Synthesis of Carbazoloquinones via Direct Palladation of 5-Anilino-2-phenylthio-1,4-benzoquinones and of 2-Anilino-1,4-naphthoquinones

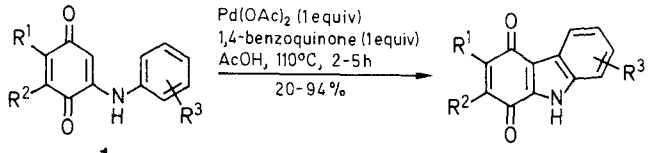
Shmuel Bittner,* Penina Krief, Tracy Massil
Department of Chemistry, Ben-Gurion University of the Negev, Beer-Sheva 84120, Israel

5-Anilino-2-phenylthio-1,4-benzoquinones and 2-anilino-1,4-naphthoquinones **1** undergo a facile one-step oxidative coupling in the presence of palladium(II) acetate to produce a series of substituted 3-phenylthiocarbazole-1,4-diones and benzo[*b*]carbazole-1,6-diones **2**.

Both palladium(II) and palladium(0) complexes have been used in the synthesis and functionalization of carbazoles.[1] Thus, ellipticine, an antitumor agent, was synthesized by direct palladation of properly substituted diphenylamine.[2] Other carbazoles have been produced in good yield from 2-halodiphenylamines by a Pd(0)-catalyzed oxidative addition/insertion process.[3] Moreover, palladium(II) also catalyzes the cyclization of *N*-allyl derivatives of 3-amino-2-bromo-1,4-benzoquinones to yield indoloquinone ring systems[4-6] common to the mitomycin antibiotics.[7]

Here we report results of the direct palladation of 5-anilino-2-phenylthio-1,4-benzoquinones and of 2-anilino-1,4-naphthoquinones which leads to the formation of a series of new carbazoloquinones.

Treatment of 5-anilino-2-phenylthio-1,4-benzoquinones **1a–g** with palladium(II) acetate in boiling acetic acid under argon for 3–5 h resulted in ring closure and formation of the carbazoloquinones **2a–g**. The process required virtually stoichiometric amounts of palladium(II) acetate even when reoxidants (e.g. 1,4-benzoquinone or chloranil) were present.



1 **2**

1,2	R^1	R^2	R^3	1,2	R^1	R^2	R^3
a	PhS	H	H	**f**	PhS	H	3-MeO
b	PhS	H	4-Me	**g**	PhS	H	4-Cl
c	PhS	H	2-Me	**h**			4-MeO
d	PhS	H	4-MeO				
e	PhS	H	2-MeO	**i**			4-Br

Both the reduced palladium and unreacted palladium(II) acetate could be recovered from the reaction mixtures.

The yield was usually good but in some cases it was low and ranged from 20–94%. The low yields were probably due to the relative instability of the quinone precursor to the somewhat severe reaction conditions. Besides **2** substantial quantities of reduced starting material were also obtained. The same general conditions were also used with the 1,4-naphthoquinone derivatives **1h–i**, yielding the benzcarbazoloquinones **2h–i**. In most cases, only a single carbazoloquinone derivative was obtained, however, palladation of the 3-methoxy compound **1f** yielded two products. One was identified as 6-methoxy-2-phenylthio-1,4-carbazoloquinone **2f** (see table) and the other product was proven to be the isomeric 8-methoxy derivative.

The UV spectra of **2** show four typical absorptions. A band of strongest intensity at λ_{max} = 253–262 nm, a somewhat weaker absorption at λ_{max} = 359–366 nm followed by a shoulder at λ_{sh} = 395–416 nm. A band with medium intensity is observed in the visible region with λ_{max} = 485–526 nm. The spectra are similar to that of the starting materials **1** with a strong hypsochromic shift in the visible region. (520–550 versus 485–526 nm).

In the IR spectra three typical absorptions are observed. The NH band at ν = 3180–3325 cm^{-1} and two carbonyl absorptions at ν = 1631–1658 and ν = 1612–1638 cm^{-1}. This pattern is typical of disubstituted quinones and is well documented.[9]

In the ^{1}H-NMR spectrum, the resonance participation by the sulfur and the nitrogen substituents causes a large shift for the quinonic protons in **2a–g**. In most compounds it is located at δ = 5.66–5.75.

In conclusion, although the yield of this coupling process is in some cases modest, and stoichiometric quantities of palladium(II) acetate are needed, the directness of the approach makes it synthetically useful and competitive with other multistep synthetic routes leading to this class of compounds.

Melting points were taken with a Thomas-Hoover capillary apparatus and are uncorrected. All substituted 1,4-benzoquinones and naphthoquinones were prepared according to literature procedures.[8]

Substituted 3-Phenylthiocarbazole-1,4-diones 2a–g and Benzo[*b*]-carbazole-1,6-diones 2h–i; General Procedure:

A mixture of 5-anilino-2-phenylthio-1,4-benzoquinone **1a–g** (0.5 mmol), or of 2-anilino-1,4-naphthoquinone **1h–i** (0.5 mmol), 1,4-benzoquinone (0.054 g, 0.5 mmol) and $Pd(OAc)_2$ (0.112 g, 0.5 mmol) in glacial AcOH (15 mL) are heated under Ar at 110°C for 2–5 h. The disappearance of starting material is monitored by TLC on silica gel plates (CH_2Cl_2/EtOH mixtures). After cooling to r.t. the mixture is filtered and the filtrate concentrated *in vacuo*. The residual solid is purified by chromatography on silica gel (Chromatotron), using the above mentioned solvent mixtures to give product **2**.

Table. Carbazoloquinone Derivatives **2a–i** Prepared

Product	Yield[a] (%)	mp (°C)	Molecular Formula[b]	IR(KBr)[c] ν (cm^{-1})	UV(CH_2Cl_2)[d] λ_{max} (nm) (log ε)	^{1}H-NMR ($CDCl_3$/TMS)[e] δ	MS(60 eV)[f] *m/z* (%)
2a	66	266–267	$C_{18}H_{11}NO_2S$ (305.4)	3227, 1631, 1616, 1560	260 (4.34), 361 (4.02), 410 (sh 3.80), 490 (3.08)	5.68 (s, 1H), 7.36–7.59 (m, 9H)	306 (MH^+, 3), 232 (32), 121 (M^+–SPh, 100)
2b	94	294–295	$C_{19}H_{13}NO_2S$ (319.4)	3247, 1638, 1623, 1518	261 (4.28), 362 (3.91), 416 (sh 3.67), 500 (3.20)	2.49 (s, 3H), 5.72 (s, 1H), 7.19–7.58 (m, 8H)	322 (M^+ + 3, 70), 321 (M^+ + 2, 72), 320 (MH^+, 100), 213 (M^+–SPh, 43)
2c	20	251–252	$C_{19}H_{13}NO_2S$ (319.4)	3296, 1639, 1612, 1553	258 (4.03), 366 (3.69), 395 (s 3.57), 490 (2.81)	2.44 (s, 3H), 5.66 (s, 1H), 7.11–8.08 (m, 8H)	322 (M^+ + 3, 51), 321 (M^+ + 2, 42), 320 (MH^+, 100), 212 (M^+–SPh, 16)
2d	60	291–292	$C_{19}H_{13}NO_3S$ (335.4)	3184, 1658, 1638, 1546	261 (4.37), 360 (3.99), 463 (3.78)	3.92 (s, 3H), 5.73 (s, 1H), 7.03–7.63 (m, 8H)	338 (M^+ + 3, 14), 337 (M^+ + 2, 23), 336 (MH^+, 100), 228 (M^+–SPh, 2)
2e	48	259–260	$C_{19}H_{13}NO_3S$ (335.4)	3275, 1645, 1623	253 (4.00)[g], 277 (3.80), 364 (3.60), 431 (3.59)	3.39 (s, 3H), 5.66 (s, 1H), 6.75–7.72 (m, 8H)	338 (M^+ + 3, 12), 337 (M^+ + 2, 19), 336 (MH^+, 100), 228 (M^+–SPh, 1)
2f	54	286–287	$C_{19}H_{13}NO_3S$[h] (335.4)	3325, 1643, 1623, 1521	264 (4.53), 372 (4.15), 526 (3.40)	3.87 (s, 3H), 5.69 (s, 1H), 6.90–7.51 (m, 8H)	338 (M^+ + 3, 67), 337 (M^+ + 2, 36), 336 (MH^+, 100), 228 (M^+–SPh, 4)
2g	24	> 300	$C_{18}H_{10}ClNO_2S$ (339.8)	3255, 1646, 1635, 1536	262 (4.44), 359 (4.14), 400 (sh 3.93), 503 (3.33)	5.75 (s, 1H), 7.04–8.20 (m, 8H)	343 (M^+ + 3, 27), 342 (M^+ + 2, 100), 341 (MH^+, 43), 340 (M^+, 88), 234 (M^+–SPh, 10)
2h	54	299–300	$C_{17}H_{11}NO_3$ (277.1)	3255, 1675, 1638, 1543	270 (4.62), 339 (3.50), 430 (3.91)	3.83 (s, 3H)[i], 7.04–7.84 (m, 7H)	279 (M^+ + 2, 13), 278 (MH^+, 100)
2i	40	> 300	$C_{16}H_8BrNO_2$ (326.1)	3198, 1668, 1638, 1575	268 (4.43), 299 (3.89), 387 (3.73)	7.56–8.30 (m, 7H)[i]	328 (M^+ + 2, 97), 326 (M^+, 100)

[a] Yield of isolated product **2** based on **1**, not optimized.
[b] Satisfactory microanalyses obtained: C ± 0.24, H ± 0.24, N ± 0.24.
[c] Recorded on Nicolet 5ZDX: FT-IR spectrophotometer.
[d] Recorded on a Perkin-Elmer Lambda 5 UV/VIS spectrophotometer.
[e] Obtained on a Bruker WP200SY spectrometer.
[f] CI in methane; recorded on a Finnigan 4020 quadropole spectrometer.
[g] This compound shows an extra absorption at 284 nm (log ε = 3.78).
[h] 6-methoxy-2-phenylthio-1,4-carbazoloquinone. The isomeric 8-methoxy compound gave m.p. > 300 (dec); ^{1}H-NMR 4.05 (s, 3H), 5.75 (s, 1H), 6.72–7.58 (m, 8H).
[i] Dissolved in DMSO-d_6.

Received: 13 August 1990; revised: 8 October 1990

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