

# A summary of research accomplishments and objectives in the Kerr group

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## Preamble

In my research group we are engaged in the development of new synthetic methods which will be of interest to the chemical community and the application of these methods to the synthesis of natural and unnatural products of biological and medicinal interest. We have gained expertise in 1) the use of ultra-high pressures to promote useful chemical reactions, 2) the Diels-Alder reactions of unusual dienophiles, 3) the synthesis and chemical reactivity of heterocyclic systems, particularly indoles, 4) the chemical synthesis of complex target molecules, particularly alkaloids, 5) the use of donor/acceptor cyclopropanes in organic synthesis and 6) the development of new cycloadditions.

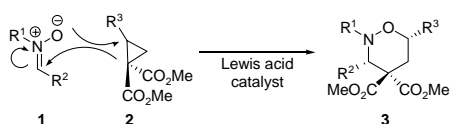
Since moving to Western in 1999 from the less research intensive environment of Acadia University, we have established one of the top synthetic organic groups in Canada. Currently I have a group of 13 graduate students who have worked very hard to achieve a level productivity and innovation I am proud of.

A short summary of our research program follows:

## The development of a homo-3+2-dipolar cycloaddition

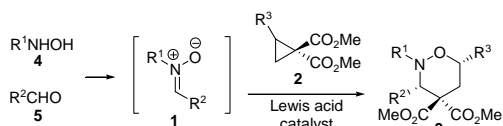
Recently we have described the reaction of nitrones with cyclopropanes in what we have termed a homo-3+2-dipolar cycloaddition.<sup>1</sup> In this reaction (Scheme 1) the combination of a nitrone with a 1,1-cyclopropanediester under the influence of a Lewis acid (most suitably a lanthanide triflate) results in the smooth formation of a tetrahydro-1,2-oxazine. This is a relatively unusual ring system and the direct synthesis of such compounds is rare. This is an unusual reaction and we have collaborated with former colleague Tom Woo in a DFT investigation of this reaction.<sup>2</sup>

## Scheme 1: A homo-3+2-dipolar cycloaddition



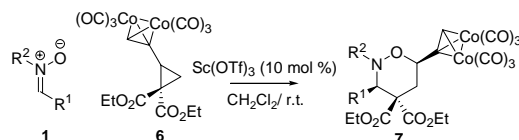
We followed this up with a three component version of this reaction whereby the requisite nitrone is formed in situ by the combination of a hydroxylamine with an aldehyde (Scheme 2).<sup>3</sup> We have also found, subsequent to our initial report, that  $MgI_2$  is an effective catalyst for the promotion of this reaction.<sup>4</sup>

## Scheme 2: A 3-component coupling



The group vicinal to the diester moiety in CDE's is integral in activating the ring-opening/cycloaddition reactions. An acetylenic cyclopropane complexed with cobalt octacarbonyl was subjected to our reaction conditions to produce oxazines in excellent yields (Scheme 2).<sup>5</sup> The dicobalt functionality was a handle for elaboration of the adducts.

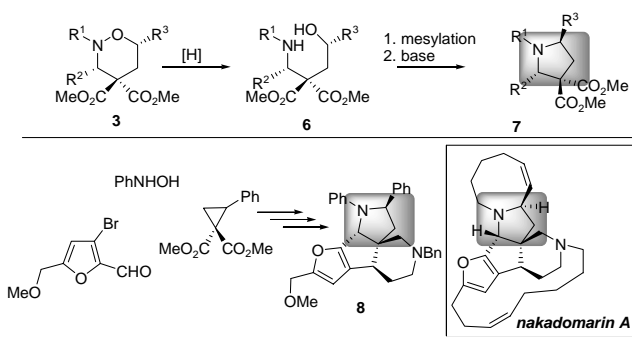
## Scheme 3: Nicholas activation of cyclopropanes



## A pyrrolidine synthesis and the synthesis of nakadomarin A

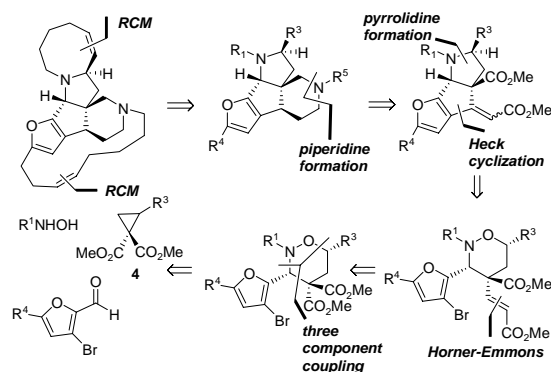
The presence of an NO bond in a ring begs the application of a reductive cleavage to form an aminoalcohol. We found this to be an unexpected challenge, however the desired transformation was accomplished by treatment with  $SmI_2$ .<sup>6</sup> The resulting 1,4-aminoalcohol was treated with mesyl chloride to effect a ring closure to a pyrrolidine with 2,5-trans stereochemistry (Scheme 3). A pyrrolidine with the substitution pattern (shaded box in Scheme 4) we end up with just happens to be a central structural feature of the beautifully complex alkaloid nakadomarin A. After illustrating that we can make a model<sup>5</sup> containing the core structure of nakadomarin A, we have, in fact, employed that methodology to the successful synthesis of the target itself.

## Scheme 4: A stereoselective pyrrolidine synthesis



Our retrosynthesis of nakadomarin A is shown in Scheme 4. It is based on our model study (vide supra) with the modification that core structure will be adorned with appendages suitable for elaboration of the 8- and 15-membered rings.

## Scheme 5: Retrosynthesis of nakadomarin A



<sup>1</sup> Young, I.S.; Kerr, M.A. *Ang. Chem. Int. Ed.* **2003**, 42, 3023.

<sup>2</sup> Wanapun, D.; Kerr, M.A.; Woo, T. *Can. J. Chem.* **2005** in press.

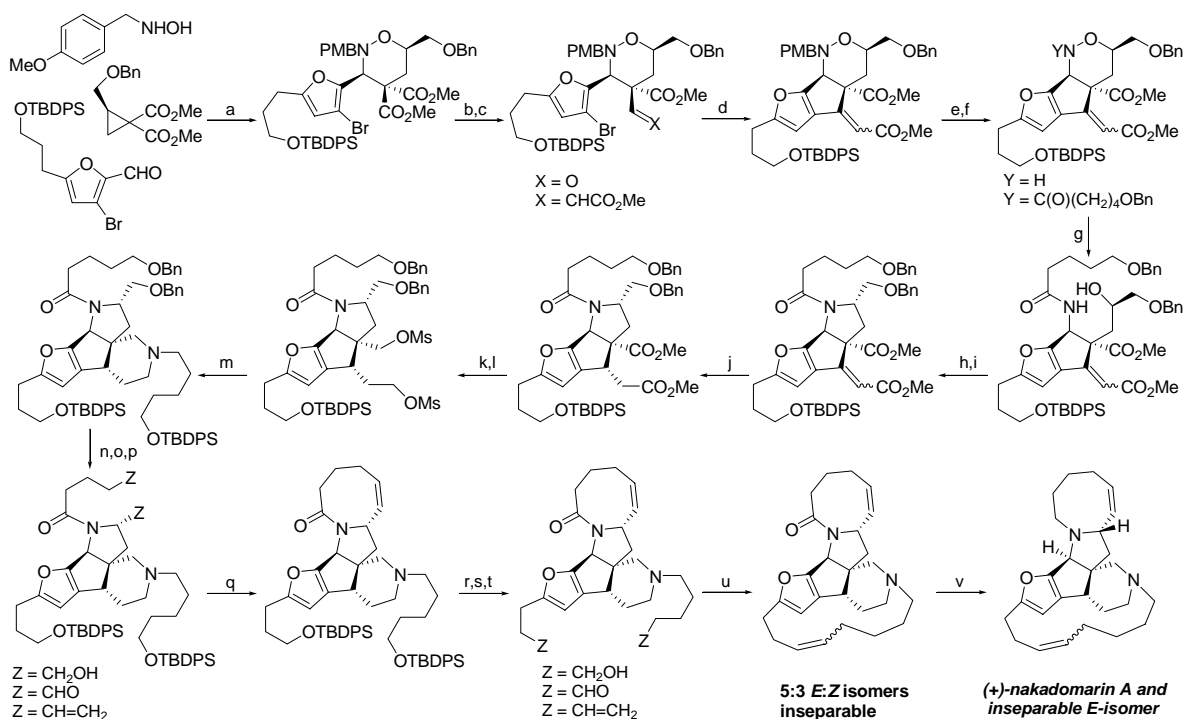
<sup>3</sup> Young, I.S.; Kerr, M.A. *Organic Letters*, **2004**, 6, 139-141.

<sup>4</sup> Ganton, M.D.; Kerr, M.A. *A J. Org. Chem.* **2004**, 69, 8554-8557.

<sup>5</sup> Lebold, T.P.; Carson, C.A.; Kerr, M.A. *Synlett* **2006**, 364.

<sup>6</sup> Young, I.S.; Williams, J.L.; Kerr, M.A. *Organic Letters* **2005**, 7, 953-955.

**Scheme 6:** Synthesis of nakadomarin A as alkene isomers.



<sup>a</sup> (a) 15% Yb(OTf)<sub>3</sub>, 4A MS, 100 °C, 87%; (b) DIBAL, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C, 87%; (c) (MeO)<sub>2</sub>P(O)CH<sub>2</sub>CO<sub>2</sub>Me, t-BuOK, THF, rt, 93%; (d) Pd(PPh<sub>3</sub>)<sub>4</sub>, Ag<sub>2</sub>SO<sub>4</sub>, NEt<sub>3</sub>, DMF, reflux, 82%; (e) DDQ, CH<sub>2</sub>Cl<sub>2</sub>/H<sub>2</sub>O 9:1, 56% after 1 recycle; (f) ClC(O)(CH<sub>2</sub>)<sub>4</sub>OBn, NEt<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C → rt, 89%; (g) 0.1M SmI<sub>2</sub>, THF, 0 °C, (5:1 ratio of double bond isomers); (h) MsCl, NEt<sub>3</sub>, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C; (i) t-BuOK, THF, -25 °C, 65% combined yield (3 steps); (j) NiCl<sub>2</sub>•6H<sub>2</sub>O, NaBH<sub>4</sub>, Na<sub>2</sub>CO<sub>3</sub>, MeOH/THF (10:1), -40 °C, 67% (14:1 diastereomers); (k) LiAlH<sub>4</sub>, THF, 0 °C; (l) MsCl, NEt<sub>3</sub>, DMAP, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C → rt, 79% (2 steps), 14:1 diastereomers; (m) TBDPSO(CH<sub>2</sub>)<sub>3</sub>NH<sub>2</sub>, EtOH/THF (10:1), reflux (74%); (n) BCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C (67%); (o) IBX, DMSO, rt; (p) t-BuOK, MePPh<sub>3</sub>I, THF, 0 °C, 55% (2 steps); (q) 20mol% Grubbs II, CH<sub>2</sub>Cl<sub>2</sub> (0.7 mM), reflux, 75%; (r) TBAF, THF, rt; (s) Dess-Martin periodinane, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C → rt; (t) t-BuOK, MePPh<sub>3</sub>I, THF, 0 °C, 31% (3 steps); (u) 40 mol% Grubbs I, CH<sub>2</sub>Cl<sub>2</sub> (0.2 mM), reflux, 5:3 mix E:Z, 66% combined; (v) Red-Al, toluene, reflux, 5:4 mix E:Z, 80% combined.

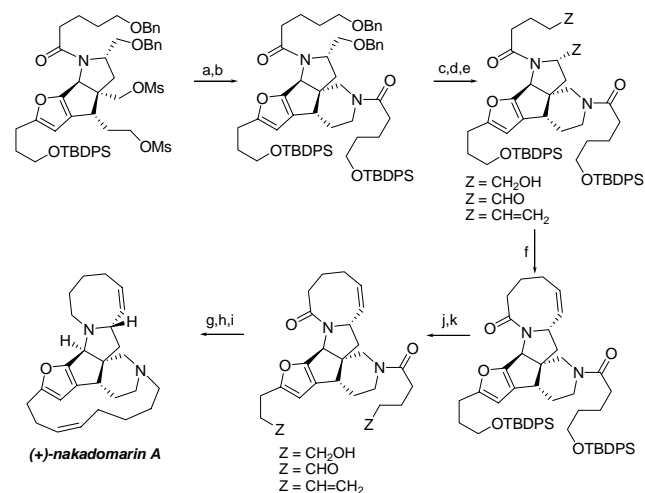
A completed synthesis of nakadomarin A is shown in Scheme 5.<sup>7</sup> All went well until the end of the synthesis where we are unable to separate the double bond isomers of the macrocyclic compound. This came as a disappointing surprise to us, however the work of Nishida gave us hope that we could retool the synthesis successfully. The only difference between our late stage compound and that of Nishida's is the fact that in his work, both nitrogen atoms are amides, whereas one of ours is an amine. The marked difference in separability of the double isomers was totally unforeseen. Scheme 7 shows how we remedied the problem by proceeding through a bis-amido intermediate. This worked as expected and we were able to prepare (+) nakadomarin A in 23 steps from the cycloaddition.

#### The synthesis of tetrahydrooxazine natural products: Total synthesis of phyllantidine

The tetrahydro-1,2-oxazine is a rare motif in natural products appearing only in FR900482 and related compounds<sup>8</sup> and in phyllantidine. It is likely that these are biooxidation products of a precursor pyrrolidine. We have shown that we can rapidly assemble the core structure of FR900482 in two steps<sup>1</sup> and have the intention of adapting our new cycloaddition to the preparation

of the natural product itself. In addition we have recently completed the synthesis of phyllantidine.<sup>16</sup>

#### Scheme 7: Successful synthesis of nakadomarin A.

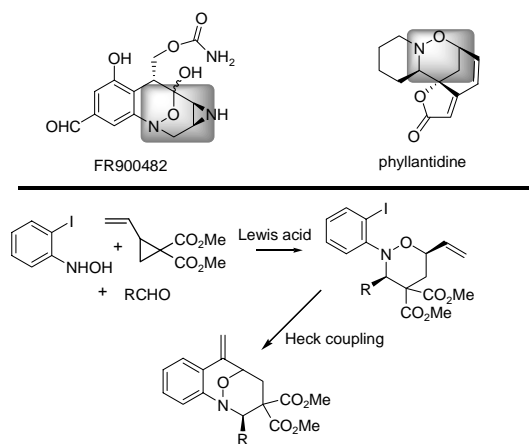


<sup>a</sup> (a) NH<sub>3</sub>, EtOH/THF (10:1), reflux; (b) ClC(O)(CH<sub>2</sub>)<sub>4</sub>OTBDPS, NEt<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C → rt, 77% (2 steps); (c) BCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, -78 °C → -50 °C → -78 °C, 71%; (d) IBX, DMSO, rt; (e) t-BuOK, MePPh<sub>3</sub>Br, THF/toluene, rt, 30-45% (2 steps); (f) 20mol% Grubbs II, CH<sub>2</sub>Cl<sub>2</sub> (0.7 mM), reflux, 84%; (g) MeOH, AcCl, rt; (h) Dess-Martin periodinane, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C → rt, 70% (2 steps); (i) t-BuOK, MePPh<sub>3</sub>Br, THF/toluene, rt; (j) 30mol% Grubbs I, CH<sub>2</sub>Cl<sub>2</sub> (0.2 mM), reflux, 28% E-isomer (2 steps), yield for Z-isomer given after reduction; (k) Red-Al, toluene, reflux (20%, 3 steps).

<sup>7</sup> Young, I.S.; Kerr, M.A. *J. Am. Chem. Soc.* **2006**, in press.

<sup>8</sup> a) M. Iwani, S. Kiyoto, H. Terano, M. Kohsaka, H. Aoki, H. Imanaka, *J. Antibiot.* **1987**, *40*, 589.; b) S. Kiyoto, T. Shibata, M. Yamashita, T. Komori, M. Okuhara, H. Terano, M. Kohsaka, H. Aoki, H. Imanaka, *J. Antibiot.* **1987**, *40*, 594.; c) I. Uchida, S. Takase, H. Kayakiri, S. Kiyoto, M. Hashimoto, *J. Am. Chem. Soc.* **1987**, *109*, 4108.

**Scheme 8:** Tetrahydro-1,2-oxazine natural products



Phyllantidine is a member of a small group of alkaloids isolated from the Euporbiaceae family of plants known as the *Securinega* alkaloids.<sup>9</sup> These compounds have an indolizidine core imbedded within an azabicyclo [3.2.1] ring system. This is fused to a butenolide moiety forming a rather interesting and structurally complex molecular framework. Securinine and its C2 epimer allosecurinine are constituents of *Securinega suffruticosa*<sup>10</sup> while the antipodal compounds virosecurinine and viroallosecurinine are found in *S. virosa*.<sup>11</sup> While these compounds show interesting CNS activity in the form of GABA receptor antagonism,<sup>12</sup> the synthetic chemist is drawn to the compact and complex architecture. Indeed several syntheses of the securinine<sup>13</sup> series of compounds have been reported. Of interest to us is not the indolizidines, but a related and much rarer alkaloid phyllantidine (isolated from *Phyllanthus discoides* and *Securinega suffruticosa*)<sup>14</sup> and its enantiomer (from *Breynia coronata*).<sup>15</sup>

<sup>9</sup> Snieckus, V. Alkaloids (Academic Press) (1973), 14 425-506.

<sup>10</sup> Original isolation: a) Murav'eva, V. I.; Ban'kovskii, A. I. *Dokl. Acad. Nauk SSSR* **1956**, *110*, 998-1000. b) Murav'eva, V. I.; Ban'kovskii, A. I. *Meditsinskaya Promyshlennost SSSR* **1956**, *10*, 27-8. Structure determination of securinine and isolation of allosecurinine: c) Satoda, I.; Murayama, M.; Tsuji, J.; Yoshii, E. *Tetrahedron Letters* **1962**, 1199-1206.

<sup>11</sup> a) Isolation of virosecurinine: Nakano, T.; Yang, T. H.; Terao, S. *Tetrahedron* **1963**, *19* 609-619. b) Isolation of viroallosecurinine: Saito, S.; Iwamoto, T.; Tanaka, T.; Matsumura, C.; Sugimoto, N.; Horii, Z.; Tamura, Y. *Chem. Ind.* **1964**, *28*, 1263-1264.

<sup>12</sup> Beutler, I. A.; Karbon, E. W.; Brubaker, A. N.; Malik, R.; Curtis, D. R.; Enna, S. J. *Brain Res.* **1985**, *330*, 135-140.

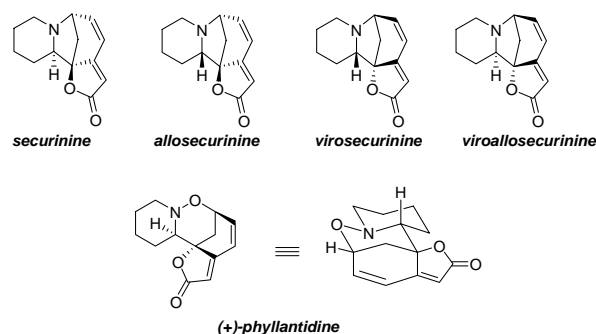
<sup>13</sup> a) Honda, T.; Namiki, H.; Watanabe, M.; Mizutani, H. *Tetrahedron Lett.* **2004**, *45*, 5211-5213. b) Alibes, R.; Ballbe, M.; Busque, F.; de March, P.; Elias, L.; Figueredo, M.; Font, J. *Org. Lett.* **2004**, *6*, 1813-1816. c) Honda, T.; Namiki, H.; Kaneda, K.; Mizutani, H. *Org. Lett.* **2004**, *6*, 87-89. d) Honda, T.; Namiki, H.; Kudoh, M.; Nagase, H.; Mizutani, H. *Heterocycles* **2003**, *59*, 169-187. e) Honda, T.; Namiki, H.; Kudoh, M.; Watanabe, N.; Nagase, H.; Mizutani, H. *Tetrahedron Lett.* **2000**, *41*, 5927-5930. f) Horii, Z.; Hanaoka, M.; Yamawaki, Y.; Tamura, Y.; Saito, S.; Shigematsu, N.; Kotera, K.; Yoshikawa, H.; Sato, Y.; Nakai, H.; Sugimoto, N. *Tetrahedron* **1967**, *23*, 1165-1174.

g) Saito, S.; Yoshikawa, H.; Sato, Y.; Nakai, H.; Sugimoto, N.; Horii, Z.; Hanaoka, N.; Tamura, Y. *Chem. Pharm. Bull.* **1966**, *14*, 313-314.

<sup>14</sup> a) Horii, Z.; Imanishi, T.; Yamauchi, M.; Hanaoka, M.; Parello, J.; Munavalli, S. *Tetrahedron Lett.* **1972**, *19*, 1877-80. b) Parello, J.; Munavalli, S. *C. R. Acad. Sci. Paris*, **1965**, *260*, 337-340.

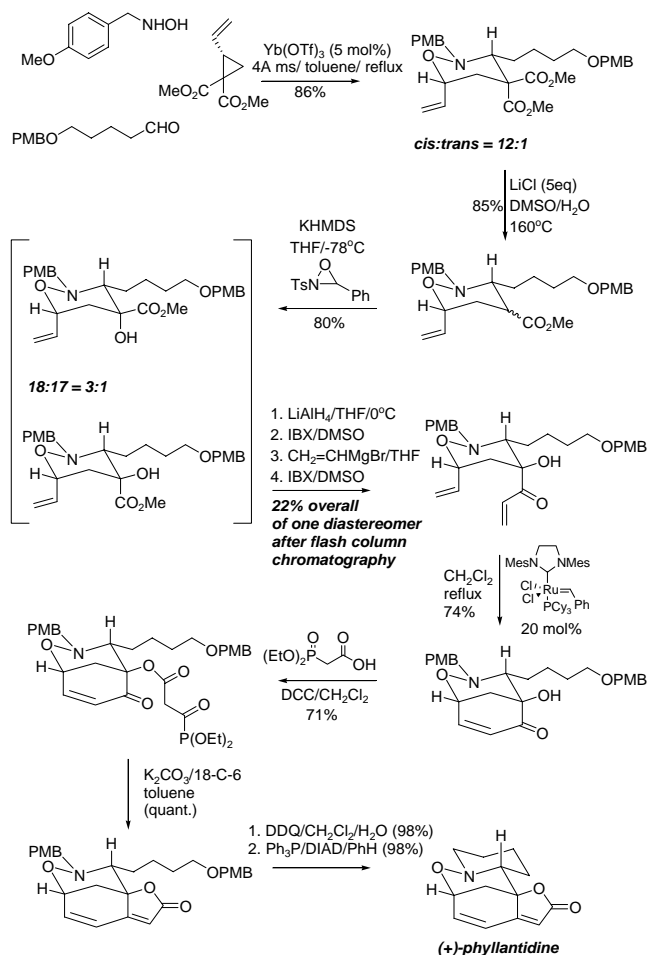
<sup>15</sup> Lajis, N.H.; Guan, O. B.; Sargent, M.V.; Skelton, B.W.; White, A.H. *Australian Journal of Chemistry* **1992**, *45*, 1893-1897.

**Figure 1:** Tetrahydro-1,2-oxazine natural products



Scheme 9 shows our recently completed synthesis of (+)-phyllantidine.<sup>16</sup> Central to the synthesis is the three component coupling of a suitable aldehyde, hydroxylamine and a cyclopropane. This rapidly assembles the central structural feature of the molecule, namely the tetrahydro-1,2-oxazine core. The overall yield of the entire total synthesis is a remarkable 6% over just 12 synthetic operations. The optically pure cyclopropane translates to an enantiospecific preparation of (+)-phyllantidine.

**Scheme 9:** The total synthesis of phyllantidine

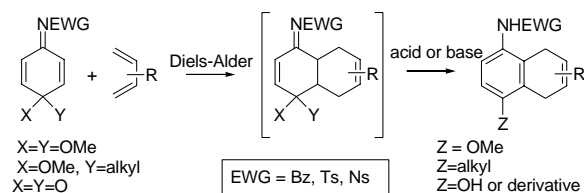


**The Diels-Alder reaction of unusual quinoid mono imines**

<sup>16</sup> Carson, C.A.; Kerr, M.A. *Angew. Chem. Int. Ed.* **2006**, *45*, 6560.

Monoimines of p-benzoquinones and their ketal derivatives are dienophiles which have received a paucity of attention from the synthetic community. We showed (Scheme 10) that the N-benzoyl ketals reacted as dienophiles under the influence of very high pressures<sup>17</sup> (13 kbar) and that the arylsulphonyl derivatives responded to thermal conditions.<sup>18</sup> The parent quinone monoimines were more reactive, cycloadding at room temperature.

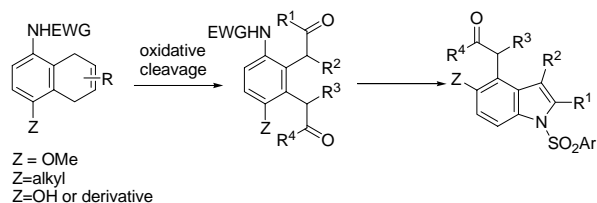
**Scheme 10:** The Diels-Alder reaction of quinoid imines



### A new synthesis of sophisticated indoles

The adducts could be subjected to oxidative cleavage of the newly formed cycloalkenyl double bond and upon treatment with acid formed indoles (Scheme 11).<sup>19</sup> The importance of this protocol lies in the fact that the synthesis of indoles with complex substitution on the benzenoid portion of the ring system remains a great unanswered challenge in heterocyclic chemistry.

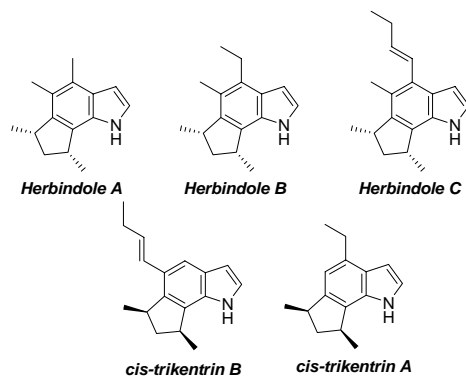
**Scheme 11:** The synthesis of sophisticated indoles



### The synthesis of polyalkylated indole natural products

Recently we adapted the indole chemistry above to the rapid synthesis of the polyalkylated indole natural products, the *cis* trikentrin and the herbindoies (Figure 2).<sup>20</sup> The very few syntheses of these compounds to date are extraordinarily lengthy and ours stand as the most general and efficient ways to assemble them. The synthesis of *cis*-trikentrin B and herbindole B have been published by us and the remaining completed syntheses represent unpublished results.

**Figure 2:** Polyalkylindole natural products



### The total synthesis of decursivine

This antimalarial compound from *Rhaphidophora decursiva*<sup>21</sup> represents an ideal application of the indole-forming methodology described in Scheme 11. The ultimately successful synthesis is detailed in Scheme 12.

**Scheme 12:** Total synthesis of decursivine

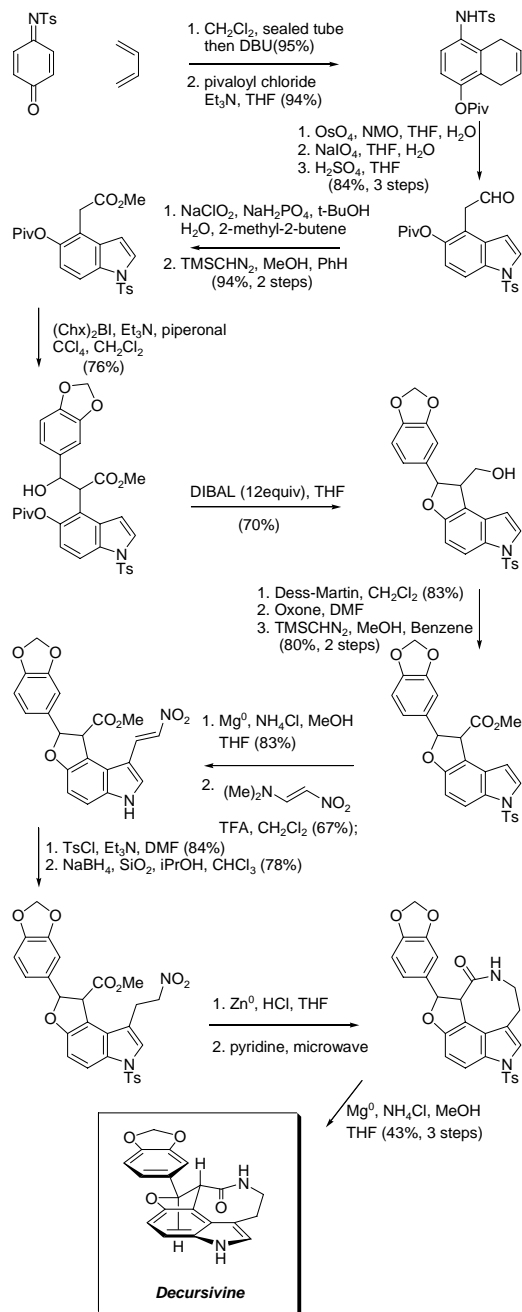
<sup>17</sup> a) Banfield, S.C.; Kerr, M.A. *Synlett* **2001**, 436-438. b) Kerr, M.A. *Synlett* **1995**, 1165-1167.

<sup>18</sup> Banfield, S.C.; Kerr, M.A. *Can. J. Chem.* **2004**, 82, 131-138.

<sup>19</sup> England, D.B.; Kerr, M.A. *J. Org. Chem.* **2005**, 70, 6519-6522. b) Zawada, P.V.; Banfield, S.C.; Kerr, M.A. *Synlett* **2003** 971. c) Banfield, S.C.; Kerr, M.A. *Organic Letters* **2001**, 3325-3327.

<sup>20</sup> Jackson, S.K.; Banfield, S.C.; Kerr, M.A. *Organic Letters* **2005**, 7, 1215-1218. b) Jackson, S.K.; Kerr, M.A. *J. Org. Chem.* **2006**, accepted.

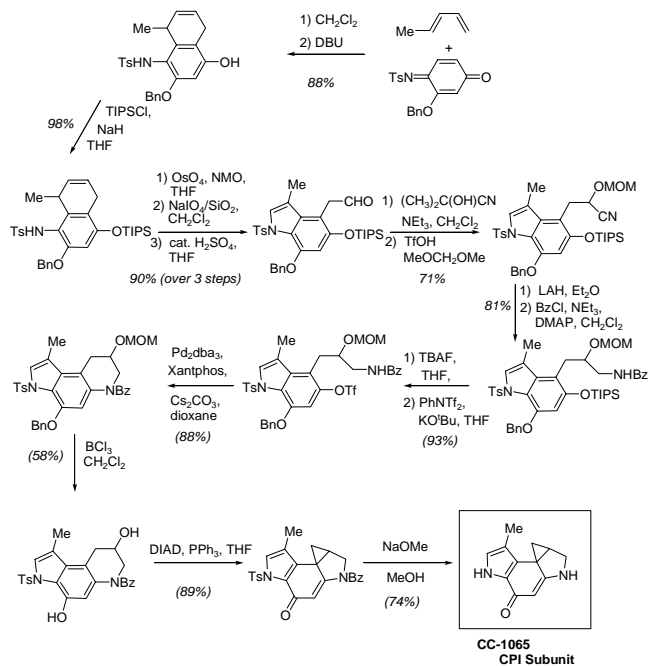
<sup>21</sup> Zhang, H.; Qiu, S.; Tamez, P.; Tan, G.T.; Aydogmus, Z.; Van Hung, N.; Cuong, N.M.; Angerhofer, C.; Soejarto, D.D.; Pezzuto, J.M.; Fong, H.H.S. *Pharm. Biol.* **2002**, 40, 221.



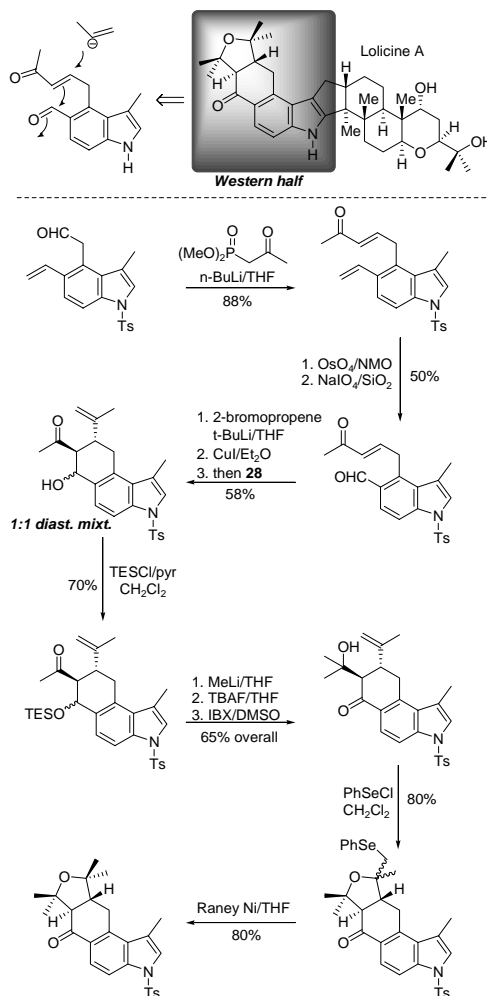
#### The synthesis of the CPI “warhead” of CC-1065.

Very recently we published an application of our indole forming methodology to the synthesis of the pharmacophore of the potent anticancer agent, CC-1065.<sup>22</sup> The synthesis is shown in Scheme 13. The key steps in the sequence are the Diels-Alder/Plieningier indolization to prepare the key intermediate and an intramolecular Buchwald/Hartwig amidation to form the key piperidine ring necessary for elaboration to the target.

#### Scheme 13: Synthesis of the CC-1065 pharmacophore.



#### Scheme 14: Synthesis of the Lolicine A Western portion



#### Synthesis of the Western half of Lolicine A

We have used our Diels-Alder/Plieningier indolization strategy for the synthesis of the indolic or “Western” portion of lolicine A. Scheme 14 summarizes our work. The starting indole was

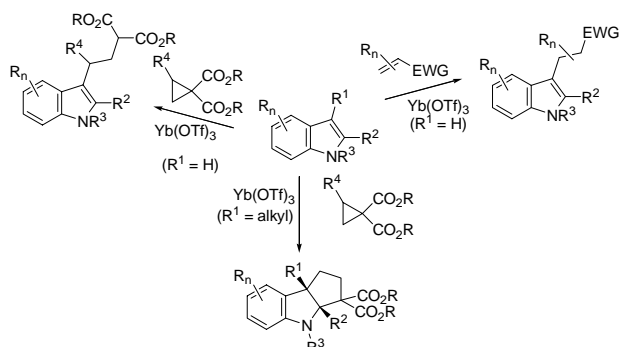
<sup>22</sup> Ganton, M.D.; Kerr, M.A. *J. Org. Chem.* **2006**, asap.

prepared by our usual methods and was converted to the target model system. Key steps include a tandem cuprate/aldol to form the tetralone ring, and a selenium mediated formation of the tetrahydrofuran.

#### Methods for the functionalization and/or synthesis of indoles

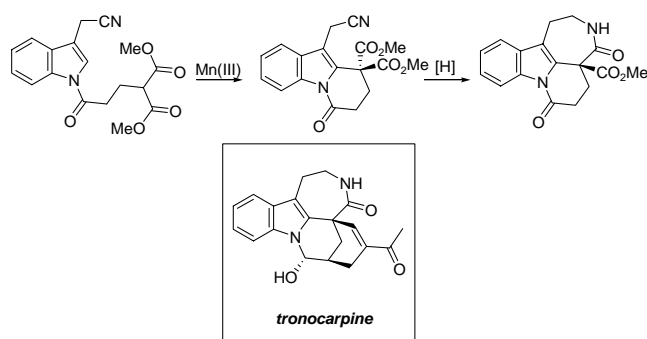
Early on in this groups existence, we discovered that lanthanide triflates were effective catalysts in the Michael addition of indoles to electron deficient olefins at either high or ambient pressures to (Scheme 15).<sup>23</sup> We followed this with a report that cyclopropanediester could engage in a homo-Michael addition by indolic nucleophiles producing malonates.<sup>24</sup> If the indole already bore substitution at the electron rich 3-position an annulation ensued.<sup>25</sup>

**Scheme 15:** Expanding the reactivity of the indole ring system



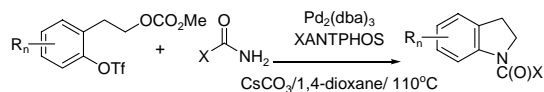
As a consequence of our work with indoles and cyclopropanes, it occurred to us that a pendant malonate residue could be made to radically add to indoles, resulting in the formation of a new carbon carbon bond.<sup>26</sup> This reaction was general however it is well represented by the transformation in Scheme 16. Oxidative radical addition leads to cyclization, which upon Raney nickel reduction gives a lactam. This represents the core structure of the natural product troncarpine.

**Scheme 16:** Mn(III) mediated cyclizations.



In the context of our work towards CC-1065, we were able to develop a tandem amidation reaction which had, as its end product indolines (Scheme 17).<sup>27</sup> These could be conveniently converted to indoles by the usual methods.

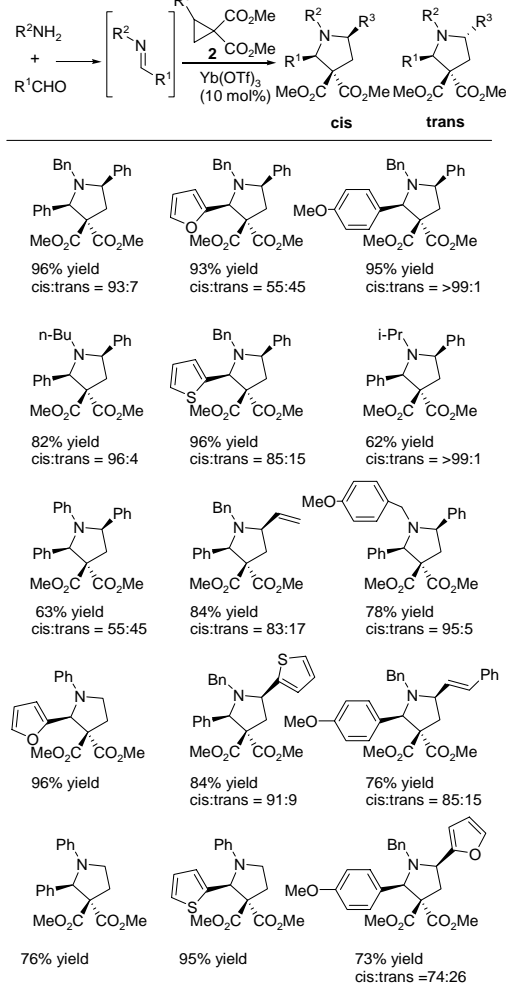
**Scheme 17:** Tandem amidation



#### New cycloaddition reactions of donor/acceptor cyclopropanes

Spurred by our successes with cyclopropane chemistry we are seeking to expand the scope of this underutilized class of molecules. Aldimines, formed *in situ* from amines and aldehydes, under the influence of Yb(OTf)<sub>3</sub> undergo smooth cycloaddition to cyclopropanediesters to yield 2,5-*cis* disubstituted pyrrolidines (Scheme 18).<sup>28</sup> This is complementary to our route to *trans* pyrrolidines via oxazine NO bond cleavage.

**Scheme 18:** Imine/cyclopropane cycloadditions



More recently we have been investigating the intramolecular cyclizations of oxime ethers with cyclopropanes (Scheme 19). Formation of the oxime ether by condensation of an alkoxyamine with an aldehyde results in oxime ether formation. Subsequent lanthanide catalyzed cyclization yields a bicyclic species. Reductive cleavage of the NO bond would yield a pyrrolidine with a 2,5-*trans* stereochemistry, in contrast to those formed in Scheme 18 by cycloaddition of imines with cyclopropanes.

**Scheme 19:** Oxime-ether/cyclopropane cycloadditions

<sup>23</sup> a) Harrington, P.E.; Kerr, M.A. *Can. J. Chem.* **1998**, *76*, 1256. b) Kerr, M.A.; Harrington, P.E. *Synlett* **1996**, 1047.

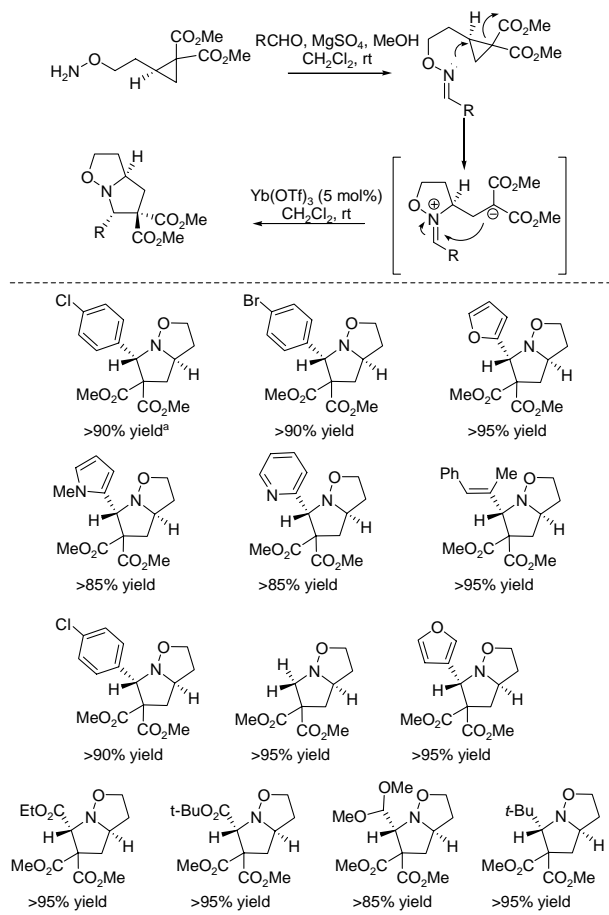
<sup>24</sup> Harrington, P.E.; Kerr, M.A. *Tetrahedron Lett.* **1997**, 5949.

<sup>25</sup> a) England, D.B.; Kuss, T.D.O.; Keddy, R.G. Kerr, M.A. *J. Org. Chem.* **2001**, *13*, 4704-4709. b) Kerr, M.A.; Keddy, R.G. *Tetrahedron Lett.* **1999**, 5671.

<sup>26</sup> Magolan, J.; Kerr, M.A. *Org. Lett.* **2006**, *8*, 4561.

<sup>27</sup> Ganton, M. D.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 4777.

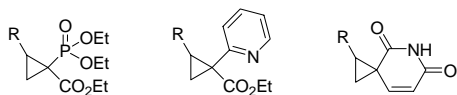
<sup>28</sup> Carson, C. A.; Kerr, M. A. *J. Org. Chem.* **2005**; *70* 8242-8244.



### Other reactions of new donor acceptor cyclopropanes

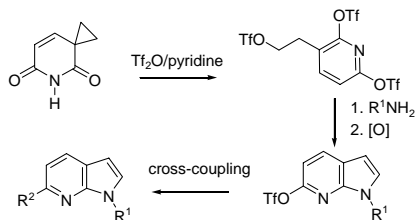
We are also investigating new donor/acceptor cyclopropanes as participants in some of the reactions described above. In addition, we are investigating new chemical reactivity for this intriguing system. Representative examples are in Figure 3.

**Figure 3:** New donor/acceptor cyclopropanes



Recently we showed that triflic anhydride may react with one of these cyclopropanes to produce a tris-trifloxy species. These compounds in turn react with primary amines to form 7-azaindoles and, upon oxidation, 7-azaindoles.<sup>29</sup> The remaining trifloxy group in the 7-azaindole may be used for cross-coupling.

**Scheme 20:** A synthesis of 7-azaindoles

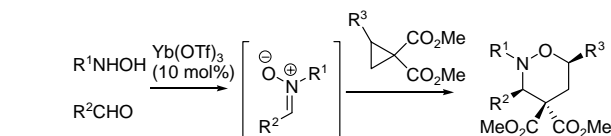


<sup>29</sup> Zheng, X.; Kerr, M.A. *Org. Lett.* **2006**, *8*, 3777.

**Summary: Synthetic methods develop by our group (1995-2006)**

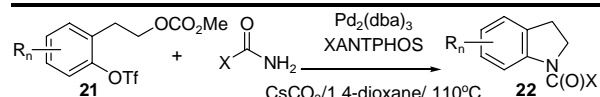
Figure 4 shows the synthetic methods developed by our group over the last decade or so. Most of these were discussed in more detail in the preceding paragraphs. Our research groups will continue to expand on some of these methods and apply them to problems encountered in the target-oriented portion of our program.

**Figure 4:** Synthetic methods (1996-2006)



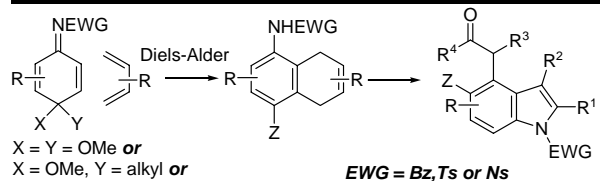
**The homo-3+2-dipolar cycloaddition of nitrones with cyclopropanes**

Lebold, T.P.; Carson, C.A.; Kerr, M.A. *Synlett* **2006**, 364.  
 Wanapun, D.; Kerr, M.A.; Woo, T. *Can. J. Chem.* **2005**, *83*, 1752.  
 Young, I.S.; Williams, J.L.; Kerr, M.A. *Org. Lett.* **2005**, *7*, 953.  
 Ganton, M.D.; Kerr, M.A. *J. Org. Chem.* **2004**, *69*, 8554.  
 Young, I.S.; Kerr, M.A. *Org. Lett.*, **2004**, *6*, 139.  
 Young, I.S.; Kerr, M.A. *Angew. Chem. Int. Ed.* **2003**, *42*, 3023.



**Domino amidation to form indolines and indoles**

Ganton, M. D.; Kerr, M. A. *Org. Lett.* **2005**, *7*, 4777.

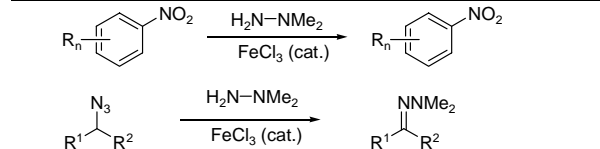


**The Diels-Alder reaction of quinoid mono imines...**

Banfield, S.C.; Kerr, M.A. *Can. J. Chem.* **2004**, *82*, 131.  
 Zawada, P.V.; Banfield, S.C.; Kerr, M.A. *Synlett* **2003**, 971.  
 Kerr, M.A. *Synlett* **1995**, 1165.

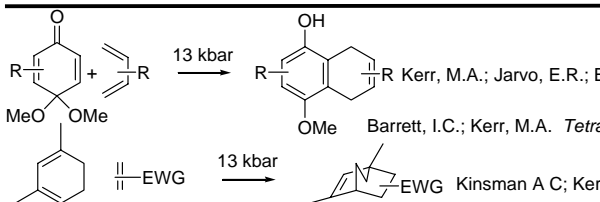
**... and the application to the synthesis of complex indoles**

England, D.B.; Magolan, J.; Kerr, M.A. *Org. Lett.* **2006**, *8*, 2209.  
 England, D.B.; Kerr, M.A. *J. Org. Chem.* **2005**, *70*, 6519.  
 Banfield S.C.; England D.B.; Kerr M.A. *Org. Lett.* **2001**, *3*, 3325.  
 Banfield, S.C.; Kerr, M.A. *Synlett* **2001**, 436.

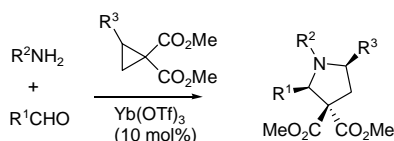


**The unusual reactivity of N,N-dimethylhydrazine**

Barrett, I.C.; Kerr, M.A. *Synlett* **2000**, 1673.  
 Barrett, I.C.; Langille, J.D.; Kerr, M.A. *J. Org. Chem.* **2000**, *65*, 6268.  
 Kerr, M.A.; Boothroyd, S.R. *Tetrahedron Lett.* **1995**, 2411.

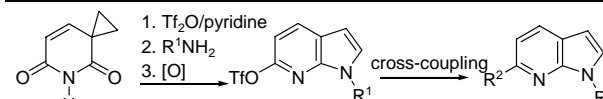


**Hyperbaric synthetic methods**



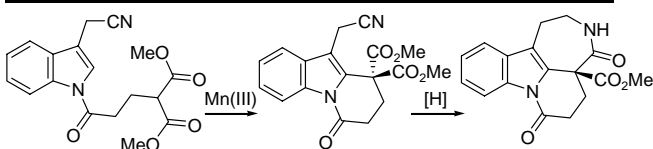
**The cycloaddition of imines with cyclopropanes to form pyrrolidines**

Carson, C. A.; Kerr, M. A. *J. Org. Chem.* **2005**; *70* 8242.



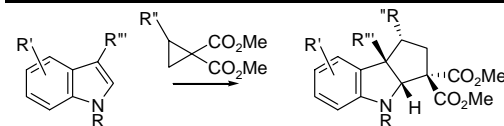
**A new cyclopropane and a synthesis of 7-azaindoles**

Zheng, X.; Kerr, M.A. *Org. Lett.* **2006**, *8*, 3777.



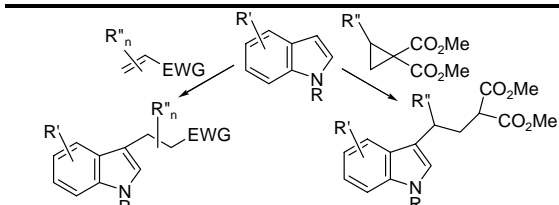
**Manganese III mediated cyclizations and an application to the synthesis of tonocarpine**

Magolan, J.; Kerr, M.A. *Org. Lett.* **2006**, *8*, 4561.



**Annulation of indoles with cyclopropanes**

Kerr, M.A.; Keddy, R.G. *Tetrahedron Lett.* **1999**, 5671.  
 England D. B.; Kuss T. D.; Keddy R. G.; Kerr M. A. *J. Org. Chem.* **2001**, *66*, 4704.



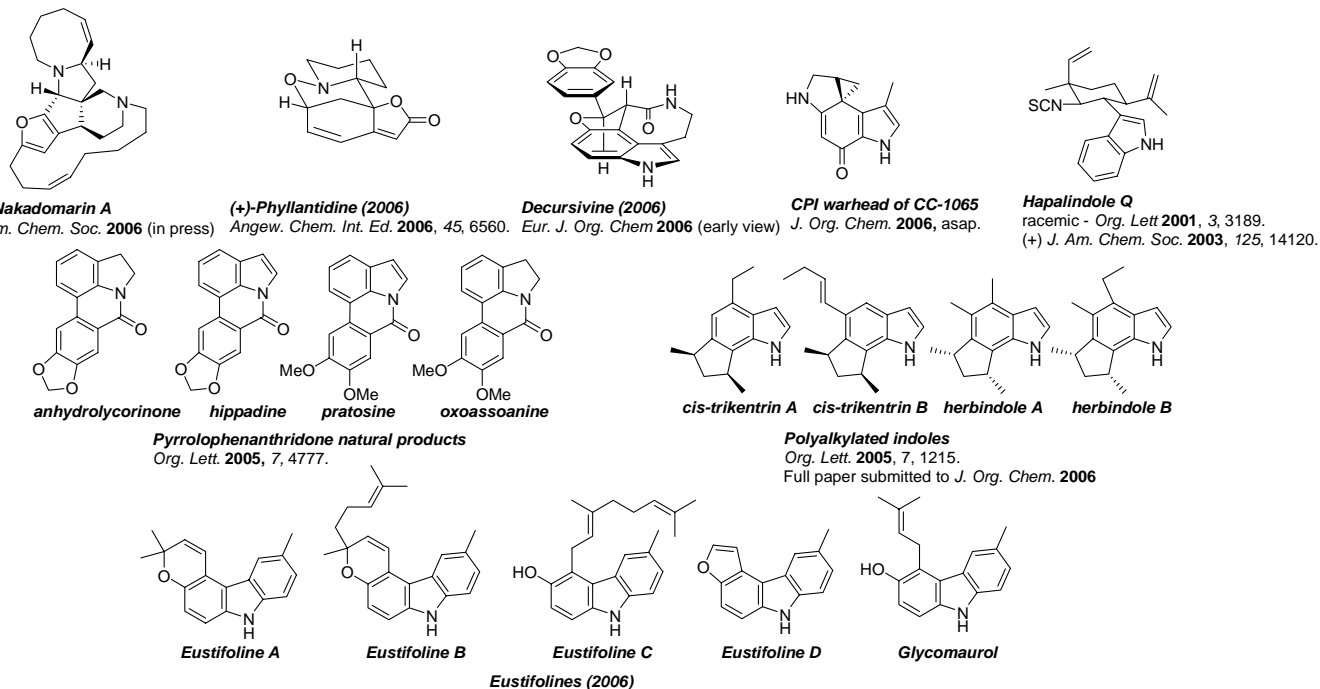
**Alkylation of indoles with Michael acceptors and cyclopropanes**

England, Dylan B.; Woo, Tom K.; Kerr, Michael A.. *Can. J. Chem.* **2002**, *80*, 992.  
 Harrington, P.E., Kerr, M.A. *Can. J. Chem.* **1998**, *76*, 1256.  
 Harrington, P.E., Kerr, M.A. *Tetrahedron Lett.* **1997**, 5949.  
 Harrington, P.E., Kerr, M.A.. *Synlett* **1996**, 1047.

### Target Oriented Synthesis: Completed targets (2001-2006)

Figure 5 shows the natural products prepared by our group in the last 5 years. Most of these molecules have employed the methodology we have developed in our group, however others were pursued with a pure target oriented motivation.

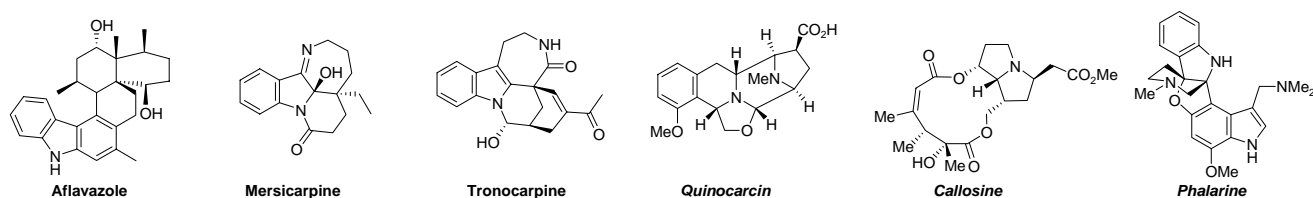
Figure 5: Natural products prepared by the Kerr group (2001-2006)



### Target Oriented Synthesis: Under construction

Figure 6 shows the natural products for which we have active routes. Some are in early stages of development, however several targets are close to completion.

Figure 6: Natural products under construction



### Summary

In our research group we have a tremendous atmosphere of scientific curiosity directed towards the development of interesting and useful synthetic methods. In addition we have active programs which employ those methods and others to address the significant challenge posed by natural products with intriguing and challenge structures.