**A Quantitative Analysis of Factors Influencing Ease of Formation and**

**σ-Bonding Strength of Oxa- and Thia-N-Heterocyclic Carbenes**

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**ABSTRACT:** The index described previously (CREF; Carbene Relative Energy of Formation) has been extended to oxygen and sulfur heterocycles. This provides a quantitative overview of factors determining ease of formation of (i) neutral N-heterocyclic carbenes (NHCs) by deprotonation of heterocyclic salts and (ii) anionic NHCs by deprotonation of heterocyclic mesomeric betaines (HMBs). The influence of the nature and ring position of oxygen and sulfur is discussed for a range of known and unknown systems. Attention is directed to unexplored systems of potential interest.

**1. INTRODUCTION**

We have previously described a DFT-computed index to quantify the relative ease of formation of neutral and anionic N-heterocyclic carbenes (NHCs) derived from nitrogen heterocycles.1 For convenience, we describe this as the CREF index (Carbene Relative Energy of Formation). To complete this study, we now report calculations of CREF index values for a wide range of NHCs derived from heterocycles containing oxygen and sulfur in addition to nitrogen. This index provides a quantitative overview of the factors affecting ease of formation of NHCs and their σ-donor strength, and directs attention to novel NHCs of potential interest. In accord with the Hammond postulate,2 we also demonstrate that the index correlates with experimentally determined rates of deprotonation/proton exchange of NHC precursors.

Using DFT (B3LYP/6-311++G(d,p)) calculated energy values (E + ZPE) in the gas phase, the CREF index is the difference in energy between the precursor and NHC product. It is a measure of the energy (hartrees) required to break heterolytically a C-H bond, and for similar heterocycles with similar solvation it is a quantitative index of the relative ease of NHC formation.

The index is illustrated in Figure 1 by application to the heterocyclic cations **1-3** which upon deprotonation give neutral NHCs. A lower index signifies easier deprotonation. The CREF values shown in structures **1-3** clearly indicate that deprotonation at position 2 is easier than at position 4. The oxazolium ring **2** is more easily deprotonated than the imidazolium ring **1** and this is attributable to the greater electronegativity of oxygen. A similar, but slightly smaller, effect is seen with sulfur (**3**) and this cannot be attributed to electronegativity. The sulfur effect must arise from d-orbital participation in the σ-bonding framework. Significantly, this is not a localised interaction between adjacent centres since a comparable effect is seen at position 4 which is remote from the sulfur.





**Figure 1.** CREF Index values for selected heterocycles

The same trends are seen in the formation of anionic NHCs. Diarylimidazolium-4-olates, e.g. **4**, are selectively deprotonated by strong base (LiHMDS) at position 2 (CREF 0.556, Figure 1).3-5 No evidence of deprotonation at position 5 (CREF 0.600) to form the alternative abnormal NHC (aNHC) has been observed. However, *N*-phenylsydnone **5** (CREF 0.572) does form an aNHC under similar conditions.6 Easier formation of an aNHC by the sydnone is reflected in the lower CREF value (0.572 vs 0.600) and this can be attributed to the greater electronegativity of oxygen, and the nitrogen at position 2. The *N*-phenylthiadiazolium-5-thiolate **6** is one of the oldest known mesoionic rings7,8 but, as far as we are aware,9,10 products derived via NHC formation have never been reported. This is interesting because the CREF value at position 2 (0.530) is particularly low.

**2. RESULTS AND DISCUSSION**

**2.1 Neutral Five-membered NHCs.** Tables 1 and 2 show calculated CREF values for NHC structures derived from 1,3-dihetero (Table 1) and 1,2-dihetero (Table 2) precursors. Some previously calculated values for nitrogen-only heterocycles are included for comparison. NHCs with two α-heteroatoms are described as classical NHCs (Table 1(i)); NHCs with only one α-heteroatom are described as nonclassical NHCs (Table 2(i)). Systems that can be represented by sextet structures are described as normal (nNHCs)(Tables 1(i) and 2(i)). Abnormal NHCs (aNHCs)(Table 1(ii)) and remote NHCs (rNHCs) (Table 2(ii)) can only be represented by dipolar resonance forms.11,12 In the latter case (rNHCs) there is no 2π-heteroatom adjacent to the carbene centre.

The ring systems shown in Tables 1 and 2 have been selected to give a broad overview of the variation of CREF index with type and position of heteroatoms. Inclusion does not imply feasible access to or inherent stability of either reactant or product.

**Table 1 Neutral NHCs: Sulfur and Oxygen Analogues of Imidazole-ylidenes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Entry** | **PRECURSOR NHC** | **E + ZPEa,b** | **CREF**  |
|  ***(i) Classical Normal NHCs (nNHCs)*** |
| 1 |  | -305.167859-304.754800 | 0.413c |
| 2 |  | -688.634081-688.216748 | 0.417 |
| 3  |  | -321.201501-320.807395 | 0.394c |
| 4 |  | -285.716448-285.328690 | 0.388 |
| 5 |  | -608.708163-608.312426 | 0.396 |
| 6 |  | -800.442510-800.041587 | 0.401 |
| 7 |  | -762.352057-761.952050 | 0.400 |
| 8 |  | -624.736835-624.359849 | 0.377 |
| 9 |  | -911.143501-910.744944 | 0.399 |
| 10 |   | -266.254393-265.903008 | 0.351 |
| 11 |   | -912.243585-911.867802 | 0.376 |
|  ***(ii) Abnormal NHCs (aNHCs)*** |  |  |
| 12 |  | -305.167859-304.725728 | 0.442c |
| 13 |  | -285.716448-285.302836 | 0.414 |
| 14 |  | -285.716448-285.294159 | 0.422 |
| 15 |  | -608.708163-608.287788 | 0.420 |
| 16 |  | -608.708163-608.287089 | 0.421 |
| 17 |  | -624.736835-624.333941 | 0.403 |
| 18 |   | -624.723513-624.323581 | 0.400 |
| 19 |  | -624.723513-624.327161 | 0.396 |
| 20 |   | -266.254393-265.866562 | 0.388 |

aHartrees, bFirst value relates to reactant and the second to product, cTaken from reference 1.

 **Table 2 Neutral NHCs: Sulfur and Oxygen Analogues of Pyrazol-ylidenes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Entry** | **PRECURSOR NHC** | **E + ZPEa,b** |  **CREF**  |
|  ***(i) Nonclassical Normal NHCs (nNHCs)*** |
| 1 |  | -305.136545-304.703725 | 0.433c |
| 2 |  | -285.676102-285.282184 | 0.394 |
| 3 |  | -285.676102-285.269021 | 0.407 |
| 4 |  | -439.319435-438.920033 | 0.399 |
| 5 |  | -439.308968-438.967464 | 0.342 |
| 6 |  | -608.695972-608.293077 | 0.403 |
| 7 |  | -608.695972-608.288722 | 0.407 |
| 8 |   | -912.250286-911.875628 | 0.375 |
| 9 |   | -928.280828-927.920783 | 0.360 |
| 1. ***Remote NHCs (rNHCs)***
 |  |  |
| 10 |  | -305.136545-304.678400 | 0.458c |
| 11 |  | -285.676102-285.248937 | 0.427 |
| 12 |  | -608.695972-608.263913 | 0.432 |
| 13 |   | -266.182595-265.794952 | 0.388 |
| 14 |   | -912.250286-911.841856 | 0.408 |
| 15 |   | -928.280828-927.883121 | 0.398 |

aHartrees, bFirst value relates to reactant and the second to product, cTaken from reference 1.

Inspection of Table 1(i) (entries 4,5 and 8) reveals that replacement of a ring NMe group by O or S results in a lower CREF value and thus greater ease of NHC formation by C-H bond cleavage, but weaker NHC σ-donor strength. Similar effects of O and S are observed for the corresponding aNHCs (Table 1(ii)) and for the pyrazol-ylidene analogues (Table 2). The effect of replacement of NMe by oxygen (ca 0.025 ±0.005 units) is attributable to oxygen’s greater electronegativity; replacement of both NMe groups by oxygen atoms approximately doubles the effect (ca 0.055 ±0.005 units). However, oxygen has disadvantages since its electronegativity facilitates nucleophilic attack and/or ring opening.13 As a result, little has been reported on the chemistry of 1,3-oxazol-ylidenes,14 although examples of transition metal complexes of 1,3-oxazol-2-ylidenes (Table 1; entry 4)15 and 1,3-oxazol-4-ylidenes (Table 1; entry 13)13 have been reported, and 1,3-oxazol-2-ylidenes (Table 1; entry 4) have been the subject of a theoretical investigation.14

For isoxazolium cations the proton at position 3 is the most acidic (Table 2; entries 2 and 3) and deprotonation at position 3 leads to rapid ring opening in accord with their use as coupling reagents.16 1,2-Benzisoxazolium salts (Table 2; entry 4) are also readily deprotonated and have also been used as coupling agents.17 It is interesting to note that the 2,1-benzisoxazolium proton (Table 2; entry 5) is significantly more acidic, which is consistent with its ease of abstraction by triethylamine.18

A ring sulfur also lowers CREF values (ca 0.02-0.03 units) relative to nitrogen without any adverse electronegativity effect. The chemistry of thiazol-2-ylidenes, for example, is well known,12,19 including the classic work on thiamine by Breslow.20 The larger effects (0.03 units) are seen in the pyrazol-ylidene analogues (Table 2). Two sulfur atoms have approximately double the effect (ca 0.04-0.06 units) (Table 1; entry 11 and Table 2; entry 14) and 1,3-dithiolylium salts (Table 1; entry 11) are easily deprotonated at position 2 (CREF 0.376).21 The effect of sulfur is often attributed to d-orbitals but this does not seem to be a simple 2p-3d interaction between adjacent atoms since remote sulfurs have similar effects to adjacent sulfurs (Table 1; entries 12, 15, 16 and Table 2; entries 10, 12, 14 ).

The influence of aza substitution is similar to that observed in the imidazole/pyrazole series.1 A pyridine-type nitrogen reduces CREF values by ca 0.02 units, indicative of a weaker C-H bond. As previously observed, the effect is smaller (ca 0.01 units) if the carbene centre is adjacent to the nitrogen σ lone pair (e.g., Table 1; entry 17 and Table 2; entry 15).1,22 Replacement of NMe by NPh results in a small increase of CREF value (ca 0.005)(Table 1; entries 2 and 6) with the phenyl substituents calculated to be twisted relative to the heterocyclic ring (30-40o).

 In accord with the variation of CREF values described above, there is good correlation between reported pKa values in water at 25 oC 23 and CREF values for the C(2)-protons of the 1,3-dimethylimidazolium, 3-methylthiazolium and 3-methyloxazolium cations (Table 3). Although limited, the linear correlation of these three pKa values with CREF (Table 3) is good (r2 0.986) and suggests that lowering CREF by 0.01 units corresponds to a reduction of pKa by 2.4. This is in accord with the measured aqueous pKa values of a series of bicyclic 1,2,4-triazolium salts which are in the range 16.5-18.5.24 These authors conclude that pKa values for triazolium salts are 5 pKa units lower than for corresponding imidazolium salts, indicating the influence of an extra ring nitrogen atom on acidity. The corresponding difference in CREF values (Table 1; entries 1 and 3) is 0.019 in good agreement with our conclusions based on the data in Table 3. Since pKa is an equilibrium property, this correlation is in accord with the definition of the CREF index,1 which is a measure of C-H bond strength.

We also find satisfactory agreement with kinetic data, in accord with the Hammond postulate for systems in which the transition state is product-like. Table 3 also compares the CREF values with rate constants (kOH) for deprotonation at C(2) of three azolium cations by OH-/H2O.23 These rate constants are in good agreement with the previously reported values for H-isotope exchange in OD-/D2O of the corresponding 4-methyl cations.25,26

**Table 3. pKa Values,23 Deprotonation Rates (kOH),23 and CREF Values for Heterocations**

|  |  |  |  |
| --- | --- | --- | --- |
| Property |  |  |  |
| pKa | 23.0 | 19.5 | 16.9 |
| kOH(M-1s-1) | 1.0 x 102 | 3.4 x 105 | 3.0 x 107 |
| CREF | 0.413 | 0.396 | 0.388 |

**Table 4. Relative Rates of H-D exchange,27 and CREF indexesa**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Property | Proton |  |  |  |
| Relative rate [CREF] | H2 | 1.0[0.396] | 3 x 103[0.377] | -- |
| Relative rate [CREF] | H4 | <10-4[0.420] | -- | 4 x 10-3[0.400] |
| Relative rate [CREF] | H5 | ̴10-4[0.421] | 2 x 10-1[0.403] | 5 x 10-1[0.396] |
| aCREF values for NMe analogues (Table 1) |

Table 4 compares the relative rates of H-D exchange for the ring protons in the 3-ethylthiazolium cation and its 4-aza and 2-aza analogues.27 The rates correlate satisfactorily with CREF values. However, some caution should be applied to protons with similar CREF values since other factors including solvent and counterion will influence reaction kinetics.

Based on the rate constants shown in Tables 3 and 4, a reduction of CREF by ca 0.02 units results in a rate increase in the range 103-104. This is in good agreement with the relative rates of exchange (3 x 104 : 1) of imidazolium C(2)-H (CREF 0.413) and pyrazolium C(3)-H (CREF 0.433) protons (Table 1; entry 1 and Table 2; entry 1).28 This conclusion is also in accord with the observation that the relative rates of proton exchange at position 2 of *N-*methyloxazolium and *N*-methylthiazolium rings (Table 1, entries 4 and 5; ΔCREF 0.008) are approximately 40 to 1.29

Based on published experimental studies of the generation of nNHCs from azolium salts, we conclude that protons with a CREF value ≤ 0.405 can probably be effectively deprotonated by triethylamine for preparative work,30-33 whereas protons with higher CREF values need a stronger base, such as tBuOK or NaH, e.g., Table 1; entry 1.34,35 This must be viewed as an approximate guideline based on published data.

**2.2 Anionic NHCs (Tables 5 and 6)** Anionic NHCs are formed by proton removal from heterocyclic mesomeric betaines (HMBs),36,37 and are of current interest as potential metal ligands. Tables 5 and 6 shows CREF values of a representative selection of anionic NHCs. The tables are subdivided according to the three fundamentally different types of HMB:37,38 conjugated (Table 5), cross-conjugated (Table 6A) and semiconjugated (Table 6B). Further subdivision is according to type of NHC (nNHC, aNHC or rNHC).

From inspection of Tables 1 and 5, it is clear that CREF values for anionic NHCs are significantly higher than those for neutral NHCs. This difference is related to the energy cost of separating a proton from the anionic species. Although similar trends between structural features and CREF values are observed for both neutral and anionic species, direct comparison of their CREF values must be cautious since solvation and counterion association for the two processes are significantly different.

*2.2.1 Conjugated Heterocyclic Mesomeric Betaines (Table 5).* For conjugated HMBs the classical nNHCs (Table 5, entries 1-18) are significantly more easy to generate than the corresponding nonclassical NHCs (Table 5; entries 19-30). Varying heteroatoms has a similar but smaller effect to that in neutral NHCs (Section 2.1). Thus, aza substitution lowers CREF values by *ca* 0.02 ± 0.005 but less if the carbene centre is next to a lone pair. Replacement of NR by S or O lowers CREF values by *ca* 0.010 ± 0.005 and 0.015 ± 0.005 units, respectively. In Section 1 we attributed the influence of electronegative oxygen and aza substitution in facilitating the formation of an anionic abnormal NHC by *N*-phenylsydnone (Table 5; entry 27).6 Similarly, the CREF value calculated for a sydnone imine (0.574)(Table 5; entry 28) is consistent with recent reports of the trapping of sydnone imine aNHCs.39

The replacement of NMe by NPh in anionic NHC rings is of some interest. This results in a lower CREF value of *ca* 0.01 units per NPh (Table 5; entries 2, 11, 20 and 27), which is the opposite to the effect in neutral NHCs (Table 1). Significantly, the NPh groups in anionic NHCs are calculated to be coplanar with the NHC ring, which presumably leads to some conjugative stabilisation. In the corresponding precursor HMBs the rings are twisted.

Since *N*-phenylsydnone (**5**) and 3-phenyl-1,3,4-thiazolium-5-thiolate (**6**) are known compounds of particular interest, we have also calculated CREF values using an *ab initio* method (MP2/aug-cc-pVDZ). The calculated CREF values (Table 5; entries 11 and 27) closely agree with those calculated by the DFT method, and the geometries of precursor and product were similar for both methods. The actual value of a computed index will always depend on the computational method used (e.g. NICS aromaticity indexes).40

**Table 5 Anionic NHCs: Conjugated HMBs**

|  |  |  |  |
| --- | --- | --- | --- |
| **Entry** |  **PRECURSOR NHC** | **E + ZPEa,b** | **CREF**  |
|  ***(i) Normal NHCs (nNHCs)*** |  |  |
| 1 |  | -380.031212-379.455354 | 0.576c |
| 2 |  | -763.491425-762.934980 | 0.556 |
| 3 |  | -360.613695-360.046979 | 0.557 |
| 4 |   | -360.601247-360.040248 | 0.561 |
| 5 |  | -683.591809-683.023727 | 0.568 |
| 6 |   | -683.590143-683.028940 | 0.561 |
| 7 |  | -396.086832-395.525576 | 0.561c |
| 8 |  | -779.547276-779.006250 | 0.541 |
| 9 |  | -376.665893-376.118299 | 0.548 |
| 10 |  | -1022.60133-1022.06421 | 0.537 |
| 11 |  | -1214.33015-1213.80030*-1211.96815**-1211.43956* | 0.530*0.529*d |
| 12 |  | -420.252178-419.679517 | 0.573c |
| 13 |  | -723.820170-723.257556 | 0.563 |
| 14 |  | -400.821266-400.261947 | 0.559 |
| 15 |  | -420.262979-419.639794 | 0.623c |
| 16 |   | -381.402610-380.800705 | 0.602 |
| 17 |   | -1027.39854-1026.80372 | 0.595 |
| 18 |   | -684.530148-683.955934 | 0.574 |
|  ***(ii) Abnormal and Remote NHCs*** |  |  |
| 19 |  | -380.031212-379.412162 | 0.619c |
| 20 |   | -763.491425-762.891366 | 0.600 |
| 21 |  | -360.613695-360.006784 | 0.607 |
| 22 |   | -360.601247-359.988060 | 0.613 |
| 23 |  | -683.591809-682.986888 | 0.605 |
| 24 |   | -683.590143-682.986182 | 0.603 |
| 25 |  | -396.063795-395.465502 | 0.598 |
| 26 |  | -376.622968-376.043373 | 0.580 |
| 27 |  | -568.350935-567.779345*-566.718290**-566.154630* | 0.572*0.564*d |
| 28 |  | -509.377363-508.802881 | 0.574 |
| 29 |   | -699.622459-699.042848 | 0.580 |
| 30 |  | -684.530148-683.940191 | 0.590 |

aHartrees, bFirst value relates to reactant and the second to product, cTaken from reference 1, dcalculated using the *ab initio* MP2/aug-cc-pVDZ method.

*2.2.2 Cross-Conjugated Heterocyclic Mesomeric Betaines (Table 6A).* Examples of the formation of NHCs from representative cross-conjugated HMBs are shown in Table 6A. The effect of replacing NR by O or S is similar to that observed in other systems. There is some interest in the use of this class of NHCs as ligands,41-43 and it is noteworthy that the CREF index values are particularly low for this class of anionic NHC, presumably because the remote anionic region has less influence on proton removal.

*2.2.3 Semi--Conjugated Heterocyclic Mesomeric Betaines (Table 6B).* The chemistry of semi-conjugated HMBs is a relatively unexplored area of heterocyclic chemistry.37 The best known examples are Type B mesoionic rings,9,10 and Table 6B shows four examples (Table 6; entries 7-10). Sulfur has a significant effect on lowering CREF index values. We are not aware of any deprotonation studies of this class of five-membered ring and ring opening may lead to complex products.

Only one example of a six-membered semi-conjugated HMB is known,44 and the chemistry of this class is unexplored.37 Four examples are shown in Table 6B (Entries 11-14). These results, and those in Table 6A, show that the effect of replacement of NR by S on ionisation is quantitatively the same in six-membered rings as in five-membered rings.

**Table 6 Anionic NHCs: Cross-Conjugated and Semi-Conjugated HMBs**

|  |  |  |
| --- | --- | --- |
| **Entry PRECURSOR NHC** | **E + ZPEa,b**  | **CREF** |
|  **A Cross-Conjugated HMBs** |  |  |
|  |  |  |  |
| 1 |  | -493.409989-492.862803 | 0.547c |
| 2 |  | -473.988335-473.446186 | 0.542 |
| 3 |  | -796.953166-796.414379 | 0.539 |
| 4 |  | -569.564356-569.028128 | 0.536c |
| 5 |  | -550.118173-549.602145 | 0.516 |
| 6 |  | -873.121162-872.597448 | 0.524 |
| **B Semi-Conjugated HMBs** |
|  |  |  |  |
| 7 |  | -379.968398-379.374961 | 0.593c |
| 8 |   | -683.550791-682.964988 | 0.586 |
| 9 |   | -683.550791-682.974953 | 0.576 |
|  |  |  |  |
| 10 |   | -987.122231-986.567183 | 0.555 |
| 11 |  | -493.382770-492.804968 | 0.578c |
| 12 |  | -796.923356-796.356153 | 0.567 |
| 13 |  | -796.923356-796.365488 | 0.558 |
| 14 |  | -1100.462391-1099.920255 | 0.540 |

aHartrees, bFirst value relates to reactant and the second to product, cTaken from reference 1.

**3. CONCLUSIONS**

Applying the CREF index over a wide range of oxygen, sulfur and nitrogen heterocycles gives a useful quantitative overview of the factors determining the ease of formation of NHCs and their σ-donor strength. These properties, which are primarily properties of the σ-bonding framework, are determined by the relative effects of ring components and substituents on reactant and product. Effectively, ionisation involves transfer of one electron from a proton environment to a carbon/heteroatom σ environment.1  Substitution of more electronegative elements in the ring (O vs NR or N vs CH) lowers the σ bond energies and increases the ease of ionisation. Substitution of ring NR by sulfur also reduces the CREF index and this cannot be attributed to a change in electronegativity. The influence of sulfur can be attributed to the mixing of empty dxy and dx2-y2 sulfur orbitals with occupied σ-bonding orbitals of suitable symmetry. This results in energy lowering in a manner similar to the mixing of unoccupied antibonding orbitals in anomeric effects. This stabilisation is not a localised effect between adjacent centres since sulfur remote from the carbene centre has a similar quantitative effect and the effect is also independent of ring size.

Where kinetic data is available, the CREF index also shows good correlation with rate constants for deprotonation and proton exchange. This empirical relationship may be attributed to product-like transition states in accord with the Hammond postulate.

We have demonstrated for a representative selection of heterocycles that the gas-phase ionisation potential expressed as an index gives a useful quantitative method of comparing and rationalising the properties of NHCs and, in accord with the main aims of theoretical studies, can direct attention to new and unexplored systems of potential interest. We also believe that it may be useful as a teaching aid.

**4. COMPUTATIONAL DETAILS**

Calculations were performed using the Gaussian 09 program,45 and the hybrid B3LYP functional,46,47 accompanied by the 6-311++G(d,p) basis set,48 was used. For comparison selected structures were optimized using the *ab initio* MP2/aug-cc-pVDZ method. All geometry optimizations were followed by frequency calculations to ensure that the stationary points obtained were true minima on the potential energy surface and to calculate the zero-point vibrational corrections (ZPE) to energy. The ZPE-corrected values were used to calculate the CREF index. As this index is based on the energy it depends on the theoretical method employed. However, the use of relative energy effectively minimises this dependence.

**ASSOCIATED CONTENT**

**Supporting Information**

Atom coordinates and absolute energies of calculated structures (PDF).

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**REFERENCES**

(1) Ramsden, C. A.; Oziminski, W. P. *J. Org. Chem.*  **2016**, *81*, 10295.

(2) Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

(3) Biju, A. T.; Hirano, K.; Fröhlich, R.; Glorius, F. *Chem. -Asian J.* **2009**, *4*, 1786.

(4) Benhamou, L.; César, V.; Gornitzka, H.; Lugan, N.; Lavigne, G. *Chem. Commun.* **2009**, 4720.

(5) Benhamou, L.; Vujkovic, N.; César, V.; Gornitzka, H.; Lugan, N.; Lavigne, G. *Organometallics*, **2010**, *29*, 2616.

(6) Wiechmann, S.; Freese, T.; Drafz, M. H. H.; Hübner, E. G.; Namyslo, J. C.; Nieger, M.; Schmidt, A. *Chem. Commun.* **2014**, *50*, 11822.

(7) Busch, M. *Chem. Ber.* **1895**, *28*, 2635.

(8) Baker, W.; Ollis, W. D.; Phillips, A.; Strawford, T. *J. Chem. Soc.* **1951**, 289.

(9) Ollis, W. D.; Ramsden, C. A. *Adv. Heterocycl. Chem.* **1976**, *19*, 1.

(10) Ollis, W. D.; Stanforth, S. P.; Ramsden, C. A. *Tetrahedron*, **1985**, *41*, 2239.

(11) Crabtree, R. H. *Coord. Chem. Rev.* **2013**, 257, 755.

(12) Schmidt, A.; Wiechmann, S.; Otto, C. F. *Adv. Heterocycl. Chem .* **2016**, *119*, 143.

(13) Ung, G.; Mendoza-Espinosa, D.; Bertrand, G. *Chem. Commun.* **2012**, *48*, 7088.

(14) Keleman, Z.; Hollóczki, O.; Oláh, J.; Nyulászi, L. *RSC Adv.***2013**, *3*, 7970.

(15) Grundy, K. R.; Roper, W. R. *J. Organomet. Chem.***1975**, *91*, C61.

(16) Woodward, R. B.; Olofson R. A. *Tetrahedron* **1966**, *22 (Supp.7*), 415.

(17) Kemp, D. S.; Wang, S-W.; Rebek Jr., J.; Mollan, R. C.; Banquer, C.; Subramanyam, G. *Tetrahedron*, **1974**, *30*, 3955.

(18) Olofson, R. A.; Meer, R. K. V.; Stournas, S. *J. Am. Chem. Soc.* **1971**, *93*, 1543.

(19) Arduengo III, A. J.; Goerlich, J. R.; Marshall, W. J. *Eur. J. Org. Chem.* **1997**, 365.

(20) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719.

(21) Lozac’h, N.; Stavaux, M. *Adv. Heterocycl. Chem.* **1980**, *27*, 151.

(22) Bernhammer, J. C.; Frison, G.; Huynh, H. V. *Chem.-Eur. J.* **2013**, *19*, 12892.

(23) Amyes, T. L.; Diver, S. T.; Richard, J. P.; Rivas, F. M.; Toth, K. *J. Am. Chem. Soc.* **2004**, *126*, 4366.

(24) Massey, R. S.; Collett, C. J.; Lindsay, A. G.; Smith, A. D.; O’Donoghue, A. C. *J. Am. Chem. Soc.* **2012**, *134*, 20421.

(25) Haake, P.; Bausher, L. P.; Miller, W. B. *J.Am. Chem. Soc.* **1969**, *91*, 1113.

(26) Ridd, J. H. *Phys. Methods Heterocycl. Chem.* **1971**, *IV*, 55.

(27) Olofson, R. A.; Landesberg, J. M. *J. Am. Chem. Soc.* **1966**, *88*, 4263.

(28) Olofson, R. A.; Thompson, W. R.; Michelman, J. S. *J. Am. Chem. Soc.* **1964**, *86*, 1865.

(29) Haake, P.; Miller, W. B. *J. Am. Chem. Soc.* **1963**, *85*, 4044.

(30) Eid, S.; Guerro, M.; Roisnel, T.; Lorcy, D. *Org. Lett.* **2006**, *8*, 2377.

(31) Haug, E.; Kantlehner, W.; Hagen, H.; Speh, P.; Bräuner, H-J. *Liebigs Ann. Chem.* **1988**, 605.

(32) Quast, H.; Hünig, S. *Angew. Chem. Internat. Edit.* **1964**, *3*, 800.

(33) Buza, D.; Gradowska, W. *Pol. J. Chem.* **1980**, *54*, 717.

(34) Schönherr, H-J.; Wanzlick, H-W. *Liebigs Ann.***1970**, *731*, 176.

(35) Arduengo III, A. J.; Harlow, R. L.; Kline, M. *J.Am. Chem. Soc.* **1991**, *113*, 361.

(36) Ollis, W. D.; Stanforth, S. P.; Ramsden, C. A. *J. Chem. Soc., Perkin Trans I* **1989**, 957.

(37) Ramsden, C. A. *Prog. Heterocyl. Chem*. **2016**, *28*, 1.

(38) Ramsden, C. A. *Tetrahedron***, 2013**, *69*, 4146.

(39) Freese, T.; Lücke, A-L.; Schmidt, C. A. S.; Polamo, M.; Nieger, M.; Namyslo, J. C.; Schmidt, A. *Tetrahedron*, **2017**, *73*, 5350.

(40) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. R. van E. *J. Am. Chem. Soc.* **1996**, *118*, 6317.

(41) César, V.; Lugan, N.; Lavigne, G. *J. Am. Chem. Soc.* **2008**, *130*, 11286.

(42) César, V.; Lugan, N.; Lavigne, G. *Chem.-Eur. J.* **2010**, *16*, 11432.

(43) Vujkovic, N.; César, V.; Lugan, N.; Lavigne, G. *Chem.-Eur. J.* **2011**, *17*, 13151.

(44) Neugebauer, F. A.; Fischer, H.; Krieger, C. *Tetrahedron Lett.* **1984**, *25*, 629.

(45) Gaussian 09, Revision D.01, 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., Jr.; 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, J. M.; 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, Inc., Wallingford CT, 2009.

(46) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(47) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

(48) Krishnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650.