*), 129.1 (2×*C*), 125.4, 94.0, 66.4 (2×*C*), 46.6 (2×*C*), 16.3.

HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{17}Br^{79}NO_2$ 310.0437; Found 310.0442.

1-(4-Bromophenyl)butane-1,3-dione (4c)[27]

Yield 405 mg (1.7 mmol, 0.56%), brown solid, mp = 85−87 °C, R_f = 0.40 (hexane/EtOAc, 3/1); *95:5 enol/keto forms*

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.07 (s, 1H), 7.72 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.6 Hz, 2H), 6.12 (s, 1H), 2.19 (s, 3H); δ (*keto form*) = 7.78 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 4.06 (s, 2H), 2.29 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 194.0, 182.3, 133.9, 132.0 (2×*C*), 128.6 (2×*C*), 127.2, 96.7, 25.9.

1-(4-Fluorohenyl)-3-morpholinobut-2-en-1-one (3d)[28]

Yield 335 mg (1.3 mmol, 45%), yellowish solid, mp = 105−108 °C

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 7.83 (dd, *J* = 8.8, 5.5 Hz, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 5.80 (s, 1H), 3.74 (t, *J* = 5.0 Hz, 4H), 3.40 (t, *J* = 5.0 Hz, 4H), 2.58 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 187.9, 164.4 (d, *J* = 250.4 Hz), 163.1, 138.7 (d, *J* = 2.8 Hz), 129.7 (d, *J* = 8.6 Hz, 2×*C*), 115.0 (d, *J* = 21.4 Hz, 2×*C*), 94.1, 66.4 (2×*C*), 46.5 (2×*C*), 16.2.

1-(4-Fluorophenyl)butane-1,3-dione (4d)[29]

Yield 443 mg (2.5 mmol, 82%), colorless solid, mp = 38−40 °C, R_f = 0.43 (hexane/EtOAc, 3/1)*; 93:7 enol/keto forms*

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.48 (br s, 1H), 8.23 (dd, *J* = 8.8, 5.5 Hz, 2H), 7.46 (t, *J* = 8.6 Hz, 2H), 6.46 (s, 1H), 2.53 (s, 3H); δ (*keto form*) = 8.31 (dd, *J* = 8.8, 5.4 Hz, 2H), 7.46 (t, *J* = 8.6 Hz, 2H), 4.41 (s, 2H), 2.64 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 193.0, 183.1, 165.5 (d, *J* = 253.5 Hz), 131.43 (d, *J* = 3.2 Hz), 129.6 (d, *J* = 9.0 Hz, 2×*C*), 115.9 (d, *J* = 21.9 Hz, 2×*C*), 96.5, 25.7.

1-(4-Methylphenyl)butane-1,3-dione (4e)[27]

Yield 355 mg (2.0 mmol, 67%), colorless oil, R_f = 0.42 (hexane/EtOAc, 3/1); *90:10 enol/keto forms*

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.19 (br s, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 6.13 (s, 1H), 2.38 (s, 3H), 2.16 (s, 3H); δ (*keto form*) = 7.81 (d, *J* = 8.2 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 2H), 4.04 (s, 2H), 2.39 (s, 3H), 2.26 (s, 3H).

^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 193.1, 183.9, 143.2, 132.3, 129.5 (2×*C*), 127.2 (2×*C*), 96.4, 25.8, 21.7.

1-(4-Methoxyphenyl)-3-morpholinobut-2-en-1-one (3f)

Yield 290 mg (1.1 mmol, 37%), yellow solid, mp = 56−58 °C

^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 7.85 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 8.4 Hz, 1H), 5.89 (s, 0H), 3.85 (d, J = 1.1 Hz, 1H), 3.77 (t, J = 4.9 Hz, 2H), 3.40 (t, J = 4.9 Hz, 2H), 2.59 (s, 1H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 188.4, 162.3, 161.8, 135.0, 129.4 (2×*C*), 113.3 (2×*C*), 94.5, 66.4 (2×*C*), 55.4, 46.4 (2×*C*), 16.1.
HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{20}NO_3$ 262.1438; Found 262.1432.

1-(4-Methoxylphenyl)butane-1,3-dione (4f)[27]

Yield 370 mg (1.9 mmol, 64%), colorless solid, mp =48−49 °C, R_f = 0.33 (hexane/EtOAc, 3/1);
88:12 enol/keto forms
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.30 (br s, 1H), 7.86 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 6.11 (s, 1H), 3.86 (s, 3H), 2.16 (s, 3H); δ (*keto form*) = 7.92 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 9.0 Hz, 2H), 4.04 (s, 2H), 3.87 (s, 3H), 2.28 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 191.7, 184.3, 163.2, 129.2 (2×*C*), 127.7, 114.1 (2×*C*), 95.9, 55.6, 25.4.

1-(3-Methoxylphenyl)butane-1,3-dione (4h)[30]

Yield 432 mg (2.3 mmol, 75%), colorless oil, R_f = 0.52 (hexane/EtOAc, 1/1); *92:8 enol/keto forms*
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.14 (br s, 1H), 7.49–7.38 (m, 2H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.05 (dd, *J* = 8.4, 3.5 Hz, 1H), 6.15 (s, 1H), 3.84 (s, 3H), 2.18 (s, 3H); δ (*keto form, selected signals*) = δ 4.06 (s, 2H), 3.80 (s, 3H), 2.28 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 193.5, 183.5, 159.9, 136.4, 129.7, 119.5, 118.5, 111.9, 96.9, 55.5, 25.8.

1-(2-Methoxylphenyl)butane-1,3-dione (4i)[31]

Yield 390 mg (2.0 mmol, 68%), white solid, mp = 32−34 °C, R_f = 0.40 (hexane/EtOAc, 3/1); *80:20 enol/keto forms*
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 16.22 (br s, 1H), 7.85 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.41 (ddd, *J* = 8.4, 7.8, 1.6 Hz, 1H), 7.00 (td, *J* = 7.5, 1.2 Hz, 2H), 6.94 (dd, *J* = 8.4 Hz, 1.2 Hz 1H), 6.42 (s, 1H), 3.88 (s, 3H), 2.16 (s, 3H); δ (*keto form*) = 7.81 (dd, J = 7.8, 1.8 Hz, 1H), 7.47 (td, *J* = 7.4, 1.6 Hz, 1H), 7.41 (ddd, *J* = 8.4, 7.8, 1.6 Hz, 1H), 7.00 (td, *J* = 7.5, 1.2 Hz, 2H), 4.03 (s, 2H), 3.85 (s, 3H), 2.23 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 194.5, 181.4, 158.4, 133.0, 130.2, 120.7, 111.6, 101.9, 55.6, 26.1; δ (*keto form*) = 202.7, 194.8, 159.0, 134.7, 130.9, 124.1, 120.9, 111.7, 58.9, 55.4, 30.3.

3-Morpholino-1-(pyridin-2-yl)but-2-en-1-one (3j)

Yield 105 mg (0.5 mmol, 15%), brown solid, mp = 73−75 °C
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 8.57 (d, *J* = 4.2 Hz, 1H), 8.11 (d, *J* = 7.9 Hz, 1H), 7.77 (td, *J* = 7.7, 1.8 Hz, 1H), 7.32 (ddd, *J* = 7.5, 4.2, 1.8 Hz, 1H), 6.78 (s, 1H), 3.85–3.70 (m, 4H), 3.62–3.48 (m, 4H), 2.67 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 187.1, 164.0, 157.6, 148.1, 136.9, 125.3, 122.0, 92.4, 66.5 (2×*C*), 46.6 (2×*C*), 16.2.
HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{17}N_2O_2$ 233.1285; Found 233.1289.

3-Morpholino-1-(pyridin-3-yl)but-2-en-1-one (3k)

Yield 145 mg (0.6 mmol, 21%), red solid, mp = 50−52 °C
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 9.03 (d, *J* = 2.0 Hz, 1H), 8.64 (dd, *J* = 4.8, 2.0 Hz, 1H), 8.13 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.33 (dd, *J* = 7.9, 4.8 Hz, 1H), 5.82 (s, 1H), 3.83–3.71 (m, 4H), 3.54–3.39 (m, 4H), 2.64 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 187.1, 163.9, 151.4, 148.8, 137.9, 135.2, 123.4, 93.9, 66.4 (2×*C*), 46.6 (2×*C*), 16.4.
HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{17}N_2O_2$ 233.1285; Found 233.1284.

1-(Pyridin-3-yl)butane-1,3-dione (4k)[31]

Yield 175 mg (1.1 mmol, 36%), yellowish solid, mp = 83−84 °C, R_f = 0.06 (EtOAc), *>97:3 enol/keto forms*
^{1}H NMR (800 MHz, 303K, $CDCl_3$): δ = 9.07 (d, *J* = 1.7 Hz, 1H), 8.73 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.17 (d, *J* = 7.9 Hz, 1H), 7.40 (dd, *J* = 7.9, 4.9 Hz, 1H), 6.19 (s, 1H), 2.23 (s, 3H). *– hydrogen-bound proton is outside the spectra area.*
^{13}C{^{1}H} NMR (201 MHz, 303 K, $CDCl_3$) δ (*enol form*): δ = 194.6, 181.3, 152.9, 148.5, 134.6, 130.8, 123.7, 97.3, 26.1.

1-(Thiophen-2-yl)butane-1,3-dione (4l)[27]
Yield 310 mg (1.9 mmol, 62%), colorless solid, mp = 28−30 °C, R_f = 0.43 (hexane/EtOAc); *87:13 enol/keto forms*
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 15.64 (br s, 1H), 7.69 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.59 (dd, *J* = 4.9, 1.2 Hz, 1H), 7.13 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.02 (s, 1H), 2.14 (s, 3H); δ (*keto form*) = 7.77–7.66 (m, 2H), 7.19–7.08 (m, 1H), 4.02 (s, 2H), 2.31 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 187.4, 181.9, 141.8, 132.5, 130.3, 128.4, 96.6, 24.0.

(1*E*)-5-Morpholino-1-phenylhexa-1,4-dien-3-one (3m)
Yield 370 mg (1.4 mmol, 48%), yellow solid, mp = 140−142 °C
^{1}H NMR (800 MHz, 300K, $CDCl_3$): δ = 7.54 – 7.50 (m, 3H), 7.34 (t, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 15.7 Hz, 1H), 5.40 (s, 1H), 3.75 (t, *J* = 4.9 Hz, 4H), 3.40 (t, *J* = 4.9 Hz, 4H), 2.61 (s, 3H).
^{13}C{^{1}H} NMR (201 MHz, 303K, $CDCl_3$): δ = 186.7, 162.7, 138.5, 136.0, 130.8, 129.3, 128.8 (2×*C*), 128.0 (2×*C*), 98.5, 66.5 (2×*C*), 46.5 (2×*C*), 16.1.
HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{20}NO_2$ 258.1489; Found 258.1485.

(*E*)-6-Phenylhex-5-ene-2,4-dione (4m)[32]
Yield 405 mg (2.2 mmol, 72%), yellow solid, mp = 76−78 °C, R_f = 0.47 (hexane/EtOAc, 3/1); *97:3 enol/keto forms*
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 15.35 (br s, 1H), 7.60 (d, *J* = 15.9 Hz, 1H), 7.55–7.46 (m, 2H), 7.43–7.32 (m, 3H), 6.47 (d, *J* = 15.9 Hz, 1H), 5.65 (s, 1H), 2.17 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 198.1, 177.0, 139.9, 135.2, 130.0, 129.0 (2×*C*), 128.0 (2×*C*), 122.9, 101.3, 27.20.

5-Morpholino-1-phenylhex-4-en-3-one (3n)
Isolated by filtration at −30 °C. Yield 390 mg (ca. 90% purity, 1.4 mmol, 45%), yellowish oil
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 7.35–7.14 (m, 5H), 5.20 (s, 1H), 3.80–3.49 (m, 4H), 3.33–3.20 (m, 4H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.67 (t, *J* = 7.8 Hz, 2H), 2.51 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 197.4, 161.2, 142.3, 128.5 (2×*C*), 128.4 (2×*C*), 125.8, 97.1, 66.4 (2×*C*), 46.4, 46.3 (2×*C*), 31.7, 15.8.
HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{22}NO_2$ 260.1645; Found 260.1649.

1-Phenylhexane-3,5-dione (4n)[20]
Yield 355 mg (1.9 mmol, 62%), colorless oil, R_f = 0.50 (hexane/EtOAc, 3/1); *84:16 enol/keto forms*
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 15.51 (br s, 1H), 7.39–7.29 (m, 2H), 7.30–7.20 (m, 3H), 5.53 (s, 1H), 2.99 (t, *J* = 7.7 Hz, 2H), 2.65 (t, *J* = 7.7 Hz, 2H), 2.09 (s, 3H); δ (*keto form*) = 7.39–7.29 (m, 2H), 7.30–7.20 (m, 3H), 3.60 (s, 2H), 3.00–2.93 (m, 2H), 2.92–2.85 (m, 2H), 2.25 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) = 193.4, 191.1, 140.8, 128.6 (2×*C*), 128.4 (2×*C*), 126.3, 100.1, 40.1, 31.6, 24.9.

1-(Cyclohexyl)-3-morpholinobut-2-en-1-one (3o)
Isolated by filtration at −30 °C. Yield 225 mg (85% purity, 0.8 mmol, 27%), yellowish oil
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 5.22 (s, 1H), 3.74–3.67 (m, 4H), 3.30 – 3.25 (m, 4H), 2.45 (s, 3H), 2.18 (tt, *J* = 11.6, 3.2 Hz, 1H), 1.87–1.60 (m, 6H), 1.37 – 1.06 (m, 4H).

$^{13}C\{^1H\}$ NMR (75 MHz, 300K, $CDCl_3$): δ = 202.2, 161.4, 96.5, 66.4 (2×*C*), 52.7, 46.3 (2×*C*), 29.9 (2×*C*), 26.2[1] (2×*C*), 22.1[6], 15.8.

HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{24}NO_2$ 238.1802; Found 238.1799.

1-Cyclohexylbutane-1,3-dione (4o)[33]

Yield 195 mg (1.2 mmol, 39%), colorless oil, R_f = 0.63 (hexane/EtOAc, 3/1); *87:13 enol/keto forms*

^1H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 15.59 (br s, 1H), 5.47 (s, 1H), 2.13 (tt, *J* = 11.4, 3.3 Hz, 1H), 2.04 (s, 3H), 1.90–1.58 (m, 4H), 1.45–1.06 (m, 6H); δ (*keto form*) =3.58 (s, 2H), 2.37 (tt, *J* = 10.8, 3.0 Hz, 1H), 2.20 (s, 3H), 1.90–1.58 (m, 10H).

$^{13}C\{^1H\}$ NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) =197.1, 192.5, 98.1, 46.4, 29.6 (2×*C*), 25.9[3], 25.8[8] (2×*C*), 25.3.

2,2-Dimethylhexane-3,5-dione (4p)[25]

Yield 192 mg (1.4 mmol, 45%), colorless oil, R_f = 0.65 (hexane/EtOAc, 3/1); *90:10 enol/keto forms*

^1H NMR (300 MHz, 300K, $CDCl_3$): δ (*enol form*) = 15.80 (s, 1H), 5.60 (s, 1H), 2.07 (s, 3H), 1.15 (s, 9H); δ (*keto form*) = 3.63 (s, 2H), 2.22 (s, 3H), 1.15 (s, 9H).

$^{13}C\{^1H\}$ NMR (75 MHz, 300K, $CDCl_3$): δ (*enol form*) =200.3, 192.6, 95.9, 39.1, 27.4 (3×*C*), 25.5.

1-Phenyl-3-pyrrolidinobut-2-en-1-one (3r)[34]

Yield 225 mg (1.1 mmol, 35%), yellow solid, mp = 155−157 °C

^1H NMR (300 MHz, 300K, $CDCl_3$) δ = 7.96–7.77 (m, 2H), 7.42–7.32 (m, 3H), 5.60 (s, 1H), 3.51 (br s, 2H), 3.36 (br s, 2H), 2.67 (s, 3H), 1.99 (br t, *J* = 5.0 Hz, 2H).

$^{13}C\{^1H\}$ NMR (75 MHz, 300K, $CDCl_3$): δ = 188.0, 161.9, 143.2, 130.2, 128.1 (2×*C*), 127.4 (2×*C*), 92.7, 48.3 (br, 2×*C*), 25.1 (br, 2×*C*), 18.1.

Chemistry of the crude enaminones

(3-(4-fluorobenzoyl)-4-morpholinophenyl)(2-hydroxyphenyl)methanone (5)

Crude reaction mixture (consisting of enaminone **3d**), obtained according to general procedure from morpholine amide **2d** (209 mg, 1.0 mmol, 1 equiv.) and propargylmagnesium bromide, was dissolved in dry acetonitrile (5 mL). 4-Oxo-4*H*-chromene-3-carbaldehyde (174 mg, 1.0 mmol, 1.0 equiv.) was added. The reaction mixture was heated at reflux with stirring for 5 h. Solvent was evaporated. The residue was subjected to a column chromatography on silica gel (eluent hexane/EtOAc, 3/1) to give aromatic compound **5** (225, 0.6 mmol, 56%) as yellowish oil, crystallizing on standing.

mp = 150-155 °C (with decomposition), R_f = 0.18 (hexane/EtOAc, 3/1)

^1H NMR (800 MHz, 303K, $CDCl_3$): δ = 11.86 (s, 1H), 7.87 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.85–7.81 (m, 2H), 7.80 (d, *J* = 2.2 Hz, 1H), 7.64 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.50 (ddd, *J* = 8.6, 7.2, 1.7 Hz, 1H), 7.14 (t, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 1H), 7.07 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.90 (ddd, *J* = 8.1, 7.2, 1.2 Hz, 1H), 3.43–3.33 (m, 4H), 3.09–3.01 (m, 4H).

$^{13}C\{^1H\}$ NMR (201 MHz, 303K, $CDCl_3$): δ = 199.4, 195.8, 166.2 (d, *J* = 256.3 Hz), 163.2, 153.9, 136.3, 133.7, 133.2, 132.95 (d, *J* = 3.1 Hz), 132.8 (d, *J* = 9.3 Hz, 2×*C*), 132.7, 131.1, 130.8, 119.3, 118.9, 118.7, 117.5, 115.7 (d, *J* = 21.9 Hz, 2×*C*), 66.4 (2×*C*), 51.9 (2×*C*).

HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{24}H_{21}FNO_4$ 406.1449; Found 406.1450.

2-Methyl-4-phenylfuran (6)[35]

Crude reaction mixture (consisting of enaminone **3a**), obtained according to general procedure from morpholine amide **2a** (191 mg, 1.0 mmol, 1.0 equiv.) and propargylmagnesium bromide, was dissolved in DMSO (8 mL); $(CH_3)_3SI$ (612 mg, 3.0 mmol, 3.0 equiv) and NaH (448 mg, 4.0 mmol, 4.0 equiv.) were added to the resulting solution at room temperature under atmosphere of dry argon. After being stirred for 12 h, the reaction mixture was poured into water (80 mL) and extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine (20 mL) and dried with anhydrous Na_2SO_4. The solution was concentrated at

reduced pressure. The residue was subjected to a column chromatography on silica gel pretreated with Et_3N[36] (eluent hexane) to give furan **6** (66 mg, 0.4 mmol, 42%) as off-white solid.
mp = 67-68 °C, R_f = 0.72 (hexane/EtOAc, 3/1).
^{1}H NMR (300 MHz, 300K, $CDCl_3$): δ = 7.60 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 6.32 (s, 1H), 2.35 (s, 3H).
^{13}C{^{1}H} NMR (75 MHz, 300K, $CDCl_3$): δ = 153.4, 136.8, 133.0, 128.9 (2×*C*), 127.4, 126.9, 125.8 (2×*C*), 105.0, 13.7.

(*E*)-3-methyl-1-phenyl-5-styryl-1*H*-pyrazole (7)[37]

Crude reaction mixture (consisting of enaminone **3m**), obtained according to general procedure from morpholine amide **2m** (215 mg, 1.0 mmol, 1.0 equiv.) and propargylmagnesium bromide, was dissolved in CH_2Cl_2 (6 mL). $PhNHNH_3^+Cl^-$ (145 mg, 1.0 mmol, 1.0 equiv.) and Et_3N (0.16 ml, 1.2 mmol, 1.2 equiv.) were added to the solution at room temperature. After completion (TLC control, generally 5 h), the reaction mixture was poured into water (20 mL) and extracted with Et_2O (3×20 mL). The combined organic layers were washed with brine (20 mL) and dried with anhydrous Na_2SO_4. The solution was concentrated at reduced pressure. The residue was subjected to a column chromatography on silica gel (eluent hexane/EtOAc, 10/1→5/1) to provide pyrazole **7** (153 mg, 0.6 mmol, 59%) as yellowish oil.
R_f = 0.48 (hexane/EtOAc, 3/1).
^{1}H NMR (800 MHz, 303K, $CDCl_3$): δ = 7.51–7.47 (m, 3H), 7.41 – 7.38 (m, 3H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 16.2 Hz, 1H), 6.88 (d, *J* = 16.2 Hz, 1H), 6.47 (s, 1H), 2.38 (s, 3H).
^{13}C{^{1}H} NMR (201 MHz, 303K, $CDCl_3$): δ = 149.6, 141.9, 139.8, 136.7, 131.8, 129.3 (2×*C*), 128.9 (2×*C*), 128.3, 127.8, 126.7 (2×*C*), 125.5 (2×*C*), 116.0, 104.0, 13.7.

Acknowledgements

This work was supported by the grant of the President of the Russian Federation № MK-736.2021.1.3.

Supplementary Material

Copies of ^{1}H and ^{13}C NMR spectra are provided in the Supplementary Material associated with this paper.

References

1. Mikhaylov, A. A.; Ikonnikova, V. A.; Solyev, P. N. *Nat. Prod. Rep*. **2021**, *38*, 1506. https://doi.org/10.1039/D0NP00082E
2. Ikonnikova, V. A.; Solyev, P. N.; Terekhov, S. S.; Alferova, V. A.; Tyurin, A. P.; Korshun, V. A.; Baranov, M. S.; Mikhaylov, A. A. *ChemistrySelect* **2021**, *6*, 11775. https://doi.org/10.1002/slct.202103755
3. Nagao, Y.; Jeong, I.-Y.; Lee, W. S.; Sano, S. *Chem*. Commun. **1996**, *53*, 19. https://doi.org/10.1039/CC9960000019
4. Martín, R.; Romea, P.; Tey, C.; Urpí, F.; Vilarrasa, J. *Synlett* **2000**, *12*, 1414. https://doi.org/10.1055/s-1997-1050

5. Hyun Choi, Y.; Soon Kim, K.; Lee, S.; Jeong, T.-S.; Lee, H.-Y.; Hae Kim, Y.; Song Lee, W. *Heterocycles* **2003**, *60*, 2499. https://doi.org/10.3987/COM-03-9869
6. Nagao, Y.; Lee, W.-S.; Kim, K. *Chem. Lett.* **1994**, *23*, 389. https://doi.org/10.1246/cl.1994.389
7. Gomtsyan, A. *Org. Lett.* **2000**, *2*, 11. https://doi.org/10.1021/ol9911122
8. Goh, J.; Ong, S. K.; Tan, Y. S.; Loh, T.-P. *Green Chem.* **2022**, *24*, 3321. https://doi.org/10.1039/D2GC00027J
9. Cromwell, N. H. *J. Am. Chem. Soc.* **1940**, *62*, 3470. https://doi.org/10.1021/ja01869a051
10. Hickmott, P. W.; Sheppard, G. *J. Chem. Soc. Perkin Trans. 1* **1972**, 1038. https://doi.org/10.1039/P19720001038
11. Khademi, Z.; Heravi, M. M. *Tetrahedron* **2022**, *103*, 132573. https://doi.org/10.1016/j.tet.2021.132573
12. Chen, J.; Xia, Y.; Lee, S. *Org. Chem. Front*. **2020**, *7*, 2931. https://doi.org/10.1039/d0qo00797h
13. Lim, D.; Fang, F.; Zhou, G.; Coltart, D. M. *Org. Lett.* **2007**, *9*, 4139. https://doi.org/10.1021/ol701599v
14. Štefane, B. *Org. Lett.* **2010**, *12*, 2900. https://doi.org/10.1021/ol100620j
15. Silva, S.; Maycock, C. D. *Tetrahedron* **2019**, *75*, 130552. https://doi.org/10.1016/j.tet.2019.130552
16. Corsaro, A.; Perrini, G.; Testa, M. G.; Chiacchio, U. *Phosphorus. Sulfur. Silicon Relat. Elem.* **1992**, *71*, 197. https://doi.org/10.1080/10426509208034512
17. Chevalley, A.; Férézou, J. P. *Tetrahedron* **2012**, *68*, 5882. https://doi.org/10.1016/j.tet.2012.04.105
18. Xu, L.; Wu, L.; Chen, T.; Xu, S.; Huang, C.; Wang, Y.; You, Q.; Shen, J. *ChemistrySelect* **2020**, *5*, 655. https://doi.org/10.1002/slct.201903792
19. Shcherbakov, R. O.; Myasnikov, D. A.; Trushkov, I. V.; Uchuskin, M. G. *J. Org. Chem.* **2023**, *88*, 8227. https://doi.org/10.1021/acs.joc.3c00203
20. Sada, M.; Matsubara, S. *J. Am. Chem. Soc.* **2010**, *132*, 432. https://doi.org/10.1021/ja910428y
21. Maslak, V.; Tokic-Vujosevic, Z.; Ferjancic, Z.; Saicic, R. N. *Tetrahedron Lett*. **2009**, *50*, 6709. https://doi.org/10.1016/j.tetlet.2009.09.113
22. Lin, H.-S.; Paquette, L. A. *Synth. Commun*. **1994**, *24*, 2503. https://doi.org/10.1080/00397919408010560
23. Barkov, A. Y.; Korotaev, V. Y.; Kutyashev, I. B.; Sosnovskikh, V. Y. *Tetrahedron* **2016**, *72*, 2026. https://doi.org/10.1016/j.tet.2016.03.005
24. Zheng, Y.; Liu, Z.-W.; Li, T.; Li, X.; Li, S.-H. *Org. Lett.* **2022**, *24*, 7533. https://doi.org/10.1021/acs.orglett.2c02824
25. Bassetti, M.; Cerichelli, G.; Floris, B. *Tetrahedron* **1988**, *44*, 2997. https://doi.org/10.1016/S0040-4020(88)90039-7
26. Lord, R. M.; Hebden, A. J.; Pask, C. M.; Henderson, I. R.; Allison, S. J.; Shepherd, S. L.; Phillips, R. M.;

McGowan, P. C. *J. Med. Chem.* **2015**, *58*, 4940.
https://doi.org/10.1021/acs.jmedchem.5b00455
27. Varun, B. V.; Gadde, K.; Prabhu, K. R. *Org. Lett*. **2015**, *17*, 2944.
https://doi.org/10.1021/acs.orglett.5b01221
28. Pratap, R.; Gupta, R. C. .; Srimal, R. C. .; Anand, N. *Indian J. Chem. Sect. B* **1980**, *19B*, 695.
29. Chassaing, S.; Isorez-Mahler, G.; Kueny-Stotz, M.; Brouillard, R. *Tetrahedron* **2015**, *71*, 3066.
https://doi.org/10.1016/j.tet.2014.10.058
30. Rajasekar, S.; Anbarasan, P. *Chem. - An Asian J.* **2019**, *14*, 4563.
https://doi.org/10.1002/asia.201901015
31. Schranck, J.; Tlili, A.; Alsabeh, P. G.; Neumann, H.; Stradiotto, M.; Beller, M. *Chem. - A Eur. J.* **2013**, *19*, 12624.
https://doi.org/10.1002/chem.201302590
32. Marx, V. M.; Stoddard, R. L.; Heverly-Coulson, G. S.; Burnell, D. J. *Chem. - A Eur. J.* **2011**, *17*, 8098.
https://doi.org/10.1002/chem.201100519
33. Roudier, M.; Constantieux, T.; Quintard, A.; Rodriguez, J. *Org. Lett.* **2014**, *16*, 2802.
https://doi.org/10.1021/ol500821c
34. Otohiko, T.; Akitaka, I. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2828.
https://doi.org/10.1246/bcsj.49.2828
35. Lin, M. H.; Huang, Y. C.; Kuo, C. K.; Tsai, C. H.; Li, Y. S.; Hu, T. C.; Chuang, T. H. *J. Org. Chem.* **2014**, *79*, 2751.
https://doi.org/10.1021/jo5001274
36. Marshall, J. A.; Sehon, C. A. *Org. Synth*. **1999**, *76*, 263.
https://doi.org/10.15227/orgsyn.076.0263
37. Jin, W.; Yu, H.; Yu, Z. *Tetrahedron Lett*. **2011**, *52*, 5884.
https://doi.org/10.1016/j.tetlet.2011.08.168