DOI: 10.1002/ejoc.200800928

2-Quinoxalinol Salen Copper Complexes for Oxidation of Aryl Methylenes

Xianghong Wu[a] and Anne E. V. Gorden*[a]

Keywords: Salen / Copper / Catalysts / Methylene / Oxidation / Chelates / Homogeneous catalysis

A copper(II) complex of the 2-quinoxalinol salen ligand (salquCu) **1** has been tested for use in catalysis. Here, an optimized method for oxidation of aryl methylenes and its potential applications are described. In organic solvents, the yields obtained are higher than with other commonly used catalytic methods. Because this methods does not require high heat or increased pressure, this presents an opportunity for more environmentally friendly or "green" chemistry in a single-phase system. Using this method, a key fragment of natural products Vitamin K_1 and K_2, 1,4-naphthoquinone, can be easily synthesized from 1,2,3,4-tetrahydronaphthalene in increased yield (65%) as compared to established methods (30–40% yield) that require higher temperatures and increased pressure.

Introduction

The development of new metal catalysts has been of wide interest in synthetic methodology;[1] however, the application of these in the pharmaceutical industry has been limited for many reasons. Developing less expensive, easier to use, or more environmentally friendly metal catalysts is a promising trend for new synthetic methods.[2] The oxidation of C–H bonds offers benefits in commercial organic synthesis in the form of "greener" chemistry by energy efficiency, and operational simplicity, while at the same time reducing wastes.[3]

The easy to prepare salen metal (Mn, Ru, Co, Cu, etc.) complexes have been used in the development of catalysts for numerous reactions,[4] among these the oxidation of activated C–H bonds; however, this reaction is limited by the low solubility of salen ligands in organic solvents resulting in low yields.[5] For these reasons, we were interested in developing a modified salen system to be used for oxidation of activated C–H bonds.

Previously, several methods of oxidation of aryl methylenes to form aryl carbonyl groups or aryl α-hydroxy groups have been described.[6] The utility of these systems has often been limited by the need for selectivity. In the 1970's, Se_2O was used as oxidant for such reactions; the reaction mechanism was determined to proceed with the formation of β-keto seleninic acids leading to numerous byproducts.[7] Oxidations with manganese salts or nitropyridinium salts were found to have a hydrogen transfer and radical mechanism, but these resulted in low yields (less than 60%).[8] Singlet oxygen has also been investigated for use as an oxidant, but because this reaction also involves radical mechanism, the products are a mixture of the α-keto and α-hydroxy group products.[9] More recently, methods of oxidation using hypervalent iodine,[10] *tert*-butyl hydroperoxide,[11] Jones reagent, DDQ, or peroxy acid[12] have been reported. Yields of these methods are still less than 80%, and these methods require rigorous controlled conditions.

For this kind of oxidation, catalysts are required for acceleration of the reaction and improvement of yields. Metal catalysts used in this way have included copper, cobalt[13] or ruthenium salts.[14] For this purpose, salen ligands have been used as manganese or copper catalyst supports.[15] One promising method developed recently is the *Gif system*, in which an iron catalyst is combined with a suitable carboxylic acid, pyridine, zinc dust (as a reductant) with oxygen as the oxidant, to acylate methylene;[16] however, less than 40% yields were obtained.[16,17] Many articles have reported high conversion rates of this oxidation as determined by GC or HPLC; however, this is not a good reflection of isolable yields, due to the different absorptions between starting materials and products. This is especially true in the oxidation of an aryl methylene group into an aryl carbonyl group which should exhibit a stronger UV absorption. For this particular oxidation, it is difficult to identify a metal catalyst possessing both good solubility in organic polar aprotic solvents (for example, CH_3CN) and non-polar solvents (for example, hexane), a bottleneck to the oxidation of non-polar compounds like steroids.

On the basis of our 2-quinoxalinol salen ligands (salqu),[18] we have developed a new copper catalyst, salquCu **1** (Figure 1).[19] This metal complex can be used as a catalyst in the conversion of aryl methylene groups into

[a] 179 Chemistry Building, Department of Chemistry and Biochemistry, College of Science and Mathematics, Auburn University,
Auburn, AL 36849-5319, USA
Fax: +1-334-884-4043
E-mail: gordeae@auburn.edu
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

aryl carbonyl groups. Here, we introduce this method, describe selectivity, and propose potential applications of the salquCu catalyst **1**.

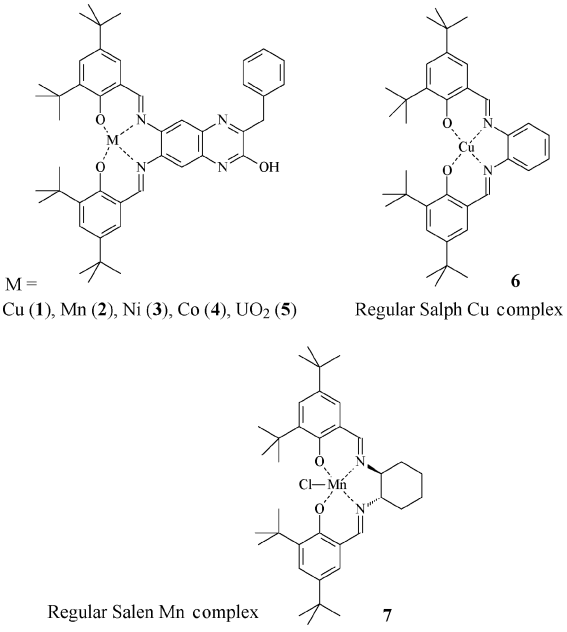


Figure 1. Structures of salen, salph and salqu copper complex catalysts **1**–**7**.

Results and Discussion

The conversion of diphenylmethane into benzophenone was selected to test the activity of the catalyst salquCu **1** and to develop optimized conditions. On the basis of previous reports with salphCu,[4] we began using the addition of 3 equiv. H_2O_2, in CH_3CN as solvent with 1% by molar of the catalyst salquCu **1**, heated to reflux temperature for 18 h. Under these conditions, the isolated yield of benzophenone is only 27%. Six experimental factors were considered for optimizing this reaction: oxidant (Figure 2), catalyst ratio (Figure 3), reaction time (Figure 4), oxidant ratio (Figure 5), solvent, and types of catalyst (Figure 6 and Table 1).

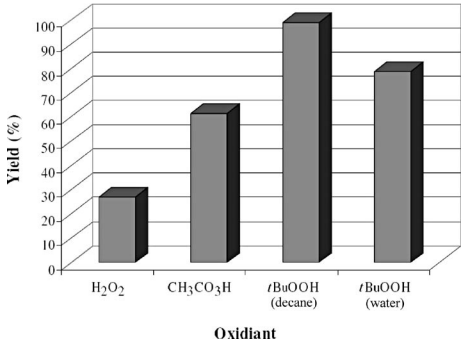


Figure 2. Oxidants for conversion of diphenylmethane into benzophenone in acetonitrile (yields are based on purification by flash-column chromatography).

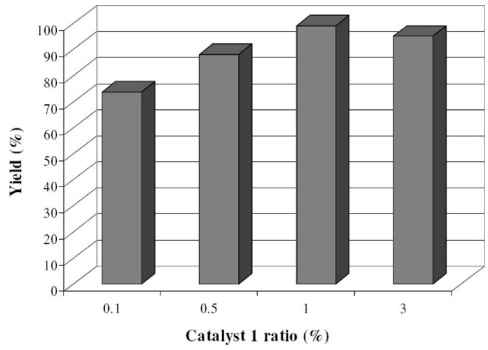


Figure 3. Catalyst ratio of **1** for conversion of diphenylmethane into benzophenone (yields are based on purification by flash-column chromatography).

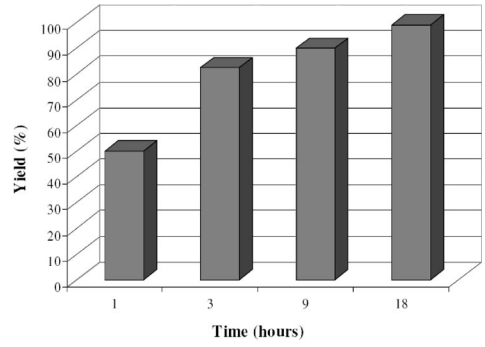


Figure 4. Reaction yields with time of the conversion of diphenylmethane into benzophenone (yields are based on purification by flash-column chromatography).

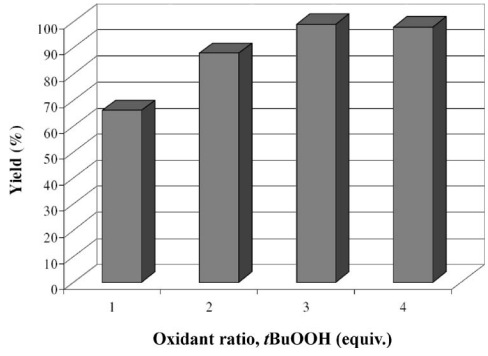


Figure 5. Oxidant ratio for the conversion of diphenylmethane into benzophenone (yields are based on purification by flash-column chromatography).

First, four oxidants were tested using CH_3CN as solvent in each case, with 1% of the catalyst **1** at reflux temperature for 18 h (Figure 2). It was found that *tert*-butyl hydroperoxide in decane was the best oxidant, quantitatively converting diphenylmethane into benzophenone. When *tert*-butyl hydroperoxide in water was used as the oxidant, the yield of the product, benzophenone, was around 80% (Figure 2). The use of *tert*-butyl hydroperoxide in decane allows for a uniform or monophasic organic soluble catalyst system, and thus further improves the optimal yield.

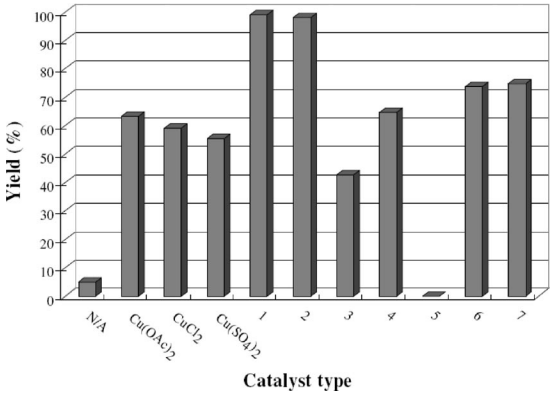
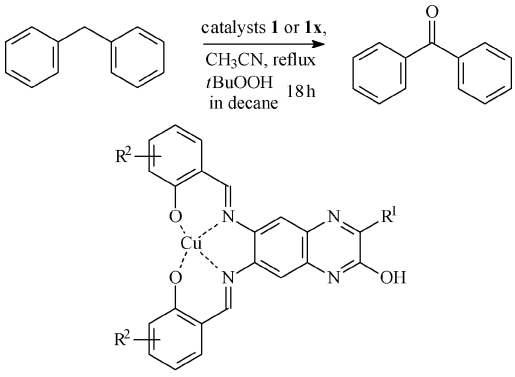


Figure 6. Reaction yields using copper salts or ligand-supported metal catalysts (salen, salph, and salqu ligands). Yields are based on separation by flash-column chromatography.

Table 1. Optimized conditions with different salqu Cu catalysts (**1x**).



	R^1	R^2	Yield (%)[a]
1	CH_2Ph	3,5-di-*tert*-butyl	99
1a	CH_2Ph	3-*tert*-butyl	92
1b	$CH_2CH(CH_3)_2$	3,5-di-*tert*-butyl	99
1c	$CH_2CH(CH_3)_2$	H	90
1d	$CH_2CH(CH_3)_2$	5-OH	80
1e	$CH(CH_3)_2$	H	90
1f	$CH(CH_3)_2$	5-OH	65
1g	$CH_2CH_2SCH_3$	3-OH	77

[a] Yields are based on separation by flash-column chromatography and mass calculation.

With *tert*-butyl hydroperoxide in decane as oxidant, the catalyst ratio was increased from 0.1% to 3% (their turnover numbers are 736, 176, 99 and 32, respectively.) It was found that 1% of catalyst **1** is best for this oxidation (Figure 3). Although 0.1% of catalyst **1** leads to the highest turnover number, using 1% of catalyst **1** results in the optimal yields within 18 h. Increasing the amount of catalyst beyond this point did not decrease the reaction time required to achieve the optimal yield of benzophenone. Using less than 1% catalyst resulted in reduced yields (Figure 3). Decreasing the reaction time or oxidant ratio also results in lower yields (Figures 4 and 5). The addition of more of the *tert*-butyl hydroperoxide oxidant also does not serve to decrease the reaction time (Figure 5).

Finally, several polar and non-polar solvents were tested. With acetonitrile, chloroform, toluene and hexane as solvents, the yields of the desired product, benzophenone, are very high (over 95%), but using THF as solvent, the yields are very low, because of the degradation of THF under oxidative conditions.[20] It is worth mentioning that when toluene was used as solvent, there were not any byproducts generated by reaction of the toluene obtained. Therefore, the optimal reaction conditions require acetonitrile (toluene, hexane or chloroform) as solvent, the addition of 3 equiv. of *tert*-butyl hydroperoxide in decane as oxidant, with 1% of the catalyst salquCu **1**. The reaction mixture heated to reflux temperature and found to be complete after 18 h.

Previously, a library of salqu ligands has been prepared using combinatorial methods.[18] These have been used to prepare stable metal complexes of broad solubility with Ni^{2+}, Co^{2+}, Cu^{2+}, Mn^{2+} or UO_2^{2+}.[19] Different metal complexes were tested as catalysts (Figure 6).

Without the addition of catalyst, oxidation using 3 equiv. of *tert*-butyl hydroperoxide in decane as oxidant in acetonitrile heated to reflux temperature for 18 h, resulted in a very modest yield. Only about 5–10% of the desired product, benzophenone, was obtained. With the addition of copper salts to the reaction mixture, 50–60% benzophenone can be obtained. The addition of the salph Cu complex **6** increased the yield of benzophenone obtained to 74%. Using the salen Mn complex **7**, produced a similar result, 75%.

The reason why the use of catalysts **6** and **7** results in lower yields than for salquCu **1** remains unclear, but two possibilities come to mind. Judging from the uranyl (UO_2^{2+}) crystal structure, the salqu metal complexes **1**–**5** have a slightly different metal coordination geometry than the salph (**6**) and salen complexes (**7**). The salqu ligand in the uranyl (UO_2^{2+}) metal complex is puckered and has the metal lifted above the plane of the ligand while the salen and salph (**6**) and salen complexes (**7**) are planar.[19] The salqu complexes also have improved solubility in numerous organic solvents.[18,19] Either characteristic of these complexes could affect the catalytic reaction mechanism and lead to the observed improved yields. The improved solubility of catalyst salquCu **1** also eliminates the need for a biphasic system, which would be useful in applying this system to larger scale applications.

As a demonstration of the importance of solubility toward the efficacy of this reaction, different salqu copper complexes were examined in catalytic studies. The results of these experiments are depicted in Table 1. Besides catalyst **1**, *tert*-butyl-functionalized copper complexes **1a** and **1b** show good catalytic effects, whereas hydroxy-functionalized complexes **1f** and **1g** lead to yields comparable with regular the manganese salen and copper salph complexes **6** and **7**. It is also possible that the hydroxy group impairs the catalytic function of Cu or Mn, leading to the lower yields. Complexes **1c** and **1e** gave a lower yield than catalysts **1**, **1a** and **1b**, probably because of reduced solubility.

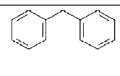
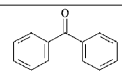
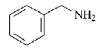
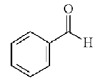
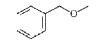
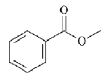
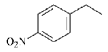
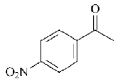
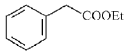
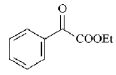
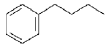
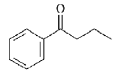
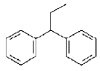
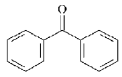
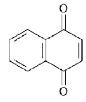
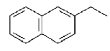
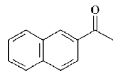
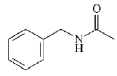
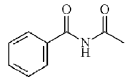
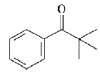
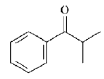
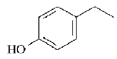
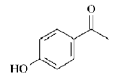
Catalyst **1** is stable to air and moisture and can be reused at least twice. Catalysts that are found to be stable both to air and moisture are much more convenient for their application. Stable capability was tested using the reaction conditions to oxidize diphenylmethane.

Diphenylmethane was treated with 1% of catalyst **1** and 3 equiv. of *tert*-butyl hydroperoxide in refluxing acetonitrile for 18 h. After 18 h, an additional equivalent of diphenylmethane, and 3 equiv. oxidant were added into the reaction system. The reaction mixture was allowed to continue refluxing for another 18 h. After this period of time, the addition was repeated. Finally, the pure benzophenone product was obtained by flash-column chromatography. The total yield is over 95% of the combined amounts of starting material. While the addition of additional material in the initial reaction (lowering the percentage of catalyst present) reduces the yield produced in 18 h, the addition of additional materials in increments indicates that the catalytic species is regenerated during the course of the reaction and that the catalyst **1** has been reused at least twice. This increases the overall lifetime of the usable catalyst and could be of benefit to reduce volumes of solvents required in larger scale reactions.

Once the optimal conditions were determined, these were used in reactions with several compounds containing aryl methylene group to be oxidized (Table 2). It was found that if there is an electron-donor group neighbouring to the methylene group to be oxidized, the yield is increased (Entries 1, 2 and 3), whereas if there is a neighbouring electron-withdrawing group the yield will decrease (Entries 4, 5). Aryl methylene compounds with neighbouring electron-withdrawing groups can be oxidized again to enhance the final yields (Table 2, method 2). Aryl methylene groups can be selectively oxidized, while other methylene groups are not affected (Entry 6). If an amino or hydroxy group is present neighbouring to the methylene group, the final product produced is an aldehyde (Entries 2 and 9). By this method, not only may the aryl methylenes be oxidized to the corresponding carbonyl groups, but an ether group can be converted to an ester in good yields (Entry 3).

If there is no aryl group neighbouring the methylene group, the expected product was not found (Entry 16). This could also be due to steric limitations on the configurational geometry of the metal complex to the catalytic mechanism. For example, when there is a bulky *tert*-butyl group on the methylene, none of the expected product found (Entries 13, 14). Compounds containing a hydroxy group were found to have no reaction (Entry 15) or lower yields (Entry 9), presumably because the oxygen atom could coordinate with the catalyst metal centre, (in this case copper), and this would block the catalyst mechanism. Remarkably, tetrahydroisoquinoline and tetrahydroquinoline were special cases. Oxidation of tetrahydroisoquinoline and tetrahydroquinoline using this method leads to isoquinoline and quinoline (Entries 17 and 18 respectively), but not α-ketoisoquinoline or α-ketoquinoline analogs. For some of the oxidation reactions found to have poor yields, the yield can be improved using a modified reaction scheme, method 2 (Entries 4, 5, 10 and 11).

Table 2. Tested aryl methylene compounds using catalyst **1**.

Entry[a]	Starting material	Final product	Yield (%)[f]
1			99[c]
2			88[c]; [e]
3			93[c]
4			50[c]; 90[d]
5			14[c]; 82[d]
6			80[c]
7			81[c]
8			80[c]
9			47[c]
10		 	26[d] 66[d]
11			60[c]; 91[d]
12			_[b]
13			_[b]
14			_[b]
15			_[b]
16			_[b]
17			56 [c]
18			66 [c]

[a] All of products have been characterized by ^{1}H and ^{13}C NMR and in agreement with their standard NMR spectrum. [b] None of the expected final product is obtained. [c] Method 1: 1% catalyst **1**, CH_3CN, 3 equiv. *t*BuOOH (in decane), reflux for 18 h. [d] Method 2: (1) 1% catalyst **1**, CH_3CN, 3 equiv. *t*BuOOH (in decane), reflux for 18 h. (2) 3 equiv. *t*BuOOH (in decane), CH_3CN, reflux for 18 h. [e] After 40 min the Schiff base product, *N*-benzylidenebenzylamine is formed. 89% of benzaldehyde was determined by adding the reacted benzaldehyde with pure isolated benzaldehyde. [f] Yields are based on separation by flash-column chromatography and mass calculation.

The oxidation of benzylamine directly into benzaldehyde by the catalyst **1** mimics the important biological process of oxidation of amine substrates to aldehydes as catalyzed by the naturally occurring metalloenzymes that contain copper, namely amine and lysyl oxidases (Entry 2).[21] Once the benzaldehyde is generated, this can react directly with any remaining unreacted benzylamine to form *N*-benzylidenebenzylamine. *N*-Benzylidenebenzylamine is a useful, costly but commercially available, indicator reagent used for organolithium assays and as an intermediate of amino acid syntheses, and this is a potentially useful as an easy, inexpensive method to prepare *N*-benzylidenebenzylamine directly from benzylamine.[22,23]

In another example of the potential utility of this catalyst, 1,4-naphthoquinone is typically prepared on an industrial scale from naphthalene using oxygen gas with a vanadium catalyst at high temperature while under pressure. This reaction typically yields no more than 40%.[24] This is an important compound as it is a key intermediate of several natural products including phylloquinone and menaquinone (vitamin K_1 and K_2),[25] the derivatives of which have been found to have broad bioactivity ranging from anticancer to antifungal.[26] Several new methods for preparing 1,4-naphthoquinone derivatives have been developed, but all of them involve more expensive metal catalysts.[27] Here, we set up a new method for preparing 1,4-naphthoquinone by using inexpensive commercial available starting material 1,2,3,4-tetrahydronaphthalene and easily prepared salquCu catalysts **1** with 63% yield (Entry 10). This conversion also mimics another crucial biological oxidization process catalyzed by galactose oxidase.[28]

This is a promising new result, but it remains to determine the specific oxidation mechanism, although the mechanism of oxidation by copper salt and THBP has been investigated.[29] This can be difficult, because if the mechanism involves a carbon cation intermediate, the methoxyl group should be better leaving group than hydrogen (Entry 3) in conversion of phenyl methyl ether to methyl benzoate. In contrast, we find that in this case, the hydrogen acts as the leaving group. Secondly, if the mechanism involves a radical intermediate, the conversion of 1,1-diphenylpropane to benzophenone can not be explained and the expected product 1,1-diphenylpropanol should be obtained as the final product (Entry 7). In addition, conversion of tetrahydroquinoline to quinoline, the expected α-ketoquinolines have not been obtained, indicating an unexpected mechanism occurs (Entries 17 and 18). Another question that arises is in the case of benzylamine (Entry 2). The expected product would be benzoic amide; however, the major product found is benzaldehyde in very good yield (>88%).

Conclusions

The unusual salquCu metal complex **1** has been developed for use in oxidation of aryl methylenes with good yields. Results of the optimization process indicate that the configuration and solubility of salqu copper complex catalyst (e.g., **1**) are key factors during the oxidation. Besides the salqu copper complex **1**, the salqu manganese complex was also found to demonstrate catalytic ability.

Using the copper catalyst **1**, an important fragment of natural compound, 1,4-naphthoquinone, can be easily obtained in high yields, and the oxidations of the metalloenzymes amine oxidase and galactose oxidase, can be mimicked. These types of catalysts present a new option for use in industry or organic syntheses because of their relative ease of preparation, low sensitivity to moisture and air, and the use of more environmentally friendly and less costly metals. They are also soluble in many common organic solvents. They possess high catalytic efficiency and can be reused at least twice. In future work, we will investigate the immobilization of the salqu metal complexes (e.g., **1**) by incorporating them into polymers for use in solid phase catalysts based on the developed solid phase extraction (SPE) technology.[30] The mechanism of this oxidation and new reactions will also be further investigated.

Experimental Section

General: All of starting materials were purchased from Acros, TCI or Alfa Aesar Inc. and were used as received. *tert*-Butyl hydroperoxide in decane (6 M) and salen Mn complex **7** were purchased from Aldrich. Salqu ligands were synthesized by a previously published procedure.[19,20,31] Solvents were purchased from Fisher Scientific and were used directly. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AC 250 spectrometer (operated at 250 and 62.5 MHz, respectively) or Bruker AV 400 spectrometer (operated at 400 and 100 MHz, respectively). The final synthesized products (Entries 1 to 19) were identified by TLC, ^{1}H and ^{13}C NMR and compared with TLC, ^{1}H and ^{13}CNMR of commercially available compounds. The known ^{1}H and ^{13}C NMR of commercial available compounds are available from spectroscopic database for organic compounds (SDBS), National Institute of Advanced Industrial Science and Technology (AIST), Japan. Chemical shifts are reported as δ values (ppm). NMR spectroscopic data were collected by using $CDCl_3$ or [D_6]DMSO. The solvents used are indicated in the experimental details. Reaction progress was monitored by thin-layer chromatography (TLC) using 0.25 mm Whatman aluminum plates precoated with silica gel 60-F254, visualization by irradiation with a Mineralight UVGL-25 lamp. The products yields are based on separation by flash-column chromatography.

General Method 1: The synthesis of the products depicted in Table 2 began with the combination of catalyst **1** (0.02 mmol, 15.2 mg) and 2.0 mmol of starting material (aryl methylene compound) dissolved in 2.0 mL acetonitrile with 1.0 mL *tert*-butyl hydroperoxide decane solution (6.0 mmol). The reaction mixture was stirred for 18 h at 70 °C and monitored by TLC. Once the starting material could no longer be seen by TLC, the reaction was considered to be complete. Pure products were obtained using flash column chromatography with a solution of hexane/ethyl acetate, 10–20:1 as the eluent. The yields of final pure products were from 45–99% (see notation in Table 2).

General Method 2: For reactions found to result in low yields (see Table 2), a modified procedure was employed. The procedure began with of the addition of catalyst **1** (0.02 mmol, 15.2 mg) and 2.0 mmol of starting materials (aryl methylene compounds) dissolved in 2.0 mL acetonitrile and 1.0 mL *tert*-butyl hydroperoxide

decane solution (6.0 mmol). The reaction mixture was stirred for 18 h at 70 °C. After 18 h, an additional 1.0 mL of *tert*-butyl hydroperoxide decane solution (6.0 mmol) was added and the solution was heated at reflux temperature for an additional 18 h. The reaction was monitored by TLC. Once the starting material can no longer be seen by TLC, the reaction was considered to be complete. Pure products are obtained by purification using flash column chromatography with a solution of hexane/ethyl acetate (10–20:1) as eluent. The yields of final pure products were from 65–92% (see notation in Table 2).

Data Section

Entry 1: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (t, 4 H), 7.62 (t, 2 H), 7.84 (d, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 137.6, 132.5, 130.1, 128.3 ppm.

Entry 2, *N*-Benzylidenebenzylamine: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.87 (s, 2 H), 7.28–7.93 (m, 10 H), 8.43 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.5, 139.0, 136.4, 134.5, 130.9, 130.6, 64.9 ppm.

Benzaldehyde: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (t, 2 H), 7.60 (t, 1 H), 7.86 (d, 2 H), 10.01 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.9, 136.0, 134.0, 129.3, 128.6 ppm.

Entry 3: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 3 H), 7.43 (t, 2 H), 7.53 (t, 1 H), 8.05 (d, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.1, 132.9, 130.2, 129.6, 128.4, 128.2, 126.9, 52.0 ppm.

Entry 4: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.71 (s, 3 H), 8.15 (d, 2 H), 8.35 (d, 2 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 196.3, 141.4, 129.3, 123.9, 27.0 ppm.

Entry 5: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, 3 H), 4.60 (q, 2 H), 7.53 (t, 2 H), 7.67 (t, 1 H), 8.01 (d, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.5, 163.9, 134.9, 132.4, 130.0, 128.9, 62.4, 14.1 ppm.

Entry 6: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, 3 H), 1.97 (m, 2 H), 2.96 (t, 2 H), 7.46 (t, 2 H), 7.53 (t, 1 H), 7.96 (d, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.4, 137.1, 132.9, 128.4, 128.2, 128.0, 40.5, 27.2, 13.9 ppm.

Entry 7: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (t, 4 H), 7.62 (t, 2 H), 7.85 (d, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 137.6, 132.4, 130.1, 128.3 ppm.

Entry 8: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57 (s, 3 H), 7.49 (t, 2 H), 7.60 (t, 1 H), 7.94 (d, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 137.3, 133.6, 129.1, 128.6, 27.2 ppm.

Entry 9: ^{1}H NMR (400 MHz $CDCl_3$): δ = 7.50 (t, 2 H), 7.60 (t, 1 H), 7.86 (d, 2 H), 10.01 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.9, 136.0, 134.0, 129.3, 128.6 ppm.

Entry 10: ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 7.02 (s, 2 H), 7.80 (dd, 2 H), 8.13 (dd, 2 H) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 185.1, 138.7, 134.0, 131.9, 126.5 ppm.

Entry 11: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.71 (s, 3 H), 7.56 (m, 2 H), 7.62 (m, 4 H), 8.05 (s, 1 H) ppm. ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 198.1, 135.6, 134.4, 132.5, 130.2, 129.6, 128.5, 128.4, 127.8, 126.8, 123.9 ppm.

Entry 17: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.96 (m, 5 H), 8.54 (d, 1 H), 9.27 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.5, 142.9, 135.8, 130.4, 127.6, 127.3, 126.5, 120.5 ppm.

Entry 18: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (m, 1 H), 7.47 (t, 1 H), 7.63 (t, 1 H), 7.73 (d, 1 H), 8.06 (m, 2 H), 8.60 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.3, 148.2, 136.0, 129.4, 128.2, 127.8, 126.5, 121.0 ppm.

Supporting Information (see also the footnote on the first page of this article): General experimental methods and ^{1}H and ^{13}C-NMR spectra of the compounds produced (see Table 2).

Acknowledgments

Funding was provided by Auburn University and the Department of Chemistry and Biochemistry. We would like to express our appreciation to Prof. C. R. Goldsmith for his helpful discussions. Literature references for ^{1}H, ^{13}C NMR spectra used for comparison were obtained from SDBSWeb: http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology, July 2008).

[1] a) R. D. Smiley, G. G. Hammes, *Chem. Rev.* **2006**, *106*, 3080; b) S. T. Connon, S. Blechert, *Angew. Chem. Int. Ed.* **2003**, *42*, 1900; c) K. C. Nicolaou, D. Vourloumis, N. Winssinger, P. S. Baran, *Angew. Chem. Int. Ed.* **2000**, *39*, 44; d) S. Caron, R. W. Dugger, S. G. Ruggeri, J. A. Ragan, D. H. B. Ripin, *Chem. Rev.* **2006**, *106*, 2943; e) R. H. Grubbs, *Angew. Chem. Int. Ed.* **2006**, *45*, 3760; f) R. R. Schrock, *Angew. Chem. Int. Ed.* **2006**, *45*, 3748; g) Y. Chauvin, *Angew. Chem. Int. Ed.* **2006**, *45*, 3741.

[2] a) P. J. Walsh, H. Li, C. A. Parrodi, *Chem. Rev.* **2007**, *107*, 2503; b) B. Notari, *Catal. Today* **1993**, *18*, 163; c) A. Butler, M. J. Clague, G. E. Meister, *Chem. Rev.* **1994**, *94*, 625; d) J. M. Aubry, S. J. Bouttemy, *J. Am. Chem. Soc.* **1997**, *119*, 5286; e) D. H. Dickman, *Chem. Rev.* **1994**, *94*, 569.

[3] a) G. Dyker, *Angew. Chem. Int. Ed.* **1999**, *38*, 1698; b) T. Naota, H. Takaya, S.-I. Murahashi, *Chem. Rev.* **1998**, *98*, 2599; c) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731; d) H. Chen, S. Schlecht, T. C. Semple, J. F. Hartwig, *Science* **2000**, *287*, 1995; e) A. S. Goldman, *Nature* **1993**, *366*, 514.

[4] a) A. Erkkila, I. Majander, P. M. Pihko, *Chem. Rev.* **2007**, *107*, 5416; b) D. Darensbourg, *Chem. Rev.* **2007**, *107*, 2388; c) N. E. Borisova, M. D. Reshetova, Y. A. Ustynyuk, *Chem. Rev.* **2007**, *107*, 49; d) S. E. Denmark, E. N. Jacobsen, *Acc. Chem. Res.* **2000**, *33*, 324; e) S. Dey, D. R. Powell, C. Hu, D. B. Berkowitz, *Angew. Chem. Int. Ed.* **2007**, *46*, 7010; f) A. Pui, J.-P. Mahy, *Polyhedron* **2007**, *26*, 3143; g) Z. Lue, M. Yuan, F. Pan, S. Gao, D. Zhang, D. Zhu, *Inorg. Chem.* **2006**, *45*, 3538.

[5] S. Velusamy, T. Punniyamurthy, *Tetrahedron Lett.* **2003**, *44*, 8955.

[6] a) H. B. Henbest, B. Nicholls, *J. Chem. Soc.* **1959**, 221; b) S. Harrison, *Chem. Commun. (London)* **1966**, 752; c) A. J. Catino, R. E. Forslund, M. P. Doyle, *J. Am. Chem. Soc.* **2004**, *126*, 13622; d) H. M. C. Ferraz Jr., L. S. Longo, *Org. Lett.* **2003**, *5*, 1337; e) R. Breslow, P. C. Scholl, *J. Am. Chem. Soc.* **1971**, *93*, 2331; f) J. Q. Yu, E. J. Coery, *J. Am. Chem. Soc.* **2003**, *125*, 3232; g) S. Tsunoi, I. Ryu, N. Sonoda, *J. Am. Chem. Soc.* **1994**, *116*, 5473.

[7] a) A. Krief, L. Hevesi, *Organoselenium Chemistry I*, Springer, NY, **1998**, 115; b) E. S. Krongauz, *Russ. Chem. Rev.* **1977**, *46*, 59; c) N. Rabjohn, *Org. React.* **1976**, *24*, 261; d) E. J. Coery, J. P. Schaefer, *J. Am. Chem. Soc.* **1960**, *82*, 918; e) K. B. Sharpless, K. M. Gordon, *J. Am. Chem. Soc.* **1976**, *98*, 300.

[8] a) J. H. Markgraf, B. Y. Choi, *Synth. Commun.* **1999**, *29*, 2405; b) J. H. Markgraf, C. A. Stickney, *J. Heterocycl. Chem.* **2000**, *37*, 109; c) S. Negele, K. Wieser, T. Severin, *J. Org. Chem.* **1998**, *63*, 1138; d) H. X. Wei, R. L. Jasoni, H. Shao, J. Hu, P. W. Pare, *Tetrahedron* **2004**, *60*, 11829.

[9] a) H. H. Wasserman, J. L. Ives, *J. Org. Chem.* **1978**, *43*, 3238; b) H. H. Wasserman, J. L. Ives, *J. Org. Chem.* **1985**, *50*, 3573; c) D. V. Rao, F. A. Stuber, H. Ulrich, *J. Org. Chem.* **1979**, *44*, 456; d) P. Li, W. M. Fong, L. C. F. Chao, S. H. C. Fung, I. D. Williams, *J. Org. Chem.* **2001**, *66*, 4087.

[10] a) J. C. Lee, H. J. Park, J. Y. Park, *Tetrahedron Lett.* **2002**, *43*, 5661; b) Z. Li, C. G. Xiu, C. Z. Xu, *Tetrahedron Lett.* **2003**, *44*, 9229; c) N. K. Sharma, K. N. Ganesh, *Tetrahedron Lett.* **2004**,

45, 1403; d) X. Zhang, A. C. Schmitt, W. Jiang, *Tetrahedron Lett.* **2001**, *42*, 5335.
[11] a) S. I. Murahashi, N. Komiya, Y. O. Kuwabara, T. Naota, *J. Org. Chem.* **2000**, *65*, 9186; b) A. R. Doumaux Jr., D. J. Trecker, *J. Org. Chem.* **1970**, *35*, 2121; c) A. J. Catino, J. M. Nichols, H. Choi, S. Gottipamula, M. P. Doyle, *Org. Lett.* **2005**, *7*, 5167; d) Y. Bonvin, E. Callens, I. Larrosa, D. A. Henderson, J. Oldham, A. J. Burton, A. G. M. Barrett, *Org. Lett.* **2005**, *7*, 4549; e) J. Mazurt, *Chem. Rev.* **1992**, *92*, 113.
[12] a) R. Rangarajan, E. J. Eisenbraun, *J. Org. Chem.* **1985**, *50*, 2435; b) H. Lee, R. G. Harvey, *J. Org. Chem.* **1988**, *53*, 4587; c) D. Ma, C. Xia, H. Tian, *Tetrahedron Lett.* **1999**, *40*, 8915.
[13] a) A. Shaabani, D. G. Lee, *Tetrahedron Lett.* **2001**, *42*, 5833; b) F. Minisci, C. Punta, F. Recupero, F. Fontana, G. F. Pedulli, *J. Org. Chem.* **2002**, *67*, 2671; c) S. Minakata, E. Imai, Y. Ohshima, K. Inaki, I. Ryu, M. Komatsu, Y. Ohshiro, *Chem. Lett.* **1996**, 19; d) M. Miyamoto, Y. Minami, Y. Ukaji, H. Kinoshita, K. Inomata, *Chem. Lett.* **1994**, 1149.
[14] a) K. Kamata, J. Kasai, K. Yamaguchi, N. Mizuno, *Org. Lett.* **2004**, *6*, 3577; b) P. H. J. Crlsen, T. Katsuki, V. S. Martin, K. B. Sharpless, *J. Org. Chem.* **1981**, *46*, 3936; c) T. C. Lau, C. K. Mak, *J. Chem. Soc., Chem. Commun.* **1993**, 766.
[15] a) N. Komiya, S. Noji, S. I. Murahashi, *Tetrahedron Lett.* **1998**, *39*, 7921; b) N. H. Lee, C. S. Lee, D. S. Jung, *Tetrahedron Lett.* **1998**, *39*, 1385.
[16] a) U. Schuchardt, M. J. D. M. Jannini, D. T. Richens, M. C. Guerreiro, E. V. Spinace, *Tetrahedron* **2001**, *57*, 2685; b) D. H. R. Barton, E. Csuhai, N. Ozbalik, *Tetrahedron Lett.* **1990**, *31*, 1657.
[17] D. H. R. Barton, *Chem. Soc. Rev.* **1996**, *25*, 237.
[18] a) X. Wu, A. E. V. Gorden, *J. Comb. Chem.* **2007**, *9*, 601; b) X. Wu, A. E. V. Gorden, S. A. Tonks, J. Z. Vilseck, *J. Org. Chem.* **2007**, *72*, 8691.
[19] X. Wu, T. H. Bray, M. S. Bharara, B. K. Tate, A. E. V. Gorden, *Inorg. Chem. Acta*, in press.
[20] R. F. Moreira, E. Y. Tshuva, S. J. Lippard, *Inorg. Chem.* **2004**, *43*, 4427.
[21] a) S. Nara, B. Gomes, K. T. Yosunobu, *J. Biol. Chem.* **1966**, *241*, 2774; b) T. Koyanagi, K. Matsumura, S. Kuroda, K. Tanizawa, *Plant Cell Physiol.* **2000**, *41*, 1259.
[22] R. G. Gillis, *J. Org. Chem.* **1956**, *21*, 805.
[23] L. Duhamel, J. C. Plaquevent, *J. Org. Chem.* **1979**, *44*, 3404.
[24] U. M. Azizov, L. I. Leonteva, *Pharm. Chem. J.* **1989**, *23*, 1017.
[25] a) S. J. Elder, D. B. Haytowitz, J. Howe, J. W. Peterson, S. L. Booth, *J. Agric. Food Chem.* **2006**, *54*, 463; b) Y. Naruta, *J. Org. Chem.* **1980**, *45*, 4097.
[26] a) I. Dai, I. Masami, Y. Yukinori, *J. Nat. Prod.* **2003**, *66*, 1611; b) T. Kazuhito, Y. Hisatsugu, N. Sei-Ichi, *J. Am. Chem. Soc.* **2007**, *129*, 12585; c) K. Barbara, Z. Wieslawa, *Bioorg. Med. Chem.* **2007**, *15*, 4144; d) E. Giaccomo, L. M. Grazia, L. Catarina, W. Vierle, S. M. Elisabeth, B. Roland, *Eur. J. Med. Chem.* **2006**, *41*, 773; e) K. Barbara, Z. Wieslawa, *Bioorg. Med. Chem.* **2007**, *15*, 4144; f) V. Claudia, M. Rui, C. G. Rita, L. Jim, J. Mohammed, T. D. Kenneth, *Bioorg. Med. Chem.* **2007**, *15*, 5340.
[27] a) C. C. Huang, N. H. Chang, *Org. Lett.* **2008**, *10*, 673; b) P. Chatchawan, K. Boonsong, K. Ngampong, *Synth. Commun.* **2007**, *37*, 1463; c) X. L. Wang, X. F. Zheng, J. Reiner, *Synlett* **2006**, *6*, 942.
[28] a) A. J. Baron, C. Stevens, C. Wilmot, K. D. Seneviratne, V. Blakeley, D. M. Dooley, S. E. V. Phillips, P. F. Knowles, M. J. Mcpherson, *J. Biol. Chem.* **1994**, *269*, 25095; b) Y. Wang, T. D. P. Stack, *J. Am. Chem. Soc.* **1996**, *118*, 13097.
[29] G. Rothenberg, L. Feldberg, H. Wiener, Y. Sasson, *J. Chem. Soc. Perkin Trans. 2* **1998**, 2429.
[30] X. Wu, A. E. V. Gorden, *Tetrahedron Lett.* **2008**, *49*, 5200.
[31] a) L. Zhang, G. Liu, S. D. Zhang, H. Z. Yang, L. Li, X. Wu, J. L. Yu, B. B. Kou, S. Xu, J. Li, G. C. Sun, Y. F. Ji, G. F. Cheng, *J. Comb. Chem.* **2004**, *6*, 431; b) X. Wu, G. Liu, J. Zhang, Z. G. Wang, S. Xu, S. D. Zhang, L. Zhang, L. Wang, *Mol. Diversity* **2004**, *8*, 165; c) G. Liu, Y. M. Fan, J. R. Calson, K. S. Lam, *J. Comb. Chem.* **2000**, *2*, 467.

Received: September 23, 2008
Published Online: December 18, 2008

