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2-Diazoacetyl-2*H*-azirines: Source of a Variety of 2*H*-Azirine Building Blocks with Orthogonal and Domino Reactivity

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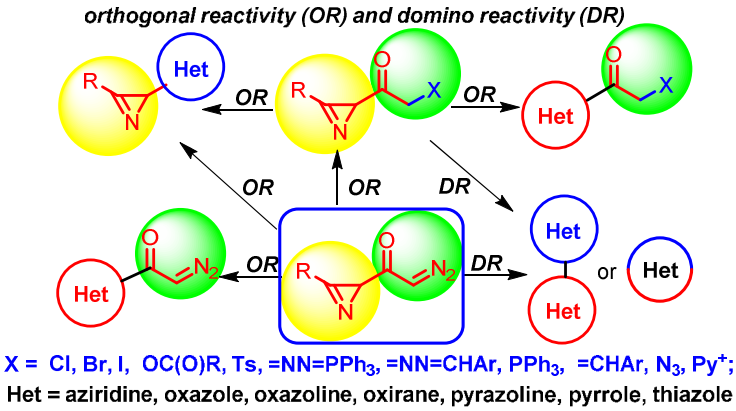


ABSTRACT: A synthesis of 2-diazoacetyl-2*H*-azirines was developed starting from 2*H*-azirine-2-carbonyl chlorides, generated by Fe(II)-catalyzed isomerization of 5-chloroisoxazoles. 2-Diazoacetyl-2*H*-azirines easily undergo reactions characteristic of α-diazo ketones with preservation of the azirine ring. Reactions with hydrohalogenic, carboxylic and *p*-toluenesulfonic acids provide novel 2-halo- and 2-(R-oxy)-1-(3-phenyl-2*H*-azirin-2-yl)ethan-1-ones in good yields. The synthesized 2*H*-azirines can offer many possibilities for chemical manipulation in heterocyclic synthesis, due to the presence of highly reactive azirine and the exocyclic –C(O)-CHN_2 or –C(O)-CH_2X functionalities, which can show orthogonal or domino reactivity. The synthetic usefulness of the developed building blocks was demonstrated by the preparation of new types of heterocyclic dyads (azirine-oxazole, azirine-pyrazoline, azirine-thiazole, azirine-oxirane, pyrrole-oxazole) as well as an azirine chalcone analogue, 2-azidoacetyl-2*H*-azirine and 2-diazoacetylaziridine derivatives.

INTRODUCTION

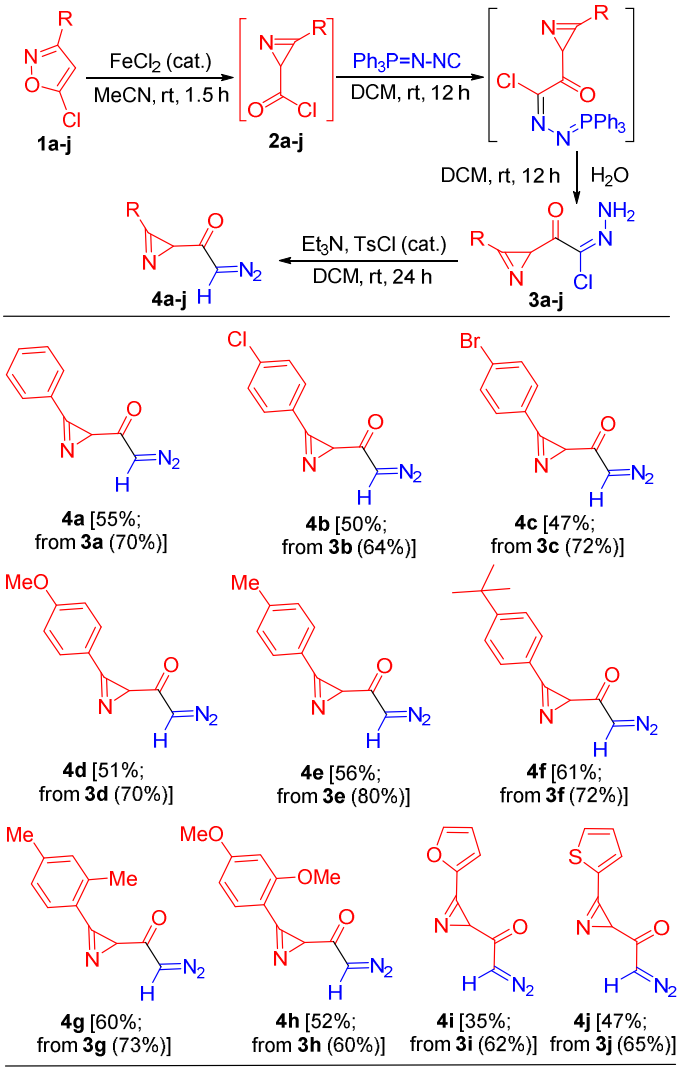
The presence in the molecule of highly reactive polynitrogen functionality such as diazo, diazonium or azide groups, or a strained ring, such as azirine, aziridine or oxirane, is the prerequisite for the implementation of synthetically useful selective reactions under mild conditions. A combination of two such highly reactive structural units in one molecule creates potentially additional opportunities for heterocyclic synthesis, especially if the structural fragments are capable of reacting both separately and jointly, demonstrating either orthogonal[1] or domino[2] reactivity. A good example of such an assemble, consisting of a strained small ring and a polynitrogen functional group, is 2-diazoacetyloxiranes,[3] which have been successfully used for the synthesis of acyclic[3a, c, d, g, h] and heterocyclic[3a, b, e, f, h, i] compounds by reactions using one of the reactive constituent elements or both in different sequences. 2*H*-Azirines are widely used as valuable starting materials for the synthesis of various nitrogen-containing heterocycles and acyclic compounds due to the high azirine ring strain, which enhances the reactivity of the C=N double bond and facilitates ring cleavage.[4] Functionalized azirines are of special interest since they permit the introduction of synthetically useful substituents into the target heterocycles.[4] The diazoacetyl function is one of the most beneficial functional groups in organic synthesis due to its very broad reactivity.[5] In particular this functionality can be transformed under mild conditions to various heterocycles, such as derivatives of pyrazole, oxazole, thiazole and pyrrole.[5] A combination of azirine and diazoacetyl moieties in one molecule can therefore provide transferring of azirine or diazo group to target molecules and the construction of various heterocyclic dyads. Diazo compounds have served as chemical probes for biological phenomena and used for modifications of proteins and nucleic acids.[6] On the other hand, azirines were recently used for the preparation of a fluorochrome,[7] which is a perspective tool for dsDNA detection in cells and tissues through high-resolution microscopy.[8] This means that azirines containing a diazo function can potentially be used for the preparation of fluorophores with a diazo moiety to enable the covalent binding to biological macromolecules.[6] All this prompted us to attempt the synthesis of 2-

diazoacetyl-2*H*-azirines, based on our recently found approach to the in situ generation of 2*H*-azirine-2-carbonyl chlorides by Fe(II)-catalyzed isomerization of 5-chloroisoxazoles.[9] In order to demonstrate the orthogonal and domino reactivity of the azirine ring and diazo group of these unique compounds, reactions which are characteristic of both the azirine and diazoacetyl constituent elements, as well as combinations of some of these reactions were studied.

RESULTS AND DISCUSSION

Since iron salts and complexes decompose diazomethane[10] for the development of one-pot approach to 2-diazoacetyl-2*H*-azirines we turned to a diazomethane-free method for the preparation of diazo ketones.[11] It involves the reaction of acid chlorides with *N*-isocyanotriphenyliminophosphorane, followed by treatment of the formed hydrazidoyl chloride with triethylamine in the presence of *p*-toluenesulfonyl chloride as catalyst. After optimization of the reaction time and temperature this two-step method, together with the generation of 2*H*-azirinecarbonyl chlorides by Fe(II)-catalyzed isomerization of 5-chloroisoxazoles, was used to prepare a series of 2-diazoacetyl-2*H*-azirines **4** bearing various aryl and hetaryl substituents at the C3 position of the cycle (Table 1). α-Ketohydrazidoyl chlorides **3a-j** were synthesized in good yields from the corresponding 5-chloroisoxazoles **1a-j** by the developed procedure. The second step yields were lower, probably because of the instability of both hydrazidoyl chlorides **3a-j** and the products **4a-j** under the reaction conditions. The method tolerates aryl groups with halogen, alkyl, methoxy substituents, including *ortho*-substition, as well as some hetaryl groups in the azirine moiety (Table 1). All the new compounds were characterized by ^{1}H, ^{13}C NMR and HRMS methods. The structure of **4a** was additionally confirmed by XRD-analysis (See Supporting information).[12] The obtained diazo ketones **4a-j** are air-stable at room temperature, non-hygroscopic yellowish solids, possessing good solubility in dichloromethane, methanol, dimethyl sulfoxide, acetonitrile and poor solubility in water.

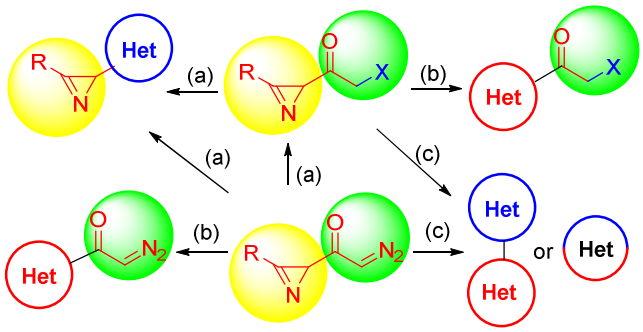
Table 1. Preparation of 1-(2*H*-Azirin-2-yl)-2-diazoethanones 4[a]



[a] Isolated yield; yield of **3** in parentheses

Our second goal was to demonstrate briefly the possibility of performing reactions of the synthesized 2-diazoacetyl-2*H*-azirines and their derivatives in different modes: (a) modification of the diazocarbonyl functionality with preservation of the azirine ring; (b) modification of the azirine ring with preservation of the exocyclic –C(O)-CHN_2/–C(O)-CH_2-X functionalities; (c) modification of both the azirine ring and exocyclic –C(O)-CHN_2/–C(O)-CH_2-X functionalities in a domino fashion (Scheme 1).

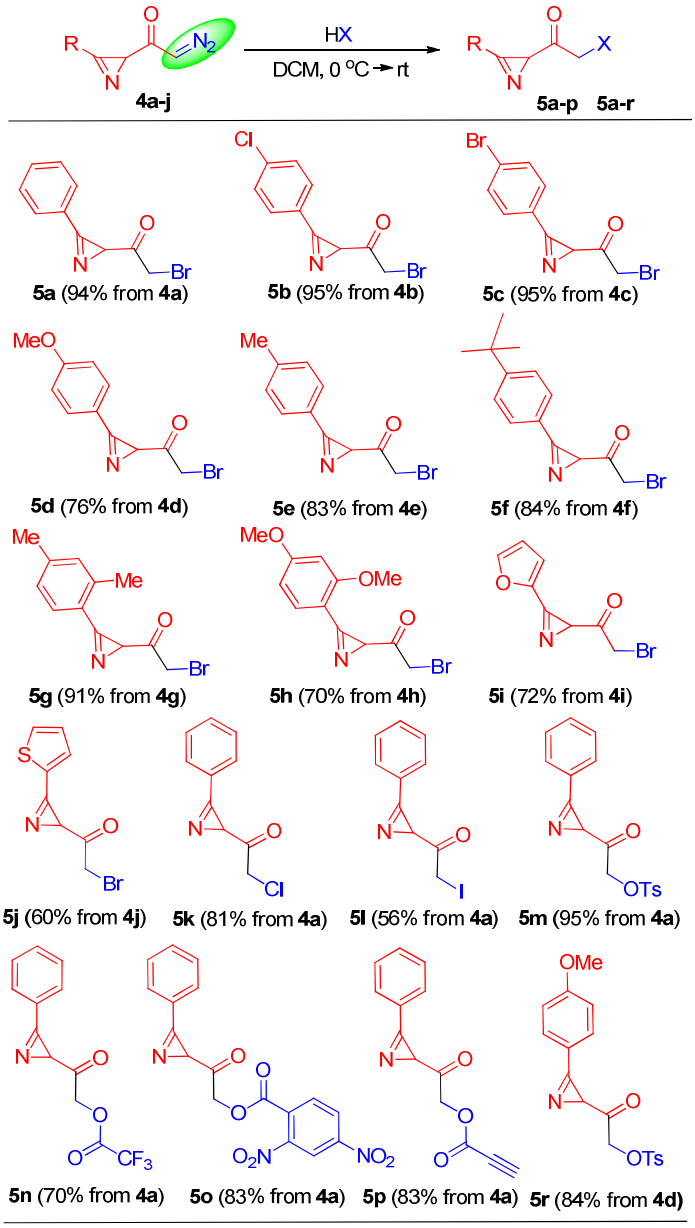
Scheme 1. Orthogonal and Domino Reactivity of Azirines with –C(O)-CHN$_2$/–C(O)-CH$_2$-X Functionalities



Firstly, using compound **4** we attempted to perform the most characteristic reactions of diazo ketones with preservation of the azirine ring. The most useful reactions of diazo ketones are (a) the Wolff rearrangement[5, 13]; (b) metal catalysed cyclopropanation of unsaturated compounds and insertion into C-H bonds;[5, 14] (c) reaction with acids, which is a very useful method for the site-selective introduction of halogen and other heteroatomic functional groups into carbonyl compounds;[5b, 15] (d) reactions leading to heterocycles either via successive formation of carbene/carbenoid, ylide and its 1,3-cyclization on a carbonyl group, or 1,3-dipolar cycloaddition of a diazo group to an activated C=C double bond;[5, 14] (e) reaction of diazo ketones with triphenylphosphane leading to azirinylphosphazines, which can be used as a method of storage of unstable diazo compounds or for their purification since the starting diazo compound can be liberated from phosphazine by reaction with methyl iodide.[5, 16, 17] Unexpectedly we failed to obtain a product typical for the diazo ketones Wolff rearrangement.[13] Only tarring of the reaction mixture was observed when compound **4a** was refluxed in methanol in the presence of Ag_2O or heated in α,α,α-trifluorotoluene in the presence of benzylamine. On the other hand, another reaction of diazo ketones, the reaction with acids was very successful. Reaction of diazo compounds **4a-j** with hydrobromic acid at rt gave the 2-bromoacetyl-2*H*-azirines **5a-j** in good to excellent yields (Table 2). The reactions with other acids were tested using diazo ketone **4a** as starting material. The 2-chloro/iodoacetyl-2*H*-azirines **5k**,**l** were obtained from **4a** by reaction with hydrochloric and hydroiodic acids (Table 2). TsOH, TFA, 2,4-

dinitrobenzoic and propiolic acids reacted with **4a** affording a new type of substituted azirine, 2-(R-oxy)acetyl-2*H*-azirines **5m-p**, in good yields (Table 2). The reactions with strong acids (hydrohalogenic acids, TsOH, TFA) proceeded fast (~2 h), whereas the reaction of the weaker acid, propiolic (pKa 1.94), took a week, and still weaker, salicylic acid (pKa 2.97) did not react at all under the same reaction conditions.

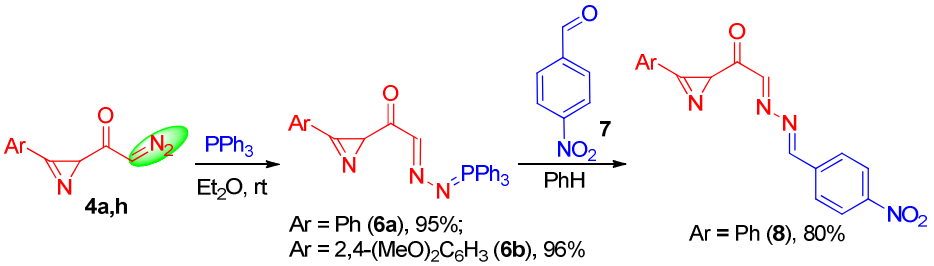
Table 2. The Reactions of Diazo Ketone 4a-j with Acids[a]



[a] Isolated yield.

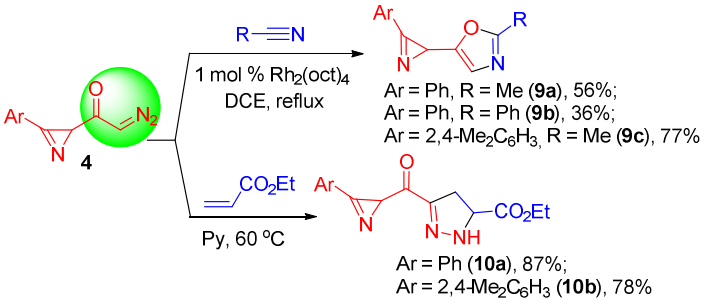
Reaction of diazo ketones **4a, h** with triphenylphosphane gave azirinylphosphazines **6a**, **b** in quantitative yield (Scheme 2). The transformation of 1-(2*H*-azirin-2-yl)-2-diazoethanones into azirinylphosphazines can be used as a method of storage of unstable diazo compounds since the starting diazo compound can be liberated from the corresponding phosphazine by reaction with methyl iodide.[17] In particular, this reaction sequence, phosphazine formation-liberation of starting diazoketone, was used in this work for the purification of compound **4h** (see the experimental section**)**. Azirinylphosphazine **6a** easily reacts with aldehyde **7** to give aza-Wittig reaction product **8** with the retention of the azirine ring.

Scheme 2. Synthesis of Azirinylphosphazine 6 and It's Aza-Wittig Reaction



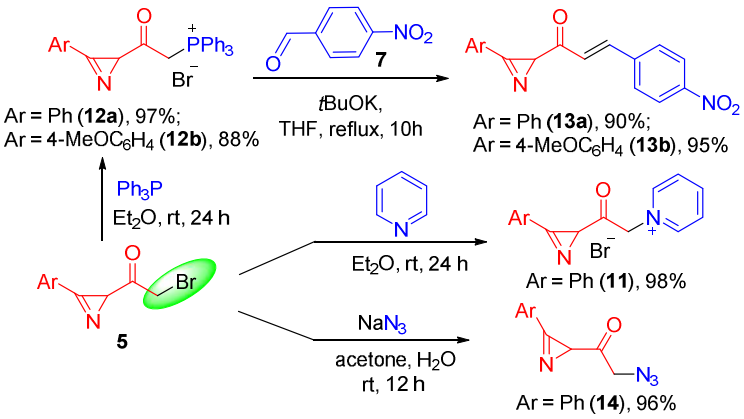
α-Diazo ketones are useful starting materials not only for selective preparation of highly sought α-functionalized ketones but also for the preparation of some hetero- and carbo-cycles, via the intermediate formation of the corresponding carbenoids under metal catalysis.[5, 14] We failed, however, to perform cyclopropanation of styrene with **4a** or C-H insertion reactions under Rh(II)-catalysis, probably due to the high reactivity of Rh-carbenoinds toward azirines,[4] leading to oligomerization. But reactions of Rh-carbenoinds derived from azirines **4a, g** with a large excess of nitrile were successful. After some optimization of the reaction conditions (see Supporting Information), the novel type of azirine-oxazole heterocyclic dyad **9a**, **b**, **c** was prepared in moderate to good yields (Scheme 3). Diazo functionality of azirines **4a, g** easily reacts as a dipole with an activated dipolarophile, ethyl acrylate, to give the 1,3-dipolar cycloaddition products, pyrazolines **10a**, **b** (*dr* ~1:1), in good yield (Scheme 3).

Scheme 3. Cycloaddition Reactions Based on 2-Diazoacetyl-2*H*-azirine 4



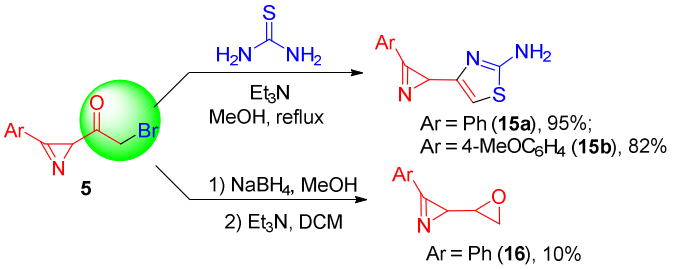
Further, the synthetic usefulness of azirine derivatives **5** containing good leaving groups was tested. It was found that pyridine reacts with bromide **5a** selectively to give pyridinium salt **11** in practically quantitative yield (Scheme 4). Analogously, compounds **5a**, **d** furnish phosphonium salts **12a**, **b** when treated with triphenylphosphane. Salt **12** could serve as a good precursor of various α,β-unsaturated azirinyl ketones. Thus, the reaction of the phosphonium ylides, generated from salts **12a**, **b**, with aldehyde **7** gave the azirine chalcone analogue, ketones **13a**, **b,** in high yield. In addition, α-bromoketones **5** are good precursors for the synthesis of α-azidoketones that possess considerable synthetic value,[18] and in particular can be potentially used to introduce an azirine ring into the various structures via azide-alkyne cycloaddition. It was found that 2-bromoacetyl-2*H*-azirine **5a** can be easily transformed into α-azidoketone **14** almost quantitatively by reaction with sodium azide in aq acetone (Scheme 4).

Scheme 4. Nucleophilic Substitution of Bromine in 2-Bromoacetyl-2*H*-azirine 5 with Preservation of the Azirine Ring



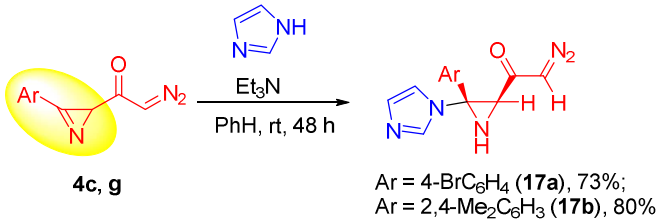
Halides **5** can be used, just like diazo compounds **4**, as building blocks in the synthesis of new types of heterocyclic dyads containing an azirine ring. For example, reaction of azirines **5a**, **d** with thiourea gives azirinylthiazoles **15a**, **b** in high yield. The reduction of the carbonyl group of **5a** with $NaBH_4$, followed by intramolecular substitution of b romine in the intermediate alcohol provides oxiranylazirine **16** (*dr* ~1:2) (Scheme 5). The low yield of oxirane **16** is probably mainly due to the instability of 2-bromo-1-(3-phenyl-2*H*-azirin-2-yl)ethan-1-ol under the reaction conditions.

Scheme 5. Synthesis of New Types of Heterocyclic Dyads 15, 16 Containing the Azirine Moiety



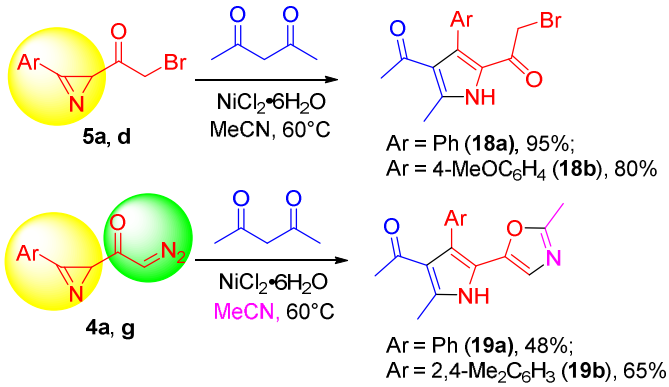
An example of the modification of the azirine ring of 2-diazoacetyl-2*H*-azirines with preservation of the exocyclic diazoacetyl function is the reaction of azirines **4c**, **g** with imidazole (Scheme 6). The addition of imidazole proceeded stereoselectively on the less hindered face of the azirine **4** to give the first representatives of 2-diazoacetylaziridine, aziridines **17a**, **b** in good yield. Addition of imidazole was previously only known to occur at the more electrophilic C=N double bond of 3-alkoxycarbonylazirines[19a] and at the less crowded C=N double bond of 3-methyl-2*H*-azirine-2-phosphonates and -phosphine oxides.[19b]

Scheme 6. The Reaction of Imidazole and Diazo Ketone 4c, g with Preservation of Diazoacetyl Function



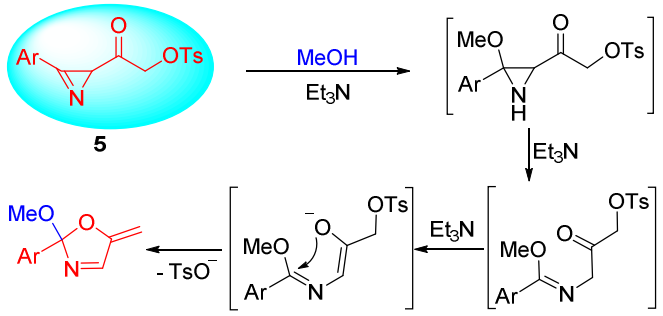
One of the useful transformations of azirines is the metal-catalyzed reaction with 1,3-dicarbonyl compounds providing pyrroles.[4, 9, 20] The possibility of a selective transformation of the three-membered ring in compounds **5** into the pyrrole system with the retention of the 2-bromoacetyl substituent is demonstrated by the synthesis of bromoacetylpyrrole **18**. The reaction of **5a**, **d** with acetylacetone under $NiCl_2 \cdot 6H_2O$ catalysis afforded pyrroles **18a**, **b** in good yield, with the $BrCH_2C(O)$ functionality ready for further transformations into different heterocycles (Scheme 7). Reaction of diazoacetylazirines **4a**, **g** under the same conditions is an example of domino modification of both the azirine ring and exocyclic –C(O)-CHN_2 functionality (Scheme 7). The pyrrole-oxazole dyads **19a**, **b** are formed probably via Ni-catalyzed formation of oxazoles **9** by reaction of acetonitrile with the diazoacetyl moiety of **4** (see Scheme 3), followed by Ni-catalyzed condensation of the azirine ring with acetylacetone or vice versa.

Scheme 7. Ni-Catalyzed Synthesis of Functionalized Pyrroles 18 and 19 from Azirines 4 and 5



Some new transformations were identified from the newly developed azirine scaffolds. When compounds **5m** or **5r** were treated with Et_3N in refluxing methanol methyleneoxazolines **20a**, **b** were isolated. Obviously oxazolines **20a**, **b** are the products of cascade reaction involving an azirine ring opening (Scheme 8).

Scheme 8. Reactions of Compounds 5m and 5r with Methanol/Et_3N



Ar = Ph (**20a**), 69%;
Ar = 4-$MeOC_6H_4$ (**20b**), 30%

In conclusion, 2-diazoacetyl-2*H*-azirines **4** were synthesized by reaction of 2*H*-azirine-2-carbonyl chlorides **2**, generated by Fe(II)-catalyzed isomerization of 5-chloroisoxazoles **1**, with *N*-isocyanotriphenyliminophosphorane followed by treatment of the formed hydrazidoyl chloride with Et_3N in the presence of TsCl-catalyst. It was found that 2-diazoacetyl-2*H*-azirines easily undergo reactions typical for α-diazo ketones with preservation of the azirine ring. In particular, reactions of **4** with hydrohalogenic, carboxylic and *p*-toluenesulfonic acids provide the corresponding 2-halo- and 2-(R-oxy)-1-(3-phenyl-2*H*-azirin-2-yl)ethan-1-ones **5** in good yields. On the other hand we failed to obtain a product typical for the diazo ketone Wolff rearrangement and cyclopropanation or C-H insertion reactions under Rh(II)-catalysis, probably due to the high reactivity of Rh-carbenoinds towards azirines. 2*H*-Azirines **4** and **5** could be used as powerful building blocks for diversity-oriented synthesis, since the highly reactive azirine moiety and the exocyclic –C(O)-CHN_2 or –C(O)-CH_2X groups permits a variety of diversity generating reactions in orthogonal and domino fashion. This was exemplified by the preparation of new types of heterocyclic dyads (azirine-oxazole, azirine-pyrazoline, azirine-thiazole, azirine-oxirane, pyrrole-oxazole), an azirine chalcone analogue, 2-azidoacetyl-2*H*-azirine and 2-diazoacetylaziridine derivatives.

EXPERIMENTAL SECTION

General Information and Methods

Melting points were determined on a melting point apparatus. ^{1}H (400 MHz), ^{31}P (162 MHz), and ^{13}C (100 MHz) NMR spectra were recorded on a NMR spectrometer in $CDCl_3$ or DMSO-d_6. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane (TMS δ = 0.00). ^{1}H NMR spectra were calibrated according to the residual peak of $CDCl_3$ (7.28 ppm) or DMSO-d_6 (2.51 ppm). For all new compounds, ^{13}C {^{1}H} and ^{13}C DEPT-135 spectra were recorded and calibrated according to the peak of $CDCl_3$ (77.00 ppm) or DMSO-d_6 (40.00 ppm). Electrospray ionization (ESI) mass spectra were recorded on a mass spectrometer, HRMS-ESI-QTOF, electrospray ionization, positive mode. Single crystal X-ray data were collected by means of diffractometer at 100 K using monochromated Cu Kα radiation. Crystallographic data for the structure **4a** (CCDC 1829758) have been deposited with the Cambridge Crystallographic Data Centre. Thin-layer chromatography (TLC) was conducted on aluminum sheets with 0.2 mm silica gel with fluorescent indicator. All solvents were distilled and dried prior to use. Acetonitrile distilled from P_2O_5, then distilled from anhydrous K_2CO_3 and stored over anhydrous K_2CO_3. Dichloromethane was distilled from CaH_2. Methanol was refluxed for 2 h with magnesium turnings and then distilled. 1,2-Dichloroethane was washed with concentrated H_2SO_4, water, then distilled from P_2O_5 and stored over anhydrous K_2CO_3. Tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone. Chloroisoxazoles **1a–j** were prepared by the reported procedure.[2f]

*3-(4-(tert-Butyl)phenyl)-5-chloroisoxazole (**1f**)*. A light brown oil, yield 4.2 g (59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 9H), 6.49 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.72 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 34.9, 99.5, 125.3, 126.0, 126.4, 154.0, 154.9, 164.1. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{13}H_{14}ClNONa^+$, 258.0656; found, 258.0647.

*5-Chloro-3-(2,4-dimethoxyphenyl)isoxazole (**1h**)*. A light yellow solid, mp 81–83 °C (hexane), yield 5.6 g (59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 3H), 3.90 (s, 3H), 6.56 (d, *J* = 2.2 Hz, 1H), 6.60 (dd, *J* = 8.6 and 2.2 Hz, 1H), 6.67 (s, 1H), 7.83 (d, *J* = 8.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 55.5, 98.8, 102.6, 105.3, 110.0, 129.8, 153.4, 158.5, 161.6, 162.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_{10}ClNO_3Na^+$, 262.0241; found, 262.0250.

*5-Chloro-3-(furan-2-yl)isoxazole (**1i**)*. A light yellow solid, mp 38–39 °C (hexane), yield 1.2 g (45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (s, 1H), 6.55 (dd, *J* = 3.4 and 1.8 Hz, 1H), 6.94 (dd, *J* = 3.5 and 0.4 Hz, 1H), 7.58 (dd, *J* = 1.7 and 0.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.1, 110.9, 111.8, 143.2, 144.4, 155.0, 156.5. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_7H_5ClNO_2^+$, 170.0003; found, 170.0006.

*5-Chloro-3-(thiophen-2-yl)isoxazole (**1j**)*. A light yellow solid, mp 36–37 °C (hexane), yield 1.4 g (30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (s, 1H), 7.14 (dd, *J* = 4.9 and 3.8 Hz, 1H), 7.46-7.48 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 99.6, 127.7, 128.0, 128.3, 129.7, 155.1, 159.4. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_7H_5ClNOS^+$, 185.9775; found, 185.9768.

General Procedure A for the Synthesis of 2-(3-Aryl-2*H*-azirin-2-yl)-2-oxoacetohydrazonoyl chlorides 3. Anhydrous $FeCl_2$ (0.2 equiv, 140 mg) was added to a solution of 5-chloroisoxazole **1** (5.6 mmol) in dry acetonitrile (50 mL) under Ar atmosphere. The mixture was stirred at rt for 1.5 h, the solvent was evaporated and dry diethyl ether (50 mL) was added to the residue. The resulting mixture was filtered through celite and the solvent was evaporated. The residue was dissolve in dry CH_2Cl_2 (100 mL) and *N*-isocyanotriphenyliminophosphorane (1.69 g, 5.6 mmol) was added. The solution was stirred at rt for 12 h, then water (3.5 mL) was added and the resulting mixture was stirred at rt for 12 h. The organic layer was separated and dried over $NaSO_4$. After filtration and concentration in vacuum the crude product, containing besides **3** Ph_3PO and a small amount of 2-diazo-1-(3-aryl-2*H*-azirin-2-yl)ethan-1-one **4**, can be used in the next step of the preparation of **4** without any purification, that does

not reduce yield of the reaction. Flash column chromatography on silica gel (EtOAc/hexane/$CHCl_3$, 1:2:3) can be used for the purification of **3**.

*2-Oxo-2-(3-phenyl-2H-azirin-2-yl)acetohydrazonoyl chloride (**3a**)*. A light brown oil, yield 864 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.98 (s, 1H), 7.01 (s, 2H), 7.53-7.57 (m, 2H), 7.60-7.64 (m, 1H), 7.84-7.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.9, 122.1, 127.2, 129.2, 130.5, 133.8, 157.2, 187.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_8ClN_3ONa^+$, 244.0248; found, 244.0251.

*2-(3-(4-Chlorophenyl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3b**)*. A colorless solid, mp 128–130 °C (Et_2O/hexane), 770 mg (64%) yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.94 (s, 1H), 7.72-7.74 (m, 2H), 7.92-7.94 (m, 2H), 8.96 (br.s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 33.0, 121.5, 123.4, 130.3, 132.3, 139.3, 157.5, 187.0. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_7Cl_2N_3ONa^+$, 277.9858; found, 277.9869.

*2-(3-(4-Bromophenyl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3c**)*. A colorless solid, mp 115–117 °C (Et_2O/hexane), yield 841 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 1H), 6.88 (s, 2H), 7.73 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.0, 121.2, 127.7, 128.9, 131.7, 132.7, 156.9, 187.3. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{10}H_8{}^{79}BrClN_3O^+$, 299.9534; found, 299.9525.

*2-(3-(4-Methoxyphenyl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3d**)*. A colorless solid, mp 146–147 °C (Et_2O/hexane), yield 841 mg (70%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.86-3.88 (m, 4H), 7.18-7.20 (m, 2H), 7.82-7.84 (m, 2H), 8.92 (br.s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 32.4, 56.2, 114.6, 115.7, 123.5, 132.8, 156.3, 164.1, 187.4. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_{10}ClN_3O_2Na^+$, 274.0354; found, 274.0364.

*2-Oxo-2-(3-(p-tolyl)-2H-azirin-2-yl)acetohydrazonoyl chloride (**3e**)*. A colorless solid, mp 87–88 °C (Et_2O/hexane), yield 974 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 3.93 (s, 1H), 7.13 (s, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 32.7,

119.1, 126.7, 129.9, 130.4, 144.8, 156.7, 187.9. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_{10}ClN_3ONa^+$, 258.0405; found, 258.0417.

*2-(3-(4-(tert-Butyl)phenyl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3f**)*. A light brown oil, yield 849 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.95 (s, 1H), 7.11 (s, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9, 32.7, 35.2, 119.2, 126.2, 127.1, 130.4, 156.7, 157.8, 187.8. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{14}H_{17}ClN_3O^+$, 278.1055; found, 278.1051.

*2-(3-(2,4-Dimethylphenyl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3g**)*. A colorless solid, mp 104–106 °C (Et_2O/hexane), yield 878 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.66 (s, 3H), 3.85 (s, 1H), 7.11 (s, 2H), 7.13-7.16 (m, 2H), 7.45 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 21.6, 31.1, 117.9, 126.9, 127.0, 131.7, 132.4, 141.5, 144.3, 155.6, 188.1. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{12}H_{13}ClN_3O^+$, 250.0742; found, 250.0740.

*2-(3-(2,4-Dimethoxyphenyl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3h**)*. Compound **3h** was obtained as a mixture with Ph_3PO (1:0.65, ^{1}H NMR) and was used without purification, yield 944 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 1H), 3.86 (s, 3H), 3.93 (s, 3H), 6.51 (d, *J* = 2.1 Hz, 1H), 6.56 (dd, *J* = 8.5 and 2.2 Hz, 1H), 7.13 (s, 2H), 7.44-7.49 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 55.6, 55.9, 98.4, 103.9, 105.6, 127.2, 134.6, 152.5, 161.9, 165.8, 188.3. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{12}H_{12}ClN_3O_3Na^+$, 304.0459; found, 304.0462.

*2-(3-(Furan-2-yl)-2H-azirin-2-yl)-2-oxoacetohydrazonoyl chloride (**3i**)*. Compound **3i** was obtained as a mixture with **4i** and was used without purification, yield 732 mg (62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 1H), 6.67 (dd, *J* = 3.4 and 1.6 Hz, 1H), 6.95 (s, 2H), 7.23 (d, *J* = 3.5 Hz, 1H), 7.80-7.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.2, 112.9, 121.5, 127.5, 139.2, 147.3, 149.0, 187.0. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_8H_7ClN_3O_2^+$, 212.0221; found, 212.0221.

*2-Oxo-2-(3-(thiophen-2-yl)-2H-azirin-2-yl)acetohydrazonoyl chloride (**3j**)*. Compound **3i** was obtained as a mixture with **4j** and was used without purification, yield 822 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (s, 1H), 7.06 (s, 2H), 7.23 (dd, *J* = 4.9 and 3.9 Hz, 1H), 7.64 (dd, *J* = 3.7 and 0.9 Hz, 1H), 7.85 (dd, *J* = 5.0 and 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.5, 124.4, 127.2, 128.4, 135.3, 135.4, 150.6, 187.1. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_8H_7ClN_3OS^+$, 227.9993; found, 227.9995.

General Procedure B for the Synthesis of 2-Diazo-1-(3-aryl-2*H*-azirin-2-yl)ethan-1-ones 4. *p*-Toluenesulfonyl chloride (149 mg, 0.78 mmol) was added to a mixture of compound **3** (3.92 mmol), dry CH_2C1_2 (50 mL) and Et_3N (396 mg, 3.92 mmol), the solution was stirred at rt for 24h and then concentrated to dryness. The residue was purified by column chromatography on silica gel (EtOAc/hexane/$CHCl_3$, 1:2:3) to give azirine **4**. 2-(Diazomethylcarbonyl)-2*H*-azirines **4** was crystallized from a mixture of hexane/Et_2O.

*2-Diazo-1-(3-phenyl-2H-azirin-2-yl)ethan-1-one (**4a**)*. A light yellow solid, mp 54–55 °C (Et_2O/hexane), yield 398 mg (55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92 (s, 1H), 5.16 (s, 1H), 7.59-7.63 (m, 2H), 7.66-7.70 (m, 1H), 7.90-7.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.3, 52.9, 122.3, 129.4, 130.5, 134.2, 160.3, 192.3. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{10}H_8N_3O^+$, 186.0662; found, 186.0670.

*1-(3-(4-Chlorophenyl)-2H-azirin-2-yl)-2-diazoethan-1-one (**4b**)*. A light yellow solid, mp 103–105 °C (Et_2O/hexane), yield 331 mg (50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92 (s, 1H), 5.18 (s, 1H), 7.60 (d, *J* = 8.5 Hz, 2H), 7.85 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.3, 53.1, 120.8, 130.0, 131.6, 140.7, 159.6, 191.8. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_6ClN_3ONa^+$, 242.0092; found, 242.0101.

*1-(3-(4-Bromophenyl)-2H-azirin-2-yl)-2-diazoethan-1-one (**4c**)*. A light yellow solid, mp 113–114 °C (Et_2O/hexane), yield 348 mg (47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 (s, 1H), 5.19 (s, 1H),

7.73-7.78 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.2, 53.2, 121.2, 129.3, 131.6, 132.9, 159.7, 191.7. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{10}H_7{}^{79}BrN_3O^+$, 263.9767; found, 263.9768.

2-Diazo-1-(3-(4-methoxyphenyl)-2H-azirin-2-yl)ethan-1-one ***(4d)***. A light yellow solid, mp 69–70 °C (Et_2O/hexane), yield 367 mg (51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (s, 1H), 3.93 (s, 3H), 5.11 (s, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 7.85 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.2, 52.5, 55.7, 114.5, 115.0, 132.6, 158.9, 164.3, 193.0. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_9N_3O_2Na^+$, 238.0587; found, 238.0595.

2-Diazo-1-(3-(p-tolyl)-2H-azirin-2-yl)ethan-1-one ***(4e)***. A light yellow solid, mp 71–72 °C (Et_2O/hexane), yield 462 mg (56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 2.88 (s, 1H), 5.12 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 36.2, 52.6, 119.4, 130.2, 130.5, 145.4, 159.8, 192.6. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_9N_3ONa^+$, 222.0638; found, 222.0649.

1-(3-(4-(tert-Butyl)phenyl)-2H-azirin-2-yl)-2-diazoethan-1-one ***(4f)***. A light brown oil, yield 450 mg (61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 9H), 2.87 (s, 1H), 5.12 (s, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9, 35.3, 36.1, 52.6, 119.3, 126.4, 130.3, 158.3, 159.6, 192.6. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{14}H_{15}N_3ONa^+$, 264.1107; found, 264.1115.

2-Diazo-1-(3-(2,4-dimethylphenyl)-2H-azirin-2-yl)ethan-1-one ***(4g)***. A light yellow solid, mp 72–73 °C (Et_2O/hexane), yield 451 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.68 (s, 3H), 2.79 (s, 1H), 5.12 (s, 1H), 7.19-7.22 (m, 2H), 7.56 (d, *J* = 7.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 21.7, 34.6, 52.5, 118.1, 127.3, 131.9, 132.7, 141.6, 144.8, 158.7, 192.9. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{12}H_{12}N_3O^+$, 214.0975; found, 214.0973.

*2-Diazo-1-(3-(2,4-dimethoxyphenyl)-2H-azirin-2-yl)ethan-1-one (**4h**)*. A special procedure was used for the purification of compound **4h**. Dry Et_2O (20 mL) and Ph_3P (1.2 equiv) were added to a mixture of 2-diazo-1-(3-(2,4-dimethoxyphenyl)-2*H*-azirin-2-yl)ethan-1-one **4h** and Ph_3PO, prepared by the general procedure B. The resulting mixture was stirred at rt for 24 h. The precipitate was filtered off, washed with diethyl ether and dried in vacuum. Methyl iodide (2 equiv) was added to a solution of the resulted 1-(3-(2,4-dimethoxyphenyl)-2*H*-azirin-2-yl)-2-((triphenyl-λ^5-phosphanylidene)hydrazono)ethan-1-one in dry THF and the mixture was stirred at rt for 24 h. The precipitate (Ph_3PMeI) was filtered off, washed with diethyl ether and the filtrate was concentrated in vacuum and purified by flash column chromatography. A light yellow solid, mp 35–36°C (Et_2O/hexane), yield 320 mg (52%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.69 (s, 1H), 3.90 (s, 3H), 3.97 (s, 3H), 5.09 (s, 1H), 6.55 (d, *J* = 2.2 Hz, 1H), 6.62 (dd, *J* = 8.6 and 2.2 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.1, 52.0, 55.7, 55.9, 98.6, 104.1, 105.7, 134.9, 155.3, 161.9, 166.2, 193.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{12}H_{11}N_3O_3Na^+$, 268.0693; found, 268.0694.

*2-Diazo-1-(3-(furan-2-yl)-2H-azirin-2-yl)ethan-1-one (**4i**)*. A light yellow solid, mp 57–58 °C (Et_2O/hexane), yield 225 mg (35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88 (s, 1H), 5.19 (s, 1H), 6.71 (dd, *J* = 3.6 and 1.7 Hz, 1H), 7.29 (m, 1H), 7.86 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.5, 53.1, 113.1, 122.2, 139.4, 149.5, 149.9, 191.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_8H_5N_3O_2Na^+$, 198.0274; found, 198.0282.

*2-Diazo-1-(3-(thiophen-2-yl)-2H-azirin-2-yl)ethan-1-one (**4j**)*. A light yellow solid, mp 38–39 °C (Et_2O/hexane), yield 315 mg (47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 (s, 1H), 5.18 (s, 1H), 7.28 (dd, *J* = 4.8 and 3.9 Hz, 1H), 7.72 (dd, *J* = 3.8 and 1.0 Hz, 1H), 7.91 (dd, *J* = 5.0 and 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.8, 52.9, 124.5, 128.7, 135.8 (2C), 153.4, 191.9. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_8H_5N_3OSNa^+$, 214.0046; found, 214.0056.

General Procedure C for the Synthesis of 2-Halo- and 2-(R-oxy)-1-(3-aryl-2*H*-azirin-2-yl)ethan-1-ones 5. Acid (1.2 equiv) was added to a stirred solution of 2-(diazomethylcarbonyl)-2*H*-azirine **4** (0.27 mmol) in methylene chloride (5 mL) at 0 °C. The mixture was stirred 30 min at 0 °C and then at rt, until 2-(diazomethylcarbonyl)-2*H*-azirines was consumed (monitoring by TLC). The reaction mixture was washed twice with water, dried over Na_2SO_4 and filtered. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (eluent hexane/EtOAc, 4:1-1:1) to give **5**.

2-Bromo-1-(3-phenyl-2H-azirin-2-yl)ethan-1-one ***(5a)***. A colorless solid, mp 41–42 °C (Et_2O/hexane), yield 60 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.16 (s, 1H), 3.83 and 3.93 (AB-q, *J* = 11.8 Hz, 2H), 7.59-7.62 (m, 2H), 7.66-7.70 (m, 1H), 7.92-7.94 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 35.6, 121.7, 129.4, 130.7, 134.2, 158.1, 199.8. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_8{}^{79}BrNONa^+$, 259.9681; found, 259.9689.

2-Bromo-1-(3-(4-chlorophenyl)-2H-azirin-2-yl)ethan-1-one ***(5b)***. A colorless solid, mp 88–89 °C (Et_2O/hexane), yield 59 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 (s, 1H), 3.83 and 3.92 (AB-q, *J* = 11.5 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 35.6, 120.2, 129.9, 131.8, 140.8, 157.4, 199.6. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_7{}^{79}BrClNONa^+$, 293.9292; found, 293.9304.

2-Bromo-1-(3-(4-bromophenyl)-2H-azirin-2-yl)ethan-1-one ***(5c)***. A colorless solid, mp 84–85 °C (Et_2O/hexane), yield 57 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 (s, 1H), 3.83 and 3.92 (AB-q, *J* = 11.5 Hz, 2H), 7.75-7.81 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 35.6, 120.7, 129.5, 131.8, 132.9, 157.7, 199.6. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_7{}^{79}Br_2NONa^+$, 337.8787; found, 337.8788.

2-Bromo-1-(3-(4-methoxyphenyl)-2H-azirin-2-yl)ethan-1-one ***(5d)***. A colorless solid, mp 96–97 °C (Et_2O/hexane), yield 47 mg (76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.09 (s, 1H), 3.80 (d, *J* = 11.8 Hz,

1H), 3.89-3.92 (m, 4H), 7.09 (d, J = 8.7 Hz, 2H), 7.87 (d, J = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 35.7, 55.6, 113.9, 115.0, 132.9, 156.9, 164.4, 200.3. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_{10}{}^{79}BrNO_2Na^+$, 289.9787; found, 289.9799.

2-Bromo-1-(3-(p-tolyl)-2H-azirin-2-yl)ethan-1-one ***(5e)***. A colorless solid, mp 55–56 °C (Et_2O/hexane), yield 52 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 3H), 3.12 (s, 1H), 3.81 and 3.91 (AB-q, J = 11.8 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 7.82 (d, J = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 30.7, 35.7, 118.9, 130.2, 130.7, 145.5, 157.8, 200.0. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{11}H_{10}{}^{79}BrNONa^+$, 273.9838; found, 273.9850.

2-Bromo-1-(3-(4-(tert-butyl)phenyl)-2H-azirin-2-yl)ethan-1-one ***(5f)***. A light yellow oil, yield 51 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.13 (s, 1H), 3.81 and 3.92 (AB-q, J = 11.9 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9, 31.0, 35.4, 35.7, 118.8, 126.5, 130.7, 157.8, 158.5, 200.0. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{14}H_{16}{}^{79}BrNONa^+$, 316.0307; found, 316.0297.

2-Bromo-1-(3-(2,4-dimethylphenyl)-2H-azirin-2-yl)ethan-1-one ***(5g)***. A colorless solid, mp 67–68 °C (Et_2O/hexane), yield 57 mg (91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 2.71 (s, 3H), 3.05 (s, 1H), 3.81 and 3.92 (AB-q, J = 11.9 Hz, 2H), 7.20-7.27 (m, 2H), 7.57 (d, J = 7.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 21.8, 30.9, 34.1, 117.7, 127.3, 132.0, 132.9, 142.0, 145.0, 156.7, 200.3. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{12}H_{12}{}^{79}BrNONa^+$, 287.9994; found, 287.9991.

2-Bromo-1-(3-(2,4-dimethoxyphenyl)-2H-azirin-2-yl)ethan-1-one ***(5h)***. A colorless solid, mp 92–93 °C (Et_2O/hexane), yield 42 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.95 (s, 1H), 3.79 (d, J = 12.2 Hz, 1H), 3.88-3.82 (m, 4H), 3.99 (s, 3H), 6.56 (d, J = 2.2 Hz, 1H), 6.64 (dd, J = 8.6 and 2.2 Hz, 1H), 7.60 (d, J = 8.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 34.0, 55.8, 56.0, 98.6, 103.6, 105.9, 134.9,

153.7, 162.0, 166.3, 200.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{12}H_{12}{}^{79}BrNO_3Na^+$, 319.9893; found, 319.9886.

2-Bromo-1-(3-(furan-2-yl)-2H-azirin-2-yl)ethan-1-one ***(5i)***. A light brown oil, yield 47 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (s, 1H), 3.83 and 3.90 (AB-q, J = 12.0 Hz, 2H), 6.72 (dd, J = 3.3 and 1.5 Hz, 1H), 7.32 (d, J = 3.5 Hz, 1H), 7.87 (d, J = 1.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.6, 35.0, 113.1, 122.6, 138.7, 148.2, 149.7, 199.2. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_8H_6{}^{79}BrNO_2Na^+$, 249.9474; found, 249.9485.

2-Bromo-1-(3-(thiophen-2-yl)-2H-azirin-2-yl)ethan-1-one ***(5j)***. A light brown oil, yield 38 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.17 (s, 1H), 3.83 and 3.92 (AB-q, J = 11.9 Hz, 2H), 7.31 (dd, J = 4.8 and 4.0 Hz, 1H), 7.78 (dd, J = 3.7 and 0.8 Hz, 1H), 7.94 (dd, J = 4.9 and 0.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 36.4, 123.9, 128.7, 136.2 (2C), 151.6, 199.5. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_8H_6{}^{79}BrNOSNa^+$, 265.9246; found, 265.9248.

2-Chloro-1-(3-phenyl-2H-azirin-2-yl)ethan-1-one ***(5k)***. A colorless solid, mp 56–57 °C (Et_2O/hexane), yield 42 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.19 (s, 1H), 3.99 and 4.16 (AB-q, J = 14.8 Hz, 2H), 7.62 (t, J = 7.5 Hz, 2H), 7.70 (t, J = 7.4 Hz, 1H), 7.90-7.93 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.7, 45.9, 121.6, 129.5, 130.7, 134.4, 158.1, 199.8. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_8ClNONa^+$, 216.0187; found, 216.0179.

2-Iodo-1-(3-phenyl-2H-azirin-2-yl)ethan-1-one ***(5l)***. A colorless solid, mp 55–56 °C (Et_2O/hexane), yield 43 mg (56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (s, 1H), 3.79 and 3.86 (AB-q, J = 9.6 Hz, 2H), 7.62 (t, J = 7.4 Hz, 2H), 7. 69 (t, J = 7.4 Hz, 1H), 7.96-7.98 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.6, 35.3, 121.8, 129.4, 130.8, 134.2, 158.4, 201.2. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_8INONa^+$, 307.9543; found, 307.9548.

*2-Oxo-2-(3-phenyl-2H-azirin-2-yl)ethyl 4-methylbenzenesulfonate (**5m**)*. A colorless solid, mp 89–91 °C (Et_2O/hexane), yield 84 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.20 (s, 1H), 4.54 and 4.67 (AB-q, *J* = 16.2 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.58-7.62 (m, 2H), 7.66-7.69 (m, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.87-7.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 34.6, 70.7, 121.3, 128.0, 129.4, 129.9, 130.7, 132.1, 134.4, 145.4, 157.2, 199.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{17}H_{15}NO_4SNa^+$, 352.0614; found, 352.0624.

*2-Oxo-2-(3-phenyl-2H-azirin-2-yl)ethyl 2,2,2-trifluoroacetate (**5n**)*. A light yellow oil, yield 51 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 (s, 1H), 4.70 (d, *J* = 16.5 Hz, 1H), 4.92 (d, *J* = 16.5 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 2H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.93-7.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 68.4, 114.3 (q, *J* = 285 Hz), 121.1, 129.7, 130.8, 134.8, 156.9 (q, *J*= 43 Hz), 158.7, 197.7. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{12}H_8F_3NO_3Na^+$, 294.0348; found, 294.0334.

*2-Oxo-2-(3-phenyl-2H-azirin-2-yl)ethyl 2,4-dinitrobenzoate (**5o**)*. A light yellow solid, mp 137–138 °C (Et_2O/hexane), yield 83 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.09 (s, 1H), 4.83 and 4.99 (AB-q, *J* = 16.7 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 2H), 7.72 (t, *J* = 7.4 Hz, 1H), 7.94-7.96 (m, 2H), 8.10 (d, *J* = 8.4 Hz, 1H), 8.56 (dd, *J* = 8.4 and 2.1 Hz, 1H), 8.83 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 68.1, 119.6, 121.3, 127.8, 129.7, 130.8, 131.7, 132.3, 134.7, 147.5, 149.1, 158.5, 163.2, 199.5. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{17}H_{11}N_3O_7Na^+$, 392.0489; found, 392.0487.

*2-Oxo-2-(3-phenyl-2H-azirin-2-yl)ethyl propiolate (**5p**)*. A colorless solid, mp 117–118 °C (Et_2O/hexane), yield 51 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (s, 1H), 3.06 (s, 1H), 4.62 and 4.77 (AB-q, *J* = 16.6 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 2H), 7.71 (t, *J* = 7.4 Hz, 1H), 7.91-7.93 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.4, 67.5, 73.7, 76.4, 121.4, 129.6, 130.8, 134.5, 151.7, 158.6, 199.3. HRMS (ESI-TOF) (m/z): $[M+Ag]^+$ calcd for $C_{13}H_9NO_3{}^{107}Ag^+$, 333.9628; found, 333.9641.

*2-(3-(4-Methoxyphenyl)-2H-azirin-2-yl)-2-oxoethyl 4-methylbenzenesulfonate (**5r**).*

A colorless solid, mp 106–107 °C (Et_2O/hexane), yield 82 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 3.11 (s, 1H), 3.93 (s, 3H), 4.49 and 4.64 (AB-q, J = 16.2 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.80-7.84 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 34.8, 55.7, 70.5, 113.5, 115.1, 128.1, 129.9, 132.3, 132.9, 145.4, 156.1, 164.5, 200.0. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{18}H_{17}NO_5SNa^+$, 382.0720; found, 382.0716.

General Procedure D for the Synthesis of 1-(3-aryl-2*H*-azirin-2-yl)-2-((triphenyl-λ^5-phosphanylidene)hydrazono)ethan-1-ones 6.

Triphenylphosphane (314 mg, 1.2 mmol) was added to a solution of azirine **4** (1 mmol) in dry diethyl ether (25 mL). The resulting mixture was stirred at rt for 24 h. The starting diazo compound **4** was completely consumed according TLC. The precipitate was filtered off, washed with diethyl ether and dried in vacuum. According to the ^{1}H, ^{31}P and ^{13}C spectra, dissolution of **6** in $CDCl_3$ is accompanied by their partial dissociation to starting diazo compound **4** and triphenylphosphane (**6a**:**4a** = 1:0.14 and **6b**:**4h** = 1:0.18). Such dissociation is characteristic of phosphazines.[16]

*1-(3-Phenyl-2H-azirin-2-yl)-2-((triphenyl-λ^5-phosphanylidene)hydrazono)ethan-1-one (**6a**).* Light yellow solid, mp 127–129 °C (Et_2O/hexane), yield 425 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.80 (s, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.52-7.58 (m, 7H), 7.63-7.68 (m, 3H), 7.72-7.76 (m, 8H), 8.14 (d, J = 2.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.9, 123.3, 127.0 (d, J = 94.4 Hz), 128.9-129.0 (m, 2C), 130.3, 132.8 (d, J = 2.7 Hz), 133.1, 133.4 (d, J = 8.4 Hz), 148.9 (d, J = 46.4 Hz), 158.6, 195.0. ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.7. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{28}H_{23}N_3OP^+$, 448.1573; found, 448.1581.

*1-(3-(2,4-Dimethoxyphenyl)-2H-azirin-2-yl)-2-((triphenyl-λ^5-phosphaneylidene)hydrazono)ethan-1-one (**6b**).* Light yellow solid, mp 150–152 °C

(Et_2O/hexane), yield 425 mg (96%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 6H), 6.45-6.47 (m, 2H), 7.30-7.33 (m, 3H), 7.50-7.54 (m, 5H), 7.61-7.64 (m, 3H), 7.71-7.76 (m, 6H), 8.12 (d, *J* = 2.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.3, 55.6, 55.7, 98.2, 105.1, 105.3, 127.1 (d, *J* = 94.1 Hz), 128.8 (d, *J* = 11.6 Hz), 132.7 (d, *J* = 2.7 Hz), 133.4 (d, *J* = 8.4 Hz), 134.6, 149.0 (d, *J* = 46.1 Hz), 153.8, 161.6, 165.2, 196.0. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{30}H_{27}N_3O_3P^+$, 508.1785; found, 508.1767.

2-((4-Nitrobenzylidene)hydrazono)-1-(3-phenyl-2H-azirin-2-yl)ethan-1-one ***(8)***. 4-Nitrobenzaldehyde (12 mg, 0.08 mmol) was added to a solution of compound **6** (40 mg, 0.09 mmol) in benzene (5 mL). The resulting mixture was stirred at rt for 4 d. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (eluent hexane/EtOAc, 4:1) to give **8** as a light yellow solid, mp 130–131 °C (Et_2O/hexane), yield 23 mg (80%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.04 (s, 1H), 7.61 (t, *J* = 7.4 Hz, 2H), 7.68 (t, *J* = 7.4 Hz, 1H), 7.92 (d, *J* = 7.1 Hz, 2H), 7.95 (s, 1H), 8.05 (d, *J* = 8.7 Hz, 2H), 8.36 (d, *J* = 8.7 Hz, 2H), 8.52 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.2, 122.0, 124.1, 129.4, 129.7, 130.7, 134.0, 138.6, 149.7, 156.3, 156.4, 158.9, 196.3. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{17}H_{12}N_4O_3Na^+$, 343.0802; found, 343.0797.

General Procedure E for the Synthesis of 2-R-5-(3-aryl-2*H*-azirin-2-yl)oxazoles 9. A portion of $Rh_2(oct)_4$ (2.3 mg, 0.03 mmol) was added to a mixture of azirine **4** (0.3 mmol) and nitrile (61.6 mmol) in DCE (75 mL). The resulting mixture was refluxed under argon for 8 min. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (eluent hexane/EtOAc, 6:1-1:1).

2-Methyl-5-(3-phenyl-2H-azirin-2-yl)oxazole ***(9a)***. A light brown oil, yield 34 mg (56%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.26 (s, 1H), 6.85 (s, 1H), 7.57-7.65 (m, 3H), 7.91-7.93 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 25.0, 123.6, 124.2, 129.3, 129.8, 133.5, 151.1, 160.7, 162.5. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{12}H_{11}N_2O^+$, 199.0866; found, 199.0872.

*2-Phenyl-5-(3-phenyl-2H-azirin-2-yl)oxazole (**9b**)*. A light brown solid, mp 74–75 °C (Et_2O/hexane), yield 29 mg (36%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.39 (s, 1H), 7.08 (s, 1H), 7.41-7.43 (m, 3H), 7.61-7.69 (m 3H), 7.90-7.99 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2, 123.5, 125.6, 126.2, 127.3, 128.7, 129.4, 129.9, 130.2, 133.7, 151.6, 160.9, 162.3. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{17}H_{12}N_2ONa^+$, 283.0842; found, 283.0850.

*5-(3-(2,4-Dimethylphenyl)-2H-azirin-2-yl)-2-methyloxazole (**9c**)*. A light brown oil, yield 52 mg (77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.44 (s, 3H), 2.67 (s, 3H), 3.12 (s, 1H), 6.82 (s, 1H), 7.19-7.22 (m, 2H), 7.63 (d, J = 7.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 19.7, 21.7, 23.0, 119.4, 123.8, 127.1, 131.9, 132.0, 141.1, 144.0, 151.7, 160.6, 161.2. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{14}H_{15}N_2O^+$, 227.1179; found, 227.1181.

General Procedure F for the Synthesis of Ethyl 3-(3-aryl-2*H*-azirine-2-carbonyl)-4,5-dihydro-1*H*-pyrazole-5-carboxylates 10.

A solution of azirine **4** (0.32 mmol) and ethyl acrylate (49 mg, 0.49 mmol) in pyridine (2 ml) was heated at 60 °C for 20 h. Pyridine and unreacted ethyl acrylate were removed under reduced pressure. The residue was dissolve in EtOAc, washed with HCl 0.1 M and dried over Na_2SO_4. After filtration and concentration in vacuum, the residue was purified by column chromatography on silica gel to give **10** (two diastereomers, *dr* ~1:1).

*Ethyl 3-(3-phenyl-2H-azirine-2-carbonyl)-4,5-dihydro-1H-pyrazole-5-carboxylate (**10a**)*. A light yellow oil, yield 80 mg (87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, J = 7.1 Hz, 3H), 3.13-3.37 (m, 2H), 3.94-3.95 (m, 1H), 4.23 (q, J = 7.1 Hz, 2H), 4.48-4.54 (m, 1H), 7.11-7.12 (m, 1H), 7.53 (t, J = 7.4 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.84-7.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (2C), 32.9, 33.0, 33.4 (2C), 61.1, 61.2, 61.9, 62.0, 122.4 (2C), 129.1 (2C), 130.4 (2C), 133.5 (2C), 150.2, 150.3, 157.2 (2C),

171.4 (2C), 191.9, 192.0. ^{15}N NMR from HMBC ^{1}H-^{15}N (100 MHz, $CDCl_3$) δ ^{15}N 142, 263, 371. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{15}H_{15}N_3O_3Na^+$, 308.1006; found, 308.1015.

*Ethyl 3-(3-(2,4-dimethylphenyl)-2H-azirine-2-carbonyl)-4,5-dihydro-1H-pyrazole-5-carboxylate (**10b**)*. A light yellow oil, yield 78 mg (78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27-1.31 (m, 3H), 2.38 (s, 3H), 2.67 (s, 3H), 3.18-3.33 (m, 2H), 3.82 (m, 1H), 4.20-4.24 (q, *J* = 7.1 Hz, 2H), 4.47-4.53 (m, 1H), 7.08-7.16 (m, 3H), 7.46 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (2C), 19.7 (2C), 21.6 (2C), 31.2, 31.3, 33.5 (2C), 61.0, 61.1, 61.9, 62.0, 118.2 (2C), 126.9 (2C), 131.6 (2C), 132.4, 132.5, 141.5 (2C) 144.0 (2C), 150.4, 150.5, 155.6, 155.7, 171.5 (2C), 192.5 (2C). HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{17}H_{19}N_3O_3Na^+$, 336.1319; found, 336.1307.

*1-(2-Oxo-2-(3-phenyl-2H-azirin-2-yl)ethyl)pyridin-1-ium bromide (**11**)*. Pyridine (7 mg, 0.088 mmol) was added to a solution of azirine **5a** (20 mg, 0.084 mmol) in dry diethyl ether (2 mL) and the resulting mixture was stirred at rt for 24 h. The precipitate was filtered off, washed with diethyl ether and dried in vacuum. A light yellow solid, mp 34–35 °C (Et_2O/hexane), yield 26 mg (98%). ^{1}H NMR (400 MHz, a mixture DMSO-d_6 and $CDCl_3$) δ 3.34 (s, 1H), 6.37 (d, *J* = 17.4 Hz, 1H), 6.95 (d, *J* = 17.4 Hz, 1H), 7.50 (t, *J* = 7.4 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.99 (t, *J* = 7.1 Hz, 2H), 8.10-8.12 (m, 2H), 8.48 (t, *J* = 7.8 Hz, 1H), 9.37 (d, *J* = 5.7 Hz, 2H). ^{13}C NMR (100 MHz, a mixture DMSO-d_6 and $CDCl_3$) δ 34.8, 67.6, 121.0, 127.5, 129.3, 131.4, 134.3, 145.7, 146.3, 156.4, 198.8. HRMS (ESI-TOF) (m/z): $[M-Br]^+$ calcd for $C_{15}H_{13}N_2O^+$, 237.1022; found, 237.1027.

General Procedure G for the Synthesis of Ethyl (2-Oxo-2-(3-aryl-2*H*-azirin-2-yl)ethyl)triphenylphosphonium bromides 12.

Triphenylphosphane (240 mg, 0.92 mmol) was added to a solution of azirine **5** (0.85 mmol) in dry diethyl ether (20 mL) and the resulting mixture was stirred at rt for 24 h. The precipitate was filtered off, washed with diethyl ether and dried in vacuum.

*(2-Oxo-2-(3-phenyl-2H-azirin-2-yl)ethyl)triphenylphosphonium bromide (**12a**)*. A light yellow solid, mp 152–155 °C (Et_2O/hexane), yield 408 mg (97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 1H), 5.59 (dd, *J* = 17.9 and 12.3 Hz, 1H), 7.07 (dd, *J* = 17.9 and 12.5 Hz, 1H), 7.53-7.66 (m, 9H), 7.72-7.76 (m, 3H), 7.86-7.91 (m, 6H), 8.11-8.13 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.7 (d, *J* = 10.1 Hz), 39.5 (d, *J* = 58.5 Hz), 118.5 (d, *J* = 89.0 Hz), 121.2, 129.3, 130.1 (d, *J* = 13.2 Hz), 131.6, 133.9 (d, *J* = 10.8 Hz), 134.0, 134.8 (d, *J* = 3.0 Hz), 156.4, 200.6 (d, *J* = 6.3 Hz). HRMS (ESI-TOF) (m/z): $[M-Br]^+$ calcd for $C_{28}H_{23}NOP^+$, 420.1512; found, 420.1530.

*(2-(3-(4-Methoxyphenyl)-2H-azirin-2-yl)-2-oxoethyl)triphenylphosphonium bromide (**12b**)*. A light yellow solid, mp 179–180 °C (Et_2O/hexane), yield 396 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56 (s, 1H), 3.82 (s, 3H), 5.58 (dd, *J* = 17.8 and 12.5 Hz, 1H), 6.79 (dd, *J* = 17.8 and 12.5 Hz, 1H), 6.99 (d, *J* = 8.5 Hz, 2H), 7.57-7.59 (m, 6H), 7.67-7.70 (m, 3H), 7.80-7.85 (m, 6H), 8.02 (d, *J* = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.5 (d, *J* = 10.0 Hz), 39.0 (d, *J* = 58.4 Hz), 55.5, 113.1, 114.8, 118.3 (d, *J* = 88.9 Hz), 130.0 (d, *J* = 13.1 Hz), 133.6, 133.8 (d, *J* = 10.8 Hz), 134.6 (d, *J* = 3.0 Hz), 154.9, 164.1, 200.6 (d, *J* = 6.3 Hz). HRMS (ESI-TOF) (m/z): $[M-Br]^+$ calcd for $C_{29}H_{25}NO_2P^+$, 450.1617; found, 450.1604.

General Procedure H for the Synthesis of 3-(4-Nitrophenyl)-1-(3-aryl-2*H*-azirin-2-yl)prop-2-en-1-ones 13.

*t*BuOK (60 mg, 0.53 mmol) was slowly added to a solution of bromide **12** (0.53 mmol) in dry THF (25 mL) under argon, followed by addition 4-nitrobenzaldehyde (75 mg, 0.5 mmol). The resulting mixture was refluxed under argon for 10 h. The reaction mixture was poured in ice water and extracted with ethyl acetate, the organic layers was collected and dried over $NaSO_4$. After filtration and concentration in vacuum, the residue was purified by column chromatography on silica gel to give **13.**

*3-(4-Nitrophenyl)-1-(3-phenyl-2H-azirin-2-yl)prop-2-en-1-one (**13a**)*. A light yellow solid, mp 133–134 °C (Et_2O/hexane), yield 139 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.27 (s, 1H), 6.91 (d, *J* =

16.0 Hz, 1H), 7.61 (t, *J* = 7.4 Hz, 2H), 7.67-7.70 (m, 3H), 7.76 (d, *J* = 16.0 Hz, 1H), 7.92 (d, *J* = 7.1 Hz, 2H), 8.23 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.4, 122.3, 124.1, 125.0, 129.0, 129.5, 130.6, 134.2, 140.4, 140.5, 148.6, 159.1, 196.4. HRMS (ESI-TOF) (m/z): $[M+Ag]^+$ calcd for $C_{17}H_{12}N_2O_3{}^{107}Ag^+$, 398.9893; found, 398.9900.

1-(3-(4-Methoxyphenyl)-2H-azirin-2-yl)-3-(4-nitrophenyl)prop-2-en-1-one ***(13b)***. A light yellow solid, mp 150–151 °C (Et_2O/hexane), yield 162 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.18 (s, 1H), 3.91 (s, 3H), 6.86 (d, *J* = 15.9 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.73 (d, *J* = 16.0 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 2H), 8.21 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.4, 55.6, 114.5, 115.0, 124.0, 124.8, 129.0, 132.7, 140.1, 140.6, 148.5, 157.7, 164.3, 196.9. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{18}H_{14}N_2O_4Na^+$, 345.0846; found, 345.0845.

2-Azido-1-(3-phenyl-2H-azirin-2-yl)ethan-1-one ***(14)***. NaN_3 (20 mg, 0.3 mmol) was added to a solution of azirine **5a** (50 mg, 0.21 mmol) in aq. acetone (3 mL) and the mixture was stirred 12 h at rt. The reaction mixture was poured into water, extracted with EtOAc, dried over Na_2SO_4 and filtered. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (eluent hexane/EtOAc, 4:1) to give azide **14** as a colorless oil, yield 41 mg (96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (s, 1H), 3.71 (d, *J* = 18.1 Hz, 1H), 3.98 (d, *J* = 18.1 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 2H), 7.70-7.74 (m, 1H), 7.90-7.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 36.0, 55.1, 121.5, 129.6, 130.6, 134.6, 158.5, 201.8. ^{15}N NMR from HMBC ^{1}H-^{15}N (100 MHz, $CDCl_3$) δ ^{15}N 63, 246, 265. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{10}H_8N_4ONa^+$, 223.0590; found, 223.0589.

General Procedure I for the Synthesis of 4-(3-aryl-2*H*-azirin-2-yl)thiazol-2-amines 15.

Triethylamine (13 mg, 0.13 mmol) was added to a mixture of azirine **5** (0.13 mmol) and thiourea (10 mg, 0.13 mmol) in dry methanol (4 mL) and the mixture was refluxed for 30 min. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to give thiazole **15**.

*4-(3-Phenyl-2H-azirin-2-yl)thiazol-2-amine (**15a**)*. A light brown solid, mp 137–139 °C (Et_2O/hexane), yield 27 mg (95%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.18 (s, 1H), 6.43 (s, 1H), 6.89 (s, 2H), 7.62-7.71 (m, 3H), 7.85-7.87 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 31.0, 102.7, 124.8, 129.9 (2C), 133.7, 152.3, 164.6, 168.6. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{11}H_{10}N_3S^+$ 216.0590; found, 216.0600.

*4-(3-(4-Methoxyphenyl)-2H-azirin-2-yl)thiazol-2-amine (**15b**)*. A light brown solid, mp 146–148 °C (Et_2O/hexane), yield 26 mg (82%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.09 (s, 1H), 3.87 (s, 3H), 6.37 (s, 1H), 6.88 (s, 2H), 7.17 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.5 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 30.5, 56.1, 102.2, 115.5, 117.1, 131.9, 152.7, 163.1, 163.5, 168.5. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{12}H_{12}N_3OS^+$ 246.0696; found, 246.0697.

*2-(Oxiran-2-yl)-3-phenyl-2H-azirine (**16**)*. $NaBH_4$ (32 mg, 0.84 mmol) was added to a solution of azirine **5a** (200 mg, 0.85 mmol) in dry methanol (25 mL) at 0 °C and the mixture was stirred at 0 °C for 2 h. The solvent was removed in vacuo and the residue was dissolve in EtOAc, washed with H_2O, saturated aq NH_4Cl, brine and dried over Na_2SO_4. After filtration the solvent was removed in vacuum and the residue was dissolve in DCM and treated with Et_3N (86 mg, 0.85 mmol). The resulting mixture was stirred at rt for 2 d. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to give azirine **16** (two diastereomers, *dr* ~1:2) as colorless oil, yield 53 mg (10%). A major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.25-2.26 (m, 1H), 2.77-2.79 (m, 1H), 2.86-2.88 (m, 2H), 7.58-7.65 (m, 3H), 7.93-7.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 46.5, 53.3, 124.5, 129.2, 129.8, 133.4, 167.8. A minor diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (d, J = 4.0 Hz, 1H), 2.63 (dd, J = 4.9 and 2.6 Hz, 1H), 2.75-2.76 (m, 1H), 3.16-3.18 (m, 1H), 7.58-7.65 (m, 3H), 7.90-7.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 43.5, 52.5, 124.7, 129.2, 129.8, 133.3, 164.8. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{10}H_{10}NO^+$, 160.0757; found, 160.0765.

General Procedure J for the Synthesis of 1-(3-aryl-3-(1*H*-imidazol-1-yl)aziridin-2-yl)-2-diazoethan-1-ones 17.

Triethylamine (42 mg, 0.42 mmol) and imidazole (26 mg, 0.38 mmol) were added to a solution of azirine **4** (0.38 mmol) in benzene (5 ml). The reaction mixture was stirred at rt for 48 h. In case **17a**, the precipitate was filtered off, washed with benzene and dried in vacuum. In case **17b**, the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel**.**

*1-((2RS,3SR)-3-(4-Bromophenyl)-3-(1H-imidazol-1-yl)aziridin-2-yl)-2-diazoethan-1-one **(17a)***. A colorless solid, mp 77-79 °C (benzene), yield 92 mg (73%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.77-4.20 (br. m, 2H), 6.59 (br. s, 1H), 6.91 (s, 1H), 7.28 (s, 1H), 7.39 (br. m, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.91 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 46.9, 56.3, 58.3, 119.3, 127.7, 129.3, 130.4, 131.8, 134.6, 137.0, 187.5. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{13}H_{11}{}^{79}BrN_5O^+$, 332.0141; found, 332.0137.

*2-Diazo-1-((2RS,3SR)-3-(2,4-dimethylphenyl)-3-(1H-imidazol-1-yl)aziridin-2-yl)ethan-1-one **(17b)**.* A light brown oil, yield 85 mg (80%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.12-2.27 (m, 6H), 3.37-3.39 (m, 2H), 6.35-6.71 (br.m, 1H), 6.86 (s, 1H), 7.00-7.06 (m, 3H), 7.42 (s, 1H), 7.62-7.65 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 18.9, 21.1, 46.5, 56.4, 58.6, 118.7, 126.9, 129.0, 129.6, 131.8, 135.6, 136.4, 137.4, 139.0, 187.3. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{15}H_{16}N_5O^+$, 282.1349; found, 282.1336.

General Procedure K for the Synthesis of 1-(4-Acetyl-5-methyl-3-aryl-1*H*-pyrrol-2-yl)-2-bromoethan-1-ones 18.

$NiCl_2 \cdot 6H_2O$ (5 mg, 0.02 mmol) was added to a mixture of azirine **5** (0.4 mmol) and acetylacetone (40 mg, 0.4 mmol) in MeCN (12 mL). The resulting mixture was heated at 60 ºC for 3 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to give **18**.

*1-(4-Acetyl-5-methyl-3-phenyl-1H-pyrrol-2-yl)-2-bromoethan-1-one (**18a**).* A colorless solid, mp 158–160 °C (Et_2O/hexane), yield 122 mg (95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.79 (s, 3H), 2.68 (s, 3H), 3.62 (s, 2H), 7.42-7.43 (m, 2H), 7.51-7.52 (m, 3H), 10.52 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 30.6, 31.9, 124.3, 125.5, 128.9, 129.0, 129.7, 133.8, 135.0, 142.6, 182.4, 195.8. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{15}H_{14}{}^{79}BrNO_2Na^+$, 342.0100; found, 342.0113.

*1-(4-Acetyl-3-(4-methoxyphenyl)-5-methyl-1H-pyrrol-2-yl)-2-bromoethan-1-one (**18b**).* A colorless solid, mp 172–173 °C (Et_2O/hexane), yield 111 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.81 (s, 3H), 2.66 (s, 3H), 3.67 (s, 2H), 3.90 (s, 3H), 7.02-7.04 (m, 2H), 7.29-7.32 (m, 2H), 10.66 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 30.6, 32.2, 55.3, 114.3, 124.4, 125.7, 126.6, 130.8, 133.8, 142.7, 160.0, 182.4, 196.0. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{16}H_{16}{}^{79}BrNO_3Na^+$, 372.0206; found, 372.0197.

General Procedure L for the Synthesis of 1-(2-Methyl-5-(2-methyloxazol-5-yl)-4-aryl-1*H*-pyrrol-3-yl)ethan-1-ones 19.

$NiCl_2 \cdot 6H_2O$ (4 mg, 0.017 mmol) was added to a mixture of azirine **4** (0.17 mmol) and acetylacetone (17 mg, 0.17 mmol) in MeCN (3 mL). The resulting mixture was heated at 60 ºC for 7 h. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to give **19**.

*1-(2-Methyl-5-(2-methyloxazol-5-yl)-4-phenyl-1H-pyrrol-3-yl)ethan-1-one (**19a**).* A colorless solid, mp 132–135 °C (Et_2O/hexane), yield 23 mg (48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90 (s, 3H), 2.41 (s, 3H), 2.62 (s, 3H), 6.13 (s, 1H), 7.31-7.33 (m, 2H), 7.41-7.47 (m, 3H), 9.11 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 14.3, 30.7, 116.6, 120.2, 122.5, 123.5, 127.9, 128.7, 130.1, 135.6, 136.1, 143.8, 159.0, 196.4. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{17}H_{17}N_2O_2^+$, 281.1285; found, 281.1288.

*1-(4-(2,4-Dimethylphenyl)-2-methyl-5-(2-methyloxazol-5-yl)-1H-pyrrol-3-yl)ethan-1-one (**19b**).* A colorless solid, mp 116–117 °C (Et_2O/hexane), yield 34 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$)

δ 1.87 (s, 3H), 2.07 (s, 3H), 2.40 (s, 3H), 2.43 (s, 3H), 2.65 (s, 3H), 5.90 (s, 1H), 7.06-7.10 (m, 2H), 7.14 (s, 1H), 8.74 (br. s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.0, 10.9, 16.3, 17.9, 27.2, 118.9, 122.4, 124.7, 125.2, 130.2, 133.3, 134.5, 135.3, 139.9, 140.4, 141.6, 147.8, 163.5, 203.4. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{19}H_{20}N_2O_2Na^+$, 331.1417; found, 331.1423.

General Procedure M for the Synthesis of 2-Methoxy-2-aryl-5-methylene-2,5-dihydrooxazoles 20.

Triethylamine (25 mg, 0.25 mmol) was added to a solution of azirine **5** (0.25 mmol) in dry methanol (4 mL) and the mixture was refluxed for 30 min. The solvent was removed in vacuo and the residue was purified by column chromatography on silica gel to give oxazoline **20**.

*2-Methoxy-5-methylene-2-phenyl-2,5-dihydrooxazole (**20a**).* A colorless oil, yield 32 mg (69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.31 (s, 3H), 4.59 (d, J = 2.5 Hz, 1H), 4.91 (d, J = 2.5 Hz, 1H), 7.39-7.40 (m, 3H), 7.59-7.61 (m, 2H), 7.90 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.1, 87.9, 125.8, 127.9, 128.3, 129.3, 137.9, 158.0, 158.8. ^{15}N NMR from HMBC ^{1}H-^{15}N (100 MHz, $CDCl_3$) δ ^{15}N 333. HRMS (ESI-TOF) (m/z): $[M+H]^+$ calcd for $C_{11}H_{12}NO_2^+$, 190.0863; found, 190.0871.

*2-Methoxy-2-(4-methoxyphenyl)-5-methylene-2,5-dihydrooxazole (**20b**).* A colorless oil, yield 16 mg (30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.29 (s, 3H), 3.83 (s, 3H), 4.56 (d, J = 2.5 Hz, 1H), 4.89 (d, J = 2.5 Hz, 1H), 6.91 (d, J = 8.9 Hz, 2H), 7.52 (d, J = 8.9 Hz, 2H), 7.87 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.1, 55.3, 87.7, 113.6, 127.2, 127.9, 130.3, 158.0, 158.5, 160.3. HRMS (ESI-TOF) (m/z): $[M+Na]^+$ calcd for $C_{12}H_{13}NO_3Na^+$, 242.0788; found, 242.0798.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.0000000. X-ray diffraction experiments, NMR spectra for all new compounds. Crystallographic data for **4a** (CIF)

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Notes

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