Pyridinium Salts Structurally Related to NAD(P)$^+$ as Enolate Transferring Agents

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The NAD(P)$^+$/NAD(P)H redox couple is known for the transfer of "hydride" equivalents. However, other anionic species, for example, CN, SR, and enolate, have been reported to add to pyridinium salts structurally related to NAD(P)$^+$.[1] For the case of thiolate, transfer in a manner resembling that involved for "hydride" has been shown.[2] We find that enolates can also be transferred by analogues of the NAD(P)$^+$/NAD(P)H system thereby allowing the realization of aldol condensations under unusually mild conditions.

Condensation of **1**[3] with acetophenone in the presence of ethanolic NaOH solution (this procedure resembles that described by Kröhnke for related condensations)[1c] gives **2** in an average isolated yield of 80%. Neither the 1,2- nor 1,6-dihydropyridine isomers of **2** were isolated. The structure of **2** was established from ^{1}H and ^{13}C NMR decoupling experiments.[4]

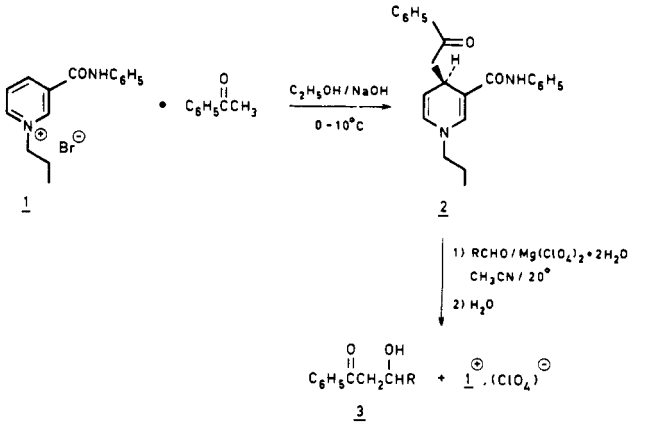
In the presence of a stoichiometric amount of $Mg(ClO_4)_2 \cdot 2H_2O$ **2** reacts at room temperature with aldehydes to afford aldol condensation products **3** and pyridinium salt **1** as shown in Scheme I.[5] The results are given in Table I.

In a typical procedure CH_3CN (2 mL) was introduced by syringe to a mixture of benzaldehyde (1 mmol), **2** (0.5 mmol), and $Mg(ClO_4)_2 \cdot 2H_2O$ (0.55 mmol, average of about 2 H_2O/molecule). The resulting solution was stirred at room temperature until the yellow color of **2** had disappeared (1 h). Excess wet $(C_2H_5)_2O$ was added and the precipitate of 1^+, ClO_4^- was removed. Workup followed by chromatography over a short column of SiO_2 gave products **3**.

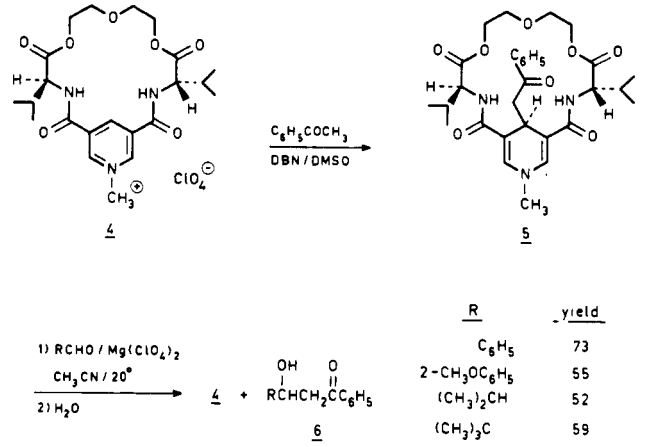
No dehydration of **3** occurred nor were other condensation products observed. Small amounts of acetophenone were formed, however. No *hydride* transfer from **2** was detected. Even a hindered aldehyde (entry e) reacts in a modest yield as does even salicylaldehyde (entry g), despite the acidic proton. Ketones are, however, poor acceptors; with acetophenone **2** gave only a 10% yield of the expected β-hydroxy ketone.

Either $BF_3 \cdot O(C_2H_5)_2$ or $SnCl_4$ (either at −40 °C in CH_2Cl_2) can also be used as electrophilic activator. $ZnCl_2$ is, however, sluggish, and $SnCl_2$ is ineffective.

Scheme I



Scheme II



R	yield
C_6H_5	73
2-$CH_3OC_6H_5$	55
$(CH_3)_2CH$	52
$(CH_3)_3C$	59

Bridged pyridinium salt **4**, which has been described by us previously,[6] reacts (DBN, Me_2SO, 25 °C) with acetophenone to provide **5**, mp 145–146 °C, $[\alpha]^{20}_D$ −44.9° (*c* 1.0, CH_2Cl_2) in 50% isolated yield. About 40% of the 1,2-isomer (not shown) is formed also in this case; separation is by recrystallization from CH_2Cl_2/hexane. Again in the presence of a stoichiometric amount of $MgClO_4 \cdot 2H_2O$ smooth aldol condensation occurs as shown in Scheme II (yields not optimized).[7] The aldol products **6** are, however, racemic, which is the expected result of reversible (at ambient temperature) carbon–carbon bond cleavage of any chiral magnesium derivatives of **6** formed initially.[8]

The opportunity for elimination of the aromatic pyridinium salts **1** or **4**, which can obviously be recycled, is clearly a driving force for these condensations. Acetophenone, benzaldehyde, and $Mg(ClO_4)_2 \cdot 2H_2O$ subjected to similar conditions fail to react. The electrophilic activator is believed to induce dissociation of **2** and **5** to an enolate and pyridinium ion prior to condensation. The isolation of acetophenone from **2** and **5** on treatment with $Mg(ClO_4)_2 \cdot 2H_2O$ alone followed by hydrolysis is consistent with this idea. Mutual association between enolate, activator, pyridinium ion, and acceptor is a prerequisite for transfer of chirality and is expected to be a sensitive function of the reaction conditions. Enantioselective reactions under unambiguous, *irreversible* conditions using acetals[9] or diacetoxy derivatives as acceptors together with extensions to other enolates are currently under investigation.

(1) See, for example: (a) Doering, W. v. E.; McEwen, W. E. *J. Am. Chem. Soc.* **1951**, *73*, 2104. (b) Kröhnke, F.; Ellegast, K.; Betram, E. *Liebigs Ann. Chem.* **1956**, *600*, 176. (c) Ahebrecht, H.; Kröhnke, F. *Ibid.* **1967**, *704*, 133. (d) Wilson, R. M.; Eberle, A. J. *J. Org. Chem.* **1974**, *39*, 2804. (e) Wenkert, E.; Chang, C.-J.; Chawla, H. P. S.; Cochran, D. W.; Hagaman, E. W.; King, J. C.; Orita, K.; *J. Am. Chem. Soc.* **1976**, *98*, 3645. (f) Zoltewicz, J. A.; Helmick, L. S.; O'Halloran, J. K. *J. Org. Chem.* **1976**, *41*, 1308. (g) Ludowieg, L.; Bhacca, N.; Levy, A. *Biochem. Biophys. Res. Commun.* **1964**, *14*, 431. (h) Marti, M.; Viscontini, M.; Karrer, P. *Helv. Chim. Acta* **1956**, *39*, 1451. (i) Wallenfels, K.; Diekmann, H. *Liebigs Ann. Chem.* **1959**, *621*, 166. (j) reviews of dihydropyridines: Eisner, U.; Kuthan, J. *Chem. Rev.* **1972**, *1*, 72. (k) Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223. (l) Weller, D. D. *Tetrahedron Lett.* **1982**, 5239.

(2) (a) Wallenfels, K.; Hofmann, D.; Shüly, H. *Liebigs Ann. Chem.* **1959**, *621*, 188. (b) Piepers, O.; Kellogg, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1147. (c) Van Keulen, B. J.; Kellogg, R. M., submitted.

(3) Nicotinamide derivatives unsubstituted at amide nitrogen on reaction with enolates give addition products in which the enolate appears to have condensed with the NH_2; **1** was chosen also for reasons of solubility and stability.

(4) All new compounds have been characterized by spectral means and have analytical data or exact masses in accord with theory.

(5) For an unusual precedent with formaldehyde as enolate acceptor, see: Steglich, W.; Höfle, G. *Chem. Ber.* **1969**, *102*, 1129.

(6) We have studied various chiral systems related to **2**: Jouin, P.; Troostwijk, C. B.; Kellogg, R. M. *J. Am. Chem. Soc.* **1981**, *103*, 2091.

(7) The 1,2-isomer of **5** appears also to transfer enolate but this reaction has not been studied in detail.

(8) (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 629–733. (b) Iwasawa, N.; Mukaiyama, T. *Chem. Lett.*, **1982**, 1441. (c) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

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Table I. Aldol Condensations of 2 with Aldehydes

entry	aldehyde	product (3)[a]	yield, %[b]
a	C_6H_5CHO	$C_6H_5CH(OH)CH_2COC_6H_5$	85, 84,[c] 78[d]
b	o-$(CH_3O)C_6H_4CHO$	o-$(CH_3O)C_6H_4CH(OH)CH_2COC_6H_5$	85
c			90[e]
d	$(CH_3)_2CHCHO$	$(CH_3)_2CH(OH)CH_2COC_6H_5$	66
e	$(CH_3)_3CCHO$	$(CH_3)_3CCH(OH)CH_2COC_6H_5$	47
f	*trans*-$C_6H_5CH=CHCHO$	*trans*-$C_6H_5CH=CHCH(OH)CH_2COC_6H_5$	67
g	o-$(HO)C_6H_4CHO$	o-$(HO)C_6H_4CH(OH)CH_2COC_6H_5$	37[f]

[a] Satisfactory spectral data were obtained for all new compounds. [b] Yields are of isolated materials homogenous by TLC. [c] With $SnCl_4$ in CH_2Cl_2 at −40 °C. [d] With $BF_3O(C_2H_5)_2$ in CH_2Cl_2 at −40 °C. [e] Yield estimated by ^1H NMR spectroscopy. [f] Yield not optimized.

To our knowledge, $NAD(P)^+/NAD(P)H$ cofactors have not (yet) been implicated in carbon–carbon bond forming counterparts of the reactions described here although the chemical validity of such processes is now firmly established. We note that enols of, for example, pyruvate, lactal, dihydroxyacetone, etc. add to NAD^+ and inhibit the redox process.[10]

Acknowledgment. The Dutch National Science Foundation (Z.W.O./S.O.N.) has provided a fellowship for S.H.M.

(9) See: (a) Mukaiyama, T.; Narasaka, K.; Bunno, K. *Chem. Lett.* **1973**, 1011. (b) Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248. (c) McNamara, J. M.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7371.

(10) For example: Florkin, M., Stotz, H. E., Eds. *Compr. Biochem.* **1966**, 1–198.

Additions and Corrections

Selectivities of π- and σ-Succinimidyl Radicals in Substitution and Addition Reactions. Appendix: Response to Walling, El-Taliawi, and Zhao [*J. Am. Chem. Soc.* **1983**, *105*, 5125]. P. S. SKELL,* R. L. TLUMAK, and S. SESHADRI

Page 5126, Table I: Column 6 [$BrCHCl_2$], M should read $BrCHCl_2$, mmol; column 7 [BPI], M should read BPI, mmol.

Page 5128, Table VIII: Row seven should read isobutane, *tert*-butyl· + SH, 5.1, 0.18; row eight should read 1-bromobutane, 1-bromo-2-butyl· + SH, 0.68, nothing.

Page 5129, Table IX: Column 4, row 8—640 should read 750; column 5, row 8—25000 should read 1.5×10^5.

Book Reviews*

Basic Analytical Chemistry. By L. Pataki and E. Zapp (Eötvös Loránd University, Budapest). Pergamon Press Ltd., Oxford. 1980. xiii + 463 pp. $55.00.

The authors of this text have endeavored to condense the features of analytical chemistry, both qualitative and quantitative analysis and classical and instrumental methods, into a single volume. They have done so in part to emphasize the unity of analytical chemistry, beginning with solution equilibria and proceeding to the group reactions used in systems of qualitative analysis. A survey of the principles of quantitative analysis and analytical instrumentation is then presented, followed by a chapter on analysis of organic compounds. The authors have made some compromises in order to reduce the amount of material to a single volume, and they have chosen to give a brief survey of many methods rather than to discuss methods and their theories to any great depth.

In spite of the title of this book, it is not really designed around the requirements of an introductory course in quantitative analysis. For example, there is no discussion on the principles and use of weights and measures. Typical laboratory manipulations and suggested experiments are not included, and the concepts of primary standards and their use in reagent preparation should be included in an introductory text. In addition, some sample problems or exercises at the ends of the chapters might help clarify concepts in solution equilibrium. The Pataki–Zapp text could probably be used for introductory quantitative analysis if supplemented by a good laboratory manual and some additional explanation by the instructor. For a course on chemical instrumentation, this text is perhaps not quite detailed enough, although most instrumental methods are mentioned. The chapters on qualitative analysis and analysis of organic compounds are quite good. Perhaps this text might best be utilized in an undergraduate advanced analytical chemistry course including both the chemistry and instrumentation of analytical chemistry.

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*Unsigned book reviews are by the Book Review Editor.

Chemical Publications: Their Nature and Use. Fifth Edition. By M. G. Mellon (Purdue University). McGraw-Hill Book Company, New York. 1982. xii + 419 pp. $24.95.

The appearance of the 5th edition of Mellon's "Chemical Publications" is a welcome event. For decades, earlier versions of this work complemented other guides to the chemical literature, including such classics as the books by Soule; Crane, Patterson, and Marr; Bottle; and Burman. In recent years, however, the 4th edition had been eclipsed by more current works on the subject, including a revision of the book by Bottle and new titles by Woodburn, Antony, Maizell, and Skolnik. Useful in their own right, none of these works precisely filled the gap left by 17 years without a new edition of Mellon, although Skolnik's more expensive "The Literature Matrix of Chemistry" (Wiley, 1982) came close. The 5th edition of "Chemical Publications" once again provides American chemists with a well-written, up-to-date guide to the burgeoning professional literature, one that simultaneously offers depth and breadth of coverage.

The book is divided into two parts. Part I (Publications: Kinds and Nature) begins with a brief description of the origin and development of the chemical literature. The next 11 chapters divide chemical publications into primary, secondary, and tertiary sources. Within these categories, Mellon discusses periodicals, technical reports (mainly government documents), patents, dissertations, trade publications, indexing and abstracting journals, reviews, bibliographies, tabular compilations, dic-