A mild oxidation of deactivated naphthalenes and anthracenes to corresponding *para*-quinones by N-bromosuccinimide

Palani Natarajan, Vinuta Devi Vagicherla, Muthana Thevar Vijayan

PII: S0040-4039(14)00725-4
DOI: http://dx.doi.org/10.1016/j.tetlet.2014.04.088
Reference: TETL 44550

To appear in: *Tetrahedron Letters*

Received Date: 26 February 2014
Revised Date: 25 April 2014
Accepted Date: 27 April 2014

Please cite this article as: Natarajan, P., Vagicherla, V.D., Vijayan, M.T., A mild oxidation of deactivated naphthalenes and anthracenes to corresponding *para*-quinones by N-bromosuccinimide, *Tetrahedron Letters* (2014), doi: http://dx.doi.org/10.1016/j.tetlet.2014.04.088

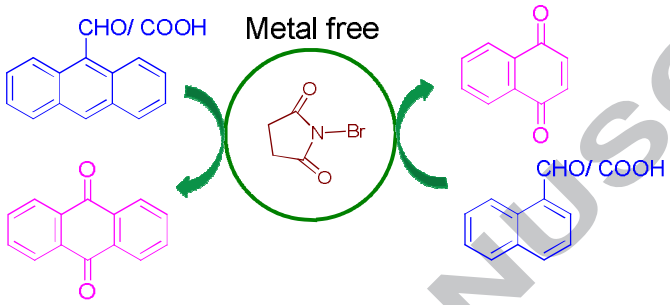
A mild oxidation of deactivated naphthalenes and anthracenes to corresponding *para*-quinones by N-bromosuccinimide

Palani Natarajan,* Vinuta Devi Vagicherla and Muthana Thevar Vijayan

Functional Materials Division, CSIR-Central Electrochemical Research Institute, Karaikudi - 630006, Tamil Nadu, India.

E-mail: pnatarajan@cecri.res.in

TOC



Abstract

A new method to synthesize 1,4-naphthoquinone and 9,10-anthraquinone from naphthalene and anthracene functionalized with either -CHO or -COOH groups, using *N*-bromosuccinimide (NBS) in aqueous *N*,*N*-dimethylformamide at 75-80 °C, has been developed. Further, -CN and -$CONH_2$ functionalized naphthalenes and anthracenes can also be transformed into respective *para*-quinones in a one pot reaction, after successive acid hydrolysis and subsequent reaction with NBS. We believe that the present finding may serve as a valuable alternative to the classical approaches for the synthesis of polycyclic quinones from polyaromatic carbaldehydes through Dakin oxidation followed by further oxidation of the resulting hydroquinone by heavy metal oxides.

In our attempt to synthesize 10-bromo-9-anthraldehyde from 9-anthraldehyde (**1A**) using *N*-bromosuccinimide (NBS, 1eq), we obtained 9,10-anthraquinone (**AQ**, mp 284-287 °C)[1] in 23 % yield, whereas 77 % of the substrate (**1A**) remained as such, even when the reaction was performed at room temperature. Intrigued by the formation of **AQ**, we reinvestigated the reaction using excess amount of NBS (6 eq). Surprisingly, the yield of **AQ** raised to 95-98 %, indicating that **1A** underwent an oxidative deformylation reaction.[2]

AQ is normally obtained in a few ways, which rely on metal catalysts, e.g., i) oxidation of the anthracene or hydroxy-anthracenes with chromium(VI) reagents,[3] ii) Lewis acid catalyzed Friedel-Craft reaction[4] between the benzene and the phthalic anhydride,[5] iii) Lewis acid catalyzed Diels-Alder reaction[6] between naphthoquinones and butadienes,[5,7] iv) oxidative demethylation reaction of anthraquinone dimethyl ethers using metal complexes such as ceric ammonium nitrate,[8] silver oxide,[9] manganese dioxide,[10] cobalt(III) fluoride[11] and others.[3] Although synthesis of **AQ** from **1A** via oxidative demethylation of 9-methoxyanthracenes and 9,10-dimethoxyanthracenes, mentioned above, involves two or three steps (Dakin oxidation,[12] etherification and subsequent re-oxidation,[13] c.f. **path b** in Scheme 1), this method has frequently been used, in the syntheses of anthraquinone-based natural products, drugs, and dyes.[3-12,14] This is mainly due to the fact that the methyl-ether precursors are stable under different reaction conditions and can be readily converted into the desired quinones in the later stages of multistep organic syntheses.[13] Except for the above mentioned multistep method (**path b** in Scheme 1), to the best of our knowledge no alternative protocol is available to synthesize **AQ** under mild conditions, without using any metal catalysts.[15] Thus we decided to examine the new-found single step oxidative deformylation reaction of **1A** into **AQ**, as shown in **path a** of Scheme 1, mediated by NBS,[16] which is often used for allylic,[17] benzylic[18] and arene[19] brominations as well as decarboxylative bromination of α,β-unsaturated carboxylic acids.[20] Remarkably, the reaction can be performed without the need

of anhydrous solvents and the product can be easily isolated, upon removal of the water soluble byproduct of scccinimide. [1-21]

Scheme 1. Synthetic routes for the 9,10-anthraquinone from the 9-anthraldehyde

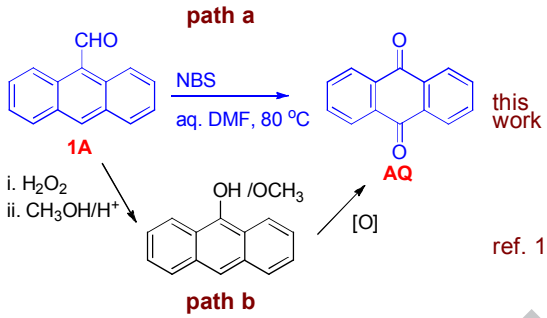
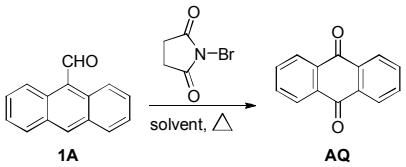


Table 1 summarizes the conversion of **1A** into **AQ**, using NBS, performed under different conditions, namely the quantity of NBS, choice of solvent, duration and the yield obtained. The reaction did not occur, when it was performed in CH_3CN, EtOAc alone or with further addition of 5 % of water (entries 10, 11, 12). Due to poor solubility, the reaction did not proceed in non-polar solvents such as CCl_4 and DCE (entries 13, 14). The reaction proceeded well in *N,N*-dimethylformamide (DMF). Surprisingly, anhydrous DMF did not result in the desired product formation (entry 6), whereas a mixture of DMF and water (95:5) was found to be a perfect solvent system for this oxidation reaction using NBS. The reaction occurred well at 75-80 °C. Upon further increase in reflux condition resulted in unidentified by-products as well as vigorous evolution of bromine/HBr. Therefore the oxidative deformylation reaction of **1A** into **AQ** was examined at 75-80 °C in the DMF-water (95:5, v/v) mixture employing different moles of NBS. When the reaction was performed with 1 mmol of NBS and **1A** each, only 24 % of **AQ** was obtained, leaving most of the substrate as such. To determine whether excess amounts (>1 eq) of NBS were essential for complete conversion of **1A** into **AQ**, experiments were conducted with 2-6 eqs of NBS (Table 1). A mechanistic analysis indicated that four mmol of NBS required for the complete conversion

of one mmol of **1A** into **AQ**. This was confirmed by the ^{1}H NMR titration experiments as well, cf. Figure 1. The easy recognizable singlet of -CHO proton of **1A** at δ = 11.54 ppm gradually disappeared with the concomitant appearance of two new peaks at δ = 7.82 ppm and δ = 8.31 ppm corresponding to the formation of the **AQ**.[1,23] When NBS concentration was increased to 4 eqs all proton signals of **1A** disappeared entirely with appearance of two new signals in the aromatic regions (Figure 1), characteristic for **AQ**.[1] Further increase in NBS (> 4 mmol) resulted significant changes neither in product yield nor in reaction time (entries 5, 7, 9). However, no reaction happened without NBS (entry 3). Thus the optimized condition[24] for a perfect oxidative deformylation of **1A** into **AQ** (**path a** of Scheme 1) is addition of 4 mmol of NBS (either gradually or at once) to a well-stirred solution of the **1A** (1mmol) in DMF-water mixture (95:5, v/v, 8 mL) at room temperature. The resultant homogeneous solution was heated at 75-80 °C for 3-4 h, during that time the color of the reaction mixture turned from yellow to brown, and then quenched with 20% aqueous $NaHCO_3$ (20-30 mL) solution. The mixture was sonicated for 15 min, the insoluble materials were isolated by filtration. A pure product of **AQ** (0.96 mmol, 96%) was obtained after successive recrystallization in ethyl acetate-hexane mixture (20:80, v/v),[1,24] cf. IR, ^{1}H and ^{13}C NMR data furnished in the Supporting Information (SI). It is worthy to mention that the unreacted NBS and its′ byproduct, succinimide, were removed from the reaction mixture gently by treating with an aqueous $NaHCO_3$ solution.[16]

Table 1. An oxidative deformylation of 9-anthraldehyde (**1A**) by NBS at various reaction conditions. All reactions were performed using 1 mmol of substrate, **1A**.



Entry	NBS mmol	Solvent (v/v)	Temp. (°C±5)	Time (h)	Product yield (%)
1	1.1	DMF	75	8	23[a]
2	1.1	DMF	20	60	17[a]
3	0	DMF	90	72	<2[b]
4	3	DMF	75	8	71
5	5	DMF	75	7	96
6	5	dry DMF[c]	75	16	<4[d]
7	5	DMF-H_2O (95:5)	75	4	97
8	4	DMF-H_2O (95:5)	75	4	96
9	6	DMF-H_2O (95:5)[e]	75	3.5	94
10	4	CH_3CN	80	12	8
11	4	CH_3CN-H_2O (95:5)	90	12	26
12	4	EtOAc-H_2O (95:5)	80	24	<10
13	4	DCE	100	24	<5
14	4	CCl_4	80	24	<5
15	4	H_2O	100	24	<10
16	2	DMF-H_2O (95:5)	75	6	47
17	3	DMF-H_2O (95:5)	75	6	73
18	4	DMF-H_2O (95:5)	80	3.5	97
19	4	DMF-H_2O (95:5)	120	3.5	76

[a] Unreacted **1A** was recovered (76-80%). [b] Unreacted **1A** was recovered (>95%). [c] DMF was purified by drying nightlong over barium oxide and vacuum distillation. [d] Reaction was not complete and **1A** remained as such. [e] Excess solvent required to make homogeneous solution.

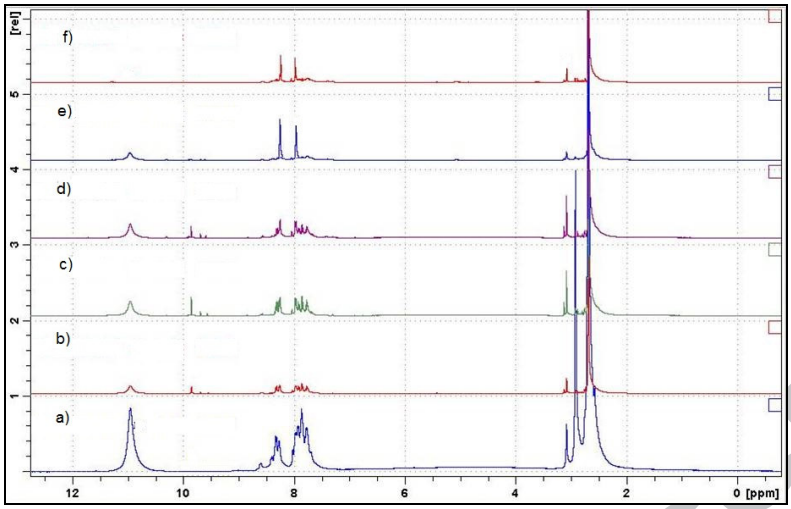
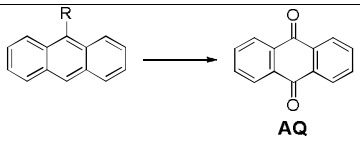
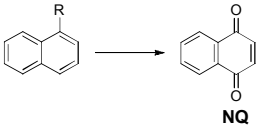
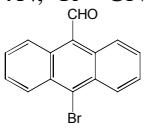
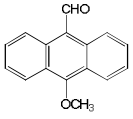
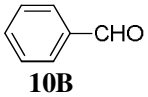
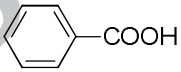
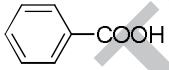
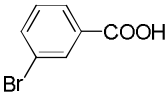
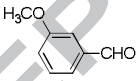
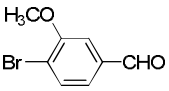
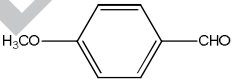
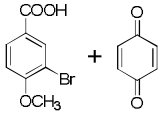
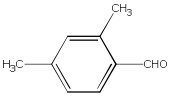
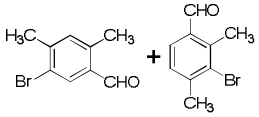
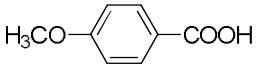
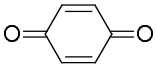
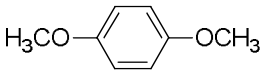
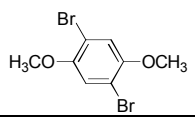


Figure 1. The ^{1}H NMR (400 MHz) spectroscopic monitoring of **1A** into **AQ** in DMF-d_7/D_2O (95:5, v/v) mixture: (a) at beginning of the reaction, (b) after 45 min, (c) after 90 min, (d) after 135 min, e) after 180 min, and f) after 240 min.

Having established the optimum condition for the oxidative deformylation reaction with NBS, the methodology was extended to a series of electron deficient anthracene, naphthalene, and benzene derivatives, which are shown in Table 2. As anticipated, 1-napthaldehyde (**5N**) also resulted in 1,4-naphthoquinone (**NQ**)[24] readily in 91 % yield under same experimental conditions. Similarly, 9-anthracene carboxylic acid (**2A**) and 1-naphthalene carboxylic acid (**6N**) underwent oxidative decarboxylation to result in **AQ** and **NQ**, respectively, in quantitative yields (Table 2). Direct reaction between NBS and the –CN and –$CONH_2$ functionalized substrates, **3A**,[25] **4A**, and **7N,** appeared sluggish, nevertheless, they provided respective *para*-quinones after hydrolysis by 30% aqueous H_2SO_4 solution.[13] In other words, –CN and –$CONH_2$ functionalized anthracenes (**3A** and **4A**) and naphthalene (**7N**) underwent an oxidative decyanation/an oxidative deamidation reaction, followed by successive acid hydrolysis and reaction with NBS. Interestingly, 9,10-disubstituted anthracenes **8A**[25] and **9A** as well underwent an oxidative deformylation smoothly under the optimized conditions yielding the expected **AQ**. In contrast to the polycyclic arenes (Table 2), the benzene derivatives (**10B**-**16B**) were found to be less reactive towards NBS mediated

oxidation reactions.[2] Among different substrates examined, **13B** and **15B** furnished expected 1,4-benzoquinone (**BQ**)[24] in low yields, whereas, **10B**-**12B**, **14B** and **16B** resulted in corresponding haloarenes under the experimental condition used. Thus the present protocol is more suitable for the oxidations of electron deficient polycyclic aromatic compounds (Table 2) than the benzene analogues.

Table 2. Synthesis of *para*-quinones via NBS mediated oxidation reactions in aqueous DMF.

S. No	Substrate [a]	Product [b]	Time (h)	Yield [c] (%)
	 **AQ**			
1	**1A**, R = CHO	AQ	4	97
2	**2A**, R = COOH	AQ	3.5	96
3	**3A**,[d] R = $CONH_2$	AQ	13	94
4	**4A**,[d] R = CN	AQ	16	83
	 **NQ**			
5	**5N**, R = CHO	NQ	16	91
6	**6N**, R = COOH	NQ	16	89
7	**7N**,[d] R = CN	NQ	36	86
8	 **8A**	AQ	4	97
9	 **9A**	AQ	3	92
10	 **10B**		60	31
11	 **11B**		72	<5
12	 **12B**		24	56
13	 **13B**		36	34 18
14	 **14B**		36	64 17
15	 **15B**		80	42
16	 **16B**		6	61

a) All reactions were performed in DMF-H_2O mixture using 1 mmol of the substrate and 4-4.2 mmol of NBS. b) Purity of compounds was established by elemental analysis and melting point determinations. c) Yields were determined from products isolated by silica gel (60-120 mesh) column chromotography. d) Compounds were hydrolysed by aqueous mineral acids before NBS oxidation.

A plausible reaction mechanism for the oxidative deformylation of **1A** into **AQ** is shown in Figure 2. We expected to isolate intermediate compounds **A**, **B** and **C**, respectively, by treatment of **1A** (1 mmol) with 1-, 2-, and 3 mmol of NBS. Nevertheless, independent to NBS concentration, temperature (20-80 °C) and the duration, **AQ** was obtained as a sole product in all of these attempts. In presence of 1 mmol of NBS, instead of reacting all starting materials to form intermediate **A** (1 mmol), exclusively 25-30% of the **1A** underwent all transformations (Figure 2) and provided 23% of **AQ** along with 77% of the starting precursor (**1A**). Likewise, about 47% and 73% of **1A**, respectively, reacted when 2- and 3 mmol of NBS employed. Obviously, when 4 mmol of NBS were added either by portionwise or all at once to the reaction mixture containing 1 mmol of the **1A**, **AQ** was obtained quantitatively (Tables 1 and 2). This indicating both the optimal NBS stoichiometry (Table 1) and the proposed reaction mechanism are fit to each other (Figures 1 and 2). From these combined findings it is discernible that once the reaction begins with a molecule, it undergoes subsequent steps (Figure 2) rapidly until **AQ** occurs by consuming 4 equivalents of NBS.[26] Similar behaviour has been observed on several oxidations[27] and substitution reactions.[28]

In an unambiguous manner all naphthalene derivatives (**5N**-**7N**) offered 1,4-naphthoquinone,[24] even there is a possibility for formation of the 1,2-naphthoquinone. This is because of combined effects of the steric-, the electronic- and the stability factors of the intermediate/s generated in the reaction, which are hardly predictable due to the finely balanced situation among them.[29] The less reactivity or the non-reactivity of the benzene derivatives (**10B**-**16B**) against NBS oxidation indicates that the reaction intermediates might

be unstable or destabilized due to the weak conjugation while compared to the naphthalene and the anthracene analogues.[30]

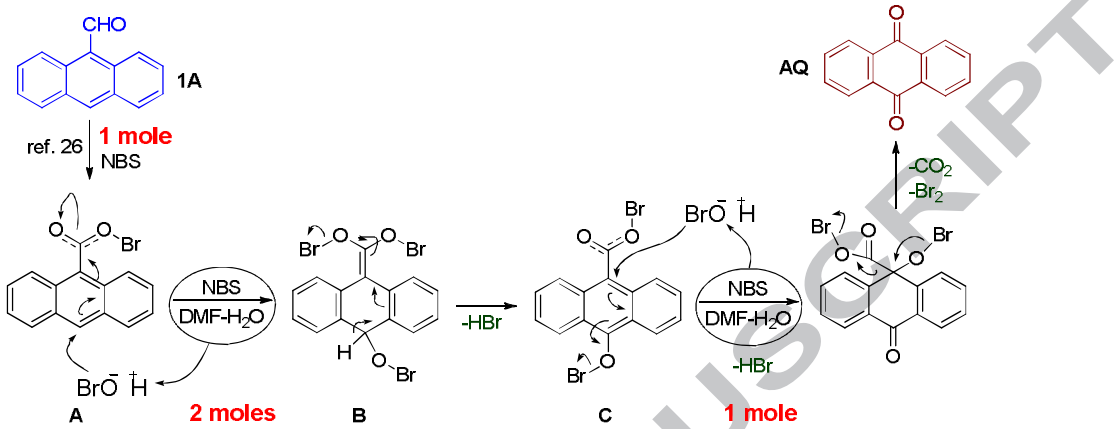


Figure 2. The proposed reaction mechanism for the oxidative deformylation of the **1A** into the **AQ**. The mechanism proposed by assuming 1 mole of the **1A** involves in the reaction. Number of mole of NBS consumed in each step is highlighted in red.

In summary, we have demonstrated a mild protocol for the oxidation of deactivated polycyclic aromatic compounds into corresponding *para*-quinones in excellent yield[31,32] by treatment with NBS in aqueous-DMF. Advantages of this method are cost effective, metal-free, the moisture and the oxygen involves, simple work-up procedure and so on. Further studies on synthetic applications of the present protocol for preparations of various biologically important qninones and the mechanistic investigations are underway in our laboratories.

Acknowledgements

P.N. gratefully acknowledges the financial support of the Department of Science & Technology (DST), India through INSPIRE Faculty Fellowship [IFA12-CH-62]. V. D. V. is grateful to CSIR-CECRI for financial support. We are indebted to Dr. Vijayamohanan K. Pillai and Dr. D. JayaKumar, CSIR-CECRI, for infrastructure facilities, and also to Dr. R. Natarajan, CSIR-IICB for help in the manuscript preparation.

Supporting Information

Supplementary Information (SI) available: [IR, ^{1}H and ^{13}C NMR spectra].

References

(1) The structure of product, 9,10-anthraquinone (AQ), formed from the reaction between 9-anthraldehyde and NBS was confirmed by IR, UV-Vis, MS, ^{1}H- and ^{13}C NMR spectra. In addition, melting point of synthesized material met with authentic compound reported in the literature; see: (a) W. Wang, W-J. Zhang, L. Wang, C. K. Quah, H-K. Fun, J-H. Xu, Y. Zhang, *J. Org. Chem.* 2013, **78**, 6211; (b) R. Joseph, C. Pulla Rao, *Chem. Rev.* 2011, **111**, 4658.

(2) The result indicates that the rate of reaction of bromination is lesser than that of oxidative decarboxylation steps under the experimental condition used; see: (a) L. F. Fieser, M. J. Haddadin, *J. Am. Chem. Soc.* 1964, **86**, 2392; (b) L. R. Gould, J. R. Lenhard, S. Farid, *J. Phys. Chem. A*, 2004, **108**, 10949; (c) H. Wang, R. Fan, *J. Org. Chem.* 2010, **75**, 6994; (d) S. Wertz, A. Studer, *Green Chem.* 2013, **15**, 3116.

(3) (a) R. A. F. Tomas, J. M. Bordado, J. F. P. Gomes, *Chem. Rev.* 2013, **113**, 7421; (b) N. Seidel, T. Hahn, S. Liebing, W. Seichter, J. Kortus, E. Weber, *New J. Chem.* 2013, **37**, 601.

(4) M. Rueping, B. J. Nachtsheim, *Beilstein J. Org. Chem.* 2010, **6**. 6.

(5) M. Phillips, *Chem. Rev.* 1929, **6**, 157.

(6) V. Nair, R. S. Menon, A. T. Biju, K. G. Abhilash, *Chem. Soc. Rev.* 2012, **41**, 1050.

(7) I. V. Nechepurenko, E. E. Shults, G. A. Tolstikov, *Russ. J. Org. Chem.* 2003, **39**, 1436.

(8) (a) B. M. O'Keefe, D. M. Mans, D. E. Kaelin-Jr., S. F. Martin, *J. Am. Chem. Soc.* 2010, **132**, 15528; (b) M. V. Bhatt, B. Periasamy, *Tetrahedron* 1994, **50**, 3575; (c) K. Toshima, Y. Maeda, H. Ouchi, A. Asai, S. Matsumura, *Bioorg. Med. Chem. Lett.* 2000, **10**, 2163.

(9) A. I. Reham, A. Elkhair, D. W. Dixon, T. L. Netzel, *J. Org. Chem.* 2009, **74**, 4712.

(10) M. N. Tam, N-H. Nam, G-Z. Jin, B-Z. Ahn, *Arch. Pharm. Res.* 2000, **23**, 283.

(11) G. Cahiez, A. Moyeux, *Chem. Rev.* 2010, **110**, 1435.

(12) (a) M. E. Jung, T. I. Lazarova, *J. Org. Chem.* 1997, **62**, 1553; (b) J. L. Zambrano, D. Romano, *Synlett.* 2003, 1545.

(13) (a) C. F. H. Allen, *Chem. Rev.* 1959, **59**, 983; (b) E. Klingsberg, *Chem. Rev.* 1954, **54**, 59; (c) K. Yates, *Acc. Chem. Res.* 1971, **4**, 136; (d) K. G. Hugentobler, F. Rebolledo, *Org. Biomol. Chem.* 2014, **12**, 615.

(14) (a) R. Devulapally, Y-S. Hon, *Tetrahedron Lett*. 2011, **52**, 3183; (b) I. Fujii, Y. Ebizuka, *Chem. Rev.* 1997, **97**, 2511; (c) R. E. Minto, C. A. Townsend, *Chem. Rev.* 1997, **97**, 2537; (d) Y. Moon, S. Hong, *Chem. Commun*. 2012, **48**, 7191; (e) D. Kim, M. Min, S. Hong, *Chem. Commun.* 2013, **49**, 4021.

15) M. Gunay, Ed. *Eco-Friendly Textile Dyeing and Finishing*; HueMetrix Inc: InTech, 2013.

(16) (a) C. Djerassi, *Chem. Rev.* 1948, **43**, 271; (b) R. Filler, *Chem. Rev.* 1963, **63**, 21; (c) O, G. Mancheno, O. Bistri, C. Bolm, *Org. Lett.* 2007, **9**, 3809; (d) D. W. Kim, H. Y. Choi, K. J. Lee, D. Y. Chi, *Org. Lett.* 2001, **3**, 445; (e) C. B. Tripathi, S. Mukherjee, *J. Org. Chem.* 2012, **77**, 1592; (f) W. Baik, H. J. Lee, J. M. Jang, S. Koo, B. H. Kim, *J. Org. Chem.* 2000, **65**, 108; (g) A. S. Mayhoub, A. Talukdar, M. Cushman, *J. Org. Chem.* 2010, **75**, 3507; (h) X.-L. Wu, J.-J. Xia, G.-W. Wang, *Org. Biomol. Chem*. 2008, **6**, 548; (i) X. Zong, Q.-Z. Zhenga, N. Jiao, *Org. Biomol. Chem*. 2013, DOI: 10.1039/C3OB42118J.

(17) (a) S. Wolfe, D. V. C. Awang, *J. Am. Chem. Soc.* 1967, **89**, 5287; (b) J. C. Day, M. J. Lindstrom, P. S. Skell, *J. Am. Chem. Soc.* 1974, **96**, 5616.

(18) (a) D. D. Tanner, N. H. Nam, *J. Org. Chem.* 1987, **52**, 4686; (b) R. P. Hanzlik, A. R. Schaefer, J. B. Moon, C. M. Judson, *J. Am. Chem. Soc.* 1987, **109**, 4926; (c) S. R. K. Pingali, S. K. Upadhyaya, B. S. Jursic, *Green Chem.* 2011, **13**, 928; (d) A. Podgorsek, S. Stavber, M. Zupan, J. Iskra, *Tetrahedron* 2009, **65**, 4429.

(19) (a) N. C. Ganguly, P. De, S. Dutta, *Synthesis* 2005, 1103; (b) E. J. Corey, M. Ishiguro, *Tetrahedron Lett.* 1979, **20**, 2745; (c) K. Rajesh, M. Somasundaram, R. Saiganesh, K. K. Balasubramanian, *J. Org. Chem.* 2007, **72**, 5867; (d) G. K. S. Prakash, T. Mathew, D. Hoole, P. M. Esteves, Q. Wang, G. Rasul, G. A. Olah, *J. Am. Chem. Soc.* 2004, **126**, 15570.

(20) (a) J. Prakash, S. Roy, *J. Org. Chem.* 2002, **67**, 7861; (b) C. Kuang, Q. Yang, H. Senboku, M. Tokuda, *Synthesis* 2005, 1319.

(21) (a) D. V. Pratt, F. Ruan, P. B. Hopkins, *J. Org. Chem.* 1987, **52**, 5053; (b) P. M. Deya, M. Dopico, A. G. Raso, J. Morey, J. M. Saa, *Tetrahedran* 1987, **43**, 3523.

(22) (a) C. Reichardt, *Chem. Soc. Rev.* 1992, **21**, 147; (b) E. Buncel, S. Rajagopal, *Acc. Chem. Res.* 1990, **23**, 226.

(23) Z. Song, H. Zhan, Y. Zhou, *Chem. Commun.* 2009, 448.

(24) **General Aspects**. Solvents were distilled prior to use and millipore water was used for the reaction. All commercial chemicals such as **1A**, **2A**, **4A**, **5N**, **6N**, **7N**, **9A**, **10B**, **11B**, **12B**, **13B**, **14B**, **15B** and **16B** were used as received, however, compounds **3A** and **8A** were synthesized according to the literature reported protocols.[25] All reactions were carried out in an open atmosphere without any precaution. Reactions were monitored by analytical thin layer chromatography (TLC) on silica gel. The products were isolated by column chromatography with silica gel (60-120 mesh). NMR spectra (400 MHz) were recorded in deuterated solvents. Chemical shifts are reported in δ-scale (ppm) and are referenced to the residual protiated solvent.

General procedure for the preparation of *para*-quinones.

To a stirred solution of starting compound (0.5-1.2 mmol) in DMF-H_2O (95:5, v/v, 8-12 mL) mixture was added NBS (4.0-4.2 mmol) at room temperature. The contents were stirred at room temperature about 10 minutes and then heated for appropriate duration mentioned in the Table 2. Progress of the reaction in every case was monitored by TLC analysis. After completion of the reaction, the reaction mixture was cooled to room temperature and quenched with aqueous $NaHCO_3$ (20%, 20-30 mL) solution. The insoluble precipitate was isolated by filtration and dried in vacuo. It was further purified by either recrystallization with ethyl acetate/n-hexane mixture or short pad silica gel column chromatography led to pure product.

The –CN and $-CONH_2$ functionalized compounds (**3A**, **4A** and **7N**) were treated with aqueous H_2SO_4 for 8-12 h before NBS mediated oxidation into quinones.

9-anthramide (**3A**).[25] Fair yellow Solid; mp >250 °C; IR (KBr cm^{-1}) 1389, 1608, 1658, 3199, 3353; ^{1}H NMR (CD_3OD, 400 MHz) δ 7.64-7.72 (m, 6H), 8.01 (d, 2H, J = 8.1 Hz), 8.21 (d, 2H, J =8.1 Hz), 8.52 (s, 1H).

10-bromo-9-anthraldehyde (**8A**). Yellow solid; mp 207-211 °C (lit. 208 °C);[25d] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63-7.76 (m, 4H), 8.61-8.69 (m, 2H), 8.85-8.93 (m, 2H), 11.52(s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 123.3, 124.1, 125.4, 128.9, 129.0, 130.8, 131.4, 135.0, 192.9.

9,10-anthraquinone (AQ). Yellow solid; mp 284-287 °C (lit. 286 °C);[1] IR (KBr, cm^{-1}) 3701, 3071, 1968, 1745, 1674, 1580, 1325, 1286; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80-7.82 (m, 4H), 8.31-8.33 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 128.2, 134.4, 135.1, 184.2; MS-EI m/z (%) 208.1 (100). Anal. Calcd for $C_{14}H_8O_2$: C, 80.76; H, 3.87; O, 15.37. Found: C, 80.74; H, 3.84.

1,4-naphthoquinone (NQ). Yellow solid; mp 124-128 °C; IR (KBr, cm^{-1}) 3703, 3308, 3058, 2961, 1981, 1752, 1660, 1588, 1295; ^{1}H NMR (CD_3OD, 400 MHz) δ 6.98 (s, 2H), 7.73-7.78 (m, 2H), 8.01-8.08 (m, 2H).

1,4-benzoquinone (BQ). Yellow solid; mp 114-116 °C; IR (KBr, cm^{-1}) 3634, 3227, 2710, 2590, 1869, 1718, 1631, 1469, 1356, 1209; ^{1}H NMR (CD_3OD, 400 MHz) δ 6.78.

(25) (a) J. S. Meek, D. R. Wilgus, J. R. Dann, *J. Am. Chem. Soc.* 1960, **82**, 2566; (b) D. H. Burns, J. D. Miller, H-K. Chan, M. O. Delaney, *J. Am. Chem. Soc.* 1997, **119**, 2125; (c) M. Frédéric, A. Gilles, L. Claude, *Synthesis* 2006, **2**, 293.

(26) L. C. Anderson, H. W. Pinnick, *J. Org. Chem.* 1978, **43**, 3417.

(27) (a) A. Chanda, V. V. Fokin, *Chem. Rev.* 2009, **109**, 725; (b) K. Tanaka, F. Toda, *Chem. Rev.* 2000, **100**, 1025.

(28) H. Abduljabbar, Ed. *Steroids – Basic Science*; InTech, 2012.

(29) (a) J. M. Sad, J. Morey, C. Rubido, *J. Org. Chem.* 1986, **51**, 4471; (b) P. S. Bailey, S. S. Bath, F. Dobinson, F. J. Garcia-Sharp, C. D. Johnson, *J. Org. Chem.* 1964, **29**, 697; (c) U. A. Spitzer, D. G. Lee, *J. Org. Chem.* 1974, **39**, 2468.

(30) (a) N. L. Holy, *Chem. Rev.* 1974, **74**, 243; (b) R. F. Guignard, S. Z. Zard, *Chem. Commun.* 2011, **47**, 12185.

(31) (a) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* 2012, **41**, 3381; (b) N. Mora-Diez, S. Keller, J. R. Alvarez-Idaboy, *Org. Biomol. Chem.* 2009, **7**, 3682; (c) Z. Zhang, G.-W. Wang, C.-B. Miao, Y.-W. Dong, Y.-B. Shen, *Chem. Commun*. 2004, 1832.

(32) (a) P. Stang, V. V. Zhdankin, *Chem. Rev.* 1996, **96**, 1123; (b) T. Miura, K. Nakashima, N. Tada, A. Itoh, *Chem. Commun*. 2011, **47**, 1875.