This article was downloaded by: [Duke University Medical Center] On: 05 October 2014, At: 05:31 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: http://www.tandfonline.com/loi/lsyc20

Anionic Fries' Type Reaction in Aryl Tetramethyldiamidophosphates

Jan H. Näsman^a & Nina Kopola^b

^a Institutionen för Organisk Kemi , Åbo Akademi Akademig. 1 Åbo, SF-20500 E-mail:

^b Neste OY, Technology Centre, PL 310, SF-06101, Porvoo, Finland Published online: 23 Sep 2006.

To cite this article: Jan H. Näsman & Nina Kopola (1992) Anionic Fries' Type Reaction in Aryl Tetramethyldiamidophosphates, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 22:17, 2491-2498, DOI: <u>10.1080/00397919208021644</u>

To link to this article: http://dx.doi.org/10.1080/00397919208021644

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with

primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <u>http://www.tandfonline.com/page/terms-and-conditions</u>

SYNTHETIC COMMUNICATIONS, 22(17), 2491-2498 (1992)

ANIONIC FRIES' TYPE REACTION IN ARYL TETRAMETHYLDIAMIDOPHOSPHATES

Jan H. Näsman* and Nina Kopola^a Institutionen för Organisk Kemi, Åbo Akademi Akademig. 1, SF-20500 Åbo, Finland Earn/Bitnet address: NASMANJ@FINABO

Summary. n-BuLi lithiates aryl tetramethyldiamidophosphates adjacent to the tetramethyldiamidophosphate group, which migrates to the adjacent position.

Metalation with lithiumreagents and quench with an electrophile has become an increasingly important reaction sequence in modern synthetic organic chemistry.¹ Recently we reported the new β -directing substituent, N,N,N',N'-tetramethyldiamidophosphate (PON), that activated furyl N,N,N',N'-tetramethyldiamidophosphate for regioselective lithiation in 3-position of the furan moiety.²

In order to establish the *ortho*-directing ability of the PON group, phenyl tetramethyldiamido phosphate 1, 1-naphtyl tetramethyldiamidophosphate 2 and 2-naphtyl tetramethyldiamidophosphate 3 have been prepared and lithiated.

To whom correspondance should be addressed. Current address: Laboratory of Polymer Technology, Åbo Akademi, Porthansgatan 3-5, SF-20500 Åbo, Finland

^a Current address: Neste OY, Technology Centre, PL 310, SF-06101 Porvoo, Finland







Scheme 2

Addition of 1.1 equiv. of *n*-BuLi at -78 °C in THF solvent to 1 followed by quench with MeI, however, did not solely give the *ortho*-methylated product. Instead also the product 4, where the PON group had migrated, was isolated, Scheme 1. All attempts to selectively methylate 1 at -78 °C were unfruitful. The same phenomenon was observed for the 1- and 2-naphtyl-PON compounds 2 and 3, Scheme 2. Thus it was possible to prepare compounds 4 - 6.

The structures 4 - 6 were assigned by comparing our ¹H-NMR and ¹³C-NMR spectra with those of reported structurally similar compounds.³⁻⁵

We observed ${}^{3}J_{PH}$ constants (to ring protons) for the compounds 4 = 10.4 Hz, 5 = 10.2 Hz and 6 = 14.4 Hz respectively. For structurally similar aryl dialkyl phosphonates coupling constants ${}^{4}J_{PH} = 6 \cdot 8$ Hz and ${}^{3}J_{PH} = 15 \cdot 16$ Hz respectively were reported.^{3a,b,e} ¹³C-NMR confirmed the proposed structures. The ¹J_{PC} coupling constant has been reported to be about 82 - 187 Hz.⁵ In all our isolated compounds a 148-150 Hz ¹J_{PC} coupling was found, i.e the PON group is attached directly to the aromatic ring. The coupling ²J_{PC} was reported to be of the order 9 - 14 Hz and ³J_{PC} 11 - 18 Hz.^{3e,5} Also similar couplings could be found in the spectral data of our compunds. For the naphtyl derivatives the chemical shifts also were in accordance, within the ppm range of 1-4 ppm, with the shifts reported for carbonyl naphtols.⁴

Considering the strong β -directing ability² of the PON group it is likely that the lithiation first occurs at the ortho carbon. The lithiated compound then collapses to give the rearranged product. Thus these results demonstrates the good activating property of the PON group also in *ortho*-lithiation of aromatic precursors.

Migrations of this type have been reported earlier for aryl dialkyltriester phosphates,³ ortho-lithio-O-trialkylsilylphenols⁶ O-aryl carbamates⁷ and 2-lithiophenyl carboxylates.⁸

Experimental

Tetrahydrofuran (THF) was distilled from sodium-benzophenone and tetramethylethylendiamine (TMEDA) was distilled from KOH prior to use. *n*-BuLi was purchased from Aldrich Chemical Company, Inc., and was titrated⁹ before use. All metalation reactions were carried out under nitrogen atmosphere. Melting points were obtained on a Gallenkamp apparatus and are uncorrected.¹³C and ¹H spectra were recorded in CDCl₃ with TMS as internal standard. ¹³C- were determined on a JEOL FX-60 instrument at 15.03 MHz. Chemical shifts in the proton noise decoupled spectra are reported in ppm downfield from TMS. The splitting pattern in the proton coupled spectra are given as s (singlet), d (doublet), t (triplet) and q (quartet) for none, one, two and three protons respectively one bond coupled to the carbon atom reported. Multiplicities in *italics* refer to carbon-phosphorious coupling in the proton noise decoupled spectra, a single (s) stands for (sxs). ¹H spectra were determined on a JEOL GX 400 instrument. Mas spectra were recorded on a VG Micromass 7070E or on a LKB 9000 instrument. Microanalysis were performed by Micro Kemi Ab Uppsala, Sweden.

1. Preparation of starting materials

Phenyl and naphtyl phosphorodiamidates were prepared from the corresponding dichloridates, which were prepared by the method of Katyshkina and Kraft¹⁰ in excellent distilled yield. Typical procedure: To one equivalent of dichloridate in MeCN, chilled in an icebath, is added a chilled solution of 4.05 equivalents of dimethylamine with stirring during one hour. After completed addition the icebath was removed and stirring was continued for 1 hour at ambient temperature. Most of the solvent was removed, ether was added and the formed dimethylamine hydrochloride was filtered off, removal of solvent and recrystallization or distillation gave pure products. The typical yield was 80 %.

(1-phenyl)-N,N,N',N'- tetramethyldiamido phosphate: distilled, bp₈: 150-152 °C; ¹H NMR 2.72 (d, 12H, ³J_{PH} = 10.1), 7.10-7.33 (m, 7H); ¹³C NMR 36.7 (dxq, J_{PC} = 3.9, J_{CH} = 136.7), 120.2 (dxd, J_{PC} = 5, J_{CH} = 162.1), 124.2 (sxd, J_{CH} = 162.1), 129.6 (sxd, J_{CH} = 161.1), 151 (dxs, J_{PC} = 7.5); MS m/e (rel.int) 228 (35), 184 (12), 135 (100), 120 (20), 94 (19), 92 (33), 77 (28)

(1-naphtyl)-N,N,N',N'- tetramethyldiamido phosphate: Recrystallized from petrol ether, bp range 60-80, and diisopropyl ether 1:1, mp 70-71 °C. ¹H NMR 2.77 (d, 12 H, ³J_{PH} = 10.1), 7.37 - 8.17 (m, 7 H); ¹³C NMR 36.8 (dxq, J_{PC} = 4, J_{CH} = 138),

114.3 (dxd, $J_{PC} = 8$, $J_{CH} = 184$), 121.5 (sxd, $J_{CH} = 163$), 123.7 (sxd, $J_{CH} = 161$), 125.9 (sxd, $J_{CH} = 162$), 126.3 (not resolved), 126.9 (not resolved), 127.8 (sxd, $J_{CH} = 162$), 134.8 (s), 147.4 (dxs, $J_{PC} = 6$); MS m/e (rel.int) 278 (44), 170 (12), 144 (12), 135 (100), 115 (7); Elemental analysis calc. for $C_{14}H_{19}N_2O_2P$ C: 60.4; H: 6.8; N: 10.0; found C: 60.8; H: 6.8; N: 10.0

(2-naphtyl)-N,N,N',N'- tetramethyldiamido phosphate: Recrystallized from diisopropyl ether mp 54-56 °C; ¹H NMR 2.75 (d, 12 H, ³J_{PH} = 10.1), 7.33 - 7.80 (m, 7 H); ¹³C NMR 36.7 (dxq, $J_{PC} = 4$), 116.3 (dxd, $J_{PC} = 5$), 120.5 (dxd, $J_{PC} = 5$, $J_{CH} = 163$), 125.0 (sxd, $J_{CH} = 161$), 126.4 (sxd, J = unresolved), 127.4 (sxd, J = unresolved), 127.6 (sxd, $J_{CH} = 159$), 129.6 (sxd, $J_{CH} = 161$), 130.6 (s), 134.2 (s), 149.1 (dxs, $J_{PC} = 6$); MS m/e (rel.int) 278 (52), 190 (14), 171 (19), 170 (22), 144 (45), 135 (100), 127 (11), 115 (14); Elemental analysis calc. for C₁₄H₁₉N₂O₂P C: 60.4; H:6.8; N:10.0; found C: 60.7; H:7.0; N:9.9.

2. Metalation procedure

The aryl tetramethyl diamido phosphate (5 mmol) was dissolved in THF and cooled to -75 °C. The lithiating agent (2.6 M *n*-BuLi in hexan (6 mmol) was added and the reaction mixture was stirred for 60 min. at -75 °C and 2 h at room temperature. The mixture was poured onto a NaHPO₄/HCl buffer. The H₂O phase was extracted with 3x100 ml ethyl acetate. The organic phase was dried over MgSO₄ and concentrated to afford the crude product.

3. Products

1-(2-hydrozy)-phenyl)-N,N,N',N'-tetramethyl phosphonic diamide; Phenyl tetramethyldiamido phosphate (1.14 g) was metalated according to the general procedure. Recrystallization from diisopropyl ether yielded the product as white crystals with mp: 69-72 °C (0.2 g, 35%). ¹H-NMR 2.67 (d, 12H, ${}^{3}J_{PH} = 10.4$), 6.85 (m, 1H), 6.95 (m, 1H), 7.22 (dxd, 1H, ${}^{3}J_{PH} = 12.8$), 7.37 (m, 1H); ${}^{13}C$ NMR 36.3 (dxq,), 110.4 (dxs, $J_{PC} = 149$), 118.0 (dxd, $J_{CH} = 164$, ${}^{3}J_{PC} = 10$), 118.7 (dxd, $J_{CH} = 164$, ${}^{3}J_{PC} = 10$), 131.2 (dxd, $J_{CH} = 158$), 133.9 (sxd, $J_{CH} = 160$), 163.1 (dxs, ${}^{2}J_{PC} =$ 6); MS m/e (rel.int) 228 (100), 185 (49), 184 (46), 167 (59), 152 (11), 140 (14), 92 (16), 77 (22); Elemental analysis; calc. for C₁₀H₁₇N₂O₂P: C: 52.6; H: 7.5; N: 12.3; found C: 52.4; H: 7.1; N: 12.1.

(3-(2-hydrozy)-naphtyl)-N,N,N',N'-tetramethyl phosphonic diamide; 1-naphtyl tetramethyl diamido phosphate (1.4 g) was metalated according to the general procedure. Recrystallization from diisopropyl ether / ethyl ether yielded the product as white crystals with mp: 132-134 °C (0.6 g, 43%). ¹H NMR 2.72 (d, 12H, ³J_{PH} = 10.4), 7.28-7.31 (m, 2H), 7.45 (m, 1H), 7.68 (d, 1H), 7.82 (d, 1H, ³J_{PH} = 14.3); ¹³C NMR 36.3 (dxq), 114.2 (dxs,¹J_{PC} = 148), 111.7 (dxd,²J_{PC} = 9, J_{CH} = 157), 123.4 (sxd, J_{CH} = 161), 126.4 (sxd, J_{CH} = 160), 128.1 (sxd, J_{CH} = 161), 128.4 (sxd, J_{CH} = 158), ca. 127 (s), 133.1 (dxd,³J_{PC} = 5, J_{CH} = 158), 137.3 (s), 158.3 (dxs, ²J_{PC} = 6); MS m/e (rel.int.) 278 (100), 233 (63), 217 (23), 190 (75), 135 (8), 127 (14), 115 (24); Elemental analysis; calc. for C₁₄H₁₉N₂O₂P C: 60.4; H: 6.8; N: 10.0; found C: 60.6; H: 6.8; N: 10.0.

(2-(1-hydrozy)-naphtyl)-N,N,N',N'-tetramethyl phosphonic diamide; 2-naphtyl tetramethyldiamido phosphate (1.4 g) was metalated according to the general procedure. Recrystallization from diisopropyl ether / diethyl ether afforded the product as white crystals with mp: 125-127 °C (0.95 g, 68%). ¹H NMR 2.70 (d, 12H, ³J_{PH} = 10.2), 7.20 (dxd, 1H, ³J_{PH} = 10.8, ³J_{HH} = 8.63), 7.28 (dxd, 1H, ⁴J_{PH} = 2.9, ³J_{HH} = 8.63), 7.51 (dxd, 1H, ³J_{HH} = 8.2, ³J_{HH} = 8.2), 7.57 (dxd, 1H, ³J_{HH} = 8.2, ${}^{3}J_{HH} = 7.9$), 7.75 (d, 1H, ${}^{3}J_{HH} = 7.9$), 8.39 (d, 4H, ${}^{3}J_{HH} = 8.2$); ${}^{13}C$ NMR 36.3 (dxq), 102.3 (dxs, ${}^{1}J_{PC} = 150$), 118.2 (dxd, ${}^{2}J_{PC} = 13$, $J_{CH} = 163$), 123.6 (sxd, $J_{CH} = 164$), 125.7 (dxd, $J_{CH} = 159$) 126.3 (sxd, $J_{CH} = 162$), 127.3 (sxd, J = not resolved), 128.5 (sxd, J = not resolved), 136.4 (s), 161.6 (dxs, ${}^{2}J_{PC} = 6$). MS m/e (rel.int.) 278 (100), 233 (100), 217 (13), 190 (73), 143 (12), 127 (11), 115 (16). Elemental analysis; calc. for C₁₄H₁₉N₂O₂P: C: 60.4; H: 6.8; N: 10.0; found C: 59.8; H: 6.6; N: 9.8

Acknowledgement. We are grateful to the Academy of Finland for fellowships and financial support. NK also thanks The Association of Finnish Chemical Societies and The Center for Technological Development (TEKES) for financial support.

REFERENCES

a) Gilman, H., Morton, J.W., Org. React. 1954, 8, 258. b) Mallan, M.J., Rebb,
 R.L., Chem. Rev. 1969, 693. c) Gschwend, H.W., Rodriguez, H.R., Org. React.
 (NY), 1979, 26, 1, Wiley. d) Narasimhan, N.S., Mali, R.S., Synthesis 1983, 965.
 e) Snieckus, V., Lect. Heterocyclic Chem. 1984, 95 - 106. f) Klumpp, G.W. Rec.
 Trav. Chim. Pays-Bas 1986, 105, 1.

2) a) Näsman, J.H. Organic Syntheses 1989, 68, 162. b) Näsman, J.H., Kopola,
N., Pensar, G., Tetrahedron Letters 1986, 27, 1391.

3 a) Dhawan, B., Redmore, D., J. Org. Chem. 1986, 51, 179. b) Dhawan, B.,
Redmore, D., Synth. Comm. 1985, 15, 411. c) Dhawan, B., Redmore, D., J.
Org. Chem. 1984, 49, 4018. d) Hammond, G.B., Calogeropoulou, T. and Wiemer,
D.F., Tetrahedron Letters 1986, 27, 4265. e) Cambie, C.R., Palmer, D.B., Aust.
J. Chem. 1982, 35, 827. f) Melvin, L.S., Tetrahedron Letters 1981, 22, 3375.

- 4) Razniewska-Lazęcka, G., Dambska, A., Janowski, A., Magn. Reson. Chem. 1986, 24(4), 366.
- 5) Modro, T., Can. J. Chem. 1977, 55, 3681.
- 6) Billedau, R.J., Sibi, M.P. and Snieckus, V., Tetrahedron Lett. 1983, 24, 4515 and references cited therein.
- 7) Sibi, M.P, Snieckus, V., J. Org. Chem. 1983, 48, 1935.
- 8) Miller, J.A., J. Org. Chem. 1987, 52, 322.
- 9) Kofron, W.G., Baclawski, L.M., J. Org. Chem. 1976, 41, 1879.
- 10) Katyshkina, V.V. and Kraft, M.J.A., as referred to in 'Houben-Weyl, Methoden

der Organischen Chemie', K. Sasse editor, Stuttgart 1964, Band 12/2 p. 216

(Received in UK 22 April, 1992)