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$Rh_2(OAc)_4$-catalyzed reaction of α-diazocarbonyl compounds with 2-carbonyl-substituted 2*H*-azirines

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ABSTRACT

The $Rh_2(OAc)_4$-catalyzed reaction of 2*H*-azirine-2-carbaldehydes with dimethyl diazomalonate proceeds via azirinium ylide formation, isomerization to 2-azabuta-1,3-dienes followed by 1,6-π-electrocyclization to give 2*H*-1,3-oxazines. According to DFT-calculations ring opening of azirinium ylides should occur stereoselectively to give 2-azadienes with the C=C bond exclusively in the *Z* configuration. Changing a formyl group for an acetyl group in the azirine leads to a lowering of stereoselectivity and the formation of azadienes with an *E* configuration of the C=C bond was observed. The reaction of 2-acyl-2-diazoacetates with 2*H*-azirine-2-carbaldehydes proceeds similarly, but the 2-acetyl-substituted 2*H*-1,3-oxazines formed are unstable under chromatographic purification and rearrange easily into pyrrole derivatives.

1. Introduction

Metal-catalyzed decomposition of diazo compounds proceeding through reactive carbenoids is an effective method for the synthesis of various heterocyclic systems. Considerable progress has been achieved in the development of methods using intramolecular reactions of metallocarbenoids, leading to cycle formation with high yields and stereoselectivity. Intermolecular reactions of carbenoids with heteroatomic molecules, which allow the use of more simple and available starting materials are also well known and extensively developed. The reactions of metallocarbenoids with monoheterocyclic substrates can result in the formation of ortho-fused[1] or bridged[2] heterocyclic systems, the products of formal C–H insertion[1d,2a,3] and recyclization, which can occur with retention of ring size,[4] ring contraction[5] or with ring enlargement. Carbenoid-mediated ring enlargement can occur as one-carbon ring expansion by formal insertion of a carbene moiety into the carbon–heteroatom bond[6] or a three-atom ring expansion. The latter reaction type implies the involvement of the atoms of a carbonyl function or an alkenyl moiety, which can be located either in the starting heterocycle[6e,7] or in the diazo compound.[8]

2*H*-Azirine derivatives are effective heterocyclic building blocks used for the construction of larger ring heterocycles.[9] There are, however, only a few examples in which 2*H*-azirine ring enlargement occurs under metallocarbenoid action. An azetine derivative was synthesized in good yield from 2,3-diphenyl-2*H*-azirine and dimethyl diazomalonate under Rh(II)-catalysis.[10] Three-atom ring expansion of the azirine ring to the 2*H*-1,4-oxazine system was observed in the reaction of aryl-substituted 2*H*-azirines with ethyl 2-acyl-2-diazoacetates carried out in the presence of $Rh_2(OAc)_4$.[11] The carbene carbon atom and two carbonyl atoms of acyl function of the diazo compound take part in a new cycle formation. To the best of our knowledge the carbenoid-mediated ring-enlargements of 2*H*-azirines with substituents on the azirine ring are unknown.

In order to broaden the scope of the applications of reactions of 2*H*-azirines with metallocarbenoids in heterocyclic synthesis the examination of the $Rh_2(OAc)_4$-catalyzed reaction of 2-carbonyl-subsituted 2*H*-azirines with dimethyl diazomalonate and ethyl 2-acyl-2-diazoacetates is the subject of the present work.

2. Results and discussion

Earlier it was found that the result of the $Rh_2(OAc)_4$-catalyzed reaction of dimethyl diazomalonate with aryl-substituted 2*H*-azirines **A** dramatically depends on a number of aryl substituents in the three-membered ring. The reaction of 2-phenyl-2*H*-azirine gives two products: 2-azadiene **B** and the product of formal double insertion of di(methoxycarbonyl)carbene into three-membered ring, pyrroline **C** (Scheme 1). The reaction of 2,3-diphenylazirine produces the product of formal insertion of di(methoxycarbonyl)

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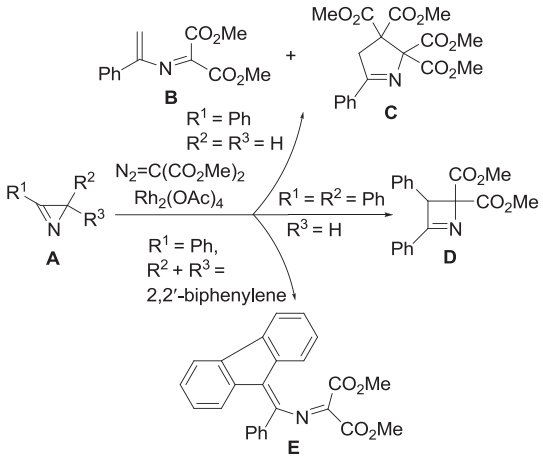
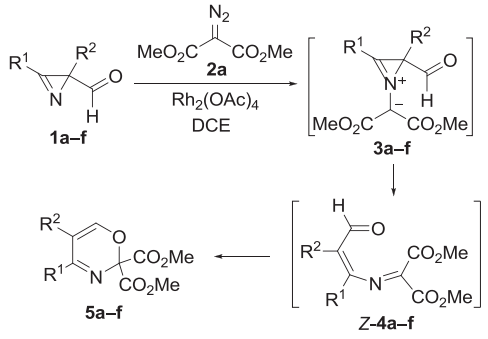


Scheme 1. $Rh_2(OAc)_4$-catalyzed reaction of aryl-substituted 2*H*-azirines with dimethyl diazomalonate.

carbene into three-membered ring, azetine **D**, while from trisubstituted azirine, 3-phenyl-2*H*,9′*H*-spiro[azirine-1,9′-fluorene] only 2-azadiene **E** was obtained as a sole product. The formation of these compounds was explained by transformations of azirinium ylides, which are primary intermediates in the reactions of carbenoids with azirines.

The introduction of a formyl group in the C2 position of the azirine ring completely changes the result of its interaction with Rh(II)-carbenoid derived from dimethyl diazomalonate (**2a**). The slow addition of diazo compound **2a** in 1,2-dichloroethane (DCE) to a solution of methyl 3-phenyl-2*H*-azirine-2-carbaldehyde (**1a**), in the presence of 5 mol % of $Rh_2(OAc)_4$ in DCE under reflux, gave 2*H*-1,3-oxazine **5a**, which was isolated in 26% yield using column chromatography on silica gel (Scheme 2). According to ^{1}H NMR spectroscopy data, no traces of products of the types **B**–**E** (Scheme 1) containing a formyl group were ever present in the reaction. The reaction mechanism can be rationalized in terms of the formation of azirinium ylide **3**, its ring-opening into 2-azadiene **4** followed by 1,6-electrocyclization with the participation of the formyl carbonyl group (Scheme 2).



Scheme 2. $Rh_2(OAc)_4$-catalyzed reaction of 2-carbonyl-substituted 2*H*-azirines **1a**–**f** with dimethyl diazomalonate **2a**.

Using this procedure 4-aryl-2*H*-1,3-oxazines **5b**–**d** were obtained in 23–42% yield (Table 1). The introduction of an additional methyl or phenyl group into position 2 of the azirine ring does not change the course of the reaction, which is controlled by the 2-formyl group to give exclusively 1,3-oxazines **5e**, **f**. In the ^{1}H NMR spectra of the reaction mixtures only traces of products containing a formyl group were observed.

All the newly obtained compounds were fully characterized using standard spectral and analytical methods. The structure of **5a** was confirmed by X-ray analysis (Fig. 1).

Table 1
The yields of 2*H*-1,3-oxazines **5a**–**f**

Azirine	R^1	R^2	Oxazine	Yield of **5**, %
1a	Ph	H	**5a**	26
1b	4-$MeOC_6H_4$	H	**5b**	23
1c	4-ClC_6H_4	H	**5c**	42
1d	4-MeC_6H_4	H	**5d**	35
1e	Ph	Me	**5e**	17
1f	Ph	Ph	**5f**	44

The azadiene *E*-**4g** along with oxazine **5g** were isolated by chromatography after reacting the 2-acetyl-substituted azirine **1g** with dimethyl diazomalonate (Scheme 3). The *E* configuration of the compound *E*-**4g** was elucidated by X-ray analysis (Fig. 1). This compound undergoes fast N-inversion in $CDCl_3$ solution, since only one singlet of the two ester methyl groups was observed in the ^{1}H NMR spectrum, as well as only one signal for two carbonyl atoms appeared in the ^{13}C NMR spectrum. Notably, the absence of an electron-withdrawing substituent at the 4-position of the 2-azabuta-2,4-diene fragment is responsible for the increase of the inversion barrier so that at ambient temperature the corresponding atoms of azadienes **B** and **E** (Scheme 1) are not equivalent.[10b]

No traces of the stereoisomer *Z*-**4g** were detected in the reaction mixtures and this can be explained by its fast cyclization into oxazine **5g** under reaction conditions. ^{1}H NMR monitoring of the reaction mixtures showed that the **5g**:*E*-**4g** ratio was 6:1 and did not change during the reaction course.

The reaction of azirinecarbaldehydes **1** with ethyl diazoacetoacetate **2b**, under Rh(II)-catalysis would produce a 2-azadiene with two carbonyl functions at the C1 and C4 atoms (acetyl and formyl groups), which both could be involved in 1,6-cyclization to give 2*H*-1,4- or 2*H*-1,3-oxazine, respectively. In order to examine the competition of these two electrocyclizations we carried out the reaction of azirine **1b** with diazo keto ester **2b** in DCE in the presence of $Rh_2(OAc)_4$. Surprisingly, neither 1,3-oxazine **8** nor 1,4-oxazine **9** but only pyrrolinone **10** was isolated after chromatographic purification of the reaction mixture (Scheme 4).

According to the ^{1}H NMR, the main component of the reaction mixture was 1,3-oxazine **8**: 2.37 (s, 3H), 3.87 (s, 3H), 6.08 (d, *J*=5.9 Hz, 1H), 6.96 (d, *J*=8.7 Hz, 2H), 7.87 (d, *J*=8.7 Hz, 2H). All attempts to separate this compound by crystallization at the lowered temperature failed. When the mixture was subjected to chromatography on silica gel the oxazine **8** was completely converted into pyrrolinone **10**. The structure of the compound **10** was verified by ^{1}H, ^{13}C NMR, IR spectroscopy, mass spectrometry, and elemental analysis. Presumably, under acidic conditions a recyclization of 1,3-oxazine via 2-azadiene **7** to 2-hydroxypyrroline **11** followed by a 1,5-sigmatropic shift is occurring.

Only pyrrole **12** was isolated in low yield in the reaction of azirine **1b** with ethyl benzoyldiazoacetate **2c** (Scheme 5). After the chromatographic work-up of the reaction mixture no products formed by 1,6-cyclizations of the intermediate 2-azadiene were observed. The structure of pyrrole **12** was determined by standard spectroscopic methods and confirmed by X-ray analysis (Fig. 1). The formation of this compound can be explained by considering the same mechanism as above giving a 2-hydroxypyrrole derivative, which then disproportionates.

The final products of the catalytic reaction of diazoacetoacetate **2c** with 2*H*-azirine-2-carbaldehydes **1** are thereby shown to be the 2-acyl-substituted 2*H*-1,3-oxazines **8**, but these then undergo a rapid rearrangement under chromatographic purification conditions. That the oxazines **8** are the preferable structures in the reaction was confirmed by quantum-chemical calculations of ring-opening of isomeric *E*- and *Z*-ylides **13** to isomeric 2-azazadienes *E*-**14** and *Z*-**14**, followed by their interconversions via N-inversion and 1,6-cyclizations to 1,3- and 1,4-oxazines **15** and **16** (Scheme 6).

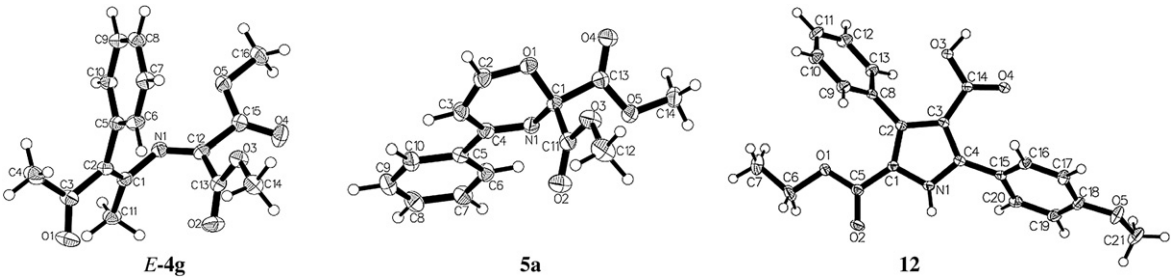
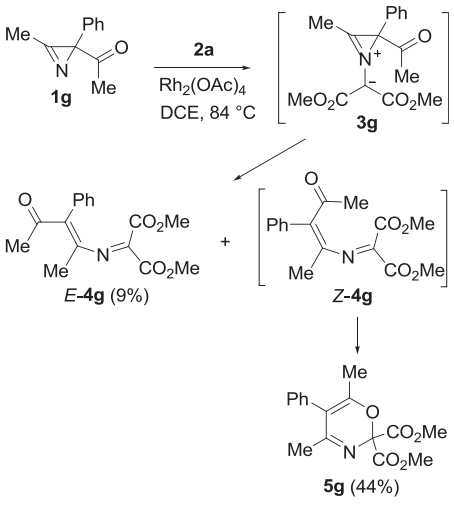
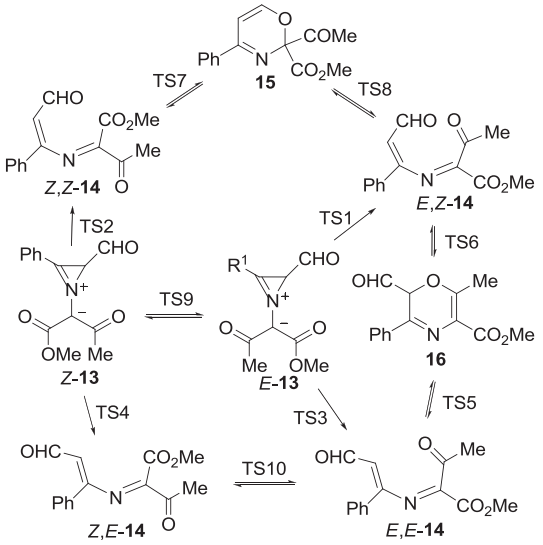


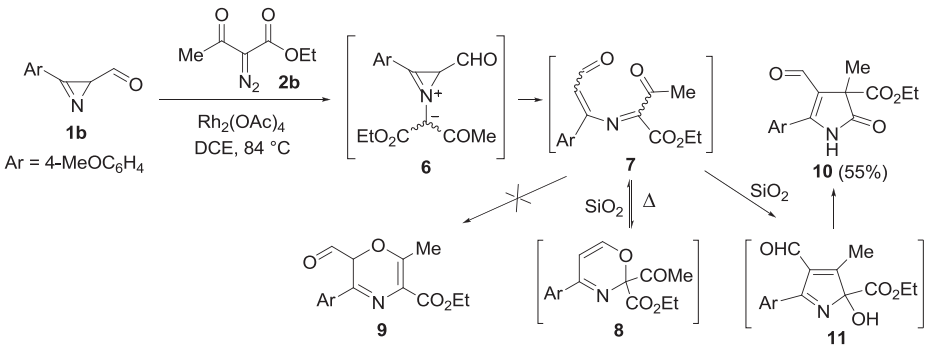
Fig. 1. X-ray structure of compounds *E*-**4g**, **5a**, and **12**.



Scheme 3. $Rh_2(OAc)_4$-catalyzed reaction of azirine **1g** with dimethyl diazomalonate **2a**.

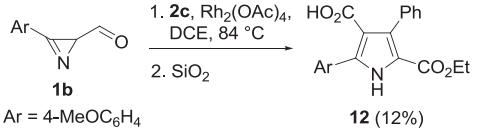


Scheme 6. The transformation of azirinium ylides *E*-**13** and *Z*-**13** into oxazines **15**, **16**.



Scheme 4. $Rh_2(OAc)_4$-catalyzed reaction of azirine **1b** with ethyl diazoacetoacetate **2b**.

The geometries of ylides *E*-**13**, *Z*-**13**, azadienes *E*,*E*-, *E*,*Z*-, *Z*,*E*-, and *Z*,*Z*-**14**, 1,3-oxazine **15**, 1,4-oxazine **16**, as well as the transition states of ring opening of ylides **13** (TS^1–TS^4), 1,6-cyclizations of azadienes **14** in oxazines **15**, **16** (TS^5–TS^8), *E*,*Z*-isomerization of ylides **6a**–**c** (TS^9) and isomerization of azadienes **14** (TS^{10}) were optimized at the DFT mPWB1K/6-31+G(d,p) level[12] using the PCM solvent model for 1,2-dichloroethane (Scheme 6).



Scheme 5. $Rh_2(OAc)_4$-catalyzed reaction of azirine **1b** with ethyl 2-benzoyl-2-diazoacetate **2c**.

The energy of the most stable conformation of each isomeric azadiene was used for calculations of the activation free energies (Fig. 2).

Computations show that the ring-opening of the isomeric ylides *E*- and *Z*-**13** to azadienes **14** must occur with high stereoselectivity to give the *E*,*Z*- and *Z*,*Z*-isomers, both having exclusively a *Z* configuration of the C=C bond: the energies of TS1 and TS2 are higher than those of TS3 and TS4 by 3–4 kcal/mol. Activation energies of azadienes *E*,*Z*- and *Z*,*Z*-**14** formation are about 9–11 kcal/mol and are comparable to the barrier values for their 1,6-cyclization to 1,3-oxazine **15** (11–12 kcal/mol). Considering that fact that the free energy for 1,3-oxazine **15** is lower than the energy of any azadiene isomer 14, one can conclude that the 1,6-cyclization of **14** to **15** is a kinetically and thermodynamically favorable process. 1,4-Oxazine **16** can be formed either from *E*,*Z*-**14** or *E*,*E*-**14**, the last of, which

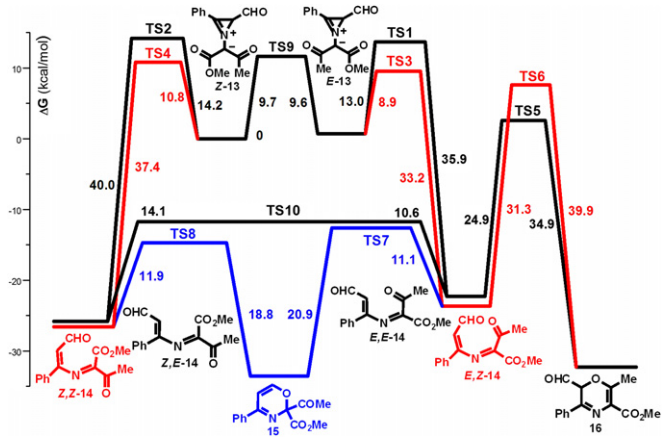


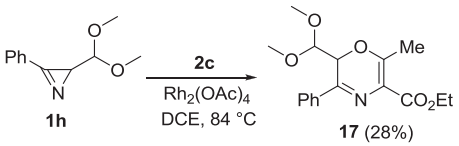
Fig. 2. Energy profiles (mPWB1K/6-31+G(d,p), kcal/mol, 357.15 K) for the transformations of ylides *E*-**13**, *Z*-**13** to oxazines **15**, **16** in 1,2-dichloroethane.

cyclizes much more rapidly. But as was mentioned above the *E*,*E*-**14** isomer does not form in the reaction, and the 1,4-oxazine **16** can therefore arise only from azadiene *E*,*Z*-**14** via transition state TS6 with an extremely high activation barrier (31.3 kcal/mol). This route of stabilization of the azadiene *E*,*Z*-**14** cannot compete with its 1,6-cyclization to 1,3-oxazine **15** proceeding with $\Delta G^{\neq}=12$ kcal/mol. On the other hand, the more preferable 1,4-oxazine **16** precursor, *E*,*E*-**14**, can be formed from *Z*,*E*-**14** via N-inversion of the C=N bond (TS10, Fig. 2), the activation barrier of, which is 14.1 kcal/mol. A sufficiently low activation barrier, however, was evaluated for ring-opening of ylide *Z*-**13** to *Z*,*Z*-isomer but not to *Z*,*E*-**14**.

From the analysis of transition states TS5, TS6 structures one can suppose that one of the reasons for such a dramatic influence of the configuration of the C=C bond of azadiene on the barrier of its cyclization to the 1,4-oxazine is in disturbance of the conjugation in the transition state of the azadiene system with the formyl group, located cis to nitrogen. According to the calculations dihedral angle C3–C4–C=O in transition state TS6 is 75.2°, while in TS5 this value is only 17.7°.

Hence, the main reason for the absence of 2*H*-1,4-oxazine derivatives among the products of the reaction is *Z*-stereoselectivity of ring opening of the ylide intermediate.

In azadiene **1h**, with a protected formyl group, derived from azirine **1h** and diazo compound **2c**, the cyclization to 1,3-oxazine is blocked, and 1,4-oxazine **17** was isolated as a sole product (Scheme 7).



Scheme 7. $Rh_2(OAc)_4$-catalyzed reaction of azirine **1h** with ethyl 2-benzoyl-2-diazoacetate **2c**.

3. Conclusions

In conclusion, we have reported the first example of a three-atom ring expansion of 2*H*-azirines to 1,3-oxazine system. This transformation is the result of the $Rh_2(OAc)_4$-catalyzed reaction of 2*H*-azirine-2-carbaldehydes with dimethyl diazomalonate. The reaction proceeds via azirinium ylides formation, ring opening to 2-azabuta-1,3-dienes followed by a 1,6-π-electrocyclization to the 2*H*-1,3-oxazines. According to DFT-calculations ring opening of azirinium ylides occurs stereoselectively to give 2-azadienes with the C=C bond exclusively in the *Z* configuration. Changing a formyl group for an acetyl group in the azirine leads to a lowering of stereoselectivity, and the formation of azadienes with an *E* configuration of the C=C bond can be observed. The analogous reaction of 2-acyl-2-diazoacetates proceeds in a similar manner, but the final 2-acetyl-substituted 2*H*-1,3-oxazines are unstable under chromatographic purification conditions and rearrange into pyrrole derivatives.

4. Experimental section

4.1. General methods

Melting points were determined on a hot stage microscope and are uncorrected. ^{1}H (300 MHz) and ^{13}C (75 or 150 MHz) NMR spectra were determined in $CDCl_3$ and DMSO-d_6. Chemical shifts (δ) are reported in parts per million downfield from tetramethylsilane. Electrospray ionization mass spectra were measured on a Bruker micrOTOF mass spectrometer. Elemental analysis was performed on a Hewlett–Packard 185B CHN-analyser. IR spectra were recorded on a SPECORD M80 spectrometer for solutions in $CHCl_3$. Single crystal X-ray data were collected on a Bruker SMART-6000 (compounds **5a** and *E*-**4g**) and on an Agilent Gemini S-Ultra (compound **12**) diffractometers equipped with Cryostream (Oxford Cryosystems) open-flow nitrogen cryostates at 120 K using graphite monochromated (MoKα)-radiation (λ=0.71073 Å). All structures were solved by direct methods and refined by full-matrix least squares on F^2 for all data using SHELXTL[13] and OLEX2[14] software. All non-hydrogen atoms were refined with anisotropic displacement parameters, H-atoms were located on the difference map and refined isotropically. Crystallographic data for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-920501 (for *E*-**4g**), CCDC-920502 (for **5a**), and CCDC-920503 (for **12**). Silica gel Merck 60 was used for column chromatography. Thin-layer chromatography (TLC) was conducted on alumina sheets precoated with SiO_2 ALUGRAM SIL G/UV_{254}. Compounds **1a**–**g**,[15] and **2a**,[16] **b**,**c**[17] were prepared by the reported procedures.

4.2. Calculation details

All calculations were performed with the mPWB1K density functional method by using the Gaussian 09 suite of quantum chemical programs.[18] Geometry optimizations of intermediates, transition states, reactants, and products in 1,2-dichloroethane were performed at the DFT mPWB1K/6-31+G(d,p) level using PCM model. Stationary points on the respective potential-energy surfaces were characterized at the same level of theory by evaluating the corresponding Hessian indices. Careful verification of the unique imaginary frequencies for transition states was carried out to check whether the frequency indeed pertains to the desired reaction coordinate. Intrinsic reaction coordinates (IRC) were calculated to authenticate the transition states.

4.3. Reactions of azirines 1a–f with diazo compounds 2a–c

4.3.1. General procedure. A 1.0 M solution of diazo compound **2a**–**c** in anhydrous 1,2-dichloroethane (DCE) was added dropwise with a syringe at a rate of 1.0 mL/h to a stirred 1.0 M solution of azirine **1a**–**f** and $Rh_2(OAc)_4$ (7 mol % on azirine) in anhydrous DCE at reflux under an argon atmosphere until the azirine was consumed completely (control by TLC). The solvent was evaporated in vacuo, and the residue was purified by column chromatography on silica gel (eluent hexane/EtOAc) to give, after crystallization from the solvent indicated below, compound **5a**–**g**.

*4.3.2. Dimethyl 4-phenyl-2H-1,3-oxazine-2,2-dicarboxylate (**5a**).* Compound **5a** was prepared according to the general procedure

from azirine **1a** (103 mg, 0.71 mmol) and diazo compound **2a** (112 mg, 0.71 mmol) as a colorless solid (50 mg, 26%). Mp 90–91 °C (hexane/Et_2O); R_f (33% EtOAc/hexane) 0.33; IR (KBr): 3089, 2966, 1756, 1632, 1580, 1534 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$): δ 3.90 (s, 6H, $2CH_3O$), 6.15 (d, 1H, J=5.8 Hz, H-5), 7.14 (d, 1H, J=5.8 Hz, H-6), 7.42–7.53 (m, 3H, ArH), 7.88–7.90 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.6 (2C, CH_3O), 90.7 (C-2), 100.4 (C-5), 127.1, 128.6, 131.5, 135.3 (Ar), 152.5 (C-6), 161.8 (C=O), 166.4 (C-4). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{14}H_{14}NO_5$, 276.0866; found 276.0854. Anal. Calcd for $C_{14}H_{13}NO_5$: C, 61.09; H, 4.76; N, 5.09. Found: C, 61.06; H, 4.60; N, 5.34. Crystal data: $C_{14}H_{13}NO_5$, M=275.25, orthorhombic, a=6.0659(3), b=7.6566(4), c=28.7710(15) Å, V=1336.25(12) $Å^3$, T=120 K, space group $P2_12_12_1$, Z=4, μ(MoKα)=0.105 mm^{-1}, 14,210 reflections measured, 1987 unique (R_{int}=0.0691) were used in all calculations. The final R_1 was 0.0447 (1519>2σ(I)), wR_2=0.1150 (all data).

*4.3.3. Dimethyl 4-(4-methoxyphenyl)-2H-1,3-oxazine-2,2-dicarboxylate (**5b**).* Compound **5b** was prepared according to the general procedure from azirine **1b** (105 mg, 0.6 mmol) and diazo compound **2a** (142 mg, 1.2 mmol) as a light yellow solid (69 mg, 23%). Mp 81–83 °C (hexane/Et_2O); R_f (50% EtOAc/hexane) 0.44; IR (KBr): 2963, 1764, 1633, 1600 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.85 (s, 3H, CH_3O), 3.89 (s, 6H, CH_3O), 6.12 (s, 1H, J=5.8 Hz, H-5), 6.93 (d, 2H, J=8.7 Hz, ArH), 7.11 (d, 1H, J=5.8 Hz, H-6), 7.86 (d, 2H, J=8.7 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.6 (2C, CH_3O), 55.4 (CH_3O), 90.7 (C-2), 100.3 (C-5), 113.8, 127.7, 128.9 (Ar), 152.2 (C-6), 160.8 (Ar), 162.4 (C-4), 166.6 (2C, C=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{15}H_{16}NO_6$, 306.0972; found 306.0968. Anal. Calcd for $C_{15}H_{15}NO_6$: C, 59.01; H, 4.95; N, 4.59. Found: C, 59.02; H, 4.80; N, 4.76.

*4.3.4. Dimethyl 4-(4-chlorophenyl)-2H-1,3-oxazine-2,2-dicarboxylate (**5c**).* Compound **5c** was prepared according to the general procedure from azirine **1c** (108 mg, 0.6 mmol) and diazo compound **2a** (95 mg, 0.6 mmol) as a light yellow oil (78 mg, 42%). ^1H NMR (300 MHz, $CDCl_3$): δ 3.90 (s, 6H, $2CH_3O$), 6.09 (d, 1H, J=5.8 Hz, H-5), 7.14 (d, 1H, J=5.8 Hz, H-6), 7.41 (d, 2H, J=8.5 Hz, ArH), 7.83 (d, 2H, J=8.5 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.7 (2C, CH_3O), 90.6 (C-2), 100.0 (C-5), 128.5, 128.8, 133.6, 137.8 (Ar), 152.8 (C-6), 160.8 (C-4), 166.2 (2C, C=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{14}H_{13}NO_5Cl$, 310.0477; found 310.0471.

*4.3.5. Dimethyl 4-(4-methylphenyl)-2H-1,3-oxazine-2,2-dicarboxylate (**5d**).* Compound **5d** was prepared according to the general procedure from azirine **1d** (70 mg, 0.44 mmol) and diazo compound **2a** (70 mg, 0.44 mmol) as a light yellow solid (45 mg, 35%). Mp 129–131 °C (Et_2O/hexane); R_f (33% EtOAc/hexane) 0.36; IR (KBr): 3086, 2966, 1769, 1754, 1629, 1530 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.40 (s, 3H, CH_3), 3.89 (s, 6H, $2CH_3O$), 6.13 (d, 1H, J=5.8 Hz, H-5), 7.12 (d, 1H, J=5.8 Hz, H-6), 7.24 (d, 2H, J=8.0 Hz, ArH), 7.79 (d, 2H, J=8.0 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.4 (CH_3), 53.6 (2C, CH_3O), 90.7 (C-2), 100.4 (C-5), 127.1, 129.2, 132.5, 142.0 (Ar), 152.3 (C-6), 161.5 (C-4), 166.5 (2C, C=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{15}H_{16}NO_5$, 290.1023; found 290.1029. Anal. Calcd for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84. Found: C, 61.99; H, 5.06; N, 5.08.

*4.3.6. Dimethyl 5-methyl-4-phenyl-2H-1,3-oxazine-2,2-dicarboxylate (**5e**).* Compound **5e** was prepared according to the general procedure from azirine **1e** (100 mg, 0.63 mmol) and diazo compound **2a** (100 mg, 0.63 mmol) as a light yellow oil (30 mg, 17%). ^1H NMR (300 MHz, $CDCl_3$): δ 1.73 (d, 3H, J=1.5 Hz, CH_3), 3.89 (s, 6H, $3CH_3O$), 6.87 (q, 1H, J=1.5 Hz, H-6), 7.42–7.51 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1 (CH_3), 53.6 (2C, CH_3O), 90.0 (C-2), 111.0 (C-5), 128.0, 128.2, 129.8, 136.6 (Ar), 148.0 (C-6), 166.6 (2C, C=O), 167.9 (C-4). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{15}H_{16}NO_5$, 290.1023; found 290.1027.

*4.3.7. Dimethyl 4,5-diphenyl-2H-1,3-oxazine-2,2-dicarboxylate (**5f**).* Compound **5f** was prepared according to the general procedure from azirine **1f** (100 mg, 0.45 mmol) and diazo compound **2a** (107 mg, 0.68 mmol) as a light yellow solid (49 mg, 31%). Mp 71–74 °C (hexane/Et_2O); R_f (33% EtOAc/hexane) 0.39; IR (KBr): 2960, 1765, 1635, 1535 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.93 (s, 6H, $2CH_3O$), 6.98–7.02 (m, 2H, ArH), 7.19–7.39 (m, 9H, H-6, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 53.7 (2C, CH_3O), 90.3 (C-2), 119.1 (C-5), 127.5, 127.8, 128.2, 128.5, 129.2, 130.1, 133.7, 136.0 (Ar), 149.9 (C-6), 165.9 (C-4), 166.4 (2C, C=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{20}H_{18}NO_5$, 352.1179; found 352.1185.

*4.3.8. Dimethyl (E)-2-[(4-oxo-3-phenylpent-2-en-2-yl)imino]malonate (E-**4g**) and dimethyl 4,6-dimethyl-5-phenyl-2H-1,3-oxazine-2,2-dicarboxylate (**5g**).* Azadiene *E*-**4g** (16 mg, 9%) and oxazine **5g** (77 mg, 44%) were prepared according to the general procedure from azirine **1g** (100 mg, 0.58 mmol) and diazo compound **2a** (131 mg, 0.83 mmol). Compound *E*-**4g**, orange solid, mp 54–55 °C (hexane/Et_2O). ^1H NMR (300 MHz, $CDCl_3$): δ 2.03 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.82 (s, 6H, $2CH_3O$), 7.07–7.10 (m, 2H, ArH), 7.28–7.35 (m, 3H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.9 (CH_3), 31.1 (CH_3), 53.1 (2C, CH_3O), 100.1 (C-3), 121.4 (C-2), 127.6, 128.5, 129.7, 136.2 (Ar), 148.5 (C=N), 153.1 (2C, C=O), 200.0 (C=O). Crystal data: $C_{16}H_{17}NO_5$, M=303.3, triclinic, space group P-1, a=8.2133(3), b=8.6001(3), c=12.2957(4) Å, α=97.967(1), β=100.663(1), γ=113.603(1)°, V=759.98(5) $Å^3$, Z=2, T=120 K, μ(MoKα)=0.099 mm^{-1}, 12,704 reflections measured, 4048 unique (R_{int}=0.0315) were used in all calculations. The final R_1 was 0.0398 (3286>2σ(I)) and wR_2 was 0.1173 (all data).

Compound **5g**, colorless solid, mp 103–104 °C (hexane/Et_2O); R_f (50% EtOAc/hexane) 0.37; IR (KBr): 2958, 2924, 2852, 1749, 1658 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.90 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 3.90 (s, 6H, CH_3O), 7.07–7.10 (m, 2H, ArH), 7.31–7.41 (m, 3H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.1 (CH_3), 23.6 (CH_3), 53.5 (2C, CH_3O), 90.2 (C-2), 115.9 (C-5), 127.8, 128.6, 130.2, 134.3 (Ar), 158.2 (C-6), 166.7 (C-4), 166.9 (2C, C=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{16}H_{18}NO_5$, 304.1179; found 304.1199.

*4.3.9. Ethyl 4-formyl-3-methyl-5-(4-methoxyphenyl)-2-oxo-2,3-dihydro-1H-pyrrole-3-carboxylate (**10**).* Compound **10** (143 mg, 55%) was prepared according to the general procedure from azirine **1d** (150 mg, 0.86 mmol) and diazo compound **2b** (334 mg, 2.14 mmol) as a light yellow solid; mp 135–137 °C (Et_2O); R_f (33% EtOAc/hexane) 0.35; IR (KBr): 3176, 2981, 2940, 1750, 1713, 1644, 1602 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.21 (t, 3H, J=7.3 Hz, CH_3), 1.72 (s, 3H, CH_3), 3.91 (s, 3H, CH_3O), 4.12–4.27 (m, 2H, CH_2), 7.06 (d, 2H, J=8.7 Hz, ArH), 7.60 (d, 2H, J=8.7 Hz, ArH), 9.26 (s, 1H, NH), 9.64 (s, 1H, HC=O). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (CH_3), 18.8 (CH_3), 55.6 (CH_3O), 56.7 (C-3), 62.0 (CH_2), 114.8, 119.3, 121.2, 130.4, 157.1, 162.7, 167.6, 178.0, 184.0 (Ar, NC=O, OC=O, HC=O). HRMS (ESI-TOF, $[M+K]^+$): calcd for $C_{16}H_{17}NO_5K$, 342.0738; found 342.0757. Anal. Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 62.96; H, 5.49; N, 4.76.

*4.3.10. 5-(Ethoxycarbonyl)-2-(4-methoxyphenyl)-4-phenyl-1H-pyrrole-3-carboxylic acid (**12**).* Compound **12** (25 mg, 12%) was prepared according to the general procedure from azirine **1d** (100 mg, 0.57 mmol) and diazo compound **2c** (311 mg, 1.43 mmol) as a light yellow solid; mp 233–235 °C (Et_2O); R_f (33% EtOAc/hexane) 0.43; IR (KBr): 3279, 2988, 1661, 1612, 1561 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 1.02 (t, 3H, J=6.9 Hz, CH_3), 3.81 (s, 3H, CH_3O), 4.04 (q, 2H, J=6.9 Hz, CH_2), 7.00 (d, 2H, J=8.7 Hz, ArH), 7.29 (s, 5H, ArH), 7.52 (d, 2H, J=8.7 Hz, ArH), 11.93 (s, 1H, NH), 12.23 (s, 1H, CO_2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 14.7 (CH_3), 56.1 (CH_3O), 60.4 (CH_2), 114.1, 115.8

(C-4), 119.8 (C-3), 124.2, 127.3, 127.7, 130.9, 131.5, 132.9 (Ar), 135.7 (C-2), 138.7, 160.2 (Ar), 161.0, 166.9 (HOC=O, EtOC=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{21}H_{20}NO_5$, 366.1336; found 366.1343. Crystal data: $C_{21}H_{19}NO_5$, M=365.37, triclinic, a=6.9306(3), b=11.6562(8), c=12.6699(10) Å, α=102.477(6), β=91.596(5), γ=106.323(5)°, V=954.79(11) Å^3, T=120 K, space group P-1, Z=2, μ(MoKα)=0.091 mm^{-1}, 11,472 reflections measured, 5312 unique (R_{int}=0.0292) were used in all calculations. The final R_1 was 0.0447 ($4168>2\sigma(I)$) and wR_2 was 0.1094 (all data).

*4.3.11. Ethyl 2-(dimethoxymethyl)-6-methyl-3-phenyl-2H-1,4-oxazine-5-carboxylate (**17**).* Compound **17** was prepared according to the general procedure from azirine **1h** (220 mg, 1.15 mmol) and diazo compound **2b** (450 mg, 2.9 mmol) as a light yellow oil (104 mg, 28%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (t, 3H, J=6.9 Hz, CH_3), 2.42 (s, 3H, CH_3), 3.26 (s, 3H, CH_3O), 3.49 (s, 3H, CH_3O), 4.32–4.40 (m, 2H, CH_2), 4.55 (d, 1H, J=7.6 Hz, CH), 5.32 (d, 1H, J=7.6 Hz, CH), 7.40–7.42 (m, 3H, ArH), 7.99–8.02 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.4 (CH_3), 17.9 (CH_3), 53.2, 56.6 (CH_3O), 60.6 (CH_2), 69.8 (C-6), 99.2 (CH), 120.1 (C-3), 127.4, 128.2, 130.2, 135.6 (Ar), 148.3 (C-2), 155.1 (C-5), 165.5 (C=O). HRMS (ESI-TOF, $[M+H]^+$): calcd for $C_{17}H_{22}NO_5$, 320.1492; found 320.1476.

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Supplementary data

^{1}H, ^{13}C NMR spectra of all new compounds and Cartesian coordinates of optimized structures can be found online. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.04.022. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Sanchez, E. L. *J. Am. Chem. Soc.* **1983**, *105*, 2021–2029; (b) Wenkert, E.; Halls, T. D. J.; Kwart, L. D.; Magnusson, G.; Showalter, H. D. H. *Tetrahedron* **1981**, *37*, 4017–4025; (c) Alonso, M. E.; Jano, P.; Hernandez, M. I.; Greebnerg, R. S.; Wenkert, E. *J. Org. Chem.* **1983**, *48*, 3047–3050; (d) Alonso, M. E.; Morales, A.; Chitty, A. W. *J. Org. Chem.* **1982**, *47*, 3747–3754.
2. (a) Davies, H. M. L.; Yong, W. B.; Smith, H. D. *Tetrahedron Lett.* **1989**, *30*, 4653–4656; (b) Davies, H. M. L.; Saikali, E.; Young, W. B. *J. Org. Chem.* **1991**, *56*, 5696–5700; (c) Davies, H. M. L.; Matasi, J. J.; Hodges, L. M.; Huby, N. J. S.; Thornley, C.; Kong, N.; Houser, J. H. *J. Org. Chem.* **1997**, *62*, 1095–1105; (d) Davies, H. M. L.; Ahmed, G.; Churchill, M. R. *J. Am. Chem. Soc.* **1996**, *118*, 10774–10780; (e) Davies, H. M. L.; Huby, N. J. S. *Tetrahedron Lett.* **1992**, *33*, 6935–6938.
3. (a) Alonso, M. E.; Garcia, M. C. *J. Org. Chem.* **1985**, *50*, 988–992; (b) Gillespie, R. J.; Porter, A. E. A. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2624–2628; (c) Maryanoff, B. E. *J. Org. Chem.* **1979**, *44*, 4410–4419; (d) Maryanoff, B. E. *J. Org. Chem.* **1982**, *47*, 3000–3002.
4. Manning, J. R.; Davies, H. M. L. *J. Am. Chem. Soc.* **2008**, *130*, 8602–8603.
5. Yoshimoto, M.; Ishihara, S.; Nakayama, E.; Soma, N. *Tetrahedron Lett.* **1972**, *13*, 2923–2926.
6. (a) Kametani, T.; Kawamura, K.; Tsubuki, M.; Honda, T. *J. Chem. Soc., Chem. Commun.* **1985**, 1324–1325; (b) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655–3669; (c) Tamura, Y.; Takebe, Y.; Mukai, C.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2978–2981; (d) Crow, W. D.; Gosney, I.; Ormiston, R. A. *J. Chem. Soc., Chem. Commun.* **1983**, 643–644; (e) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; van Leusen, D. *J. Org. Chem.* **1984**, *49*, 1917–1925; (f) Manning, J. R.; Davies, H. M. L. *Tetrahedron* **2008**, *64*, 6901–6908.
7. (a) Vedejs, E.; Hagen, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 6878–6879; (b) Vedejs, E.; Hagen, J. P.; Roach, B. L.; Spear, K. L. *J. Org. Chem.* **1978**, *43*, 1185–1190; (c) Nickon, A.; Rodriguez, A. D.; Ganguly, R.; Shirhatti, V. *J. Org. Chem.* **1985**, *50*, 2767–2777; (d) Ceré, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1981**, *46*, 486–490.
8. (a) Kametani, T.; Kanaya, N.; Mochizuki, T.; Honda, T. *Tetrahedron Lett.* **1983**, *24*, 221–224; (b) Meth-Cohn, O.; Vuorinen, E. *J. Chem. Soc., Chem. Commun.* **1988**, 138–140; (c) Yamagata, K.; Ohkubo, K.; Yamazaki, M. *Liebigs Ann. Chem.* **1995**, 187–190; (d) Kametani, T.; Kanaya, N.; Mochizuki, T.; Honda, T. *Tetrahedron Lett.* **1983**, *24*, 1511–1512; (e) Kametani, T.; Kanaya, N.; Nakayama, A.; Yokohama, S.; Honda, T. *J. Org. Chem.* **1986**, *51*, 1120–1123.
9. (a) Palacios, F.; Ochoa de Retana, A. M.; Marigorta, E. M.; de los Santos, J. M. In *Recent Developments in Heterocyclic Chemistry*; Pinho e Melo, T. M. V. D., Rocha-Gonsalves, A. M. A., Eds.; Research Signpost: Trivandrum, India, 2007; pp 27–58; (b) Alves, M. J.; Teixeira Costa, F. In *Heterocyclic Targets in Advanced Organic Synthesis*; do CarmoCarreiras, M., Marco-Contelles, J., Eds.; Research Signpost: Trivandrum, India, 2011; pp 145–172; (c) Pinho e Melo, T. M. V. D.; d'A Rocha Gonsalves, A. M. *Curr. Org. Synth.* **2004**, *1*, 275–292; (d) Padwa, A. *Adv. Heterocycl. Chem.* **2010**, *99*, 1–31; (e) Padwa, A. In *Comprehensive Heterocyclic Chemistry III*; Elsevier: Oxford, UK, 2008; Vol. 1, pp 82–95.
10. (a) Khlebnikov, A. F.; Novikov, M. S.; Amer, A. A. *Tetrahedron Lett.* **2004**, *45*, 6003–6006; (b) Khlebnikov, A. F.; Novikov, M. S.; Amer, A. A.; Kostikov, R. R.; Magull, J.; Vidovic, D. *Russ. J. Org. Chem.* **2006**, *42*, 515–526.
11. Khlebnikov, V. A.; Novikov, M. S.; Khlebnikov, A. F.; Rostovskii, N. V. *Tetrahedron Lett.* **2009**, *50*, 6509–6511.
12. Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 6908–6918.
13. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **2008**, *64*, 112–122.
14. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Crystallogr.* **2009**, *42*, 339–341.
15. Brahma, S.; Ray, J. K. *J. Heterocycl. Chem.* **2008**, *45*, 311–317.
16. Julian, R. R.; May, J. A.; Stoltz, B. M.; Beauchamp, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 4478–4486.
17. Davies, J. R.; Kane, P. D.; Moody, C. J. *Tetrahedron* **2004**, *60*, 3967–3977.
18. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision C.01*; Gaussian: Wallingford, CT, 2010.