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A Novel Heterobicyclic Framework by Successive Ene Reactions

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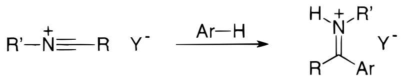
Introduction

Nitrilium ions are intermediates in numerous reactions, e.g., in the Beckmann rearrangement[1] and in the Ritter,[2] von-Braun,[3] Bischler−Napieralski,[3] Houben−Hoesch,[4] Gattermann,[5] and Schmidt reactions.[6] Isolated nitrilium salts undergo various types of reactions with alkenes,[7] alkynes,[8] carbonyl compounds,[9] and 1,3-dipoles.[10] Arenes react with *N*-aryl- or *N*-alkylnitrilium salts to give iminium ions[7a,11] where the incoming aryl group is located in the position cis to the N-substituent (Houben−Hoesch reaction, eq 1).[7a,12]

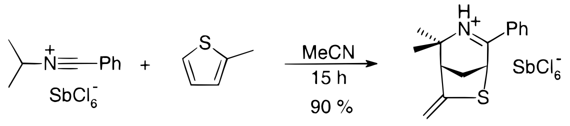


$$R'-\overset{+}{N}\equiv R\quad Y^- \xrightarrow{Ar-H} R(Ar)C=\overset{+}{N}(H)R'\quad Y^- \qquad (1)$$

In this paper, we report on a novel reaction mode of nitrilium ions with arenes, an ene reaction with inverse electron demand, where the nitrilium ion acts as the ene and the arene as the enophile.

Results and Discussion

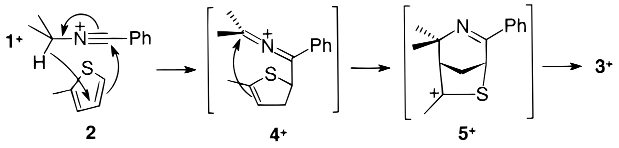
N-Isopropylbenzonitrilium hexachloroantimonate (**1**−$SbCl_6$), obtained from benzonitrile, isopropyl chloride, and antimony pentachloride,[13] reacts with 2-methylthiophene (**2**) in acetonitrile at 20 °C to yield 90% of the bicyclic product **3**−$SbCl_6$ (eq 2), which was characterized by X-ray crystallography[14] (see the Supporting Information).



1-$SbCl_6$ **2** **3**-$SbCl_6$ (2)

The reaction of $\mathbf{1}^+$ with **2** is suggested to proceed via concerted or stepwise ene reaction with the formation of an intermediate 2-azoniaallene[7b,8a] ($\mathbf{4}^+$). Since only signals of the reactants $\mathbf{1}^+$ and **2** and of the product $\mathbf{3}^+$ were detectable when monitoring the reaction by ^{1}H NMR spectroscopy, the formation of long-lived intermediates is ruled out. We, therefore, conclude that $\mathbf{4}^+$ cyclizes immediately to yield $\mathbf{5}^+$, which gives $\mathbf{3}^+$ by a proton shift (Scheme 1). Alternatively, the formation of $\mathbf{3}^+$ from $\mathbf{4}^+$ can be considered as a concerted 6-(3,5) ene cyclization,[15] a variation of Oppolzer's intramolecular ene reaction type I,[16a] classified as type IV by Snider.[16b]

Scheme 1



To our knowledge, the reaction of **1**−$SbCl_6$ with **2** is the first example of an ene reaction of a nitrilium ion with an aromatic compound. The scope of this new reaction type is not yet clear. Since reactions of *N*-methyl and *N*-ethylnitrilium salts with 2-methylthiophene (**2**) and other arenes gave exclusively Houben−Hoesch-type products,[12a] it is assumed that ene-type reactions are typical for *N*-isopropylnitrilium ions, particularly since Jochims also observed ene reactions when *N*-isopropylnitrilium salts were combined with alkenes[7b] and alkynes.[8a]

Experimental Section

General Methods. All reactions were run under an atmosphere of dry nitrogen. The nitrilium salt **1**−$SbCl_6$ was synthesized from benzonitrile, isopropyl chloride, and $SbCl_5$ according

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(1) (a) Craig, D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ley, S. V., Eds.; Pergamon Press: Oxford, 1991; Vol. 7, Chapter 5.2, pp 689−702. (b) Gawley, R. E. *Org. React.* **1988**, *35*, 1−420.

(2) (a) Bishop, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Winterfeldt, E., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, Chapter 1.9, pp 261−300. (b) Benz, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Winterfeldt, E., Eds.; Pergamon Press: Oxford, 1991; Vol. 6, Chapter 2.3, pp 381−417. (c) Krimen, L. I.; Cota, D. J. *Org. React.* **1969**, *17*, 213−325. (d) Johnson, F.; Madroñero, R. *Adv. Heterocycl. Chem.* **1966**, *6*, 95−146.

(3) Fodor, G.; Nagubandi, S. *Tetrahedron* **1980**, *36*, 1279−1300.

(4) (a) Heaney, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, Chapter 3.2, pp 733−752. (b) Ruske, W. In *Friedel−Crafts and Related Reactions*; Olah, G. A., Ed.; Wiley: New York, 1964; Vol. 3, pp 383−497.

(5) Truce, W. E. *Org. React.* **1957**, *9*, 37−72.

(6) Banthorpe, D. V. In *The Chemistry of the Azido Group*; Patai, S., Ed.; Wiley: London, 1971; Chapter 7, pp 397−440.

(7) (a) Moustafa, A. H.; Hitzler, M. G.; Lutz, M.; Jochims, J. C. *Tetrahedron* **1997**, *53*, 625−640. (b) Moustafa, A. H.; Wirschun, W.; Freyhardt, C. C.; Jochims, J. C.; Abu-El-Halawa, R. *J. Prakt. Chem.* **1997**, *339*, 615−622. (c) Schmidt, R. R. *Angew. Chem.* **1973**, *85*, 235−247; *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 212−223.

(8) (a) Abu-El-Halawa, R.; Jochims, J. C. *Synthesis* **1992**, 871−874. (b) Al-Talib, M.; Jochims, J. C.; Wang, Q.; Hamed, A.; Ismail, A. E. *Synthesis* **1992**, 875−878.

(9) (a) Lukyanov, S. M. In *The Chemistry of Enamines − Part 2*; Rappoport, Z., Ed.; Wiley: Chichester, 1994; Chapter 24, pp 1441−1506. (b) Al-Talib, M.; Zaki, M.; Hehl, S.; Stumpf, R.; Fischer, H.; Jochims, J. C. *Synthesis* **1996**, 1115−1121.

(10) (a) Quast, H.; Hergenröther, T. *Liebigs Ann. Chem.* **1992**, 581−590. (b) Abu-El-Halawa, R.; Shrestha-Dawadi, P. B.; Jochims, J. C. *Chem. Ber.* **1993**, *126*, 109−116.

(11) (a) Eyley, S. C.; Giles, R. G.; Heaney, H. *Tetrahedron Lett.* **1985**, *26*, 4649−4652. (b) Amer, M. I.; Booth, B. L.; Noori, G. F. M.; Proença, M. F. J. R. P. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1075−1082.

(12) (a) Henninger, J. Dissertation, Ludwig-Maximilians-Universität München, 1999. (b) Hegarty, A. F. *Acc. Chem. Res.* **1980**, *13*, 448−454.

(13) Meerwein, H.; Laasch, P.; Mersch, R.; Spille, J. *Chem. Ber.* **1956**, *89*, 209−224.

(14) Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-138484. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223/336-033; e-mail: deposit@ccdc.cam.ac.uk).

(15) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021−1050.

(16) (a) Oppolzer, W.; Snieckus, V. *Angew. Chem.* **1978**, *90*, 506−516; *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476−486. (b) Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 1.1, pp 1−27.

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to ref 13. 2-Methylthiophene (**2**) is commercially available and was distilled prior to use. ^{1}H (400 MHz) and ^{13}C NMR (100.6 MHz) spectra of solutions in CD$_3$CN were calibrated to the solvent signals (δ_H 1.93, δ_C 1.30).

2,2-Dimethyl-7-methylene-4-phenyl-3-azonia-6-thiabicyclo[3.2.1]octa-3-ene Hexachloroantimonate (3−SbCl$_6$). 2-Methylthiophene (**2**, 0.83 g, 8.5 mmol) was added to a solution of **1**−SbCl$_6$ (0.96 g, 2.0 mmol) in 3 mL of dry acetonitrile at ambient temperature. After steering for 15 h, the volatile components were removed in vacuo, and the residue was recrystallized from CH$_2$Cl$_2$/pentane to yield 1.04 g of **3** (1.8 mmol, 90%): orange needles; mp 180 °C; ^{1}H NMR (CD$_3$CN) δ 1.54, 1.58 (2 s, 2 × 3 H, 2 × CH$_3$), 2.48−2.54, 2.85−2.88 (2 m, 2 × 1 H, 8-H$_2$), 3.24−3.25 (m, 1 H, 1-H), 4.95 (m$_c$, 1 H, 5-H), 5.27−5.29, 5.46−5.47 (2 m, 2 × 1 H, =CH$_2$), 7.65−7.69 (m, 2 H, Ph), 7.82−7.86 (m, 3 H, Ph), 10.29 (br t, $J_{N,H} \approx 47$ Hz, 1 H, NH); ^{13}C NMR (CD$_3$CN) δ 27.6, 28.0 (2 q, 2 × CH$_3$), 33.2 (t, C-8), 45.2 (d, C-5), 52.0 (d, C-1), 63.2 (s, C-2), 110.7 (t, =CH$_2$), 129.4 (s, Ph), 130.4, 130.7, 137.3 (3 d, Ph), 145.2 (s, C-7), 183.1 (s, C-4) (signal assignments are based on 2D NOE, ^{1}H,^{1}H- and ^{1}H,^{13}C−COSY experiments); MS (FAB, Ar, 5−6 kV) *m/z* 246, 245, 244 (6, 18, 89) [M − SbCl$_6$]. Anal. Calcd for C$_{15}$H$_{18}$Cl$_6$NSSb: C, 31.12; H, 3.13; Cl, 36.75; N, 2.42; S, 5.54. Found: C, 31.49; H, 3.21; Cl, 36.47; N, 2.43; S, 5.68.

Crystallization from diethyl ether yields **3**−SbCl$_6$ as gold-yellow needles with approximately 0.75 equiv of ether in the crystals.

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Supporting Information Available: ORTEP diagram and details of the X-ray crystallographic study of **3**−SbCl$_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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Additions and Corrections

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Ryo Takeuchi,* Keisuke Tanabe, and Shigeru Tanaka. Stereodivergent Synthesis of (*E*)- and (*Z*)-2-Alken-4-yn-1-ols from 2-Propynoic Acid: A Practical Route via 2-Alken-4-ynoates.

Page 1558. We inadvertently overlooked the related work of Uguen and co-workers in ref 12: Zoller, T.; Uguen, D. *Tetrahedron Lett.* **1998**, *39*, 6719.

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