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Directed *ortho* Metalation of Ferrocenes. Ring-substituted Fulvenes by Nesmeyanov Ferrocenylcarbenium Ion Fragmentation

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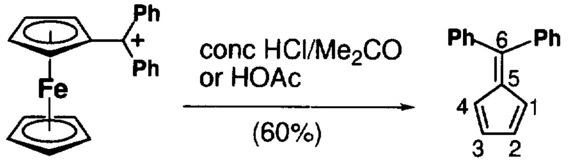
Abstract: A convenient and general synthesis of 6-aryl and 6,6-diaryl ring-functionalized fulvenes from ferrocenyl amide carbinols *via* a combined Directed *ortho* Metalation – acid catalyzed fragmentation (**Scheme 2**) is reported.

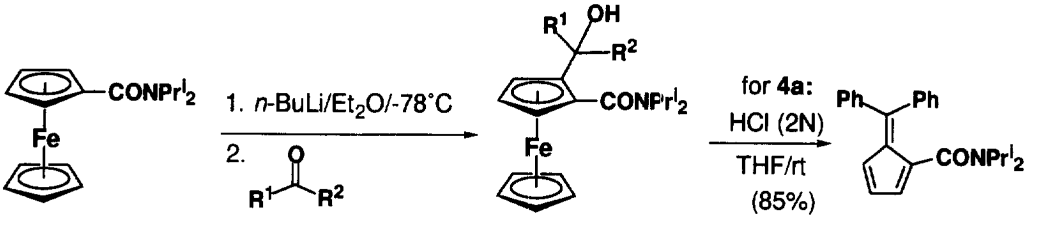
Since 1900, when Thiele coined the term,[2] (penta)fulvenes have enjoyed a rich history in chemical education[3] and research as exemplary nonbenzenoid aromatics with high polar character, cycloaddition reactivity, and potential charge transfer properties.[4] More recently, fulvene building blocks have been employed in natural product synthesis.[5] The voluminous literature on ferrocenyl carbenium ions[6] contains the observation by Nesmeyanov that 6,6-diphenyl fulvene **2** is rapidly formed from **1** (or the corresponding carbinol) (**Scheme 1**).[7] Herein we report a general Directed *ortho* Metalation (D*o*M) - Nesmeyanov fragmentation sequence to ring-substituted 6-aryl and 6,6-diaryl fulvenes, **3** → **4** → **5** (**Scheme 2**). Among synthetic approaches to such fulvenes,[8] only a Friedel-Crafts protocol provides ring-functionalized fulvene derivatives.[4c]



1 **2**

Scheme 1

In the course of studies on sparteine-mediated synthesis of planar chiral ferrocenes, **3** → **4**,[9] we observed by chance that treatment of ferrocenyl alcohol **4a** with p-TsOH•H_2O in PhH at reflux or 2N aq HCl in THF gave the brick-red fulvene amide **5a** in quantitative yield (**Scheme 2**).



3 **4** **5a**

4a: $R^1 = R^2 = Ph$; **4b**: $R^1 = R^2 = Et$; **4c**: $R^1 = CH_2{=}CH_2$, $R^2 = H$

Scheme 2

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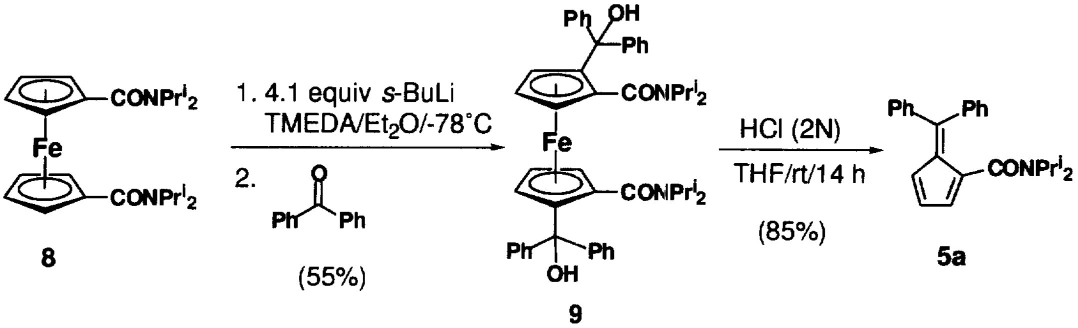
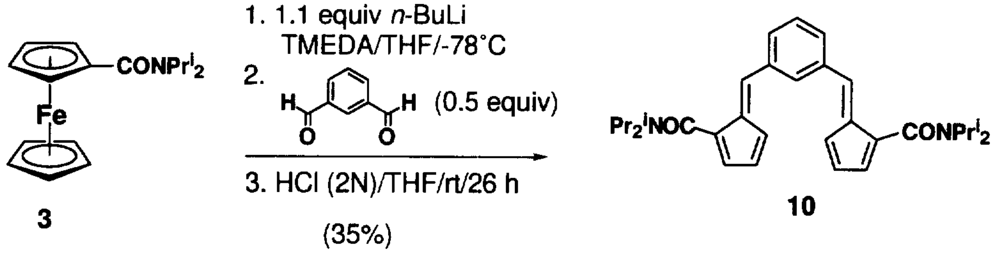
The reaction was generalized under the aq HCl conditions and the results are depicted in the Table. Treatment of the diethyl ketone and acrolein adducts (**4b**, **4c**) under the standard acidic conditions resulted in extensive decomposition and inability to isolate the expected products. Thus carbocation-stabilizing groups R^1 and R^2 in **6** appear to be critical for clean transformation to fulvene amides **7**. On the other hand, aryl aldehyde and diaryl ketone adducts underwent smooth conversion to the corresponding fulvenes (entries 1-3). Structurally attractive 6,6-dipyridyl (entry 4), -fluorenyl (entry 5), and -xanthenyl (entry 6) fulvenes were readily obtained in good to excellent yields. Variation of tertiary amide was demonstrated (entries 7-9) and, more interestingly, a 1-phosphinyl fulvene (entry 10) was obtained by this route.[10]

Double deprotonation – excess benzophenone condensation of the ferrocenyl bisamide[11] **8** gave adduct **9**, which upon HCl treatment furnished fulvene **5a** whose stoichiometry represents a double fragmentation reaction (**Scheme 3**).



Scheme 3

As a further extension, metalation of **3** was followed by quenching with 0.5 equiv of isophthalic dicarboxaldehyde to afford the symmetrical fulvene bisamide **10** (**Scheme 4**) of potential interest in charge transfer property studies.

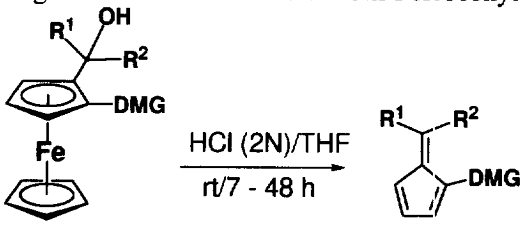


Scheme 4

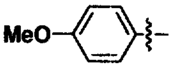
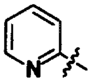
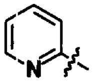
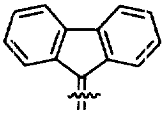
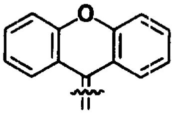
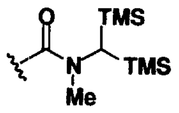
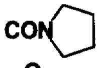
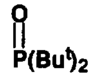
In summary, a highly versatile method for the construction of 6-aryl and 6,6-diaryl fulvenes has been devised by a combined D*o*M – Nesmeyanov fragmentation tactic. The scope of the reaction includes amide and phosphinyl (**Table**, entry 10) ring substituents, and 2:1 condensation modes (**Scheme 4**), all of which suggest general availability of interesting new fulvene derivatives for physicochemical studies.

Acknowledgments. We are grateful to NSERC Canada and Monsanto for support under the Industrial Research Chair and Research Grant programs. We thank Radek Laufer for a sample of compound **8** and Dr. Prakash Patil and Brian Chapell for intellectual contribution to and practical advice on the synthesis of fulvenes depicted in entries 8 and 10 (**Table**) respectively.

Table. Synthesis of Ring-substituted Fulvenes **7** from Ferrocenyl Carbinols **6**



6 **7**

Entry	6,[a] DMG	R1	R2	7, yld%[b]
1	$CONPr^i_2$	Ph	H	62
2	$CONPr^i_2$		H	80[c]
3	$CONPr^i_2$	Ph	Ph	78
4	$CONPr^i_2$			70
5	$CONPr^i_2$			85
6	$CONPr^i_2$			90
7	$CONEt_2$	Ph	Ph	78
8		Ph	Ph	78
9		Ph	Ph	78
10	 $P(O)(Bu^t)_2$	Ph	Ph	78

[a] Starting ferrocenyl carbinols were obtained by described D*o*M chemistry (refs 1a, 9). [b] Yields are of isolated materials. All new compounds show analytical and spectral (^1H NMR, ^{13}C NMR, MS) data consistent with the depicted structures. [c] Stereochemistry established by an NOE experiment.

References and Footnotes

1. a) Taken, in part, from the M.Sc. Thesis of Miao, B. University of Waterloo, **1998**. b) Present address: Additives Research, CIBA, 180.154, CH-1723 Marly, Switzerland. c) Present address: Department of Chemistry, Queen's Univeristy, Kingston, ON, Canada K7L 3N6, Fax: 613-544-2837, email: baderadm@chem.queensu.ca.

2. Thiele, J. Chem. Ber. **1990**, *33*, 666.

3. Carey F. A.; Sundberg R. J. *Advanced Organic Chemistry*, 3rd Ed. Part A, Plenum, New York, **1990**, pp 528-530. For a witty account, see Nickon, A.; Silversmith, E. F. *Organic Chemistry: The Name Game*, Pergamon Press, New York, **1987**, p 287.

4. For reviews, see a) Bergmann, E. D. *Chem. Rev.* **1968**, *68*, 41-84. b) Zeller, K. P. *Houben-Weyl: Methoden der Organischen Chemie*; **1985**, Vol.5/2C, p 504-684. c) Neuenschwander, M. In*The Chemistry of Double-Bonded Functional Groups*; Suppl. A. Patai, S. Ed.; Wiley, New York, **1989**, p 1131-1268.

5. For leading references, see Büchi, G.; Berthet, D.; Decorzant, R.; Grieder, A.; Hauser. A. *J. Org. Chem.* **1976**. *41*, 3208. Little, R. D.; Carroll, G. L.; Petersen, J. L. *J. Am. Chem. Soc.* **1983**, *105*, 928. Nyström, J. -E.; Helquist, P. *J. Org. Chem.* **1989**, *54*, 4695. Sternbach, D. D.; Ensinger, C. L. *J. Org. Chem.* **1990**, *55*, 2725. Wang, Y.; Mukherjee, D.; Birney, D.; Houk, K. N. *J. Org. Chem.* **1990**. *55*, 4504. Lei, B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 4609. Siderberg, B. C.; Austin, L. R.; Davis, C. A.; Nystîm, J. -E.; Vügberg, J. O. *Tetrahedron* **1994**, *50*, 61. Rawal, V. H.; Fabré, A.; Iwasa, S. *Tetrahedron Lett.* **1995**, *36*, 6851. For the synthesis of natural and unnatural fulvenoid terpenes, see McMorris, T. C.; Yu, J.; Hu, Y.; Estes, L. A.; Kelner, M. J. *J. Org. Chem.* **1997**, *62*, 3015 and McMorris, T.C.; Hu, Y; Yu, J.; Kelner, M.J. *J. Chem. Soc., Chem. Commun.* **1997**, 315.

6. Watts, W. E. *J. Organometal. Chem. Libr.* **1979**, *7*, 399.

7. a) Nesmeyanov, A. N.; Sazonova, V. A.; Drozd, V. N. *Doklady Akad. Nauk SSSR*, **1964**, *154*, 1393; *Chem. Abstr.* **1964**, *60*, 11937d. b) Nesmeyanov, A. N.; Sazonova, V. A.; Drozd, V. N.; Rodinova, N. A. *Doklady Akad. Nauk SSSR*, **1965**, *160*, 355, Engl. Edit., p 62; *Chem. Abstr.* **1965**, *62*, 14725b. c) Nesmeyanov, A. N.; Sazonova, V. A.; Zudkova, G. I.; Isaeva, L. S. *Isz. Akad. Nauk SSSR, Ser. Chim.* **1966**, 2017, Engl. Edit. p 1949, *Chem. Abstr.* **1967**, *66*, 76133d.

8. For ring unsubstituted fulvenes, the prominent methods are: a) base-mediated condensation of cyclopentadienes with carbonyl compounds (Thiele reaction): Little, R. D.; Stone, K. J. *J. Org. Chem.* **1984**, *49*, 1849 and extensive citations therein. For a modification and synthesis of vinylfulvenes, see Erden, I.; Xu, F. -P.; Sadoun, A.; Smith, W.; Sheff, G.; Ossun, M. *J. Org. Chem.* **1995**, *60*, 813; b) electrophilic substitution, Straud, P. A.; Meuche, D.; Heilbronner, E. *Helv. Chim. Acta* **1966**, *49*, 517. d) photochemical method of potential greater value, Nesmeyanov, A. N.; Sazonova, V. A.; Gerasimenko A. V.; Sazonova, N. S. *Doklady Akad. Nauk SSSR*, **1963**, *149*, 1354, Engl. Edit. p. 376, *Chem. Abstr.* **1963**, *59*, 3460h.

9. Tsukazaki, M.; Tinkl, M.; Roglans, A.; Chapell, B. J.; Taylor, N. J.; Snieckus, V. *J. Am. Chem. Soc.* **1996**, *118*, 685.

10. Synthesis of the ferrocenyl phosphine oxide precursor: Chapell, B. J.; Snieckus, V. unpublished results.

11. Laufer, R. M.Sc. thesis, University of Waterloo, **1998**.