A Simple Route to Benz[a]acridinium Salts

Horst Hartmann

Department Chemie, Technische Universität Dresden, 01062 Dresden, Germany

Reprint requests to Prof. Dr. Horst Hartmann. Fax: ++49-351-4633 9485. E-mail: Hartmann@iapp.de

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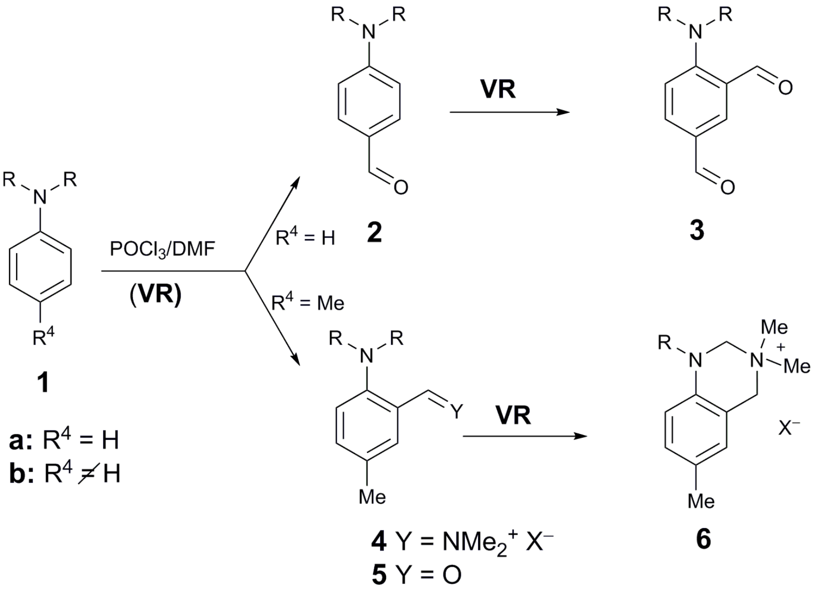
Dedicated to Prof. Dr. Dr. hc mult. Siegfried Hünig to the occasion of his 90th birthday

By reaction of *N*-substituted *N*-phenyl-2-naphthylamimes with the Vilsmeier reagent *N*-substituted benz[a]acridinium salts are formed in satisfactory yields.

Key words: Vilsmeier Reaction, *N*-Substituted 2-(*N*-Phenyl)-naphthylamines, Benz[a]acridinium Perchlorates

Introduction

As has been known for a long time, the Vilsmeier reaction (VR), usually performed with a mixture of DMF and $POCl_3$, is a versatile method for preparing aromatic or heteroaromatic aldehydes in an enormous variety [1]. For instance, by starting with 4-unsubstituted *N,N*-dialkylanilines **1a**, *N,N*-disubstituted 4-aminobenzaldehydes **2** or, under more rigorous conditions, corresponding *N,N*-disubstituted 4-amino-terephthalaldehydes **3** are formed [2]. However, by starting with 4-substituted *N,N*-dialkylanines **1b**, instead of expected *N,N*-disubstituted 2-amino-benzaldehydes **5**, the 1,3,3,4-tetrahydro-3-quinazolinium salts **6** were obtained [3]. These compounds arise by cyclisation of the corresponding dimethyliminium salts **4** intermediately formed in the course of the VR and can be regarded as undesired by-products in the Vilsmeier aldehyde synthesis (Scheme 1). In contrast, the mono-formyl compounds **2** and the bis-formyl derivatives **3** are important starting materials for a variety of products with some practical interest, such as organic dyes with intense absorption in the visible or near infrared region [4], with highly non-linear optical properties [5], or with a high two-photon cross section [6].



Scheme 1. VR = Vilsmeier reaction.

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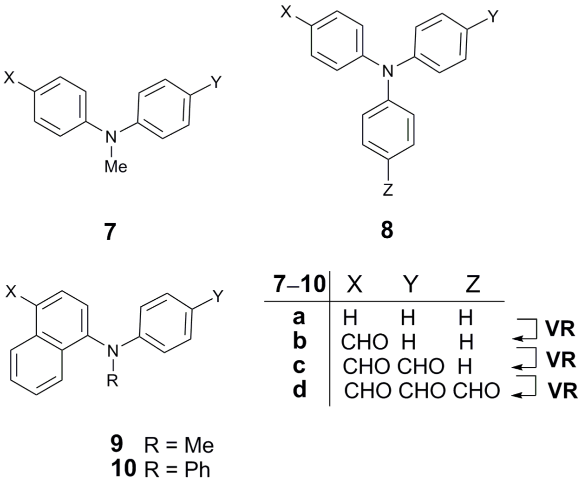


7–10	X	Y	Z
a	H	H	H
b	CHO	H	H
c	CHO	CHO	H
d	CHO	CHO	CHO

Scheme 2.

The Vilsmeier formylation of *N,N*-dialkylanilines **1** outlined here starts similarly with *N*-monoaryl- and *N,N*-diaryl-substituted aniline derivatives and gives rise to the formation of corresponding *N*-monoaryl- and *N,N*-diaryl-substituted aldehydes or their dimethyliminium salt precursors (Scheme 2). Thus, *N*-methyl-diphenylamine **7a**, triphenylamine **8a**, *N*-methyl-*N*-phenyl-1-naphthylamine **9a**, and *N,N*-diphenyl-1-naphthylamine **10a** were converted by a VR into the corresponding *N*-methyl-*N*-phenyl-4-aminobenzaldehyde **7b** [7], *N,N*-diphenyl-4-aminobenzaldehyde **8b** [8], *N*-methyl-*N*-phenyl-4-amino-1-naphthaldehyde **9b** [9], and *N,N*-diphenyl-4-amino-1-naphthaldehyde **10b** [10], respectively. Under more rigorous conditions the bis-formyl derivatives **7c**–**10c** as well as the tris-formyl derivative **8d** were formed [8a, 11].

Results and Discussion

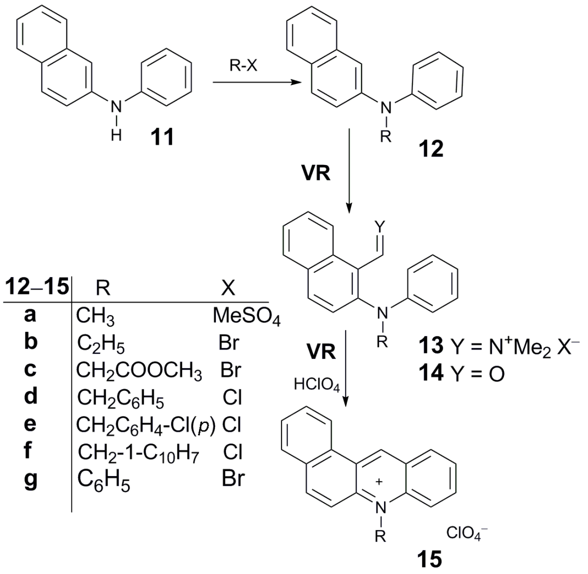
A quite different result has been found, however, when *N*-phenyl-substituted 2-naphthylamines **12** were used as reactants in the VR. Instead of the corresponding formyl compounds **14** (or their corresponding dimethyliminium salt precursors **13**) benz[a]acridinium salts of the general structure **15** were obtained (Scheme 3).

The reaction can be advantageously performed by heating a mixture of the Vilsmeier reagent with the appropriate *N*-phenyl-substituted 2-naphthylamine **12** at 80–90 °C for several hours and quenching the reaction mixture after cooling by pouring into methanol. The benz[a]acridinium salts **15** so formed could be isolated after addition of aqueous perchloric acid to the reaction mixture and were obtained in rather high yields.

The necessary *N*-substituted *N*-phenyl-2-naphthylamines **12** are commercially not available, but they can be synthesised easily from the *N*—unsubstituted *N*-phenyl-2-naphthylamine parent compound **11** by addition of an appropriate alkylating agent of the general formula R-X before starting the Vilsmeier formylation. The *N,N*-diphenyl-2-naphthylamine **10g** was prepared, however, by a palladium-catalysed *C-N* cross coupling from *N*-phenyl-2-naphthylamine and bromobenzene [12].

The benz[a]acridinium salts **15** so prepared are pale-yellow solids. Their structures follow unambiguously from the analytic data. For instance, all salts exhibit in the mass spectra *m/z* values which are in accord with the cationic moieties, and in the ^{1}H NMR spectra they show characteristic signals between $\delta = 7.8-9.5$ and ~ 10.0 ppm. Whereas the former signals originate from the protons at the carbocyclic rings, the latter signals can be attributed to the protons at C12 of the heterocyclic azine ring in the benzo[c]acridinium salts **15**.

In contrast to acridines [13], acridinium salts are hitherto sparsely known and usually prepared by alkylation of their non-ionic parent compounds [14]. Because they are of some interest for various applications, *e. g.* as chemotherapeutics (*e. g.* Acriflavine), as fluorescent stains [15], or as organic dyes [16], the simple access described will make further studies on these compounds much easier.



12–15	R	X
a	CH_3	$MeSO_4$
b	C_2H_5	Br
c	CH_2COOCH_3	Br
d	$CH_2C_6H_5$	Cl
e	$CH_2C_6H_4$-Cl(*p*)	Cl
f	CH_2-1-$C_{10}H_7$	Cl
g	C_6H_5	Br

Scheme 3.

Experimental Section

^{1}H NMR spectra were recorded in trifluoroacetic acid with a Bruker DRX 500 P instrument at 500.13 MHz. The melting points were measured with a Boetius heating-table microscope. Mass spectra were recorded with a Bruker Esquire-LC 00084 instrument at 10 V with electrospray ionisation using methanol containing 0.1 % ammonium acetate.

*Preparation of N,N-diphenyl-2-naphthylamine (**12g**)*

To a solution of *N*-phenyl-2-naphthylamine (**11**, 54.8 g, 0.25 mol), bromobenzene (39.3 g, 0.25 mol) and Na-*tert.*-butanolate (28.8 g, 0.3 mol) in toluene (500 mL) a solution of palladium-bis-(tri-*tert.*-butylphosphane) (10 mL, 10 %) in toluene was added dropwise under argon at r. t. After refluxing the resulting mixture for 8 h, it was cooled to r. t. and mixed with water (500 mL). The organic phase was separated and the aqueous solution extracted twice with diethyl ether (250 mL). The organic solutions were combined, dried with $MgSO_4$, and evaporated *in vacuo*. The product so obtained in a yield of 74 g was purified by recrystallisation from a toluene/cyclohexane mixture. M. p. 120 °C (Lit. [17]: 120 – 121 °C). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.05 (dt, 2H), 7.12 (t, 1H), 7.15 (t, 2H), 7.25 – 7.27 (m, 5H), 7.30 (t, 1H), 7.37 (dt, 2H), 7.42 (t, 1H), 7.58 (d, J = 10.0 Hz, 1H), 7.73 (dd, J = 11.2, J = 4 Hz, 2 H).

*Preparation of the benz[a]acridinium perchlorates **15** (General procedure)*

To a solution of *N*-phenyl-2-naphthylamine (**11**, 2.2 g, 10 mmol) in DMF (25 mL) the corresponding alkylating reagent R-X (15 mmol) was added and the resulting mixture heated at 120 °C for 30 min. After cooling, $POCl_3$ (3.2 g, 20 mmol) was added dropwise to the reaction mixture which was subsequently heated at 90 °C for 2 h and then cooled to r. t. After addition of methanol (50 mL), perchloric acid (70 %, 2 mL) was added to the resulting mixture under cooling. The precipitate formed after addition of some ethyl acetate was isolated by suction and recrystallised, after drying at air, from acetic acid. The following benz[a]acridinium perchlorates were prepared:

*7-Methyl-benzo[a]acridinium perchlorate (**15a**)* in a yield of 80 %. M. p. 320 – 324 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 5.32 (s, 3H, CH_3), 8.35 (t, 1 H), 8.46 (t, 2 H), 8.56 (d, J = 10.0 Hz, 1H), 8.70 – 8.81 (m, 2H), 8.95 (dd, J = 12.8 Hz, J = 4.0 Hz, 2H), 9.08 (d, J = 12.8 Hz, 1H), 9.39 (d, J = 10.8 Hz, 1 H), 10.76 (s, 1H). – MS ((+)ESI): *m/z* = 244.0 (calcd. 244.31 for $C_{18}H_{14}N^+$, $[M–ClO_4^-]^+$). – $C_{18}H_{14}ClNO_4$ (343.76): calcd. C 62.89, H 4.10, Cl 10.31, N 4.20, O 18.62; found C 62.44, H 4.18, N 4.20.

*7-Ethyl-benzo[a]acridinium perchlorate (**15b**)* in a yield of 86 %. M. p. 293 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 1.80 (t, 3H, CH_3), 5.99 (q, 2H, CH_2), 7.78 (t, 1H), 7.81 – 7.93 (m, 2H), 8.00 (d, J = 7.9 Hz, 1H), 8.15 (d, J = 9.7 Hz, 1H), 8.26 (t, 1H), 8.37 (d, J = 9.2 Hz, 1H), 8.44 (d, J = 8.2 Hz, 1H), 8.53 (d, J = 9.8 Hz, 1H), 8.84 (d, J = 8.3 Hz, 1H), 10.19 (s, 1H). – MS ((+)ESI): *m/z* = 258.1 (calcd. 258.34; for $C_{19}H_{16}N^+$, $[M–ClO_4^-]^+$). – $C_{19}H_{19}ClNO_4$ (357.79): calcd. C 63.78, H 4.51, Cl 9.91, N 3.91, O 17.89; found C 63.64, H 4.81, N 4.55.

*7-Methoxycarbonylmethyl-benzo[a]acridinium perchlorate (**15c**)* in a yield of 75 %. M. p. 290 – 292 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 4.47 (s, 3H, CH_3), 6.71 (s, 2H, H_2), 8.39 (t, 1H), 8.49 – 8.61 (m, 4H), 8.74 – 8.85 (m, 2H), 9.03 (d, J = 11.2 Hz, 1H), 9.12 (d, J = 12.8 Hz, 1H), 9.43 (d, J = 11.2 Hz, 1H), 10.87 (s, 1H). – MS ((+)ESI): *m/z* = 302.1 (calcd. 302.35 for $C_{20}H_{16}NO_2{}^+$, $[M–ClO_4^-]^+$). – $C_{20}H_{16}ClNO_6$ (401.80): calcd. C 59.78, H 4.01, Cl 8.82, N 3.49, O 23.89; found C 59.24, H 4.01, N 3.45.

*7-Benzyl-benzo[a]acridinium perchlorate (**15d**)* in a yield of 92 %. M. p. 288 – 289 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 7.02 (s, 2H, CH_2), 7.56 (d, J = 12.0 Hz, 2H), 7.80 (m, 2H), 8.36 (t, 1H), 8.47 – 8.61 (m, 3H), 8.72 (t, 1H), 8.20 (d, J = 12.0 Hz, 1H), 8.99 (t, 2H), 9.46 (d, J = 11.6 Hz, 1H), 10.88 (s, 1H). – MS ((+)ESI): *m/z* = 320.2 (calcd. 320.41 for $C_{24}H_{18}N^+$, $[M–ClO_4^-]^+$). – $C_{24}H_{18}ClNO_4$ (419.86): calcd. C 68.66, H 4.32, Cl 8.44, N 3.34; O 15.24; found C 69.04, H 4.31, N 3.54.

*7-(4-Chlorobenzyl)-benzo[a]acridiniumperchlorate (**15e**)* in a yield of 96 %. M. p. 299 – 300 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 6.62 (s, 2H, CH_2), 7.13 (d, J = 11.2 Hz, 2H), 7.42 (d, J = 11.2 Hz, 2H), 8.01 (t, 1H), 8.11 – 8.22 (m, 4H), 8.36 (m, 2H), 8.67 (t, 2H), 9.09 (d, J = 10.8 Hz, 1H), 10.49 (s, 1H). – MS ((+)ESI): *m/z* = 354.2, 355.1, 356.1, 357.1 (calcd. 354.85 for $C_{24}H_{17}ClN^+$, $[M–ClO_4^-]^+$). – $C_{24}H_{17}Cl_2NO_4$ (454.30): calcd. C 63.45, H 3.77, Cl 15.61, N 3.08, O 14.09; found C 63.49, H 3.31, N 3.20.

*7-(1-Naphthylmethyl)-benz[a]acridinium perchlorate (**15f**)* in a yield of 90 %. M. p. 297 – 300 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 7.07 (s, 3H, CH_2), 7.79 (t, 1H), 7.90 (t, 1H), 7.97 – 8.20 (M, 7H), 8.29 (d, J = 4.8 Hz, 2H), 8.35 (d, J = 10.8 Hz, 1H), 8.57 (d, J = 12.8 Hz, 1H), 8.73 (d, J = 11.2 Hz, 1H), 9.15, d, J = 11.6 Hz, 1H), 10.57 (s, 1H). – MS ((+)ESI): *m/z* = 370.2 (calcd. 370.47 for $C_{28}H_{20}N^+$, $[M–ClO_4^-]^+$). – $C_{18}H_{14}ClNO_4$ (469.92): calcd. C 71.57, H 4.29, Cl 7.54, N 2.98, O 13.62; found C 71.30, H 4.37, N 3.00.

*7-Phenyl-benz[a]acridinium perchlorate (**15g**)* in a yield of 82 %. M. p. 335 °C. – ^{1}H NMR (400 MHz, CF_3COOH): δ = 7.37 (d, J = 12.8 Hz, 1H), 7.49 (d, J = 12.0 Hz, 1H), 7.82 – 7.86 (m, 2H), 8.02 (d, J = 9.6 Hz, 1H), 7.95 – 7.98 (m, 3H), 8.10 – 8.19 (m, 2H), 8.25 – 8.31 (m, 2H), 8.64 (d, J = 12.8 Hz, 1H), 8.80 (dd, J = 10.8 Hz, 1H). – MS ((+)ESI): *m/z* = 306.1 (calcd. 306,38 for $C_{23}H_{16}N^+$, $[M–ClO_4^-]^+$). – $C_{23}H_{16}ClNO_4$ (405.83): calcd. C 68.07, H 3.97, Cl 8.74, N 3.45, O 15.77; found C 68.01, H 3.97, N 3.52.

[1] G. Jones, S. P. Stanforth, *Org. React.*, Vol. 49, John Wiley & Sons, London, **1997**, pp. 1 – 330.

[2] C. Grundmann, J. M. Dean, *Angew. Chem.* **1965**, *77*, 966 – 967; *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 955 – 956.

[3] a) Y. Cheng, O. Meth-Cohn, D. Taylor, *J. Chem. Soc., Perkin Trans. 1* **1998**, 1257 – 1262; b) O. Meth-Cohn, D. Taylor, *J. Chem. Soc., Chem. Commun.* **1995**, 1463 – 1464; c) O. Meth-Cohn, *Adv. Heterocycl. Chem.* **1996**, *65*, 1 – 37; d) L. D. Patsenker, I. G. Ermolenko, I. A. Feyunyaeva, N. A. Popova, B. M. Krasovitskii, *Chem. Heterocycl. Comp.* **2000**, *36*, 623 – 625; e) L. D. Patsenker, I. G. Ermolenko, O. N. Lyubrenko, I. A. Fedyunyaeva, N. A. Popova, O. S. Galkina, A. V. Mazepa, B. M. Krasovitskii, *Chem. Heterocycl. Comp.* **2003**, *39*, 525 – 533; f) O. N. Semenova, Y. Y. Artyukhova, I. G. Yermolenko, L. D. Patsenker, *Funct. Mater*. **2003**, *10*, 730 – 738.

[4] a) J. Fabian, H. Nakazumi, M. Matsuoka, *Chem. Rev.* **1992**, *92*, 1197 – 1226; b) J. Fabian, *J. Prakt. Chem.* **1991**, *333*, 197 – 222.

[5] C. Bosshard, K. Sutter, P. Pretre, J. Hulliger, M. Flörsheimer, P. Kaatz, P. Günter, *Adv. Nonlinear Optics, Vol. 1*; Gordon & Breach, Basel, **1995**, pp. 1 – 247.

[6] a) S. J. Chung, M. Rumi, V. Alain, S. Barlow, J. W. Perry, S. R. Marder, *J. Am. Chem. Soc.* **2005**, *127*, 10844 – 10845; b) B. Strehmel, A. M. Sarker, H. Detert, *ChemPhysChem* **2003**, *4*, 249 – 259.

[7] H. Jenny, DE 1060375, **1961**; *Chem. Abstr.* **1961**, *55*, 70758.

[8] a) T. Mallegol, S. Gmouh, M. A. A. Meziane, M. Blanchard-Desce, O. Mongin, *Synthesis* **2005**, 1771 – 1774; b) H.-Y. Wang, *Austr. J. Chem.* **2010**, *63*, 712 – 718; c) H.-Y. Wang, *Synth. Metals* **2010**, *160*, 1065 – 1072; d) Y.-J. Wang, H.-S. Sheu, C. K. Lai, *Tetrahedron* **2007**, *63*, 1695 – 1705; e) K. C. Majumdar, B. Chattopadhyay, P. K. Shyam, N. Pal, *Tetrahedron Lett.* **2009**, *50*, 6901 – 6905.

[9] R. S. Gairns, A. A. Watson, GB 2249789, **1992**; *Chem. Abstr.* **1992**, *117*, 212314.

[10] T. B. Brantly, C. J. Fox, DE 1908346, **1969**; *Chem. Abstr.* **1970**, *72*, 31416.

[11] a) K. C. Majumdar, B. Chattopadhyay, S. Chakravorty, N. Pal, R. K. Sinha, *Tetrahedron Lett.* **2008**, *49*, 7149 – 7152; b) H. Niegel, M. Zeiler, H. G. Wirth, DD 136146, **1979**; *Chem. Abstr.* **1979**, *91*, 212576.

[12] P. Gerstner, D. Rohde, H. Hartmann, *Synthesis* **2002**, 2487 – 2489.

[13] U. Kuckländer, *Acridine* in *Houben-Weyl, Meth. Organ. Chem., Hetarene II*, Part 2, Vol. E7b (Ed. R. Kreher), Georg Thieme, Stuttgart, **1992**, pp. 115 – 156.

[14] K. Lehmstedt, H. Hundertmark, *Ber. Dtsch. Chem. Ges*. **1931**, *64*, 2386 – 2394.

[15] I. Weeks, I. Beheshti, F. McCapra, A. K. Campbell, J. S. Woodhead, *Clin. Chem*. **1983**, *29*, 1474 – 1479.

[16] a) A. E. Porai-Koshiz, G. S. Ter-Sarkisyan, *Isv. Akad. Nauk. SSSR, Ot. Khim*. **1951**, 771 – 776; b) A. E. Porai-Koshiz, G. S. Ter-Sarkisyan, *Isv. Akad. Nauk. SSSR, Ot. Khim*. **1951**, 601 – 604; c) J. Griffith, Z. Li, *Dyes Pigm*. **1993**, *21*, 205 – 216.

[17] C.-Y. Gao, X. Cao, L.-M. Yang. *Org. Biomol. Chem.* **2009**, *7*, 3922 – 3825.