Note

Nonstabilized Azomethine Ylides in the Mannich Reaction. Synthesis of 3,3-Disubstituted Pyrrolidines, Including Oxindole Alkaloids

Evgeny M. Buev, Vladimir S. Moshkin, and Vyacheslav Y. Sosnovskikh

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02193 • Publication Date (Web): 19 Oct 2017

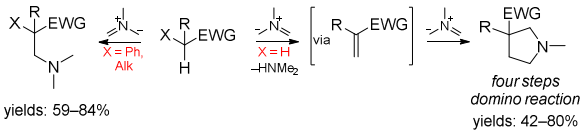
Nonstabilized Azomethine Ylides in the Mannich Reaction. Synthesis of 3,3-Disubstituted Pyrrolidines, Including Oxindole Alkaloids

Evgeny M. Buev, Vladimir S. Moshkin*, and Vyacheslav Y. Sosnovskikh

Institute of Natural Sciences and Mathematics, Ural Federal University, 620000 Ekaterinburg, Russian Federation

Keywords: Nonstabilized azomethine ylides; Saturated azaheterocycles; Pyrrolidines; Oxindole alkaloids; Horsfiline; [3+2] Cycloaddition; Mannich reaction; Domino reaction.

Graphical Abstract



ABSTRACT: Active methylene compounds react with in situ generated nonstabilized azomethine ylides via domino Mannich reaction–dipolar cycloaddition to form 3,3-disubstituted pyrrolidines, including oxindole alkaloids. When starting material possesses a single activated hydrogen the reaction terminates at the Mannich base stage. The developed methodology was applied in short and efficient synthesis of (±)-horsfiline and N-protected (±)-coerulescine.

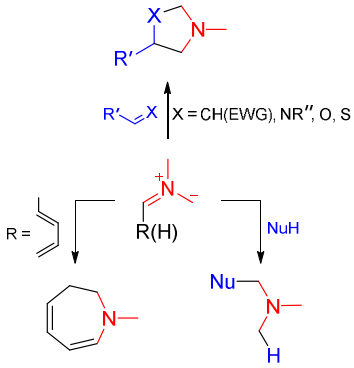
Reactions of nonstabilized azomethine ylides are one of the most convenient methods for a synthesis of various nitrogen containing compounds. Their use in the synthesis of five-membered azaheterocycles by [3+2] cycloadditions to multiple bonds of dipolarophiles is attractive and frequently utilized methodology.[1] The significant advantages of this approach are the easy of in situ generation of starting ylides, the formation of two new covalent bonds of the product by single cycloaddition step, as well as the selectivity of this process, which allows to create few chiral centers with a specific configuration simultaneously. All aspects mentioned above make them an indispensable tool in the synthesis of natural and biologically active compounds. A combination of [3+2] cycloaddition of these ylides with subsequent one-two stage one-pot transformations of primary adducts opens especially broad prospects. Thus, methods based on the reactions of nonstabilized azomethine ylides for the synthesis of adrenergic 2-alkylamino-1-arylethanols and 3-arylpyrrolidines, containing conformationally fixed phenethylamine moiety, tetrahydroisoquinoline alkaloids, showing antihypertensive and antidepressive effects, and

**E-mail:* mvslc@mail.ru (V. S. Moshkin).

tetrahydro-γ-carbolines, structurally related to antihistamine medicinal compounds, were developed previously by a number of research groups including ours.[2]

Synthetic potential of nonstabilized azomethine ylides is not limited by the [3+2] cycloadditions (Scheme 1). Examples of 1,5- and 1,7-electrocyclizations of conjugated azomethine ylides are also known in the literature.[3] The reactions of azomethine ylides with various nucleophilic compounds in the presence of H^+ are intensively studied by Seidel and other authors over the last 10 years.[4] In the latter case, the initially formed azomethine ylide is not involved into pericyclic reaction, but acts as a base. Iminium cation formed by this process then reacts with internal or external C-, N-, O-, P- or S-nucleophile. This direction within the scope of simplest symmetric nonstabilized azomethine ylides with C-nucleophiles was previously little studied.[4] Whereas, in perspective it should appear to be a modification of the Mannich reaction, and thus became the subject of the present work. To the best of our knowledge, the first example of such process was the reaction of ethyl 6-phenylcomanoate with *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine described in 1999.[5a] Later there was another instance of the similar reaction of *p*-hydroxybenzaldehyde.[5b] However, in both cases, observed reactions were side processes and have not been further developed.

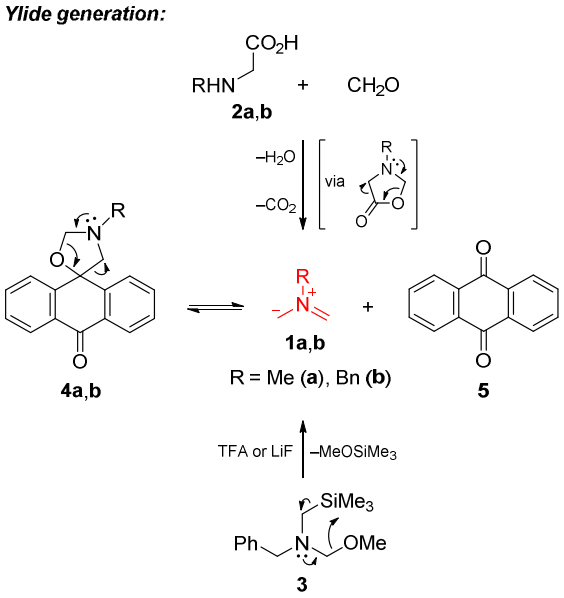
Scheme 1. General synthetic possibilities of azomethine ylides



For the implement of our investigation, frequently utilized methods of simple nonstabilized azomethine ylides **1a**,**b** generation were used (Scheme 2). They are decarboxylative condensation of *N*-alkyl-α-amino acids **2a**,**b** with carbonyl compounds[6] and desilylation of *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine (**3**) in the presence of TFA or LiF.[7] Moreover, recently we discovered new precursors of these ylides – spiroanthraceneoxazolidines **4a**,**b**, which are readily available from anthraquinone **5**, *N*-substituted glycines **2a**,**b** and formaldehyde.[8] These at room temperature stable oxazolidines have an unique ability to undergo

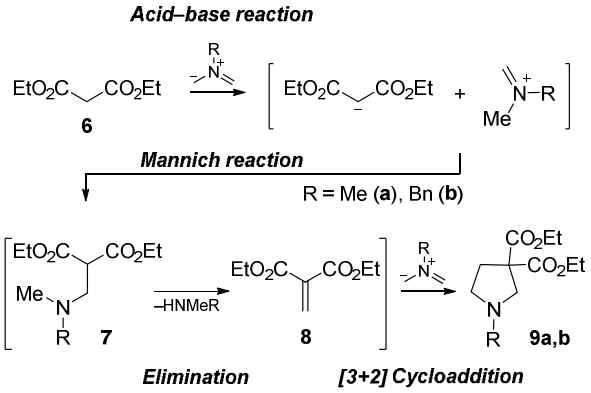
a cycloreversion in a presence of other dipolarophiles at high temperature and previously proved to be useful and convenient reagents for the synthesis of substituted pyrrolidines.

Scheme 2. Useful methods for the generation of nonstabilized azomethine ylides



As a model experiment, we carried out the reaction of diethyl malonate **6** with *N*-methylazomethine ylide **1a**, generated in situ from sarcosine **2a** and formaldehyde at reflux for 2 h in the mixture of DMF and *o*-xylene (1:1). Remarkably, this reaction did not stop at the formation of the Mannich base **7**, as it could be initially assumed. It proceeded further through the elimination of dimethylamine from intermediate **7** and the following [3+2] cycloaddition of formed methylenemalonate **8** with another equivalent of starting ylide **1a** (Scheme 3; Table 1, entry 1,2). The above process led to the formation of simple diethyl 1-methylpyrrolidine-3,3-dicarboxylate (**9a**) previously unknown in the literature.

Scheme 3. New domino reaction leading to pyrrolidine ring



It is noteworthy that using of malonate **6** and excess of spiroanthraceneoxazolidine **4a** in a microwave reactor at 210 °C for 45 min allowed to substantially increase the yield of product **9a** (Table 1, entry 3,4). Attempts to perform the reaction at lower temperatures (refluxing in *o*-xylene or toluene), including those with an addition of acid or base as potential catalysts, were not successful (Table 1, entry 5–8). On the other hand, it was discovered that reaction with spirooxazolidine **4a** can be carried out without the microwave reactor by heating of the reagents in *N*-methylpyrrolidone (NMP) at 210 °C, however, the yield of the product was only 25% (Table 1, entry 9). Thus, we propose scalable and easy for practical implementation one-pot synthesis from readily available reagents which appears to be a new, fairly competitive method for the synthesis of various 3,3-disubstituted pyrrolidines.

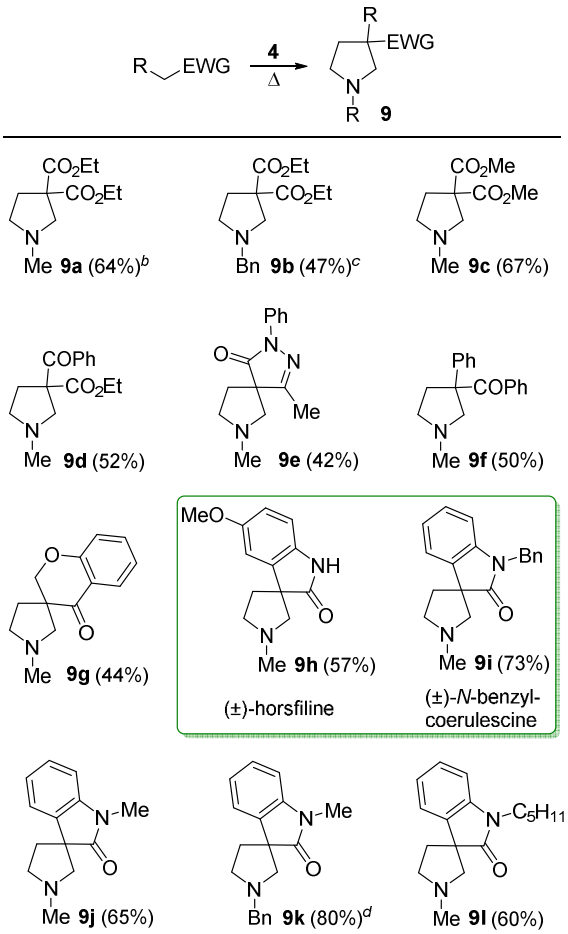
Table 1. Optimization of the reaction conditions

entry	conditions	yield **9** (%)
1	**2a** (1.5 equiv.), CH_2O (2.3 equiv.), DMF/*o*-xylene (1:1), reflux, 2 h	37
2	**2a** (3 equiv.), CH_2O (5 equiv.), DMF/*o*-xylene (1:1), reflux, 2 h	38
3	**4a** (2.5 equiv.), *o*-xylene, MW, 210 °C, 90 min	50
4	**4a (2.3 equiv.), *o*-xylene, MW, 210 °C, 45 min**	**64**
5	**4a** (2.3 equiv.), *o*-xylene, reflux, 2 h	–[a]
6	**4a** (2.3 equiv.), *o*-xylene, reflux, 5 h	–[a]
7	**4a** (2.3 equiv.), $PhCO_2H$ (0.1 equiv.), toluene, reflux, 5 h	–[b]
8	**4a** (1.1 equiv.), *t*-BuOK (0.5 equiv.), toluene, reflux, 2 h	–[b]
9	**4a** (2.5 equiv.), NMP, 210 °C, 45 min	25
10	**3** (2.5 equiv.), LiF (4 equiv.), DMF, MW, 210 °C, 45 min	47[c]

[a]Mixture of product **9a** and starting oxazolidine **4a** 1:1 determined by ^{1}H NMR spectroscopy data. [b]According to ^{1}H NMR data, the reaction mixture was in general starting **4a**. [c]In contrast to product **9a** synthesis (entry 1-4,9) it was necessary to purify product **9b** by column chromatography.

We also managed to carry out this domino process using previously mentioned *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine (**3**) as the precursor of nonstabilized azomethine ylide **1b** (R = Bn) in a presence of LiF in the microwave reactor at 210 °C for 45 min. However, pyrrolidine **9b** was formed as a mixture with side benzylamines and, unlike to **9a**, was isolated after the purification by column chromatography in 47% yield (Table 1, entry 10; Table 2).

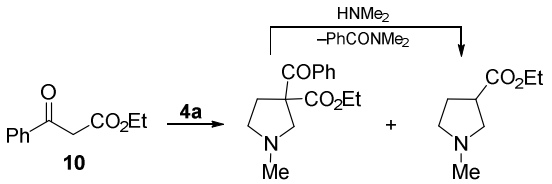
Table 2. Synthesis of 3,3-disubstituted pyrrolidines **9**[a]



[a]Reaction conditions: methylene active compound (1.0 mmol), **4** (2.3 mmol), *o*-xylene, MW, 210 °C, 45 min. Isolated yields of chromatographically purified compounds are specified. [b]Product **9a** was obtained without chromatographic purification. [c]*N*-(MeOCH$_2$)-*N*-(Me$_3$SiCH$_2$)benzylamine (**3**) was used. [d]*N*-Benzyl substituted spiroanthraceneoxazolidine **4b** was used.

In the next step of our research, we investigated the reaction of spiroanthraceneoxazolidines **4** with other active methylene compounds (Table 2). As expected, we obtained dimethyl 1-methylpyrrolidine-3,3-dicarboxylate (**9c**) in good yield. Furthermore, ethyl benzoylacetate **10** was successfully converted into pyrrolidine **9d** which was observed in a mixture with debenzoylated product **9′d**. The quantity of latter was depended on the duration of the reaction (Scheme 4). Probably, nucleophilic dimethylamine eliminated from the Mannich base or traces of water in the reaction mixture attacked benzoyl group of the main product **9d**. Subsequent retro-Claisen reaction gave 3-ethoxycarbonylpyrrolidine **9′d**. Pure pyrrolidine **9d** was isolated by column chromatography in 52% yield.

Scheme 4. Reaction of spiroanthraceneoxazolidine **4a** with ethyl benzoylacetate



	9d	NMR ratio	9′d	
MW, 210 °C, 90 min	2		1	(58%)[a]
MW, 210 °C, 45 min	4.5		1	(73%)[a]

[a]Yields of the mixture of products

5-Methyl-2-phenylpyrazol-3-one, containing imino moiety as a second activating group, also reacted with oxazolidine **4a** to give spiropyrrolidine **9e** in moderate yield. It was possible to carry out the reaction with benzyl phenyl ketone containing activating carbonyl and phenyl groups that resulted in pyrrolidine **9f**. Moreover, chroman-4-one, having only one activating keto-group conjugated with electron-donating oxygen, also reacted with oxazolidine **4a** and allowed to isolate spiro-fused pyrrolidine **9g**. In spite of this, reactions of **4a** with methyl phenylacetate as well as with phenylacetonitrile were not successful. Thus, substrates with conformationally free weak activating groups are not suitable for this process.

A point of special interest was the investigation of the reaction between spirooxazolidines **4** and indolin-2-ones that could lead to the formation of oxindole alkaloids coerulescine and horsfiline **9h** (Table 2). The latter was isolated from the plant *Horsfieldia superba* and has attracted significant attention of scientific society as analgesic medicinal compound.[9] We discovered that unsubstituted indolin-2-one reacted with spiroanthraceneoxazolidine **4a** to form hard to purify coerulescine in low yield. The cause of this is, presumably, a competitive acidic amide moiety. Nevertheless, 5-methoxyindolin-2-one reacted readily due to the presence in its structure of one electron-donating substituent in the para position relative to 1-NH that, apparently, decreases its acidity. As the result, (±)-horsfiline **9h** was obtained in 57% yield.

Gratifyingly, 1-substituted indolin-2-ones smoothly reacted with azomethine ylides precursors **4** to give spirooxindoles **9i–l** in good to high yields (60–80%). Taking into account the fact that method for a debenzylation of **9i** in high yield (83%) is known in the literature,[10] such two-step approach to the synthesis of coerulescine is pretty attractive.

Unfortunately, attempt to involve in this process such conformationally free ketone as acetophenone was not successful. The reactions failed also with acidic compounds which are capable to a self-condensation (acetylacetone, indan-1,3-dione, diethyl 3-ketoglutarate, malononitrile). In general, it can be concluded that only one keto-group in conformationally fixed methylene active compound or two electron-withdrawing groups in conformationally free substrate are sufficient for this process. Despite these limits, it is obvious that discovered domino

reaction could be achieved on a wide range of CH_2-acidic compounds. Thus, proposed azomethine ylide methodology for the rapid construction of the spirocyclic systems in one stage provides an efficient and straightforward access to various spiropyrrolidines, which are difficult to synthesize by other methods.

In view of the fact that probable intermediate of this domino process is unstable Mannich base **7** (Scheme 3), we decided to isolate it using substituted CH-acidic substrates which are unable to eliminate dimethylamine. For this purpose, we carried out the reaction of spiroanthraceneoxazolidine **4a** with diethyl benzylmalonate **11a** (Scheme 5).

Scheme 5. Dimethylaminomethylation of **11a** by spiroanthraceneoxazolidine **4a**

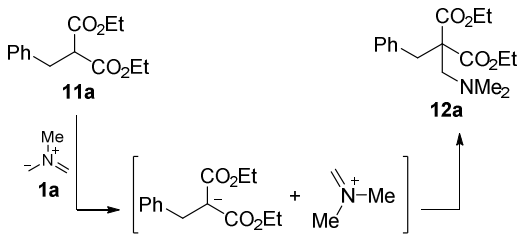


Table 3. Optimization of the reaction conditions

entry	conditions	yield (%) **12a**
1	**4a** (2.3 equiv.), *o*-xylene, MW, 210 °C, 45 min	–[a]
2	**4a** (1.4 equiv.), *o*-xylene, MW, 210 °C, 60 min	67[b]
3	**4a (1.0 equiv.), 11a (1.5 equiv.), *o*-xylene, MW, 210 °C, 45 min**	**65**[c]
4	sarcosine **2a** (1.5 equiv.) and formaldehyde (2.25 equiv.), DMF/*o*-xylene (1:1), reflux, 2 h	22

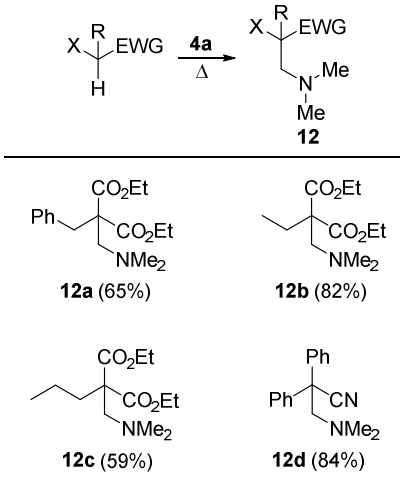
[a]Mixture of product **12a** and starting oxazolidine **4a** 2:1 (determined by ^{1}H NMR spectroscopy data). [b]Product **12a** was contaminated with difficult to separate initial oxazolidine **4a**. [c]Isolated yield based on the starting spiroanthraceneoxazolidine **4a**.

Indeed, previously found conditions for the annulation (2.3 equiv. of spiro-fused oxazolidine **4a**, heating at 210 °C) resulted in the insertion of azomethine ylide into C–H bond. However, obtained product **12a** was in the mixture with initial spiroanthraceneoxazolidine **4a**. A simple modification of the reaction conditions consisted in using of 1.5 equiv. excess of starting benzylmalonate allowed us to isolate pure Mannich base **12a** in 65% yield. As a side note, nonstabilized azomethine ylide **1a**, generated in situ from sarcosine and formaldehyde, also

reacted with diethyl benzylmalonate **11a** to give Mannich adduct **12a** but in significantly lower yield (Table 3, entry 4).

In connection with these results, we examined such reaction on a number of other CH-acidic compounds and successfully obtained corresponding amines **12b–d** in 59–84% yields (Table 4). Notably, this synthesis does not require chromatographic purification. Due to a simple implementation, discovered dimethylaminomethylation reaction is an unusual modification of Mannich reaction. Spiro-oxazolidine **4a** can be considered as the basic analog of Eschenmoser salt in this light.

Table 4. Synthesis of Mannich products **12**[a]



[a]Reaction conditions: CH-acidic compound (1.5 mmol), **4a** (1.0 mmol), *o*-xylene, MW, 210 °C, 45 min. Isolated yields based on starting spiroanthraceneoxazolidine **4a**.

In summary, it could be concluded that reactions of CH-acidic compounds with nonstabilized azomethine ylides possess a general nature and depending on number of reactive hydrogens either stop on the Mannich base formation or proceed through the domino process resulted in the formation of new pyrrolidine ring. In the first case, *N*-alkylazomethine ylides are protonated and act as Mannich iminium cations, while in the second one, they act as a synthetic equivalent of formaldehyde and as 1,3-dipole. The application of strained spiroanthraceneoxazolidines **4** was especially effective in these reactions that allowed to significantly expand synthetic possibilities of nonstabilized azomethine ylides. Discovered approach is particularly actual in view of new perspective way to biologically active spiro-oxindole alkaloids and related to them 3,3-disubstituted pyrrolidines.

EXPERIMENTAL SECTION

General Experimental Details. All solvents used were dried and distilled per standard procedures. Microwave syntheses were performed in a sealed tube in Biotage Initiator+, temperature was monitored by external surface sensor. Column chromatography was performed with silica gel (40–63 μm, ASTM). Chloroform, mixture of chloroform and ethanol (from 200/1 to 20/1), mixture of dichloromethane and ethanol (20/1) were used as eluents. NMR spectra were recorded on Bruker DRX-400 (^{1}H – 400 MHz and ^{13}C – 101 MHz) and Bruker Avance III-500 (^{1}H – 500 MHz and ^{13}C – 126 MHz) spectrometers in DMSO-d_6, $CDCl_3$. The chemical shifts are reported in ppm relative to internal standard TMS (^{1}H NMR) and to residual signals of the solvents (^{13}C NMR). The HRMS spectra were obtained using UHR-Qq TOF mass spectrometer maX is Impact HD (Bruker Daltonics) installed in the Institute of Organic Synthesis UB RAS. Electrospray ionization with direct sample inlet (flow rate 240 μL/h) was used. The mass spectrometer was operating in positive mode in the mass range of 50–1550 Da.

General procedure for the synthesis of pyrrolidines 9a-l and Mannich adducts 12a-d. A 10 mL microwave reaction tube was charged with a stir bar, the corresponding active methylene compound (1.0 mmol), 10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4** (2.3 mmol),[8a] dry *o*-xylene (3 mL) and was filled with an argon atmosphere, before it was sealed with a cap. After pre-stirring for 3 min the mixture was heated in microwave reactor at 210 °C for 45 min with stirring. After cooling with a compressed air flow the resulting mixture was diluted with PhMe (5 mL). The precipitate was filtered off. The solution was extracted with cold 1 M HCl (10 mL) and aqueous phase was washed with PhMe (2 × 5 mL). The aqueous layer was basified with $NaHCO_3$ to pH = 8–9, extracted with PhMe (2 × 5 mL), dried over Na_2SO_4 and evaporated under reduced pressure to give the desired product. The latter, if necessary, was purified by column chromatography.

Specific procedures for the synthesis of pyrrolidines from diethyl malonate by action of various nonstabilized azomethine ylide precursors. Procedure A for the synthesis of pyrrolidines without microwave reactor. A 10 mL round-bottom flask was charged with a stir bar, diethyl malonate **6** (160 mg, 1.0 mmol), 3′-methyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4a** (610 mg, 2.3 mmol), dry *N*-methyl-2-pyrrolidone (3 mL), reflux condenser and $CaCl_2$ tube. Mixture was heated on oil bath at 210 °C for 45 min with stirring. After cooling to room temperature the resulting mixture was diluted with H_2O (15 mL) and extracted with PhMe (2 × 5 mL). The precipitate was filtered off. The organic phase was extracted with cold 1 M HCl (10 mL). The aqueous phase was washed with PhMe (2 × 5 mL) and then it was basified with $NaHCO_3$ to pH = 8–9, extracted with PhMe (2 × 5 mL), dried over Na_2SO_4 and evaporated under

reduced pressure to give the desired diethyl 1-methylpyrrolidine-3,3-dicarboxylate **9a** in 25% yield (57 mg).

Procedure B for the synthesis of pyrrolidines using sarcosine and paraformaldehyde. A mixture of the diethyl malonate **6** (160 mg, 1.0 mmol), finely ground sarcosine **2a** (267 mg, 3.0 mmol), and paraformaldehyde (150 mg, 5.0 mmol of formaldehyde) was heated at reflux in the mixture of dry *o*-xylene and dry DMF (1:1, 8 mL) in a 25 mL round-bottom flask fitted with a Dean-Stark trap for 2 h on oil bath previously warmed up to 170 °C. After cooling to room temperature the resulting mixture was washed with H_2O (3 × 5 mL). The solution was extracted with cold 1 M HCl (10 mL). The aqueous phase was washed with PhMe (2 × 5 mL) and then it was basified with $NaHCO_3$ to pH = 8–9, extracted with PhMe (2 × 5 mL), dried over Na_2SO_4 and evaporated under reduced pressure to give the desired diethyl 1-methylpyrrolidine-3,3-dicarboxylate **9a** in 38% yield (87 mg).

Procedure C for the synthesis of pyrrolidines using *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine. A 10 mL microwave reaction tube was charged with a stir bar, diethyl malonate **6** (160 mg, 1.0 mmol), *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine (**3**) (2.5 mmol, 592 mg),[7e] lithium fluoride (104 mg, 4.0 mmol), dry DMF (3 mL) and was filled with an argon atmosphere, before it was sealed with a cap. After pre-stirring for 3 min the mixture was heated in microwave reactor at 210 °C for 45 min with stirring. After cooling with a compressed air flow the resulting mixture was diluted with PhMe (8 mL) and was washed with H_2O (3 × 5 mL). The solution was extracted with cold 1 M HCl (10 mL). The aqueous phase was washed with PhMe (2 × 5 mL) and then it was basified with $NaHCO_3$ to pH = 8–9, extracted with PhMe (2 × 5 mL), dried over Na_2SO_4 and evaporated under reduced pressure to give the crude product. The latter was purified by column chromatography (eluent: chloroform; R_f (chloroform/methanol, 100/2) = 0.6) to give pure diethyl 1-benzylpyrrolidine-3,3-dicarboxylate **9b** in 47% yield (144 mg).

Diethyl 1-methylpyrrolidine-3,3-dicarboxylate (9a). Compound **9a** was synthesized according to the **general procedure** from diethyl malonate. Light brown oil, yield 147 mg (64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (q, *J* = 7.1 Hz, 4H, $2CO_2CH_2CH_3$), 3.03 (s, 2H, 2-CH_2), 2.62 (t, *J* = 6.8 Hz, 2H), 2.44 (t, *J* = 6.8 Hz, 2H), 2.35 (s, 3H, MeN), 1.25 (t, *J* = 7.1 Hz, 6H, $2CO_2CH_2CH_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4 (2C=O), 62.6 (2-CH_2), 61.7 ($2CH_2O$), 59.8 (3-C), 55.9 (5-CH_2), 41.8 (CH_3N), 33.2 (4-CH_2), 14.1 ($2CH_3$). HRMS (ESI) calcd for $(C_{11}H_{20}NO_4)^+$ $[M+H]^+$: 230.1387, found: 230.1391.

Diethyl 1-benzylpyrrolidine-3,3-dicarboxylate (9b). Compound **9b** was synthesized according to the **procedure C** from diethyl malonate **6** (160 mg, 1.0 mmol) and *N*-(methoxymethyl)-*N*-(trimethylsilylmethyl)benzylamine (**3**) (2.5 mmol, 592 mg). Crude product was purified by

column chromatography (eluent: chloroform; R_f (chloroform/methanol, 100/2) = 0.6). Light yellow oil, yield 144 mg (47%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.28 (m, 4H, Ph), 7.26–7.22 (m, 1H, Ph), 4.19 (q, *J* = 7.1 Hz, 4H, $2CO_2CH_2CH_3$), 3.64 (s, 2H, $PhCH_2$), 3.05 (s, 2H, 2-CH_2), 2.67 (t, *J* = 6.8 Hz, 2H), 2.44 (t, *J* = 6.8 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 6H, $2CO_2CH_2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4 (2C=O), 138.8 (C), 128.7 (2CH), 128.4 (2CH), 127.1 (CH), 61.7 ($2CH_2O$), 60.1, 59.54, 59.45, 53.5 (CH_2), 32.7 (4-CH_2), 14.2 ($2CH_3$). HRMS (ESI) calcd for $(C_{17}H_{24}NO_4)^+$ $[M+H]^+$: 306.1700, found: 306.1703.

Dimethyl 1-methylpyrrolidine-3,3-dicarboxylate (9c). Compound **9c** was synthesized according to the **general procedure** from dimethyl malonate. Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/1; R_f (chloroform/ethanol, 100/2) = 0.2). Yellow oil, yield 135 mg (67%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 3.66 (s, 6H, $2CO_2Me$), 2.89 (s, 2H, 2-CH_2), 2.48 (t, *J* = 6.9 Hz, 2H), 2.29 (t, *J* = 6.9 Hz, 2H), 2.21 (s, 3H, MeN); ^{13}C NMR (126 MHz, DMSO-d_6) δ 171.0 (2C=O), 61.9 (2-CH_2), 59.1 (3-C), 55.0 (5-CH_2), 52.8 ($2CH_3O$), 41.1 (CH_3N), 32.5 (4-CH_2). HRMS (ESI) calcd for $(C_9H_{16}NO_4)^+$ $[M+H]^+$: 202.1074, found: 202.1077.

Ethyl 3-benzoyl-1-methylpyrrolidine-3-carboxylate (9d). Compound **9d** was synthesized according to the **general procedure** from ethyl benzoylacetate. Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/1; R_f (chloroform/ethanol, 100/2) = 0.3). Light yellow oil, yield 136 mg (52%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.4, 1.1 Hz, 2H, 2,6-HPh), 7.54 (t, *J* = 7.4 Hz, 1H, 4-HPh), 7.43 (t, *J* = 7.8 Hz, 2H, 3,5-HPh), 4.10 (q, *J* = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 3.32 (d, *J* = 10.0 Hz, 1H, 2-CH*H*), 3.09 (d, *J* = 10.0 Hz, 1H, 2-C*H*H), 2.74–2.68 (m, 1H), 2.66–2.61 (m, 2H), 2.58 (dd, *J* = 9.3, 6.0 Hz, 1H), 2.39 (s, 3H, MeN), 1.02 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.3 (*C*OPh), 173.2 (*C*OOEt), 135.2 (C), 133.0 (CH), 129.0 (2CH), 128.7 (2CH), 63.7 (3-C), 62.5 (CH_2), 61.8 (CH_2), 56.2 (CH_2), 41.9 (CH_3N), 33.8 (4-CH_2), 13.8 (CH_3). HRMS (ESI) calcd for $(C_{15}H_{20}NO_3)^+$ $[M+H]^+$: 262.1438, found: 262.1440.

4,7-Dimethyl-2-phenyl-2,3,7-triazaspiro[4.4]non-3-en-1-one (9e). Compound **9e** was synthesized according to the **general procedure** from 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one. Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/1; R_f (chloroform/ethanol, 100/2) = 0.25). Yellow oil, yield 102 mg (42%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.83 (dd, *J* = 8.7, 1.1 Hz, 2H, 2,6-HPh), 7.42 (app dd, *J* = 8.7, 7.3 Hz, 2H, 3,5-HPh), 7.18 (tt, *J* = 7.3, 1.1 Hz, 1H, 4-HPh), 3.01 (d, *J* = 10.0 Hz, 1H, 6-CH*H*), 2.94 (ddd, *J* = 8.4, 7.4, 3.8 Hz, 1H, 8-CH*H*), 2.5–2.4 (masked, 1H, 8-C*H*H), 2.45 (d, *J* = 10.0 Hz, 1H, 6-C*H*H), 2.32 (s, 3H, 7-MeN), 2.14 (s, 3H, 1-Me), 2.15–2.08 (m, 1H, 9-CH*H*), 2.04 (ddd, *J* = 13.1, 7.8, 3.8 Hz, 1H, 9-C*H*H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.5 (C=O), 164.6

(C=N), 138.0 (C), 128.9 (2CH), 124.5 (CH), 118.0 (2CH), 62.3 (2-CH_2), 58.5 (3-C), 55.8 (5-CH_2), 41.0 (CH_3N), 33.4 (4-CH_2), 13.8 (CH_3). HRMS (ESI) calcd for $(C_{14}H_{18}N_3O)^+$ $[M+H]^+$: 244.1445, found: 244.1448.

(1-Methyl-3-phenylpyrrolidin-3-yl)(phenyl)methanone (9f). Compound **9f** was synthesized according to the **general procedure** from 1,2-diphenylethan-1-one, except that a mixture of cold 1 M HCl (10 mL) and MeOH (2 mL) was used for the extraction of corresponding pyrrolidine from the reaction mixture instead of 1 M HCl (10 mL). Crude product was purified by column chromatography (eluent: chloroform/ethanol from 100/1 to 100/5; R_f (chloroform/ethanol, 100/2) = 0.1). Light yellow oil, yield 133 mg (50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 8.3, 1.1 Hz, 2H, Ph), 7.39 (t, *J* = 7.4 Hz, 1H, Ph), 7.34–7.29 (m, 4H, Ph), 7.26 (t, *J* = 7.8 Hz, 2H, Ph), 7.24–7.20 (m, 1H, Ph), 3.33 (d, *J* = 10.0 Hz, 1H, 2-CH*H*), 2.98 (d, *J* = 10.0 Hz, 1H, 2-C*H*H), 2.90 (ddd, *J* = 13.5, 7.7, 5.6 Hz, 1H, 4-CH*H*), 2.74 (td, *J* = 8.2, 5.6 Hz, 1H, 5-CH*H*), 2.65 (q, *J* = 7.7 Hz, 1H, 5-C*H*H), 2.36 (s, 3H, MeN), 2.32 (ddd, *J* = 13.5, 7.7, 6.5 Hz, 1H, 4-C*H*H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1 (C=O), 144.4 (C), 135.7 (C), 132.1 (CH), 130.2 (2CH), 129.2 (2CH), 128.2 (2CH), 126.8 (CH), 125.9 (2CH), 66.4 (2-CH_2), 62.4 (3-C), 56.6 (5-CH_2), 42.4 (CH_3N), 37.3 (4-CH_2); HRMS (ESI) calcd for $(C_{18}H_{20}NO)^+$ $[M+H]^+$: 266.1540, found: 266.1536.

1′-Methylspiro[chromane-3,3′-pyrrolidin]-4-one (9g). Compound **9g** was synthesized according to the **general procedure** using chroman-4-one. Crude product was purified by column chromatography (eluent: chloroform/ethanol from 100/1.5 to 100/4; R_f (chloroform/ethanol, 100/3) = 0.14). Light brown oil, yield 96 mg (44%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.9, 1.7 Hz, 1H, 5-HAr), 7.48 (ddd, *J* = 8.3, 7.5, 1.7 Hz, 1H, 7-HAr), 7.03 (t, *J* = 7.6 Hz, 1H, 6-HAr), 6.97 (d, *J* = 8.3 Hz, 1H, 8-HAr), 4.39 (d, *J* = 11.3 Hz, 1H, 2-CH*H*), 4.27 (d, *J* = 11.3 Hz, 1H, 2-C*H*H), 2.93–2.90 (m, 1H, 5′-CH*H*), 2.90 (d, *J* = 9.8 Hz, 1H, 2′-CH*H*), 2.59 (d, *J* = 9.8 Hz, 1H, 2′-C*H*H), 2.53 (q, *J* = 8.3 Hz, 1H, 5′-C*H*H), 2.39 (s, 3H, 1′-NMe), 2.34 (ddd, *J* = 12.9, 7.7, 3.6 Hz, 1H, 4′-CH*H*), 1.73 (dt, *J* = 12.9, 7.9 Hz, 1H, 4′-C*H*H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.8 (C=O), 161.5 (C-O), 136.0 (CH), 128.0 (CH), 121.6 (CH), 120.2 (C), 117.9 (CH), 73.9 (CH_2O), 60.7 (2′-CH_2), 56.2 (5′-CH_2), 52.5 (3-C), 41.8 (CH_3N), 31.0 (4′-CH_2). HRMS (ESI) calcd for $(C_{13}H_{16}NO_2)^+$ $[M+H]^+$: 218.1176, found: 218.1180.

Horsfiline (5-methoxy-1′-methylspiro[indoline-3,3′-pyrrolidin]-2-one) (9h). A 10 mL microwave reaction tube was charged with a stir bar, 5-methoxyindolin-2-one (1.0 mmol), 3′-methyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4a** (2.5 mmol, 663 mg), dry *o*-xylene (3 mL) and was filled with an argon atmosphere, before it was sealed with a cap. After pre-stirring for 3 min the mixture was heated in microwave reactor at 225 °C for 45 min with stirring. After cooling with a compressed air flow the resulting mixture was diluted with PhMe (5 mL). The precipitate was filtered off. The solution was extracted with cold 1 M HCl (10 mL) and aqueous

phase was washed with PhMe (2 × 5 mL). The aqueous layer was basified with $NaHCO_3$ to pH = 10, extracted with DCM (2 × 5 mL), dried over Na_2SO_4 and evaporated under reduced pressure. The residue was dissolved in MeOH (5 mL) and 11.5 M HCl (3 mmol, 0.26 mL) was added. Mixture was refluxed for 1.5 h, cooled to rt, basified with $NaHCO_3$ to pH = 10, extracted with DCM (2 × 5 mL), dried over Na_2SO_4 and evaporated under reduced pressure. Crude product was purified by column chromatography (eluent: dichloromethane/ethanol, 100/5; R_f (dichloromethane/methanol, 9/1) = 0.4) and then it was recrystallized from hexane with small amount of acetone. Beige powder, yield 132 mg (57%), mp 153–156 °C (in ref 10 mp 154–156 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.92–6.90 (m, 1H, 4-HAr), 6.8–6.7 (m, 2H, 7,6-HAr), 3.70 (s, 3H, OMe), 3.01 (td, J = 7.9, 4.1 Hz, 1H, 5′-CH*H*), 2.74 (d, J = 9.0 Hz, 1H, 2′-C*H*H), 2.57 (d, J = 9.0 Hz, 1H, 2′-C*H*H), 2.50–2.43 (m, 1H, 5′-C*H*H), 2.34 (s, 3H, 1′-NMe), 2.16 (ddd, J = 12.3, 7.9, 4.1 Hz, 1H, 4′-CH*H*), 1.90 (dt, J = 12.3, 7.9 Hz, 1H, 4′-C*H*H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 180.8 (C=O), 155.1 (C-O), 137.9 (C), 134.4 (C), 112.1 (CH), 110.0 (CH), 109.4 (CH), 66.0 (2′-CH_2), 56.1 (5′-CH_2), 55.4 (CH_3O), 53.5 (3-C), 41.5 (CH_3N), 37.3 (4′-CH_2). HRMS (ESI) calcd for $(C_{13}H_{17}N_2O_2)^+$ $[M+H]^+$: 233.1285, found: 233.1287.

1-Benzyl-1′-methylspiro[indoline-3,3′-pyrrolidin]-2-one (9i). Compound **9i** was synthesized according to the **general procedure** using 1-benzylindolin-2-one, except that a mixture of cold 1 M HCl (10 mL) and MeOH (2 mL) was used for the extraction of corresponding pyrrolidine from the reaction mixture instead of 1 M HCl (10 mL). Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/0.5; R_f (DCM/ethanol, 100/2) = 0.27). Viscous light yellow oil, yield 213 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.4 Hz, 1H, 4-HAr), 7.34–7.23 (m, 5H), 7.15 (t, J = 7.5 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H, 5-HAr), 6.70 (d, J = 7.7 Hz, 1H, 7-HAr), 4.91 (s, 2H, 1-NCH_2Ph), 3.22 (br s, 1H), 3.09 (br s, 1H), 2.94 (d, J = 9.6 Hz, 1H, 2′-C*H*H), 2.89 (q, J = 8.3 Hz, 1H, 5′-C*H*H), 2.56 (s, 3H, 1′-NMe), 2.43 (ddd, J = 12.7, 7.5, 3.7 Hz, 1H, 4′-CH*H*), 2.28–2.18 (m, 1H, 4′-C*H*H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 180.5 (C=O), 142.1 (C), 136.1 (C), 135.7 (C), 128.9 (2CH), 127.8 (CH), 127.7 (CH), 127.4 (2CH), 123.3 (CH), 123.1 (CH), 108.9 (CH), 66.4 (2′-CH_2), 56.8 (5′-CH_2), 53.4 (3-C), 43.9, 42.0, 38.2 (CH_2). HRMS (ESI) calcd for $(C_{19}H_{21}N_2O)^+$ $[M+H]^+$: 293.1649, found: 293.1653.

1,1′-Dimethylspiro[indoline-3,3′-pyrrolidin]-2-one (9j). Compound **9j** was synthesized according to the **general procedure** from 1-methylindolin-2-one. Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/1; R_f (chloroform/ethanol, 100/6) = 0.35). Viscous light yellow oil, yield 140 mg (65%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.36 (dd, J = 7.5, 0.6 Hz, 1H, 4-HAr), 7.27 (td, J = 7.6, 0.6 Hz, 1H, 6-HAr), 7.04 (t, J = 7.6 Hz, 1H, 5-HAr), 6.98 (d, J = 7.7 Hz, 1H, 7-HAr), 3.13 (s, 3H, 1-NMe), 3.03 (td, J = 8.1, 4.3 Hz, 1H, 5′-C*H*H), 2.72 (d, J = 9.0 Hz, 1H, 2′-C*H*H), 2.60 (d, J = 9.0 Hz, 1H, 2′-C*H*H), 2.52 (q, J = 8.1 Hz,

1H, 5′-C*H*H), 2.34 (s, 3H, 1′-NMe), 2.18 (ddd, *J* = 12.5, 8.1, 4.3 Hz, 1H, 4′-CH*H*), 1.91 (dt, *J* = 12.5, 7.6 Hz, 1H, 4′-C*H*H); ^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ 178.9 (C=O), 142.6 (C), 135.8 (C), 127.6 (CH), 122.6 (CH), 122.5 (CH), 108.1 (CH), 66.0 (2′-CH_2), 56.1 (5′-CH_2), 52.6 (3-C), 41.5 (1′-NCH_3), 37.3 (4′-CH_2), 26.1 (1-NCH_3). HRMS (ESI) calcd for $(C_{13}H_{17}N_2O)^+$ $[M+H]^+$: 217.1336, found: 217.1339.

1′-Benzyl-1-methylspiro[indoline-3,3′-pyrrolidin]-2-one (9k). Compound **9k** was synthesized according to the **general procedure** using 1-methylindolin-2-one (1.0 mmol, 147 mg) and *N*-benzyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4b** (2.5 mmol, 853 mg), except that a mixture of cold 1 M HCl (10 mL) and MeOH (2 mL) was used for the extraction of corresponding pyrrolidine from the reaction mixture instead of 1 M HCl (10 mL). Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/0.5; R_f (chloroform/ethanol, 100/2) = 0.28). Beige solid, yield 234 mg (80%), mp 92–93 °C. ^{1}H NMR (500 MHz, DMSO-*d*$_6$) δ 7.44 (dd, *J* = 7.4, 0.8 Hz, 1H, 4-HAr), 7.37 (d, *J* = 7.3 Hz, 2H, Ph), 7.32 (t, *J* = 7.5 Hz, 2H, Ph), 7.27 (td, *J* = 7.7, 0.8 Hz, 1H, 6-HAr), 7.24 (t, *J* = 7.6 Hz, 1H, Ph), 7.07 (t, *J* = 7.6 Hz, 1H, 5-HAr), 6.98 (d, *J* = 7.8 Hz, 1H, 7-HAr), 3.72 (d, *J* = 13.2 Hz, 1H, 1′-NCH*H*Ph), 3.69 (d, *J* = 13.2 Hz, 1H, 1′-NC*H*HPh), 3.12 (s, 3H, 1-NMe), 3.08 (td, *J* = 8.1, 4.2 Hz, 1H, 5′-CH*H*), 2.73 (d, *J* = 9.0 Hz, 1H, 2′-CH*H*), 2.65 (d, *J* = 9.0 Hz, 1H, 2′-C*H*H), 2.59 (q, *J* = 8.1 Hz, 1H, 5′-C*H*H), 2.20 (ddd, *J* = 12.7, 8.3, 4.2 Hz, 1H, 4′-CH*H*), 1.93 (dt, *J* = 12.7, 7.7 Hz, 1H, 4′-C*H*H); ^{13}C NMR (126 MHz, DMSO-*d*$_6$) δ 178.6 (C=O), 142.6 (C), 139.0 (C), 135.8 (C), 128.4 (2CH), 128.2 (2CH), 127.7 (CH), 126.9 (CH), 122.6 (CH), 122.5 (CH), 108.2 (CH), 63.7 (CH_2), 58.7 (CH_2), 53.6 (CH_2), 52.0 (3-C), 36.5 (4′-CH_2), 26.1 (1-NCH_3). HRMS (ESI) calcd for $(C_{19}H_{21}N_2O)^+$ $[M+H]^+$: 293.1649, found: 293.1639.

1′-Methyl-1-pentylspiro[indoline-3,3′-pyrrolidin]-2-one (9l). Compound **9l** was synthesized according to the **general procedure** using 1-pentylindolin-2-one. Crude product was purified by column chromatography (eluent: chloroform/ethanol, 100/2; R_f (chloroform/ethanol, 100/5) = 0.27). Viscous light yellow oil, yield 163 mg (60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62–7.55 (m, 1H, 4-HAr), 7.27 (td, *J* = 7.7, 1.0 Hz, 1H, 6-HAr), 7.09 (t, *J* = 7.5 Hz, 1H, 5-HAr), 6.83 (d, *J* = 7.8 Hz, 1H, 7-HAr), 3.71 (dt, *J* = 14.5, 7.4 Hz, 1H, 1-NCH*H*), 3.67 (dt, *J* = 14.5, 7.4 Hz, 1H, 1-NC*H*H), 3.34 (br s, 1H), 3.25 (br s, 1H), 3.00 (br s, 1H), 2.93 (d, *J* = 9.7 Hz, 1H, 5′-C*H*H), 2.63 (s, 3H, 1′-NMe), 2.35 (ddd, *J* = 12.7, 7.2, 3.2 Hz, 1H, 4′-C*H*H), 2.30 (br s, 1H), 1.68 (quint, *J* = 7.4 Hz, 2H, CH_2), 1.39–1.30 (m, 4H, 2CH_2), 0.90 (t, *J* = 7.0 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.2 (C=O), 142.4 (C), 136.2 (C), 127.7 (CH), 123.3 (CH), 122.7 (CH), 108.1 (CH), 66.5 (2′-CH_2), 56.9 (5′-CH_2), 53.4 (3-C), 42.0, 40.2, 38.1 (CH_2), 29.1 (CH_2), 27.2 (CH_2), 22.4 (CH_2), 14.1 (CH_3). HRMS (ESI) calcd for $(C_{17}H_{25}N_2O)^+$ $[M+H]^+$: 273.1961, found: 273.1964.

Diethyl 2-benzyl-2-((dimethylamino)methyl)malonate (12a). Compound **12a** was synthesized according to the **general procedure** using *N*-methyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4a** (1.0 mmol, 265 mg) and diethyl 2-benzylmalonate **11a** (1.5 mmol, 375 mg) without additional purification. Product decomposes on silica-gel (column chromatography eluent – chloroform) with the formation of starting compound probably by retro-Mannich reaction. Light yellow oil, yield 200 mg (65% based on starting oxazolidine **4a**). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.27 (t, J = 7.3 Hz, 2H, 3,5-HPh), 7.22 (t, J = 7.3 Hz, 1H, 4-HPh), 7.12 (d, J = 7.3 Hz, 2H, 2,6-HPh), 4.10 (app q, J = 7.1 Hz, 4H, $2CO_2CH_2CH_3$), 3.24 (s, 2H, $PhCH_2$), 2.60 (s, 2H, NCH_2), 2.16 (s, 6H, NMe_2), 1.16 (t, J = 7.1 Hz, 6H, $2CO_2CH_2CH_3$); ^{13}C NMR (126 MHz, DMSO-d_6) δ 170.1 (2C=O), 136.1 (C), 129.9 (2CH), 128.1 (2CH), 126.8 (CH), 61.0 ($2CH_2O$), 59.7 (CH_2N), 58.6 (C), 46.3 ($(CH_3)_2N$), 36.2 (CH_2Ph), 13.8 ($2CH_3$). HRMS (ESI) calcd for $(C_{17}H_{26}NO_4)^+$ $[M+H]^+$: 308.1857, found: 308.1856.

Diethyl 2-((dimethylamino)methyl)-2-ethylmalonate (12b). Compound **12b** was synthesized according to the **general procedure** using *N*-methyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4a** (1.0 mmol, 265 mg) and diethyl 2-ethylmalonate (1.5 mmol, 282 mg) without additional purification. Light yellow oil, yield 200 mg (82% based on starting oxazolidine **4a**). ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.10 (q, J = 7.1 Hz, 4H, $2CO_2CH_2CH_3$), 2.77 (s, 2H, NCH_2), 2.13 (s, 6H, NMe_2), 1.92 (q, J = 7.5 Hz, 2H, CH_2CH_3), 1.16 (t, J = 7.1 Hz, 6H, $2CO_2CH_2CH_3$), 0.75 (t, J = 7.5 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.4 (2C=O), 60.6 ($2CH_2O$), 59.4 (CH_2N), 58.1 (C), 46.9 ($(CH_3)_2N$), 23.8 (CH_2), 13.9 ($2CH_3$), 8.3 (CH_3). HRMS (ESI) calcd for $(C_{12}H_{24}NO_4)^+$ $[M+H]^+$: 246.1700, found: 246.1697.

Diethyl 2-((dimethylamino)methyl)-2-propylmalonate (12c). Compound **12c** was synthesized according to the **general procedure** using *N*-methyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4a** (1.0 mmol, 265 mg) and diethyl 2-propylmalonate (1.5 mmol, 303 mg) without additional purification. Light yellow oil, yield 153 mg (59% based on starting oxazolidine **4a**). ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.10 (q, J = 7.1 Hz, 4H, $2CO_2CH_2CH_3$), 2.77 (s, 2H, NCH_2), 2.13 (s, 6H, NMe_2), 1.87–1.82 (m, 2H, $CH_2CH_2CH_3$), 1.15 (t, J = 7.1 Hz, 6H, $2CO_2CH_2CH_3$), 1.13–1.07 (m, 2H, $CH_2CH_2CH_3$), 0.88 (t, J = 7.2 Hz, 3H, $CH_2CH_2CH_3$); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.5 (2C=O), 60.7 ($2CH_2O$), 60.0 (CH_2N), 57.7 (C), 46.9 ($(CH_3)_2N$), 33.1 (CH_2), 16.9 (CH_2), 14.3 (CH_3), 13.8 ($2CH_3$). HRMS (ESI) calcd for $(C_{13}H_{26}NO_4)^+$ $[M+H]^+$: 260.1857, found: 260.1857.

3-(Dimethylamino)-2,2-diphenylpropanenitrile (12d). Compound **12d** was synthesized according to the **general procedure** using *N*-methyl-10*H*-spiro[anthracene-9,5′-oxazolidin]-10-one **4a** (1.0 mmol, 265 mg) and 2,2-diphenylacetonitrile (1.5 mmol, 289 mg) without additional purification. Brown viscous oil, yield 210 mg (84% based on starting oxazolidine **4a**), it was

previously known in ref 11. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.45–7.37 (m, 8H, Ph), 7.35–7.30 (m, 2H, Ph), 3.40 (s, 2H, NCH_2), 2.16 (s, 6H, NMe_2); ^{13}C NMR (101 MHz, DMSO-d_6) δ 139.4 (2C), 128.8 (4CH), 127.8 (2CH), 126.9 (4CH), 122.5 (C≡N), 66.0 (CH_2N), 52.7 (C), 46.8 ($(CH_3)_2N$). HRMS (ESI) calcd for $(C_{17}H_{19}N_2)^+$ $[M+H]^+$: 251.1543, found: 251.1540.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
NMR Spectra (PDF).

AUTHOR INFORMATION

Corresponding Author

*E-mail: mvslc@mail.ru

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

This work was financially supported by the Russian Science Foundation (Grant 17-73-20070). We also thank Sergey Usachev for his remarks.

REFERENCES

(1) (a) Tsuge, O.; Kanemasa, S. *Adv. Heterocycl. Chem.* **1989**, *45*, 231. (b) Harwood, L. M.; Vickers, R. J. *In Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products; Chemistry of Heterocyclic Compounds,* Vol. 59; Padwa, A., Pearson, W. H., Eds.; Wiley: Chichester, 2002; p 169. (c) Nájera, C.; Sansano, J. M. *Curr. Org. Chem.* **2003**, *7*, 1105. (d) Coldham, I.; Hufton, R. *Chem. Rev.* **2005**, *105*, 2765. (e) Pandey, G.; Banerjee, P.; Gadre, S. R. *Chem. Rev.* **2006**, *106*, 4484. (f) Mirzayans, P. M.; Krenske, E. H.; Williams, C. M. *Aust. J. Chem.* **2014**, *67*, 1309. (g) Meyer, A. G.; Ryan, J. H. *Molecules* **2016**, *21*, 935.

(2) (a) Rizzi, G. P. *J. Org. Chem.* **1970**, *35*, 2069. (b) Nyerges, M.; Fejes, I.; Virányi, A.; Groundwater, P. W.; Töke, L. *Synthesis* **2001**, 1479. (c) Moshkin, V. S.; Sosnovskikh, V. Y. *Tetrahedron Lett.* **2013**, *54*, 2455. (d) Moshkin, V. S.; Sosnovskikh, V. Y. *Tetrahedron Lett.* **2013**, *54*, 2699. (e) Moshkin, V. S.; Sosnovskikh, V. Y. *Tetrahedron Lett.* **2013**, *54*, 5869. (f) Moshkin, V. S.; Sosnovskikh, V. Y. *Tetrahedron Lett.* **2014**, *55*, 6121.

(3) (a) Pinho e Melo, T. M. V. D. *Eur. J. Org. Chem.* **2006**, 2873. (b) Nyerges, M.; Tóth, J.; Groundwater, P. W. *Synlett* **2008**, 1269. (c) Anaç, O.; Güngör, F. Ş. *Tetrahedron* **2010**, *66*, 5931. (d) Deb, I.; Seidel, D. *Tetrahedron Lett.* **2010**, *51*, 2945.

(4) (a) Zhang, C.; De, C. K.; Mal, R.; Seidel, D. *J. Am. Chem. Soc.* **2008**, *130*, 416. (b) Zheng, L.; Yang, F.; Dang, Q.; Bai, X. *Org. Lett.* **2008**, *10*, 889. (c) Bi, H.-P.; Zhao, L.; Liang, Y.-M.; Li, C.-J. *Angew. Chem., Int. Ed.* **2009**, *48*, 792. (d) Yang, D.; Zhao, D.; Mao, L.; Wang, L.; Wang, R. *J. Org. Chem.* **2011**, *76*, 6426. (e) Chen, W.; Wilde, R. G.; Seidel, D. *Org. Lett.* **2014**, *16*, 730. (f) Seidel, D. *Acc. Chem. Res.* **2015**, *48*, 317, and references cited therein. (g) Zhu, Z.; Seidel, D. *Org. Lett.* **2017**, *19*, 2841.

(5) (a) Rudas, M.; Fejes, I.; Nyerges, M.; Szöllõsy, Á.; Tõke, L.; Groundwater, P. W. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1167. (b) Ryan, J. H.; Spiccia, N.; Wong, L. S.-M.; Holmes, A. B. *Aust. J. Chem.* **2007**, *60*, 898.

(6) (a) Grigg, R.; Idle, J.; McMeekin, P.; Vipond, D. *J. Chem. Soc., Chem. Commun.* **1987**, 49. (b) Tsuge, O.; Kanemasa, S.; Ohe, M.; Takenaka, S. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4079. (c) Grigg, R.; Idle, J.; McMeekin, P.; Surendrakumar, S.; Vipond, D. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2703. (d) Orsini, F.; Pelizzoni, F.; Forte, M.; Destro, R.; Gariboldi, P. *Tetrahedron* **1988**, *44*, 519. (e) Častulík, J; Marek, J.; Mazal, C. *Tetrahedron* **2001**, *57*, 8339.

(7) (a) Vedejs, E.; Martinez, G. R. *J. Am. Chem. Soc.* **1979**, *101*, 6452. (b) Terao, Y.; Kotaki, H.; Imai, N.; Achiwa, K. *Chem. Pharm. Bull.* **1985**, *33*, 896. (c) Vedejs, E.; West, F. G. *Chem. Rev.* **1986**, *86*, 941. (d) Tsuge, O.; Kanemasa, S.; Hatada, A.; Matsuda, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2537. (e) Padwa, A.; Dent, W. *J. Org. Chem.* **1987**, *52*, 235. (f) D'Souza, A. M.; Spiccia, N.; Basutto, J.; Jokisz, P.; Wong, L. S.-M.; Meyer, A. G.; Holmes, A. B.; White, J. M.; Ryan, J. H. *Org. Lett.* **2011**, *13*, 486. (g) Buev, E. M.; Moshkin, V. S.; Sosnovskikh, V. Y. *Tetrahedron Lett.* **2015**, *56*, 6590. (h) Chen, S.; Bacauanu, V.; Knecht, T.; Mercado, B. Q.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2016**, *138*, 12664.

(8) (a) Buev, E. M.; Moshkin, V. S.; Sosnovskikh, V. Y. *Org. Lett.* **2016**, *18*, 1764. (b) Buev, E. M.; Moshkin, V. S.; Sosnovskikh, V. Y. *Tetrahedron Lett.* **2016**, *57*, 3731.

(9) (a) Jossang, A.; Jossang, P.; Hadi, H. A.; Sévent, T.; Bodo, B. *J. Org. Chem.* **1991**, *56*, 6527. (b) Pellegrini, C.; Strässler, C.; Weber, M.; Borschberg, H.-J. *Tetrahedron: Asymmetry* **1994**, *5*, 1979. (c) Hsieh, J.-C.; Cheng, A.-Y.; Fu, J.-H.; Kang, T.-W. *Org. Biomol. Chem.* **2012**, *10*, 6404. (d) Le Goff, R.; Lawson, A. M.; Daïch, A.; Comesse, S. *Org. Biomol. Chem.* **2013**, *11*, 1818. (e) Palmisano, G.; Annunziata, R.; Papeo, G.; Sisti, M. *Tetrahedron: Asymmetry* **1996**, *7*, 1.

(10) Lizos, D. E.; Murphy, J. A. *Org. Biomol. Chem.* **2003**, *1*, 117.

(11) Zaugg, H. E.; Horrom, B. W.; Vernsten, M. R. *J. Am. Chem. Soc.* **1953**, *75*, 288.