ORGANIC
LETTERS

2013
Vol. 15, No. 18
4627–4629

Reaction of Benzopinacol with Non-ionic Bases: Reversing the Pinacol Coupling

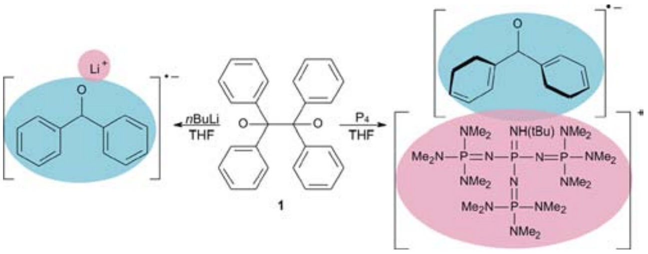
Michal Zalibera,[†] Peter Nesvadba,[‡] and Georg Gescheidt*,[†]

Institute of Physical and Theoretical Chemistry, Graz University of Technology, Stremayrgasse 9, 8010 Graz, Austria, and BASF Schweiz AG, 4002 Basel, Switzerland

g.gescheidt-demner@tugraz.at

Received August 7, 2013

ABSTRACT



The reaction of benzopinacol with the non-ionic bases butyllithium and phosphazene P_4 leads to the formation of the corresponding ketyl radical anions, which have been characterized by EPR/ENDOR spectroscopy. This conversion has a high efficiency. Such a reversed pinacol reaction can be used for a controlled release of ketyl radicals. Moreover, the nature of the base has a marked effect on the association of the ketyl radical anion and the counterions. This illustrates the importance of ion pairing for reductive coupling.

Reductive coupling processes, for example, the pinacol or the McMurry reaction, are frequently utilized synthetic methologies.[1] Generally, such reactions involve ketyl-type radicals (radical ions), although this has been questioned in some cases. Astonishingly, there is not ample mechanistic insight into these reactions.[2] Early investigations have shown that dimeric pinacol precursors can cleave in the presence of strong bases in DMSO, yielding ketyl-type radical anions.[3] More recently, the continuing interest in the chemistry of ketyls revealed novel structural features, in terms of their interactions with counterions.[4]

Here, we investigate the reaction of 1,1,2,2-tetraphenyl-1,2-ethanediol (benzopinacol, **1**) with butyllithium (*n*-BuLi) and the sterically hindered base 1-*tert*-butyl-4,4,4-tris(dimethylamino)-2,2-bis[tris(dimethylamino)-phosphoranylidenamino]-2λ^5,4λ^5-catenadi(phosphazene) (P_4).[5]

The reaction of 2 equiv of *n*-BuLi with **1** in THF under high vacuum yielded the characteristic deeply blue-colored solution (λ_{max} = 630 nm), which gave rise to intense and well-resolved electron paramagnetic resonance (EPR) spectra. An unambiguous simulation of the EPR spectra becomes possible by the use of the electron nuclear double resonance (ENDOR) technique directly providing isotropic hyperfine coupling constants (a).[6] The a_H values (lines centered at ν_H = 14.56 MHz) are in very good agreement with those published for the benzophenone radical anion (**B**, Table 1).[7]

The patterns of the EPR spectra shown in Figure 1 are substantially dependent on the temperature. This is

---

[†] Graz University of Technology.

[‡] BASF Schweiz AG.

(1) (a) Furstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed.* **1996**, *35*, 2442. (b) Iqbal, J.; Bhatia, B.; Nayyar, N. K. *Chem. Rev.* **1994**, *94*, 519. (c) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513. (d) Perchyonok, V. T.; Lykakis, I.; Postigo, A. *Streamlining Free Radical Green Chemistry*; RSC Publishing: Cambridge, U.K., 2011.

(2) (a) Livingston, A. J.; Lindsay, H. A.; Milletti, M. C. *J. Coord. Chem.* **2012**, *65*, 1484. (b) Stahl, M.; Pidun, U.; Frenking, G. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2234.

(3) Russell, G. A.; Young, M. C. *J. Am. Chem. Soc.* **1966**, *88*, 2007.

(4) (a) Hou, Z. M.; Jia, X. S.; Fujita, A.; Tezuka, H.; Yamazaki, H.; Wakatsuki, Y. *Chem.—Eur. J.* **2000**, *6*, 2994. (b) Jones, C.; McDyre, L.; Murphy, D. M.; Stasch, A. *Chem. Commun.* **2010**, *46*, 1511. (c) Murphy, D. M.; McDyre, L. E.; Carter, E.; Stasch, A.; Jones, C. *Magn. Reson. Chem.* **2011**, *49*, 159.

(5) (a) Schwesinger, R.; Schlemper, H. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1167. (b) Schwesinger, R.; Hasenfratz, C.; Schlemper, H.; Walz, L.; Peters, E. M.; Peters, K.; Vonschnering, H. G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1361. (c) Schwesinger, R.; Schlemper, H.; Hasenfratz, C.; Willaredt, J.; Dambacher, T.; Breuer, T.; Ottaway, C.; Fletschinger, M.; Boele, J.; Fritz, H.; Putzas, D.; Rotter, H. W.; Bordwell, F. G.; Satish, A. V.; Ji, G.-Z.; Peters, E.-M.; Peters, K.; von Schnering, H. G.; Walz, L. *Liebigs Ann. Chem.* **1996**, *1996*, 1055.

(6) (a) Feher, G. *Phys. Rev.* **1956**, *103*, 834. (b) Höfer, P. In *Electron Paramagnetic Resonance: A Practitioner's Toolkit*; Brustolon, M., Giamello, E., Eds.; John Wiley & Sons, Inc.: Hoboken, NJ, 2008; p 37. (c) Kurreck, H.; Kirste, B.; Lubitz, W. *Electron Nuclear Double Resonance Spectroscopy of Radicals in Solution: Application to Organic and Biological Chemistry*; Wiley-VCH: Weinheim, 1988.

10.1021/ol402253s

Table 1. Hyperfine Coupling Constants (a/mT) of **1**/n-BuLi, **1**/P_4 (solvent THF), and the Corresponding Reference Data

	1/nBuLi[a]	**1**/P_4[b]	**B**/electrolysis[c]
$a_{H(para)}$	−0.350 (2 H)	−0.351 (2 H)	0.332 (2 H)
$a_{H(ortho)}$	−0.282 (4 H)	−0.269/−0.216 (2 H/2 H)	0.249 (4 H)
$a_{H(meta)}$	+0.101 (4 H)	+0.079/+0.069 (2 H/2 H)	0.083 (4 H)
a_{Li}[d]	0.056		

[a] Determined by ENDOR, T = 220 K, **1**/n-BuLi = 1:2. [b] Determined by ENDOR, signs by general TRIPLE, T = 175 K, **1**/P_4 = 1:2. [c] a values from ref 7b, electrolysis in 0.1 M tetraethylammonium perchlorate/CH_3CN, T = 293 K. [d] Determined for 220 K.

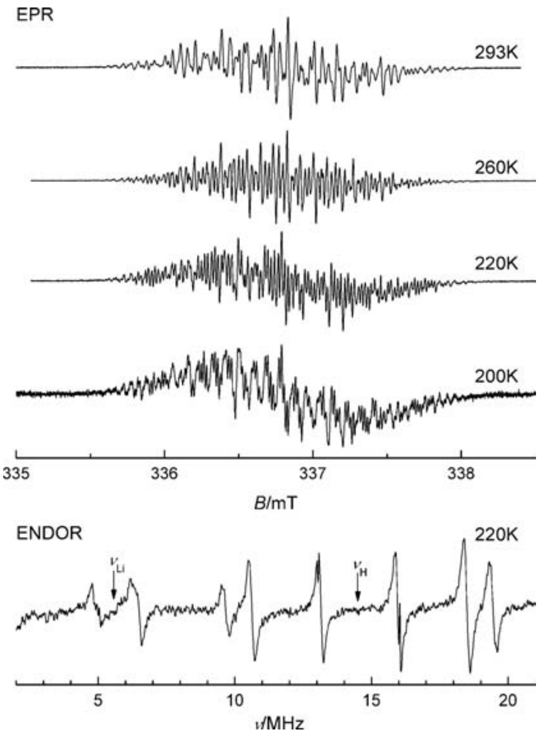


Figure 1. EPR spectra of **1**/n-BuLi in THF at various temperatures and the corresponding ENDOR spectrum at 220 K.

predominately caused by ion pairing with the Li^+ counterions, in line with previous investigations[7a,b] and corroborated by ENDOR spectra showing resonances of ^7Li nuclei ($I = 3/2$, 92.5% natural abundance, lines centered at ν_{Li} = 5.6 MHz; see Figure 1). The size of the lithium hyperfine coupling (a_{Li}) critically depends on the temperature and on the **1**:n-BuLi ratio (Figure S3 in the Supporting Information).

Very intense and resolved EPR spectra are also observed when **1** reacts with P_4 in THF (Figure 2a). Here, the color of the solution turns green (λ_{max} = 785 nm). Again, ENDOR allows determining the a_H values. Additionally, the intensity patterns of electron nuclear nuclear triple resonance (general TRIPLE and special TRIPLE) spectra provide the information of the signs and multiplicities of the coupling constants.[6b,c,8] The a_H values are again compatible with **B**, but the number of the detected coupling constants is five instead of three (for the reaction of **1** with n-BuLi, Figure 2b–d, Table 1).

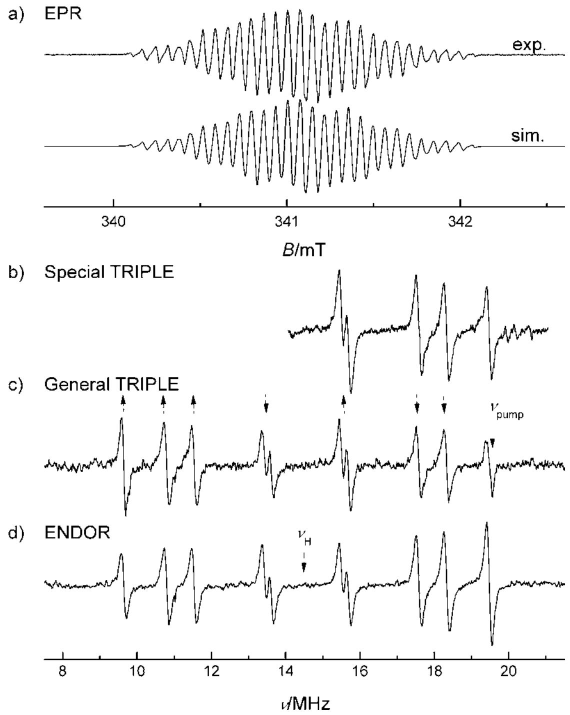


Figure 2. (a) EPR spectrum of **1**/P_4 1:2 in THF, together with the simulation and the corresponding (T = 175 K), (b) special TRIPLE, (c) general TRIPLE, and (d) ENDOR spectra (T = 175 K).

Significantly, the homolytic cleavage of the central bond, followed by the formation of the benzophenone radical anion (**B**),[7b] is observed for both bases, as illustrated by the EPR data. Ion-pairing interactions of ketyl radical anions with metal cations are well-established.[9] It is remarkable that association phenomena are also detectable, when the bulky base P_4 is used. At low temperatures, the *ortho* and the *meta* hydrogens possess only pairwise equivalency, a phenomenon that is not observed with n-BuLi. This shows that the rotation of the phenyl groups is restricted (abstract figure). Upon raising the temperature, the EPR spectra indicate dynamic phenomena, and the simulation of the spectra using a two-jump model for chemical exchange[10] yielded an activation energy for the rotation of the phenyl groups of 28.8 ± 0.8 kJ mol^{-1} (Figures S4, S5 in the Supporting Information). This points to an interaction between the (protonated) base P_4

---

(7) (a) Ayscough, P. B.; Wilson, R. *Proc. Chem. Soc.* **1962**, 229. (b) Ayscough, P. B.; Wilson, R. *J. Chem. Soc.* **1963**, 5412. (c) Rieger, P. H.; Fraenkel, G. K. *J. Chem. Phys.* **1962**, *37*, 2811. (d) Hirota, N. *J. Chem. Phys.* **1962**, *37*, 1884. (e) Wilson, R. *Can. J. Chem.* **1966**, *44*, 551.

(8) Dinse, K. P.; Biehl, R.; Mobius, K. *J. Chem. Phys.* **1974**, *61*, 4335.

(9) (a) Baskaran, D.; Mueller, A. H. E. *Prog. Polym. Sci.* **2007**, *32*, 173. (b) Roth, H. D. *Tetrahedron* **1986**, *42*, 6097. (c) Tidwell, T. T. *Angew. Chem., Int. Ed.* **2001**, *40*, 331.

(10) (a) Freed, J. H.; Fraenkel, G. K. *J. Chem. Phys.* **1963**, *39*, 326. (b) Stoll, S.; Schweiger, A. *J. Magn. Reson.* **2006**, *178*, 42–55.

and the benzophenone ketyl radical anion via the π system of **B**, an effect that does not appear, when alkali-metal cations act as counterions.

In summary, we have shown that non-ionic bases are able to reverse the pinacol coupling, inducing cleavage of the central bond in benzopinacol and producing ketyl radical anions.

From a mechanistic point of view, our results show that ion pairing is a central aspect for coupling reactions involving radical ions.[11]

Remarkably, the reaction proceeds in a very clean way, as can be shown by NMR spectroscopy of the quenched reaction solution (Figure S6 in the Supporting Information). Accordingly, this reaction paves a way for the use of non-ionic bases for efficient and controlled release of ketyl radicals. Here, pinacols would serve as caged precursors. Thus, it will be interesting to explore P_4 and related organic superbases, in terms of their application beyond deprotonation reactions,[12] that is, for a controlled release of ketyl radicals for (radical) polymerizations, nonsymmetric coupling reactions, and in "base induced" electron-transfer reactions.

Acknowledgment. The financial support of TU Graz is duly acknowledged.

Supporting Information Available. UV−vis spectra of the reaction mixture **1**/*n*-BuLi and **1**/P_4 in THF, simulations of the variable-temperature EPR of **1**/P_4, and NMR of the quenched reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

---

(11) (a) Scholz, M.; Gescheidt, G.; Daub, J. *Chem. Commun.* **1995**, 803. (b) Shohoji, C., M. *Tetrahedron Lett.* **1995**, *36*, 6167. (c) Alberti, A.; Seconi, G.; Pedulli, G. F.; Degl'Innocenti, A. *J. Organomet. Chem.* **1983**, *253*, 291.

(12) (a) Hirono, Y.; Kobayashi, K.; Yonemoto, M.; Kondo, Y. *Chem. Commun.* **2010**, *46*, 7623. (b) Lo, R.; Singh, A.; Kesharwani, M. K.; Ganguly, B. *Chem. Commun.* **2012**, *48*, 5865. (c) Kanazawa, C.; Ito, A.; Terada, M. *Synlett* **2009**, 638.