

Cite this: *Chem. Sci.*, 2017, 8, 5482

# Ground-state dioxygen undergoes metal-free [3 + 2]-annulations with allenes and nitrosoarenes under ambient conditions†

Jinxian Liu,<sup>‡ab</sup> Manisha Skaria,<sup>‡a</sup> Pankaj Sharma,<sup>a</sup> Yun-Wei Chiang<sup>id</sup><sup>a</sup> and Rai-Shung Liu<sup>id</sup><sup>\*a</sup>

The cycloadditions of molecular dioxygen with neutral  $\pi$ -bond motifs rely heavily on singlet-state  $^1\text{O}_2$ , whereas ground state  $^3\text{O}_2$  is chemically inactive. Here we report novel [3 + 2]-annulations among ground-state  $^3\text{O}_2$  (1 bar), allenes, and nitrosoarenes at low temperatures, efficiently yielding dioxygen-containing oxacycles. With less hindered 1-aryllallene derivatives, these dioxygen species undergo skeletal rearrangement to 3-hydroxy-1-ketonyl-2-imine oxides. These cycloadditions represent valuable one-pot *O,N,O*-trifunctionalizations of allenes. Our EPR experiments confirm the presence of 1,4-diradical intermediates from an allene/nitrosoarene mixture, which manifest the hidden diradical properties of nitrosoarenes.

Received 20th April 2017  
Accepted 20th May 2017

DOI: 10.1039/c7sc01770g

rsc.li/chemical-science

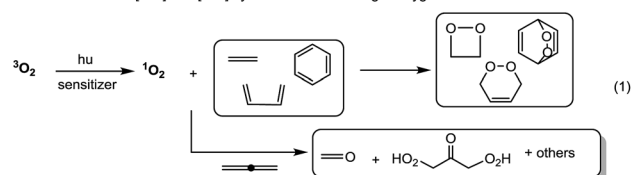
## Introduction

Cycloadditions of two or three  $\pi$ -bond molecules are powerful tools to access carbo- or heterocycles. Ground-state  $^3\text{O}_2$  has low-lying LUMO orbitals, but its triplet state greatly reduces its chemical reactivity toward neutral molecules<sup>1</sup> unless a metal catalyst is present. The cycloadditions of  $^3\text{O}_2$  dioxygen rely nearly exclusively on prior photo-activation to form singlet-state  $^1\text{O}_2$  (ref. 1) that reacts with dienes,<sup>2</sup> olefins<sup>3</sup> or even arenes<sup>4</sup> in [n + 2]-cycloadditions ( $n = 2$  and 4, Scheme 1, eqn (1)). This photolytic process requires a sensitizer in a cold bath ( $-40\text{ }^\circ\text{C}$ ) over a protracted period (>12 h) because highly energetic  $^1\text{O}_2$  might produce byproducts from the oxygen-ene reactions<sup>5</sup> and oxidative C=C cleavages.<sup>6</sup> In the case of allenes, singlet dioxygen afforded a complicated mixture of undesired compounds.<sup>7a,b</sup>

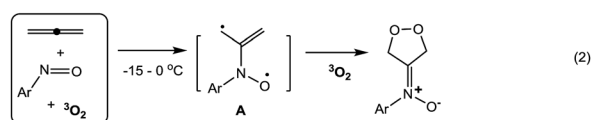
As ground-state  $^3\text{O}_2$  is a free  $\pi$ -molecule and is available everywhere; its metal-free [n + 2]-cycloadditions with commonly used unsaturated hydrocarbons would provide a clean and cheap synthesis of valuable 1,*n*-diols, although there is no literature precedence. As far as we are aware, only 1,4-diradical precursors such as *o*-benzocyclobutanes,<sup>8</sup> 1,2,6,7-octatetraenes,<sup>9</sup> 2,3-dimethylbicyclo[2.2.0]hexane<sup>10</sup> and other 1,4-diazo species<sup>11</sup> reacted with ground-state  $^3\text{O}_2$  in thermal [4 + 2]-

cycloadditions; these precursors are too uncommon to show general utility. We recently achieved metal-catalyzed annulations of *N*-hydroxy allenylamines with nitrosoarenes *via* a single radical process.<sup>7d</sup> In search of a breakthrough in dioxygen chemistry, we developed facile [3 + 2]-cycloadditions among nitrosoarenes, allenes and ground-state  $^3\text{O}_2$  to efficiently afford *N*-(1,2-dioxolan-4-ylidene)aniline oxides (eqn (2)). Particularly notable are the ambient conditions:  $-15$  to  $0\text{ }^\circ\text{C}$ ,  $^3\text{O}_2$  (1 bar), no light, no catalyst and no additive. Importantly, these facile spin-forbidden dioxygen annulations reveal a new role of nitrosoarenes as effective diradical precursors that is synthetically significant in nitroso chemistry.<sup>12</sup> In the context of nitroso/alkene and nitroso/alkyne reactions,<sup>13</sup> theoretical calculations by Houk<sup>12e,f</sup> suggested the intermediacy of the diradical species, but these transient species could not be trapped with dioxygen or other small molecules.

Current reactions: [2+2] and [4+2]-cycloadditions with singlet oxygen



This work: [3+2]-annulations involving 3O2



Scheme 1 Cycloadditions of unsaturated hydrocarbons with  $^1\text{O}_2$  and  $^3\text{O}_2$ .

<sup>a</sup>Department of Chemistry, National Tsing-Hua University, Hsinchu, Taiwan, Republic of China. E-mail: rslu@mx.nthu.edu.tw

<sup>b</sup>College of Chemistry & Materials Science, Longyan University, Fujian, China

† Electronic supplementary information (ESI) available. CCDC 1507477, 1507478, 1510902 and 1540299. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7sc01770g

‡ These authors contributed equally to this work.



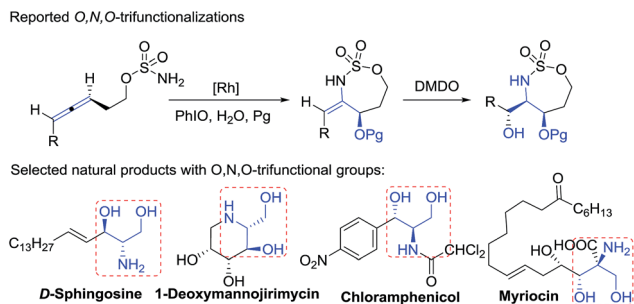


Fig. 1 *O,N,O*-Trifunctionalizations of allenes and selected natural products.

2-Amino-1,3-diols are present in numerous natural products with diverse biological activity (Fig. 1).<sup>14</sup> Catalytic *O,N,O*-trifunctionalization of allenes is a new appealing tool to assess these motifs, as noted by the work of Schomaker, who reported Rh-catalyzed intramolecular cyclizations of homo-allenylsulfamate esters *via* a two-step sequence.<sup>15a</sup> In contrast, our one-pot intermolecular *O,N,O*-functionalizations employ common and cheap nitrosoarenes, allenes and oxygen.

## Results and discussion

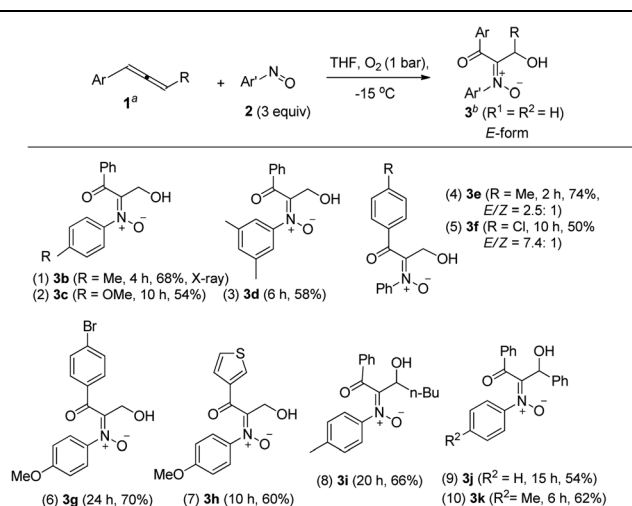
Table 1 presents the optimized yields of a *O,N,O*-trifunctionalized molecule **3a** from a mixture of allene **1a**, nitrosobenzene **2a** (*n* equiv.) and O<sub>2</sub> (1 bar). When 1.5 equiv. of nitrosobenzene **2a** was used in cold THF (−15 °C), the yield was 43% (entry 1). The yield of **3a** increased to 63% with nitrosobenzene in three fold proportions (entry 2). In other solvents, the yields of **3a** were 50% in toluene, 54% in CH<sub>3</sub>CN, and 58% in DCM (entries 3–5). The yield of **3a** decreased substantially to 10% in THF at 25 °C (entry 6). The reaction under N<sub>2</sub> failed to yield the desired product **3a** in a traceable amount (entry 7).<sup>16</sup> Compound **3a** assumes an *E*-configuration with its hydroxyl *cis* to the nitron oxygen to form a hydrogen bond. This structure was inferred from X-ray diffraction measurements of its relative **3b**<sup>17</sup> (Table 2 entry 1).

Table 1 Optimization of reaction conditions

Entry	Solvent <sup>a</sup>	Gas	<i>n</i>	<i>T</i> (°C)	<i>t</i> (h)	Yield <sup>b</sup> (%)
1	THF	O <sub>2</sub>	1.5	−15	2	43
2	THF	O <sub>2</sub>	3	−15	2	63
3	Toluene	O <sub>2</sub>	3	−15	2	50
4	MeCN	O <sub>2</sub>	3	−15	2	54
5	DCM	O <sub>2</sub>	3	−15	2	58
6	THF	O <sub>2</sub>	3	25	2	10
7	THF	N <sub>2</sub>	3	−15	10	—

<sup>a</sup> [**1a**] = 0.1 M. <sup>b</sup> Product yields are reported after purification using a silica column.

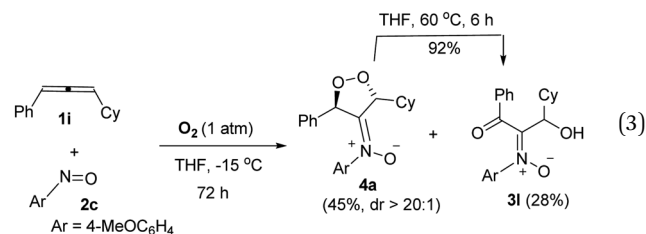
Table 2 *O,N,O*-Trifunctionalizations of allenes with O<sub>2</sub> and ArNO<sup>a,b</sup>



<sup>a</sup> [**1**] = 0.1 M. <sup>b</sup> Product yields are reported after purification using a silica column.

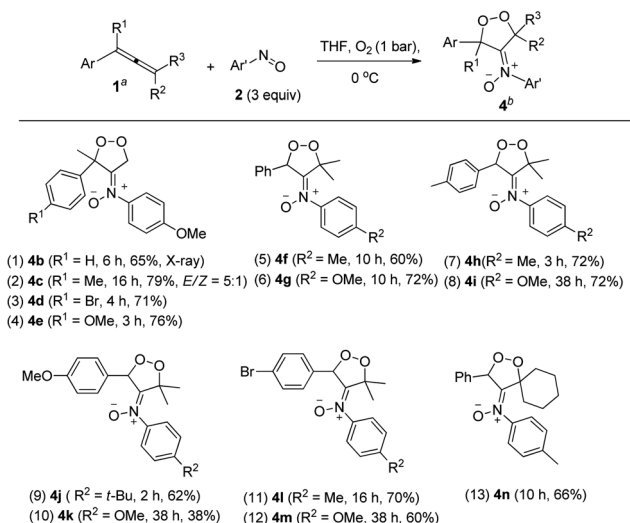
To assess the reaction scope, we applied these optimized conditions to additional mono- and 1,3-disubstituted allenes **1b–1g**; Table 2 summarizes the results. For phenylallene **1a**, its corresponding reactions with 4-methyl-, 4-methoxy- and 3,5-dimethylphenylnitroso species afforded 3-hydroxy-1-ketonil-2-imine oxides **3b–3d** in 54–68% yields (entries 1–3). Varied arylallenes **1b–1e** (Ar = 4-MeC<sub>6</sub>H<sub>4</sub>, 4-ClC<sub>6</sub>H<sub>4</sub>, 4-BrC<sub>6</sub>H<sub>4</sub> and 3-thienyl) yielded desired compounds **3e–3h** in satisfactory yields (50–74%, entries 4–6). 3-Substituted phenylallenes **1f** and **1g** (R = *n*-Bu and Ph) were also effective substrates for these cycloadditions (entries 8–10).

Notably, the reaction of sterically hindered 3-cyclohexyl-1-phenylallene **1i** with 4-methoxyphenylnitroso **2c** and O<sub>2</sub> (1 bar) afforded dioxygen-containing oxacycle **4a** together with desired product **3l**; the yields were 45% and 28%, respectively. Species **4a** assumes an anti-configuration (*dr* > 20 : 1) according to its <sup>1</sup>H NOE spectra; this new compound was efficiently converted to compound **3l** in hot THF (eqn (3)), *via* a Kornblum-DeLaMare rearrangement.<sup>22</sup>



The kinetic stability of dioxygen-containing oxacycle **4a** is enhanced with a suitable steric environment. We further tested the reactions on various 1-aryl-1-methylallenes **1j–1m** with 4-methoxyphenylnitroso **2c** and O<sub>2</sub> (1 bar) in THF (0 °C), generating dioxygen-containing compounds **4b–4e** (Ar = 4-RC<sub>6</sub>H<sub>4</sub>, R = H, Me, MeO, Br) in satisfactory yields (Table 3, entries 1–4). The molecular structure of compound **4b** was confirmed by its X-ray

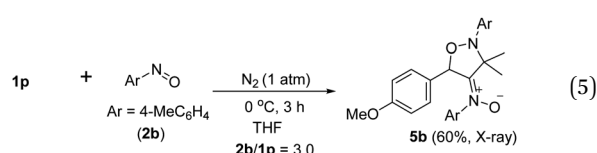
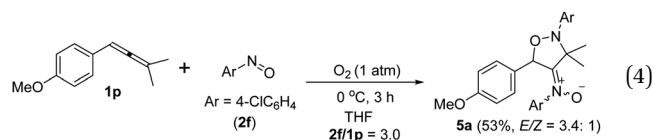
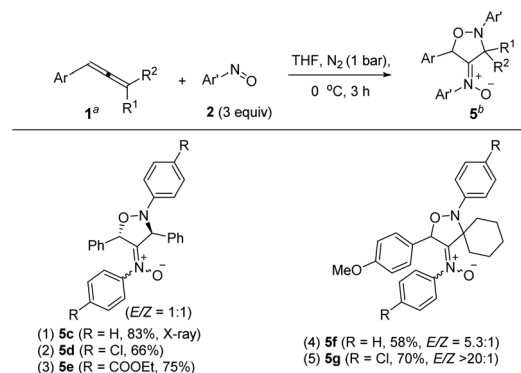


Table 3 [3 + 2]-Cycloadditions among O<sub>2</sub>, allenes and nitrosoarenes<sup>a,b</sup>

<sup>a</sup> [1] = 0.1 M. <sup>b</sup> Product yields are reported after purification using a silica column.

diffraction pattern.<sup>17</sup> Various 1-aryl-3,3-dimethylallenes **1n–1q** (Ar = 4-RC<sub>6</sub>H<sub>4</sub>, R = H, Me, MeO, Br), electron-rich nitrosoarenes and O<sub>2</sub> were also amenable to such cycloadditions, yielding desired compounds **4f–4m** in satisfactory yields (60–72%, entries 5–12) except **4k** in only 38% yield. This dioxygen cycloaddition was applicable to cyclohexylidene-derived phenylallene **1r**, affording compound **4n** in 66% yield (entry 13). Compounds **4** serve as the first examples of the cycloadditions of ground-state <sup>3</sup>O<sub>2</sub> with unsaturated hydrocarbons at low temperatures.

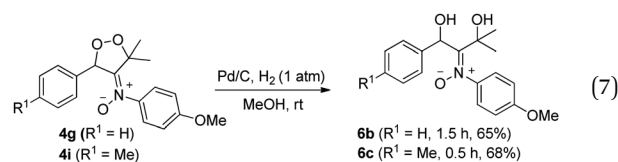
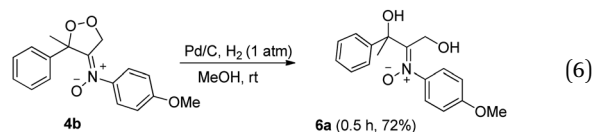
An electron-deficient nitrosoarene is an inapplicable substrate, as shown by eqn (4). Under O<sub>2</sub>, the reaction of trisubstituted allene **1p** with 4-chlorophenyl nitroso species **2f** in cold THF (0 °C) afforded nitroso-containing cycloadduct **5a** in 53% yield; the dioxygen-containing product, *ca.* 5%, was unstable for isolation (eqn (4)). In contrast, the same allene **1p** could deliver dioxygen-containing species **4j** and **4k** using electron-rich nitrosoarenes under the same conditions (entries 9–10, Table 3).

Table 4 [3 + 2]-Cycloadditions among allenes and nitrosoarenes under N<sub>2</sub><sup>a,b</sup>

<sup>a</sup> [1] = 0.1 M. <sup>b</sup> Product yields are reported after purification using a silica column.

Under nitrogen, trisubstituted allene **1p** reacted with 4-methylphenylnitroso **2b** in cold THF to form nitroso-containing cycloadduct **5b** in 60% yield (eqn (5)). The stereochemistry and its E-configuration of this new compound was confirmed by its X-ray diffraction pattern.<sup>17</sup> Such a new reaction represents a new and useful O,*N,N*-functionalization of allenes. A preliminary survey of the reaction scope is summarized in Table 4. We tested the reactions on 1,3-di- and 1,1,3-trisubstituted allenes **1g** and **1t** that reacted with nitroso-arenes (R = H, Cl, CO<sub>2</sub>Et) to afford nitroso-containing cycloadducts **5c–5g** in reasonable yields (58–83%). Furthermore, the anti-configuration of compound **5c** was determined by X-ray diffraction.<sup>17</sup>

Dioxygen-containing heterocycles **4** are readily reduced with Pd/C, H<sub>2</sub> (1 atm) in MeOH (23 °C)<sup>18</sup> to cleave their O–O bonds, satisfactorily yielding desired 1,3-dihydroxy-2-imine oxides **6**. These reductions highlight the utility of molecular oxygen to afford 1,3-dihydroxy-2-amino derivatives. Several instances of affording tertiary 1,3-alcohol derivatives are illustrated in eqn (6) and (7); their chemical yields exceed 65%. Under these reductions, the valuable nitron functionalities of these acyclic 1,3-diols remain intact as indicated by their HRMS and <sup>13</sup>C-NMR spectra.



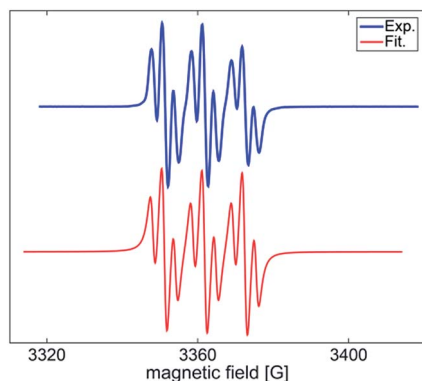
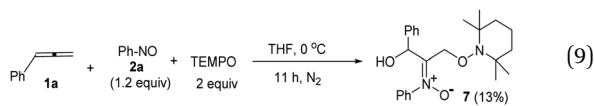
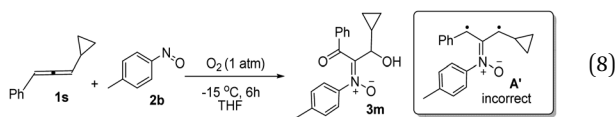
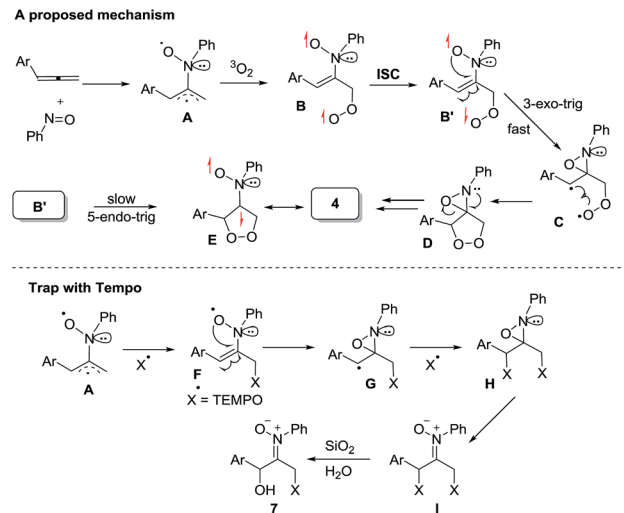


Fig. 2 Observed and simulated EPR spectra.

The facile cycloadditions among allenes, nitrones and ground-state  $O_2$  are very astonishing because an intersystem crossing (ISC) must be involved for one key intermediate. To investigate the mechanism, we examined the reaction of 1-phenyl-3-cyclopropylallene **1s** with 4-methylphenylnitroso species **2b** under  $O_2$ , yielding compound **3m** in 71% yield; this transformation did not induce cyclopropane cleavage because of the stability of the phenylallylic radical **A** (eqn (8)).<sup>19</sup> We thus exclude the intermediacy of the dicarbon radical **A'**, although analogous carbon radicals were postulated for the *o*-quinodimethine species.<sup>8</sup> We isolated compound **7** in 13% yield from the reaction of 1-phenylallene **1a** with PhNO (1.2 equiv.) and TEMPO (2 equiv.) under  $N_2$ , indicating the formation of diradical intermediates (eqn (9)). We employed EPR to characterize the diradical species from a mixture of 3,3-dimethyl-1-phenylallene **1n** and nitrosobenzene **2a** in THF at 0 °C (0.5 h). Fig. 2 (top) shows the EPR signal of the diradical species; the intensity of this signal remains unchanged for 5 h under  $N_2$ . The simulation analysis was performed using the EasySpin program.<sup>20</sup> The satisfactory fit was achieved with a two-component simulation (bottom). The abundant component (70%) corresponds to nitrogen-centered diradicals ( $g = 2.00616$ ,  $a_N = 10.7$  G and 3.0 G).<sup>21</sup> The minor component corresponds to a monoradical nitroxide with  $a_N = 10.7$  G. Notably, when recorded at  $T < 130$  K, the spectrum exhibits a well-known nitroxide rigid-limit lineshape in accordance with the above simulation result; the coupling of unpaired electrons with the nitrogen center is evident.



Scheme 2 depicts a plausible mechanism to rationalize the remarkable facility of such dioxygen annulations. We postulate



Scheme 2 A plausible mechanism.

that allene **1** reacts initially with nitrosobenzene to form 1,4-diradical species **A**, which is likely to be a major component, as detected in the EPR spectra; its nitroso and allylic radicals are expected to couple with nitrogen in two magnitudes, *i.e.*  $a_N = 10.7$  G and 3.0 G respectively.<sup>21</sup> The capture of molecular dioxygen  $^3O_2$  by 1,4-diradical species **A** forms peroxy diradical **B** in a triplet state, as the two radical centers of species **B** are remote from each other, rendering an intersystem crossing (ISC) feasible. After a change of spin state, singlet-state diradical **B'** is expected to form primary 1,2-oxaziridine diradical **C** through a 3-*exo-trig* cyclization that is more feasible than an alternative 5-*endo-trig* cyclization.<sup>23</sup> A final radical-radical coupling of resulting species **C** forms precursor **D**, and ultimately yields desired 1,2-dioxolanes **4**. This proposed path rationalizes the formation of compound **7** from the TEMPO experiment (eqn (9)) well. The trapping of the 1,4-biradical generates single radical species **F** that undergoes a rapid 3-*exo-trig* cyclization to form benzylic radical **G**. A second trapping of this species with the TEMPO radical is expected to yield species **I** that is prone to hydrolysis on a silica column to yield observed product **7**.

## Conclusions

Prior to this work, singlet state oxygen  $^1O_2$  failed to react with allenes to give useful oxygenated products.<sup>7</sup> This study reports the first examples of metal-free [3 + 2]-cycloadditions among allenes, nitrosoarenes and ground-state  $^3O_2$  (1 bar) at low temperatures, efficiently yielding dioxygen-containing oxacycles.<sup>24</sup> With less hindered 1-arylallene derivatives, the resulting oxacycles undergo skeletal rearrangement to 3-hydroxy-1-ketonyl-2-imine oxides. These transformations highlight a cheap, efficient and clean synthesis of 1,3-dihydroxy-2-amino derivatives. Our experimental data indicate that an initial attack of a nitrosoarene at an allene generates a diradical species that is detectable with EPR. We envisage that the concept of nitrosoarenes as diradical precursors will inspire new synthetic concepts.

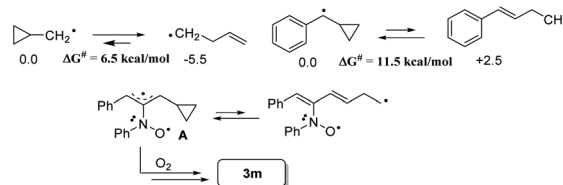


## Acknowledgements

The authors thank the National Science Council and the Ministry of Education, Taiwan, for supporting this work.

## Notes and references

- For reviews see: (a) P. R. Ogilby, *Chem. Soc. Rev.*, 2010, **39**, 3181; (b) J. Sivaguru, M. R. Solomon, T. Poon, S. Jockusch, S. G. Bosio, W. Adam and N. Turro, *Acc. Chem. Res.*, 2008, **41**, 387; (c) A. Greer, *Acc. Chem. Res.*, 2006, **39**, 797; (d) A. G. Leach and K. N. Houk, *Chem. Commun.*, 2002, 1243.
- (a) J. A. Celaje, D. Zhang, A. M. Guerrero and M. Selke, *Org. Lett.*, 2011, **13**, 4846; (b) E. Salamci, H. Seçen, Y. Sütbeyaz and M. Balci, *J. Org. Chem.*, 1997, **62**, 2453; (c) K. M. Davis and B. K. Carpenter, *J. Org. Chem.*, 1996, **61**, 4617.
- (a) K. Ohkubo, T. Nanjo and S. Fukuzumi, *Org. Lett.*, 2005, **7**, 4265; (b) W. Adam, C. R. Saha-Moeller and S. B. Schambony, *J. Am. Chem. Soc.*, 1999, **121**, 1834; (c) K. A. Zaklika, B. Kaskar and A. P. Schaap, *J. Am. Chem. Soc.*, 1980, **102**, 386.
- (a) M. Klaper and T. Linker, *Chem.-Eur. J.*, 2015, **21**, 8569; (b) W. Fudickar and T. Linker, *J. Am. Chem. Soc.*, 2012, **134**, 15071; (c) H. Kotani, K. Ohkubo and S. Fukuzumi, *J. Am. Chem. Soc.*, 2004, **126**, 15999.
- (a) A. Eske, B. Goldfuss, A. G. Griesbeck, A. Kiff, M. Kleczka, M. Leven, J.-M. Neudorfl and M. Vollmer, *J. Org. Chem.*, 2014, **79**, 1818; (b) W. Adam and M. J. Richter, *J. Org. Chem.*, 1994, **59**, 3335; (c) L. M. Stephenson, *Acc. Chem. Res.*, 1980, **13**, 419.
- W. Adam and H. Rebollo, *Tetrahedron Lett.*, 1981, **22**, 3049.
- (a) K. Gollnick and A. Schnatterer, *Tetrahedron Lett.*, 1985, **26**, 5029; (b) I. Erden and T. R. Martinez, *Tetrahedron Lett.*, 1991, **32**, 1859; (c) R. K. Howe, *J. Org. Chem.*, 1968, **33**, 2848; (d) P. Sharma and R. S. Liu, *Org. Lett.*, 2016, **18**, 412.
- (a) J. Drujon, R. Rahmani, V. Heran, R. Blanc, Y. Carissan, B. Tuccio, L. Commeiras and J. Parrain, *Phys. Chem. Chem. Phys.*, 2014, **16**, 7513; (b) W. R. Roth, T. Ebbrecht and A. Beitat, *Chem. Ber.*, 1988, **121**, 1357.
- (a) W. R. Roth, R. Longer, M. Bartmann, B. Stevermann, G. Maier, H. P. Reisenauer, R. Sustmann and W. Müller, *Angew. Chem., Int. Ed.*, 1987, **26**, 256; (b) W. R. Roth, B. P. Scholz, R. Breuckmann, K. Jelich and H. W. Lennartz, *Chem. Ber.*, 1982, **115**, 1934.
- W. R. Roth and B. P. Scholz, *Chem. Ber.*, 1982, **115**, 1197.
- (a) W. Adam, S. Grabowski and H. Platsch, *J. Am. Chem. Soc.*, 1989, **111**, 751; (b) W. Adam, K. Hannemann and R. M. Wilson, *J. Am. Chem. Soc.*, 1986, **108**, 929; (c) W. Adam, K. Hannemann and R. M. Wilson, *J. Am. Chem. Soc.*, 1984, **106**, 1646; (d) W. R. Roth, M. Biermann, G. Erker, K. Jelich, W. Gerhartz and H. Görner, *Chem. Ber.*, 1980, **113**, 586.
- (a) H. Yamamoto and N. Momiyama, *Chem. Commun.*, 2005, 3514; (b) W. Adam and O. Krebs, *Chem. Rev.*, 2003, **103**, 4131; (c) P. Zuman and B. Shah, *Chem. Rev.*, 1994, **94**, 1621; (d) K. Mikami and M. Shimizu, *Chem. Rev.*, 1992, **92**, 1021; (e) A. G. Leach and K. N. Houk, *Org. Biomol. Chem.*, 2003, **1**, 1389; (f) A. G. Leach and K. N. Houk, *J. Am. Chem. Soc.*, 2002, **124**, 14820; (g) D. J. Fisher, G. L. Burnett, R. Velasco and J. R. de Alaniz, *J. Am. Chem. Soc.*, 2015, **137**, 11614.
- (a) G. Ieronimo, A. Mondelli, F. Tibiletti, A. Maspero, G. Palmisano, S. Galli, S. Tollari, N. Masciocchi, K. M. Nicholas, S. Tagliapietra, G. Cravotto and A. Penoni, *Tetrahedron*, 2013, **69**, 10906; (b) A. Penoni, G. Palmisano, Y. L. Zhao, K. N. Houk, J. Volkman and K. M. Nichols, *J. Am. Chem. Soc.*, 2009, **131**, 653.
- (a) M. Kurano, K. Tsukamoto, M. Hara, R. Ohkawa, H. Ikeda and Y. Yatomi, *J. Biol. Chem.*, 2015, **290**, 2477; (b) E. Ogier-Denis, A. Blais, J. J. Hourri, T. Voisin, G. Trugnan and P. Codogno, *J. Biol. Chem.*, 1994, **269**, 4285; (c) O. N. Kostopoulou, E. C. Kouvela, G. E. Magoulas, T. Garnelis, I. Panagoulas, M. Rodi, G. Papadopoulos, A. Mouzaki, G. P. Dinos, D. Papaioanmou and D. L. Kalpaxis, *Nucleic Acids Res.*, 2014, **42**, 8621; (d) E. N. Glaros, W. S. Kim, B. J. Wu, C. Suarna, C. M. Quinn, K.-A. Rye, R. Stocker, W. Jessup and B. Garner, *Biochem. Pharmacol.*, 2007, **73**, 1340.
- Triple functionalizations of allenes are focused extensively on their double epoxidations,<sup>15c-e</sup> and other reactions are very few.<sup>15a,b</sup> See: (a) C. S. Adams, R. D. Grigg and J. M. Schomaker, *Chem. Sci.*, 2014, **5**, 3046; (b) W. Zhao and J. Montgomery, *J. Am. Chem. Soc.*, 2016, **138**, 9763; (c) C. S. Adams, C. D. Weatherly, E. G. Burke and J. M. Schomaker, *Chem. Soc. Rev.*, 2014, **43**, 3136; (d) S. D. Lotesta, S. Kiren, R. R. Sauers and L. J. Williams, *Angew. Chem., Int. Ed.*, 2007, **46**, 7108; (e) P. Ghosh, S. D. Lotesta and L. J. Williams, *J. Am. Chem. Soc.*, 2007, **129**, 2438–2439.
- R. K. Howe, *J. Org. Chem.*, 1968, **33**, 2848.
- Crystallographic data of **3b**, **4b**, **5b** and **5c** were deposited at the Cambridge Crystallographic Data Centre (**3b** CCDC 1507478, **4b** CCDC 1507477, **5b** CCDC 1510902, **5c** CCDC 1540299).
- T. V. Robinson, D. S. Pedersen, D. K. Taylor and R. T. Tiekink, *J. Org. Chem.*, 2009, **74**, 5093.
- The rearrangement of cyclopropylmethyl radicals to homoallylic radicals is seriously affected by the radical substituents; this process is reversible. Previous studies by Bowry indicate that stable cyclopropylbenzyl radicals are reluctant to form the corresponding homoallylic radicals. In our system, key intermediate **A** is a very stable phenylallylic radical that has many resonance forms. The equilibrium of this rearrangement is expected to be favourable for initial radicals **A** that can be trapped by O<sub>2</sub> to yield the observed product **3m**. For the nature of this radical rearrangement, see the leading reference, A. J. Beckwith and V. W. Bowry, *J. Am. Chem. Soc.*, 1994, **116**, 2710–2716.



- 20 S. Stoll and R. D. Britt, *Phys. Chem. Chem. Phys.*, 2009, **11**, 6614.
- 21 (a) L. Jonkman, H. Muller and J. Kommandeur, *J. Am. Chem. Soc.*, 1971, **93**, 5833; (b) V. Branchadell, J. Font, A. G. Moglioni, C. O. de Echagulen, A. Oliva, M. Rosa, R. M. Ortuno, J. Veciana and J. Vidal-Gancedo, *J. Am. Chem. Soc.*, 1997, **119**, 9992; (c) P. Astolfi, P. Carloni, E. Damiani, L. Greci, M. Marini, C. Rizzoli and P. Stipa, *Eur. J. Org. Chem.*, 2008, 3279.
- 22 (a) N. Kornblum and H. E. DeLaMare, *J. Am. Chem. Soc.*, 1951, **73**, 880; (b) S. T. Staben, X. Linghu and F. D. Toste, *J. Am. Chem. Soc.*, 2006, **128**, 12658.
- 23 (a) J. E. Baldwin, *J. Chem. Soc., Chem. Commun.*, 1976, 734; (b) J. E. Baldwin, J. Cutting, W. Dupont, L. Kruse, L. Silberman and R. C. Thomas, *J. Chem. Soc., Chem. Commun.*, 1976, 736; (c) C. Chatgililoglu, C. Ferreri, M. Guerra, V. Timokhin, G. Froudakis and T. Gimisis, *J. Am. Chem. Soc.*, 2002, **124**, 10765.
- 24 For metal-catalyzed oxidations of 5-hydroxy-1-enes with O<sub>2</sub> to yield tetrahydrofuran products, see (a) S. Inoki and T. Mukayama, *Chem. Lett.*, 1990, 67–70; (b) C. Palmer, N. M. Morra, A. C. Stevens, B. Bajtos, B. P. Machin and B. L. Pagenkopf, *Org. Lett.*, 2009, **11**, 5614–5617; (c) R. M. Trend, Y. K. Ramtohl, E. M. Ferreira and B. M. Stoltz, *Angew. Chem., Int. Ed.*, 2003, **42**, 2892; (d) X. Xie and S. S. Stahl, *J. Am. Chem. Soc.*, 2015, **137**, 3767; (e) S. L. Zultanski, J. Zhao and S. S. Stahl, *J. Am. Chem. Soc.*, 2016, **138**, 6416.

