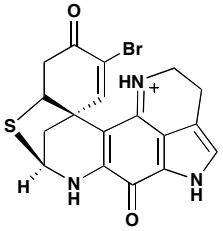
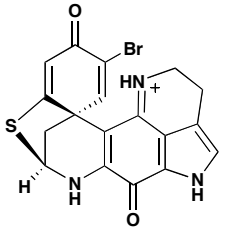
# The Discorhabdin Alkaloids

*Paul Krawczuk*

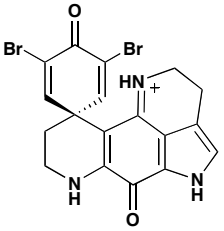
**Representative Structures of the Discorhabdin Alkaloid Family:**



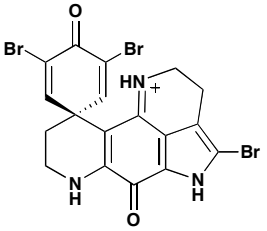
Discorhabdin A



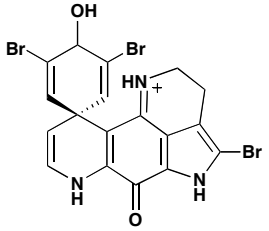
Discorhabdin B



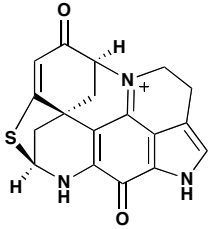
Discorhabdin C



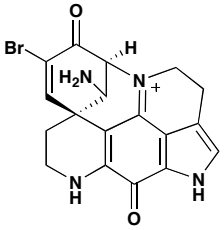
14-bromo-Discorhabdin C



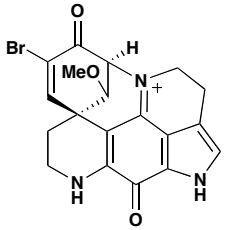
14-bromo-3-dihydro-
7,8-dehydro-Discorhabdin C



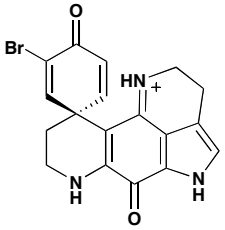
Discorhabdin D



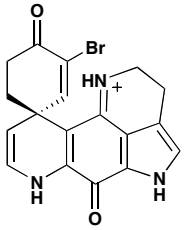
1-amino-Discorhabdin D



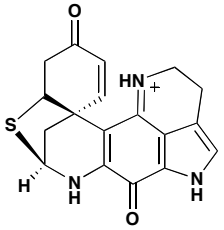
1-methoxy-Discorhabdin D



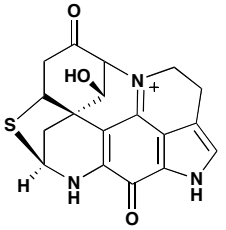
Discorhabdin E



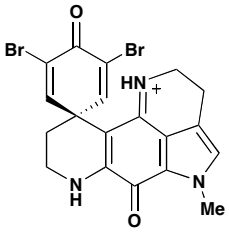
Discorhabdin G



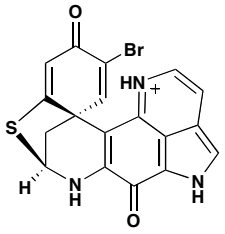
Discorhabdin I



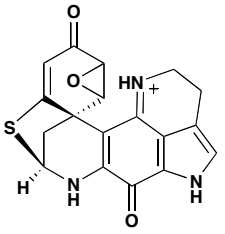
Discorhabdin L



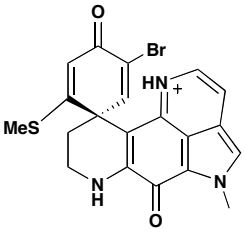
Discorhabdin P



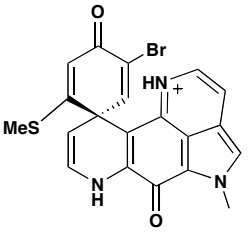
Discorhabdin Q



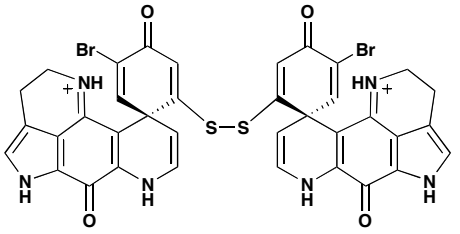
Discorhabdin R



Discorhabdin S



Discorhabdin T



Discorhabdin W

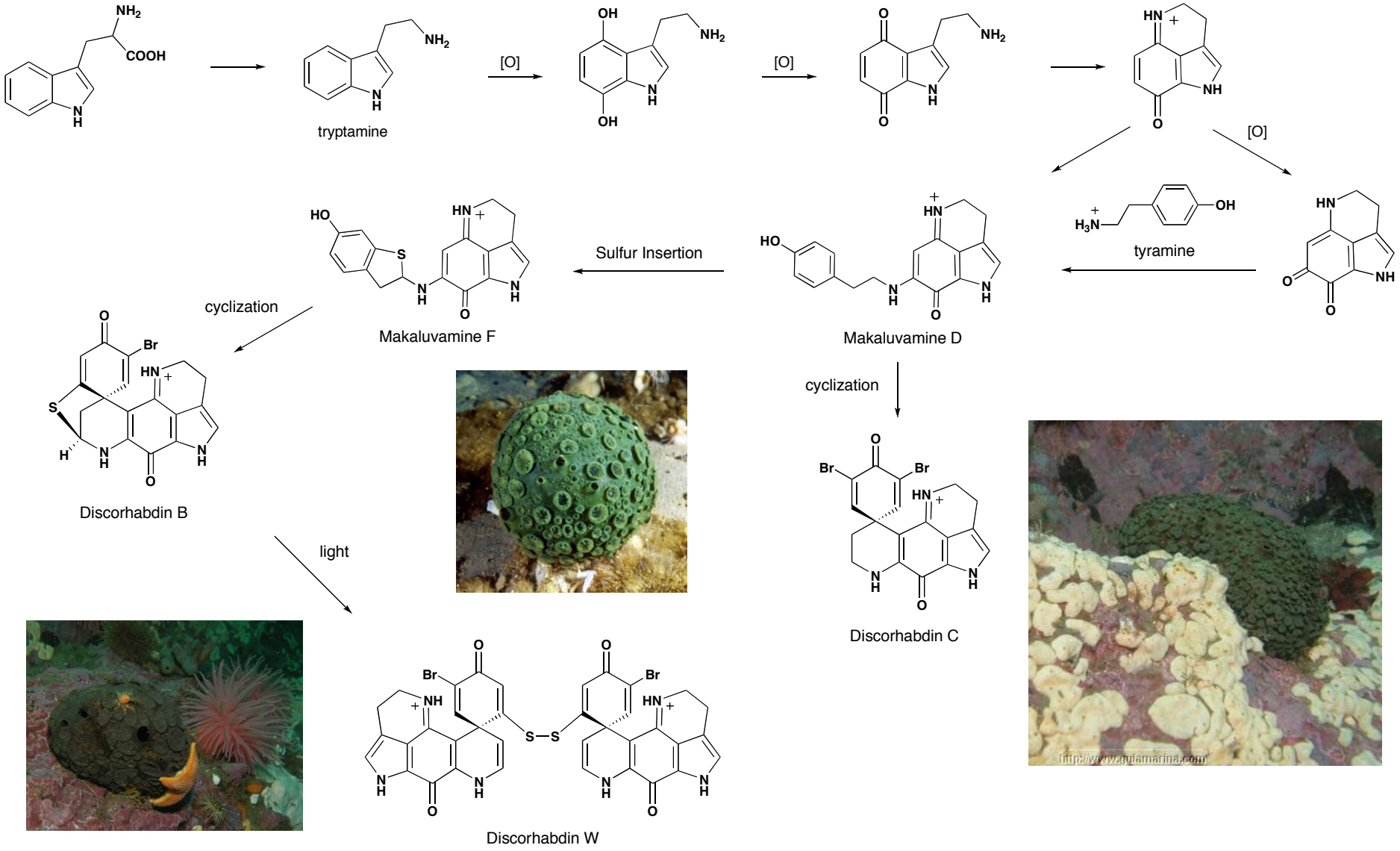
For a comprehensive review see: Y. Harayama, Y. Kita. *Curr. Org. Chem.* **2005,** 9, 1567-1588.

# The Discorhabdin Alkaloids

*Paul Krawczuk*

**Proposed Biosynthesis of the Discorhabdin core:**

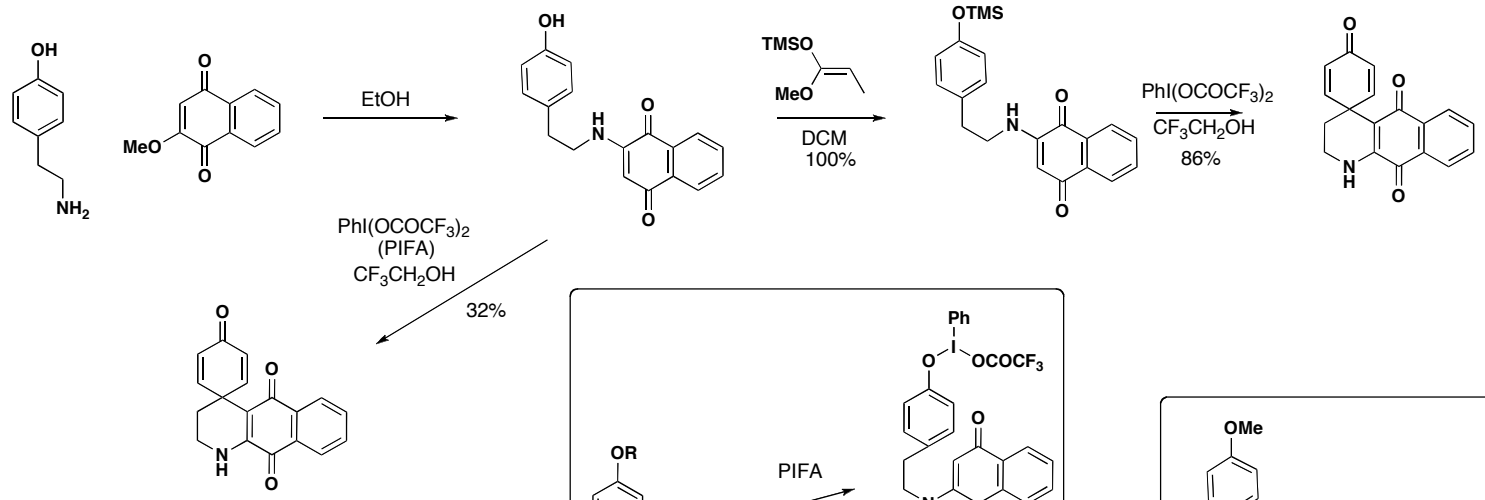
M. Munro, *J. Nat. Prod.* **1995,** 58, 306-311.

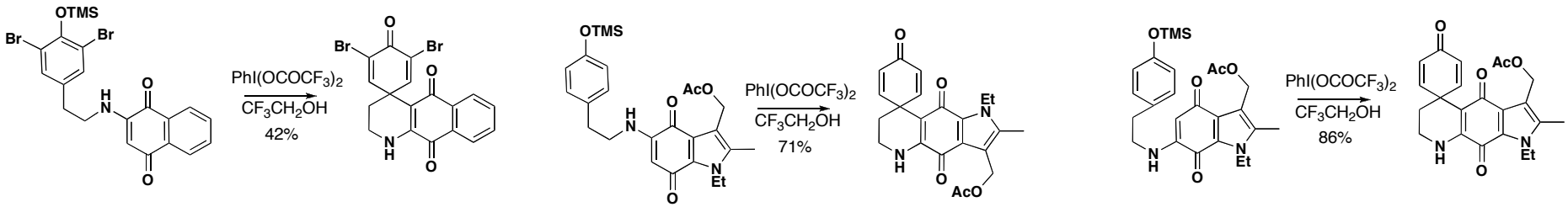


# The Discorhabdin Alkaloids

*Paul Krawczuk*

**First Sythetic Approach to the Discorhabdin Alkaloids:**
Y. Kita et al *Tet. Lett.* **1989**, 30, 1119-1120.



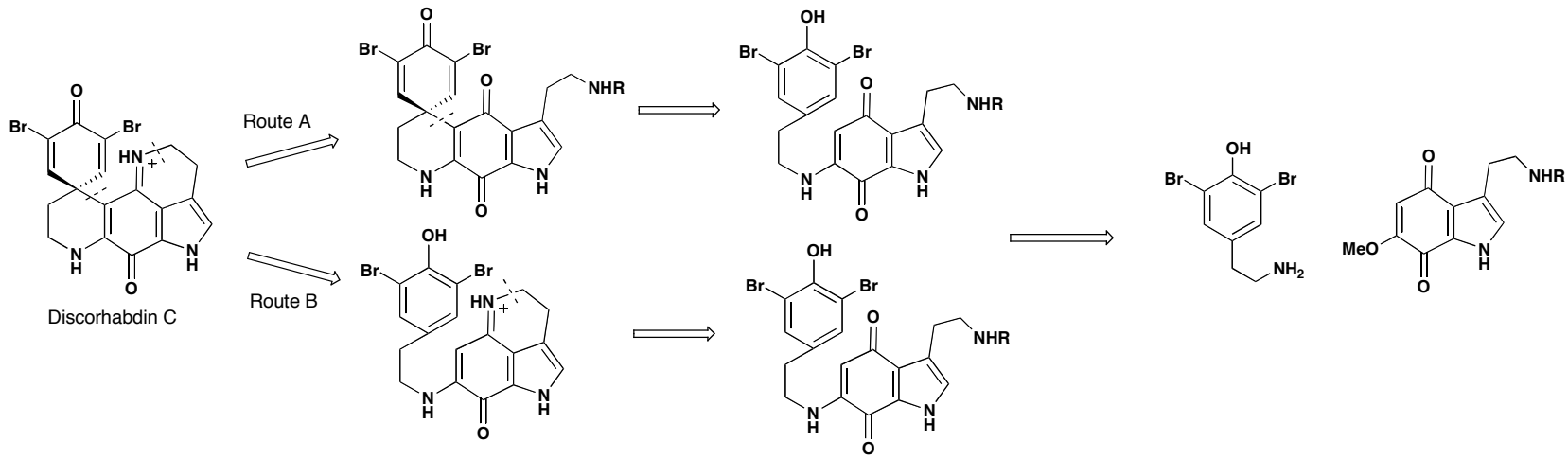



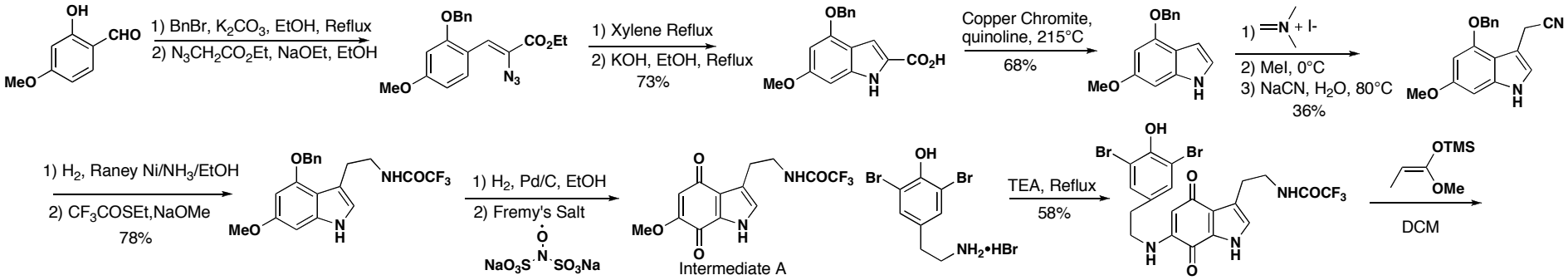
# The Discorhabdin Alkaloids

*Paul Krawczuk*

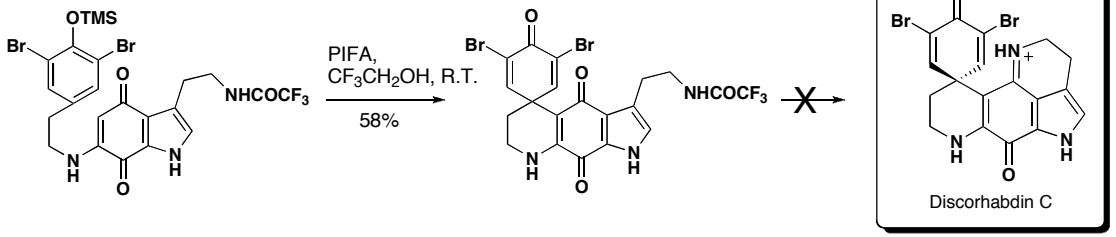
**First Total Synthesis of Discorhabdin C:**

Y. Kita et al *J. Am. Chem. Soc.* **1992**, 114, 2175-2180.




Fremy's Salt Review:
*Chem. Rev.* **1971,** 71, 229-246.



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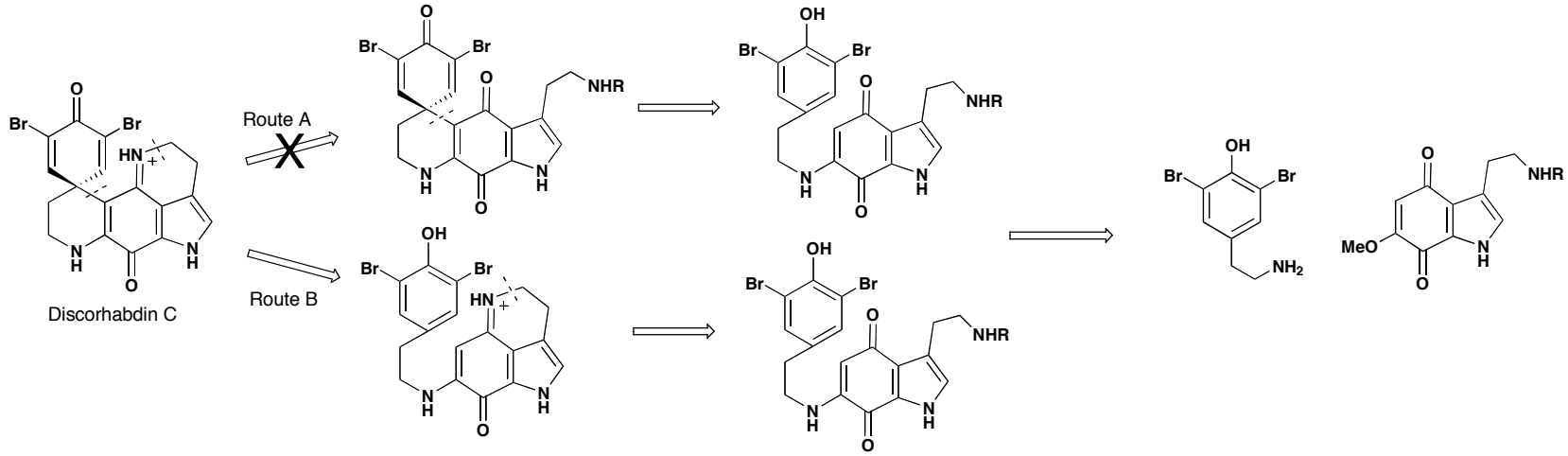
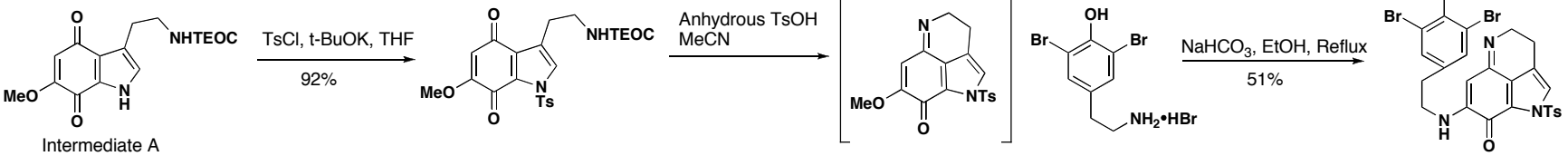
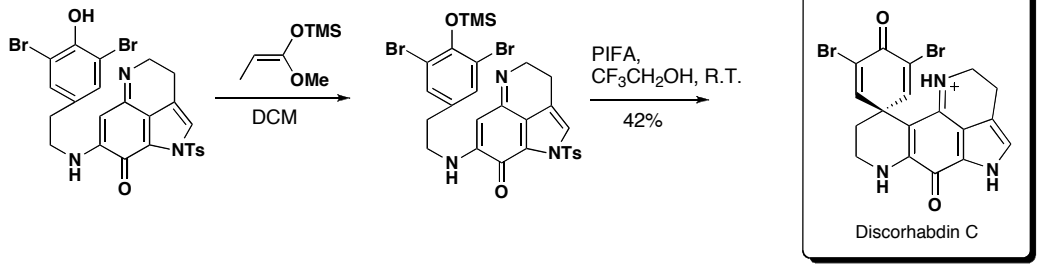


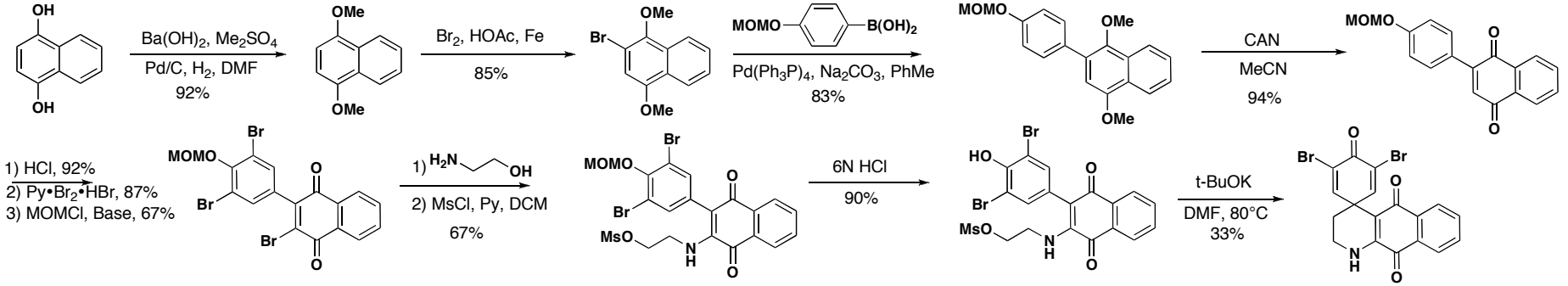
*Baran Group Meeting*

# The Discorhabdin Alkaloids

*Paul Krawczuk*

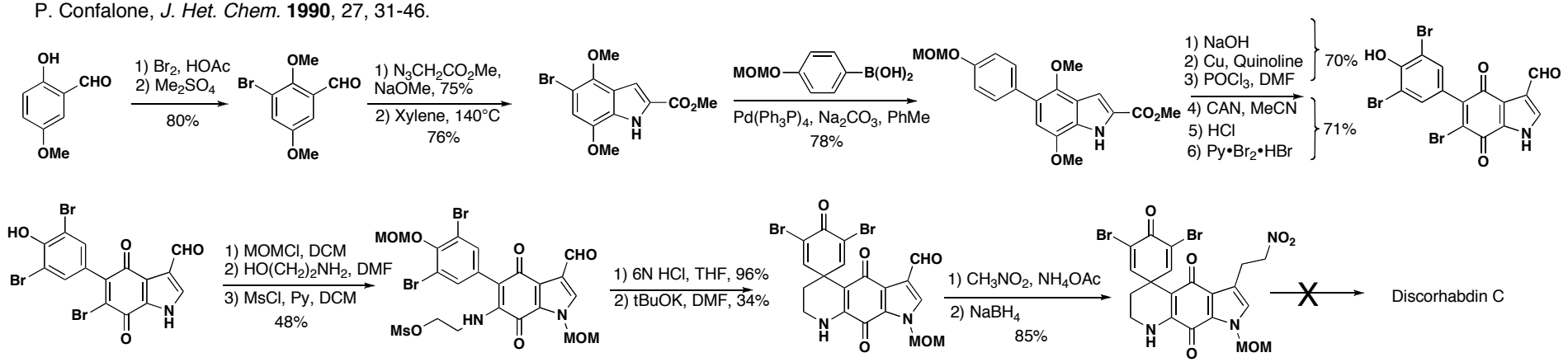
**The Preparation of the Aza-Spirobicyclic System of Discorhabdin C via an Intramolecular Phenolate Alyklation:**

G. Kubiak, P. Confalone, *Tet. Lett.* **1990**, 31, 3845-3848.

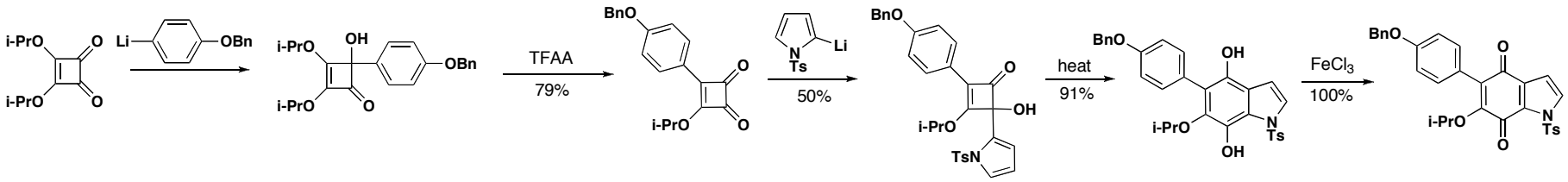



**The Use of Hetrocyclic Chemistry in the Synthesis of Natural and Unnatural Products: Discorhabdin C**

P. Confalone, *J. Het. Chem.* **1990**, 27, 31-46.



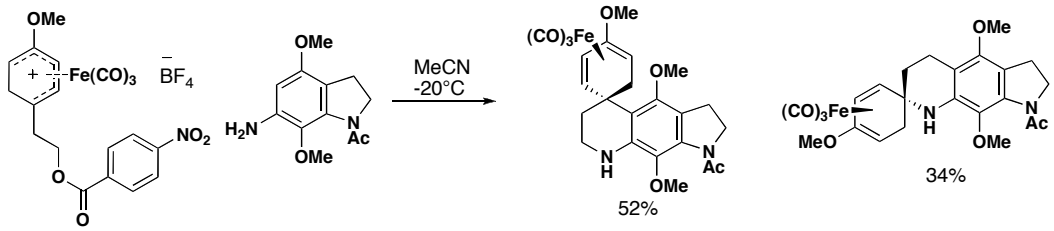

An alternative squaric acid approach:



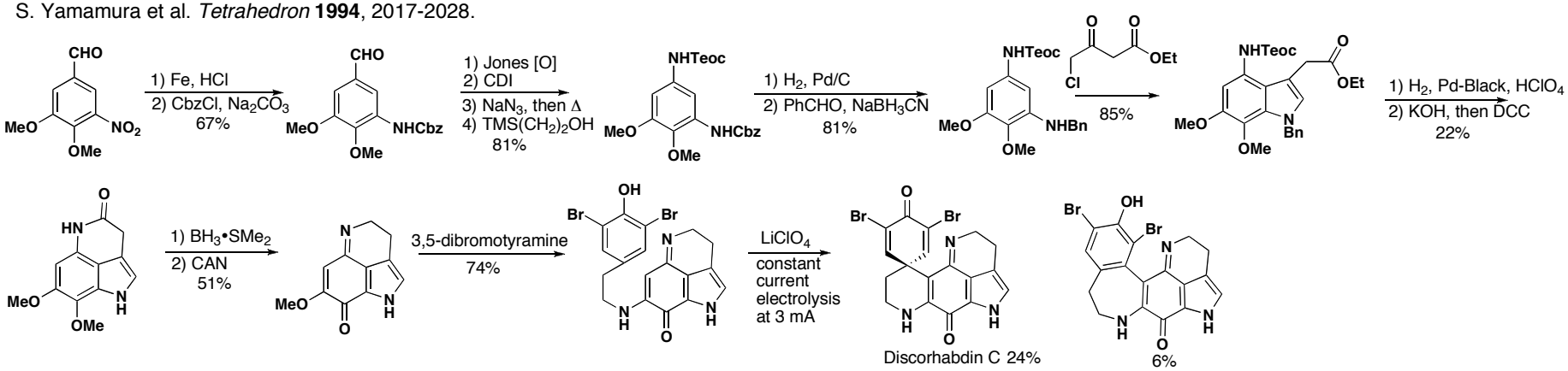
# The Discorhabdin Alkaloids

*Paul Krawczuk*

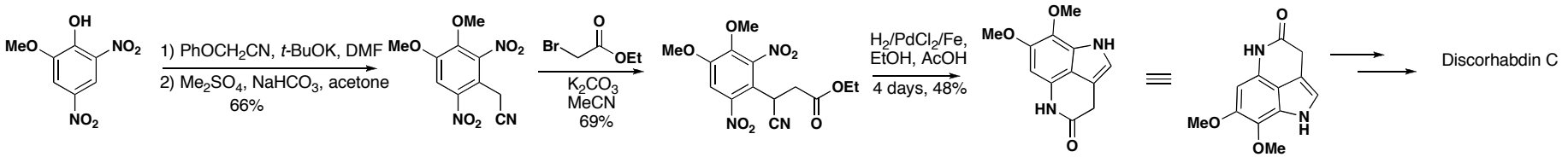
**Transition Metal-Diene Complexes in Organic Sythesis: Iron Mediated Approach to the Discorhabdin and Prianosin Alkaloids:**
H. Knölker, K. Hartmann, *Synlett* **1991**, 428-430.




**Synthetic Studies on Tetrahydropyrroloquinoine-containing Natural Products: Synthesis of Discorhabdin C, Batzelline C and Isobatzelline C:**
S. Yamamura et al. *Tetrahedron* **1994**, 2017-2028.



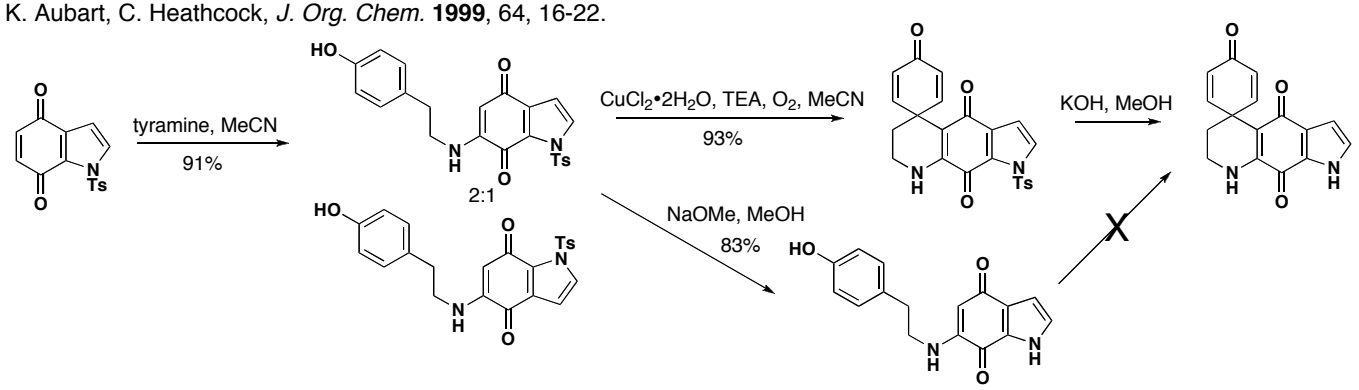

**Synthetic of 7,8-Dimethoxy-2-oxo-1,3,4,5-tetrahydropyrrolo[4,3,2-de]quinoline: A key Intermediate en Route to Discorhabdin C:**
M. Makosza et al. *Synthesis* **1997**, 1131-1133.

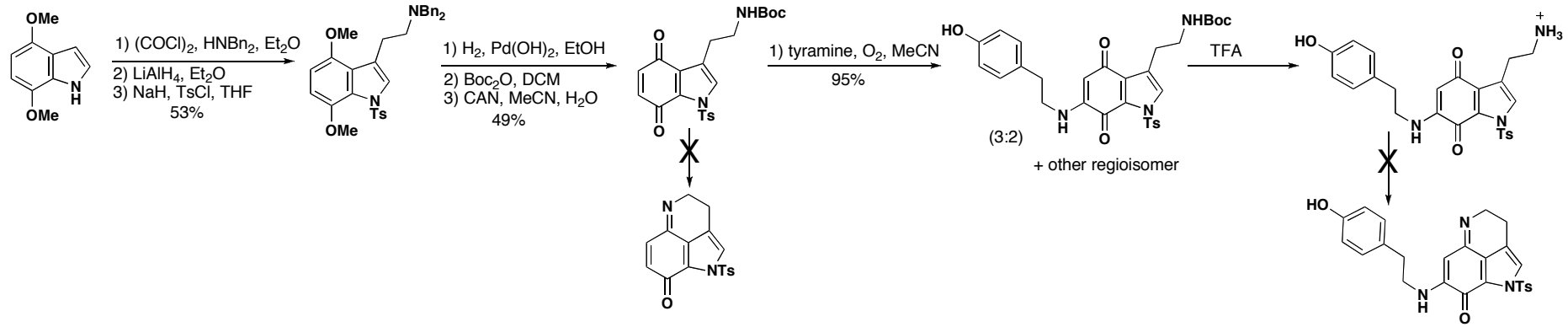


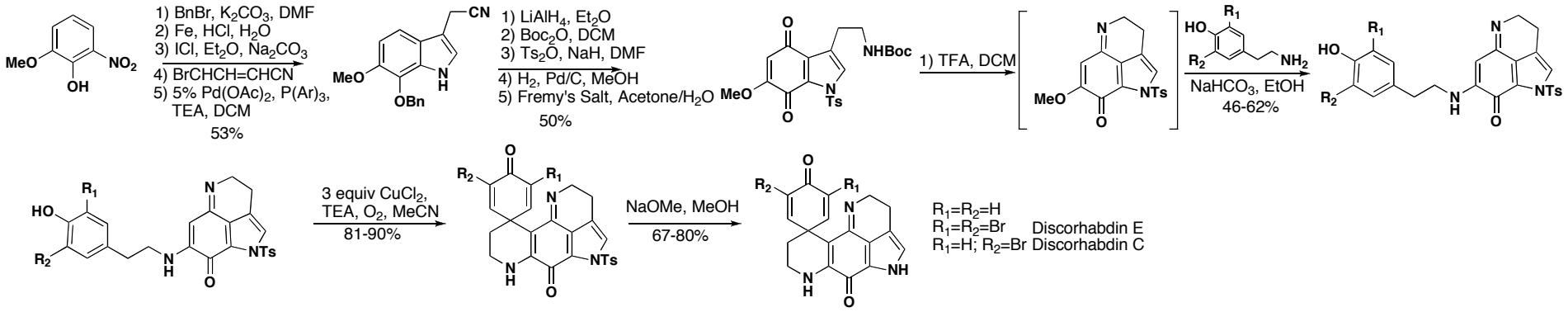
# The Discorhabdin Alkaloids

*Paul Krawczuk*

**A Biomimetic Approach to the Discorhabdin Alkaloids: Total syntheses of Discorhabdins C and E and Dethiadiscorhabdin D:**
K. Aubart, C. Heathcock, *J. Org. Chem.* **1999**, 64, 16-22.



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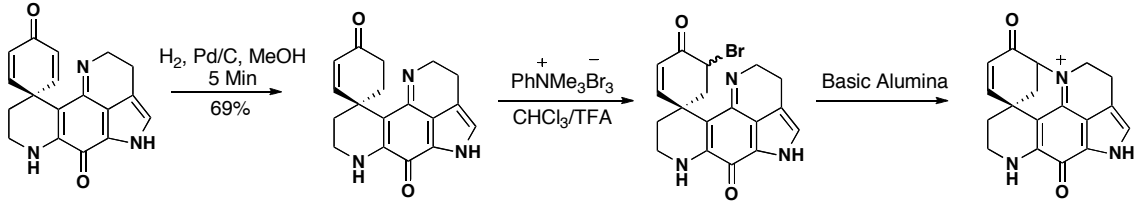
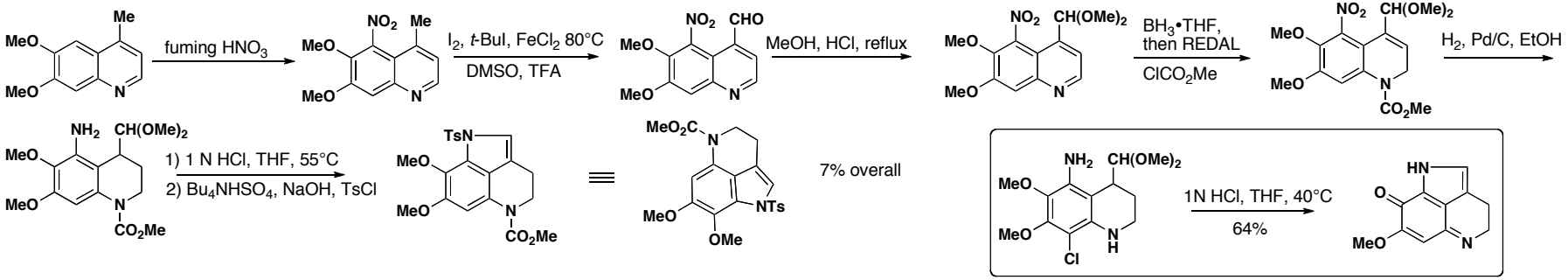
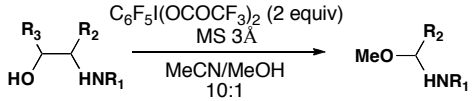


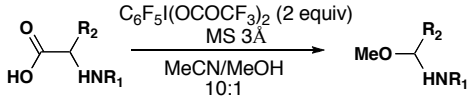

**Formal Total Synthesis of Damirones A and B, Batzelline C, Isobatzelline C, Discorhabdin C, and Makaluvamines A-D:**
J. Joule et al. *J. Org. Chem.* **1997**, 62, 568-577.



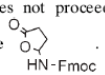

**Direct Synthesis of N,O-Acetal Compounds as Key Intermediates of Discorhabdin A:**
Y. Kita et al. *Chem. Eur. J.* **2006**, 12, 4893-4899.

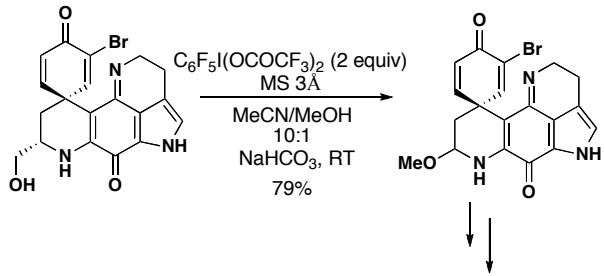



| Entry | Reactant | $R^1$ | $R^2$ | $R^3$ | *t* [h] | Yield [%] |
|---|---|---|---|---|---|---|
| 1 | **1a** | Fmoc | $CO_2Me$ | H | 5 | 89 |
| 2 | **1b** | Fmoc | $CO_2Me$ | $CH_3$ | 1 | 98 |
| 3 | **1c** | Fmoc | H | H | 3 | 90 |
| 4 | **1d** | Fmoc | $CH_3$ | H | 0.5 | 63 |
| 5 | **1e** | Fmoc | $CH(CH_3)_2$ | H | 0.5 | 76 |
| 6 | **1f** | Cbz | $CO_2Me$ | H | 7 | 80 |
| 7 | **1g** | Cbz | $CO_2Bn$ | $CH_3$ | 1 | quant. |
| 8 | **1h** | Bz | $CO_2Me$ | $CH_3$ | 2 | 47 |




| Entry | Reactant | $R^1$ | $R^2$ | *t* [h] | Yield [%] |
|---|---|---|---|---|---|
| 1 | **3a** | Fmoc | H | 1 | 73 |
| 2 | **3b** | Fmoc | $CH_3$ | 0.25 | 54 |
| 3 | **3c** | Fmoc | $CH_2CH_2CO_2Me$ | 0.25 | 55 |
| 4 | **3d** | Cbz | $CO_2Et$ | 1 | 46 |
| 5 | **3e** | Fmoc | $CH_2CH_2CO_2H$ | 0.5 | 73[b] |

[a] The reaction does not proceed at room temperature. [b] Without MeOH. Product = **4e**  .

# The Discorhabdin Alkaloids

*Paul Krawczuk*

**The First Total Synthesis of Discorhabdin A:**

Y. Kita et al. *Angew. Chem. Int. Ed.* **2002**, 41, 348-350. and Y. Kita et al. *J. Am. Chem. Soc.* **2003**, 125, 11235-11240.

