Tetrahedron Letters 50 (2009) 5896–5902

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

'On water': unprecedented nucleophilic substitution and addition reactions with 1,4-quinones in aqueous suspension

Vishnu K. Tandon *, Hardesh K. Maurya

Department of Chemistry, Lucknow University, Lucknow 226 007, India

ARTICLE INFO

Article history:
Received 12 May 2009
Revised 28 July 2009
Accepted 30 July 2009
Available online 3 August 2009

Keywords:
Quinone
Naphthoquinones
Water
Green synthesis
Amines
Thiols
Amino acids

ABSTRACT

Unique nucleophilic substitution and addition reactions of 1,4-quinones in aqueous suspension with aromatic amines, primary aliphatic amines, amino acid, ester of amino acid, heterocyclic amines, hydrazine, amide, and thioethers are described in absence of catalyst against the traditional synthetic routes of these reactions in non-aqueous medium in presence of catalyst.

Water is the most desirable solvent for chemical reactions due to its profound economic, environmental, safety, and societal implications leading further to development of ideology of Green chemistry. Recently organic reactions performed in water have attracted considerable attention with respect to the unique properties of water in promoting reactions and enhancing selectivity. Most recently several reactions have been reported in water with substantial rate acceleration even though water-insoluble substrate was used in a suspension.[1]

The development of transformations of C–H bonds into C–O, C–X, and C–C bonds has been extensively studied in water.[1] The first rhodium-catalyzed 1,4-addition of organo boron reagents represents a powerful method of transition-metal-catalyzed asymmetric C–C bond formation.[2] The regioselective and stereoselective hydroxylation of steroids in water using manganese porphyrins and β-cyclodextrins as catalysts and iodosobenzene as oxidant have led to the formation of C–O bond.[3] Most notably the unique reactivity of organic compounds in aqueous suspension has been elegantly demonstrated by Sharpless et al.[4]

In recent years Wittig reaction,[5] Mannich type reaction,[6] intramolecular Diels–Alder reaction,[7] and many such reactions have been studied in H_2O.

The nucleophilic substitution (Fig. 1) of 2,3-dichloro-1,4-naphthoquinone (**1a**) and 2,3-dibromo-1,4-naphthoquinone (**1b**) and addition reactions of 1,4-benzoquinone (**1c**), 1,4-naphthoquinone (**1d**), naphthazarine (**1e**), and 2-hydroxy-1,4-naphthoquinone (**1f**) (Fig. 2) have been extensively[8–17] studied in non-aqueous media. In connection with our studies on nucleophilic addition and substitution reactions of 1,4-naphthoquinones in non-aqueous media,[18–23] we encountered a mixture of products in most of these reactions leading to unsatisfactory yields.

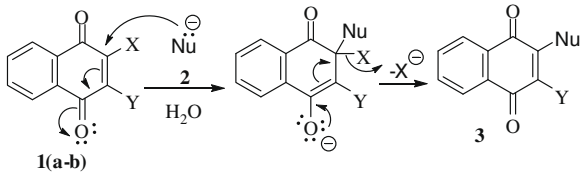


Figure 1. Nucleophilic substitution of 2,3-dichloro-1,4-naphthoquinone (**1a**) and 2,3-dibromo-1,4-naphthoquinone (**1b**).

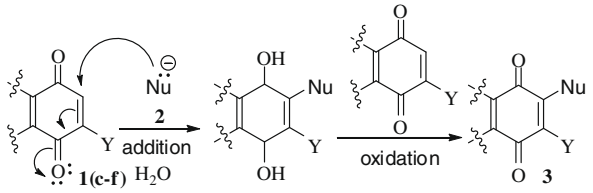


Figure 2. Addition reactions of 1,4-benzoquinone (**1c**),[27] 1,4-naphthoquinone (**1d**), naphthazarine (**1e**), and 2-hydroxy-1,4-naphthoquinone (**1f**).

* Corresponding author. Tel.: +91 9415066847; fax: +91 522 2684388.
E-mail address: vishnutandon@yahoo.co.in (V.K. Tandon).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.07.149

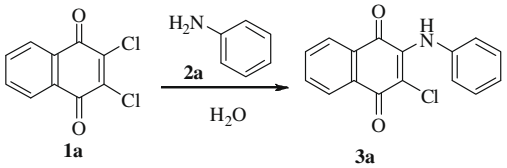
Organic solvent usage is often an integral part of chemical or manufacturing processes of amino and mercapto derivatives of quinone since more than a century[28] for miscellaneous applications.[8–27] Different organic solvents such as EtOH,[19–25] MeOH,[29] C_6H_6, $CHCl_3$, CH_2Cl_2, DMF, DMSO, ether, THF, AcOEt, and toluene[12,30] have been used for the synthesis of amino and mercapto derivatives of quinone.

In connection with our studies on the reactivity of quinone with nucleophiles 'on water', we first explored the preparation of 2-anilino-3-chloro-1,4-naphthoquinone (**3a**) from 2,3-dichloro-1,4-naphthoquinone (**1a**) by the nucleophilic substitution reaction with aniline (**2a**) synthesized by Lien et al.[12] as depicted in Figure 1.

The typical reaction conditions involve heating **1a** with aniline (**2a**) in benzene at 50 °C for 30 min to afford product **3a** in 81% yield. Sarhana et al.[31] reported 73% yield by change of nonpolar solvent to polar solvent MeOH. However use of excess of absolute ethanol at room temperature for 1 h afforded 90% yield of **3a**. In contrast, when a mixture of **1a** and **2a** is stirred 'on water' the reaction is complete within 50 min at ambient temperature and 15 min at 50 °C leading to the formation of **3a** in 100% yield as shown in Table 1. Here, we find that water alone is the medium of choice. The reactions are completed in shorter times than in other protic and nonprotic solvents and the pure product precipitates and can be isolated by simple filtration. Bhattacharyya[32] has reported the synthesis of 2-chloro-3-(4-morpholino)-1,4-naphthoquinone (**3n**) by refluxing a solution of 2,3-dichloro-1,4-naphthoquinone (**1a**) and morpholine (**2i**) in ethanol and using anhydrous K_2CO_3 as base in 16 h under an atmosphere of nitrogen. The corresponding reaction of 2,3-dichloro-1,4-naphthoquinone (**1a**) and morpholine (**2i**) 'on water' is complete within 30 min at 50 °C (Table 2). The nucleophilic substitution of aniline (**2a**) with 2,3-dichloro-1,4-naphthoquinone (**1a**) demonstrates that 'on water' method consists of simply heating the reactants with stirring. It is pertinent to note that both solid reactants can also be utilized, as reaction of **1a** with *p*-hydroxy aniline (**2b**), L-alanine ethyl ester (**2f**), glycine (**2e**), 5-(4-nitrophenyl)-1,3,4-oxadiazole-2-thiol (**2m**), and 2-phenylacetamide (**2k**) (Table 3) afforded excellent results, showing that vigorous stirring promotes the reaction, most likely by increasing the area of surface contact between the organic and aqueous phases.

Change in amount of water does not alter the observed rate acceleration till sufficient water is present for clear phase separation or filtration. In cases where clear phase separation does not occur, such as in small-scale reactions, liquid extraction or evaporation of water and purification may be necessary as shown in workup process (**W**) in Table 3. We have found that the high reactivity of quinones (**1**) 'on water' is not limited to these nucleophilic substitutions with primary and secondary amino groups containing reactants.

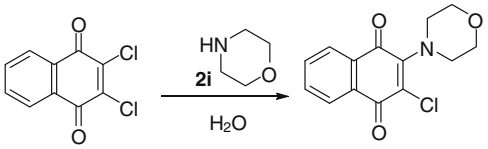
Table 1
Comparison of water versus organic solvents for a typical nucleophilic substitution reaction of 2,3-dichloro-1,4-naphthoquinone (**1a**) with aniline (**2a**)[35]



1a **3a**

Solvent	*T* (°C)	*t*	Yield (%)
Benzene	50–60	30 min	81[12]
MeOH	—	—	73[31]
EtOH	rt	1 h	90
On H_2O	rt	50 min	100
On H_2O	50	15 min	100

Table 2
Reaction of 2,3-dichloro-1,4-naphthoquinone (**1a**) with morpholine (**2i**)[35]



1a **3n**

Solvent	b	*t*	Yield (%)
EtOH	K_2CO_3	16 h	68[32]
On H_2O	—	30 min	98

Thiols also respond effectively to conditions of aqueous suspension compared to reaction in organic solvents. We have explored the reaction of **1a** with ethyl thioglycolate (**2n**) to achieve the nucleophilic substitution reaction in excess of absolute ethanol by prolonged vigorous refluxing at 80–90 °C for 8–10 h to afford the product **3v** in 95–97% yield.[21] In contrast, the reaction performed 'on water' was complete in 2 h at 50 °C and afforded the product **3v** in 100% yield. On the basis of the above results we have performed reactions of different quinones (**1**) with thiophenol (**2l**), 5-(4-nitrophenyl)-1,3,4-oxadiazole-2-thiol (**2m**), ethyl thioglycolate (**2n**), diethyl 2-mercaptosuccinate (**2o**), and ethane-1,2-dithiol (**2p**) affording **3(l–p)** in good to excellent yields (Table 5).

Wang and co-workers[33] reported palladium-catalyzed amination of 2,3-dichloro-1,4-naphthoquione with nitro-substituted arylamines in presence of *t*-BuONa as a base which is entirely different to the nucleophilic substitution carried out by us 'on water'. The palladium-catalyzed amination involves oxidative addition followed by transmetalation and reductive elimination.[33] In order to explore the reactivity of thiophenol with 2-anilino-3-chloro-1,4-naphthoquinone (**3a**), we observed that the reaction with thiophenol (**2l**) 'on water' afforded 98% yield of **3s** in an hour without using any catalyst or base at room temperature. On further study of rate acceleration for reactions on H_2O, we attempted to explore reaction of methyl amine (**2d**) with **3v** 'on water' at 50 °C using Et_3N as base. This resulted in the formation of 3-hydroxy-4-methyl-4*H*-naphtho[2,3-*b*][1,4] thiazine-5,10-dione (**3f**) in shorter duration of time.[21] The mechanism of formation of **3f** involves nucleophilic displacement followed by intramolecular nucleophilic addition–elimination and cyclization.[21]

The nucleophilic addition reactions depicted in Tables 3 and 4 proceed by mechanism outlined in Figure 2. The mechanism of oxidation proceeds by redox process of 1,4-quinones which is well documented in literature.[27] Reoxidation with remaining starting material leads to excellent yields of the nucleophilic substitution product as depicted in Figure 2. Oxygen in the media presumably accelerates the process of oxidation since no quinol intermediate is left in the reaction mixture.

Thus a variety of nucleophilic substitution (Fig. 1) and addition reactions (Fig. 2) of quinones **1** with a variety of aromatic amines (**2a** and **b**), primary aliphatic amines (**2c and d**), amino acid (**2e**), ester of amino acid (**2f**), heterocyclic amines (**2g–i**), hydrazine (**2j**), amide (**2k**) (Table 3), and thiols (**2l–p**) (Table 5) can be efficiently carried out in aqueous suspension with the most dramatic effects observed for the second nucleophilic substitution of **2l** with thiophenol without using any base and formation of product **3s** in aqueous suspension. In absence of water, the rate of completion of reaction is extremely slow especially with nucleophiles having high boiling point. As with nucleophilic substitution reactions, the 'on water' protocol provides the best of conditions in terms of efficiency, safety, and convenience, even when rate accelerations are not large. Thus a variety of nucleophilic substitution and addition reactions can be efficiently carried out in aqueous suspension,

Table 3
Reaction conditions of water-assisted reaction of quinones **1** with aromatic amines (**2a** and **b**), primary aliphatic amines (**2c** and **d**), amino acid (**2e**), ester of amino acid (**2f**), heterocyclic amines (**2g–i**), hydrazine (**2j**), and amide (**2k**)[35]

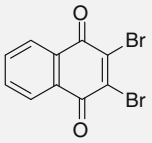
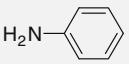
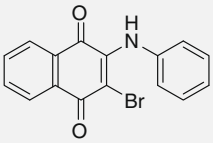
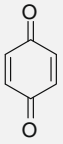
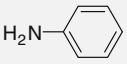
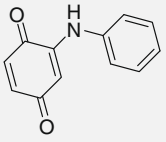
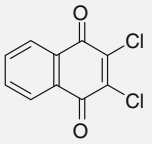
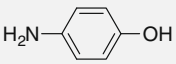
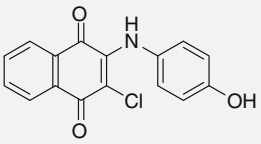
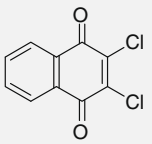
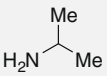
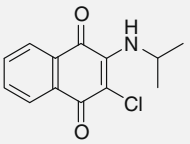
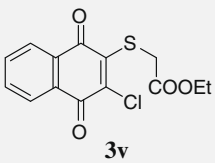
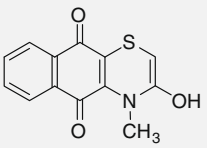
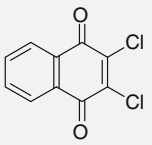
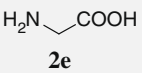
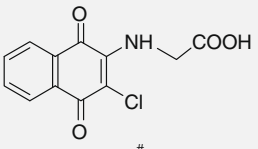
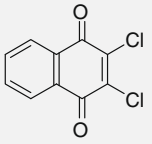
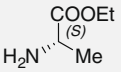
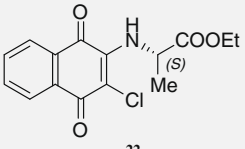
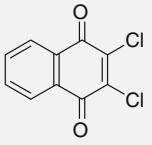
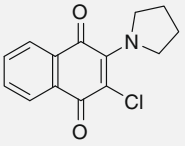
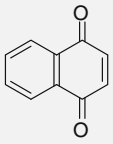
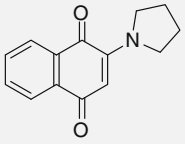
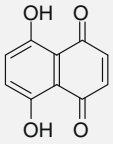
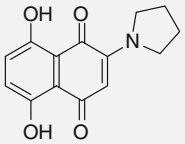
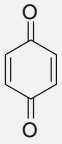
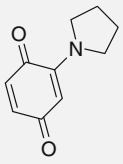
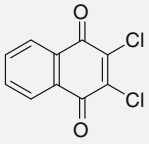
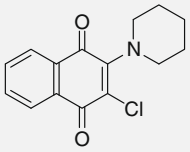
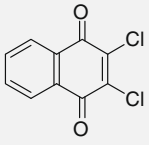
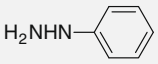
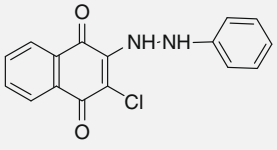
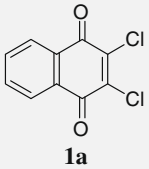
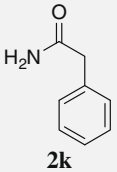
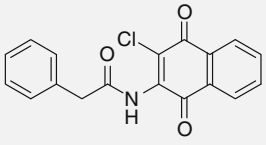
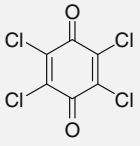
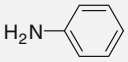
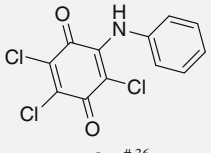
Entry	1	2	Time	b	*T* (°C)	Product 3	Yield (%)	*c*	W
1	 **1b**	 **2a**	30 min	N	50	 **3b**	100	100	A
2	 **1c**	 **2a**	20 min	N	rt	 **3c**[#]	98	100	A
3	 **1a**	 **2b**	1 h	N	50	 **3d**	95	100	A
4	 **1a**	 **2c**	15 min	N	rt	 **3e**[#]	80	100	B
5	 **3v**	 **2d**	10 h	Et_3N	50	 **3f**[#]	30	90	C
6	 **1a**	 **2e**	2 h	Et_3N	50	 **3g**[#]	89	91	D
7	 **1a**	 **2f**	3 h	Et_3N	50	 **3h**[22]	85	90	C
8	 **1a**	 **2g**	10 min	N	rt	 **3i**	99	100	A

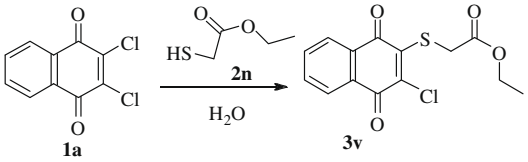
Table 3 (*continued*)

Entry	1	2	Time	b	*T* (°C)	Product 3	Yield (%)	*c*	W
9	 **1d**	 **2g**	30 min	N	rt	 **3j**	98	100	A
10	 **1e**	 **2g**	15 min	N	rt	 **3k**	98	100	A
11	 **1c**	 **2g**	30 min	N	rt	 **3l**[#]	92	100	D
12	 **1a**	 **2h**	10 min	N	rt	 **3m**	98	100	A
13	 **1a**	 **2j**	4 h	N	50	 **3o**	96	95	C
14	 **1a**	 **2k**	12 h	N	rt	 **3p**	98	89	C
15	 **1g**	 **2a**	20 min	N	rt	 **3w**[#,36]	77	100	C

b: base, N: not required.

[#]Other product was not isolated, *c*: conversion% of [**1**], W: workup process, A: product directly filtered, B: product filtered as ppt [**3**], C: product filtered and purified by column chromatography, D: water was evaporated or extracted with suitable solvent and purified by column chromatography using silica gel in hexane and ethyl acetate.

Table 4
Nucleophilic substitution reaction of quinone (**1a**) with ethyl thioglyconate (**2e**) 'on water'[35]



1a **3v**

Solvent	*T* (°C)	*t* (h)	Yield (%)
EtOH	80–90	8–10	95–97[21]
On H_2O	50	2	100

with the most dramatic effects observed for the substitution and addition of nucleophiles to 1,4-benzoquinone and 1,4-naphthoquinones. Clearly solubility is not essential for nucleophilic substitution and addition reactions 'on water' even if two reactants are solids. The unique reactivity and selectivity of these reactions 'on water' through the interaction of nonpolar or hydrophobic regions of reactants are of utmost significance.[34] The reactivity of nucleophiles toward nucleophilic substitution and addition has immediate practical implications. The derivatives of naphthoquinones and benzoquinone are widely studied in organic synthesis.[8] The amino and thioether derivatives of naphthoquinones are a component of molecular frame work of several biologically active compounds. These compounds have been found to possess marked

Table 5
Reaction conditions of water-assisted thioethers of quinone **1**[35]

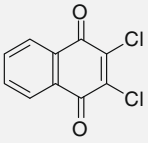
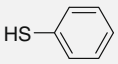
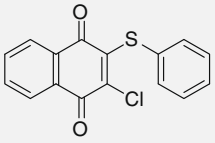
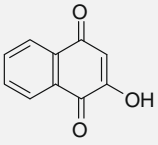
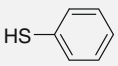
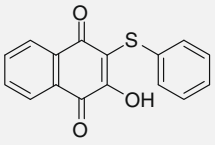
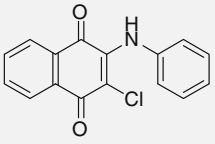
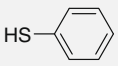
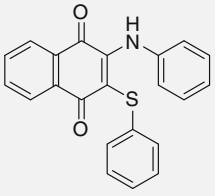
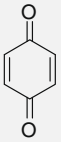
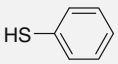
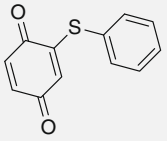
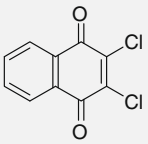
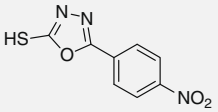
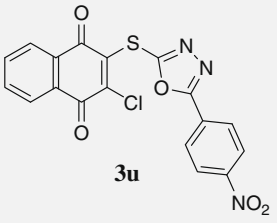
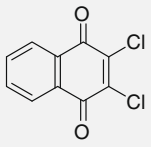
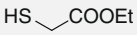
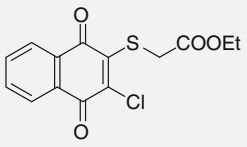
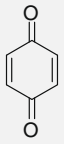
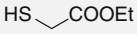
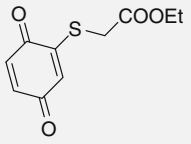
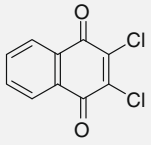
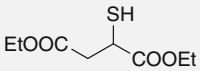
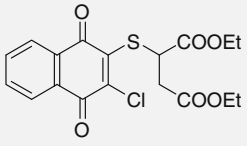
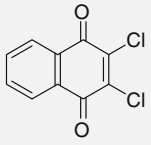
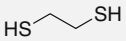
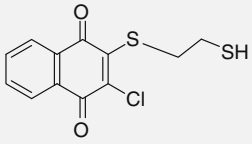
Entry	1	2	*t*	b	*T* (°C)	Product 3	Yield (%)	*c*	W
1	 **1a**	 **2l**	10 min	N	rt	 **3q**[#]	60	80	C
2	 **1f**	 **2l**	4 h	N	50	 **3r**	98	100	D
3	 **3a**	 **2l**	1 h	N	rt	 **3s**	98	100	A
4	 **1c**	 **2l**	1 h	N	rt	 **3t**[#]	80	100	D
5	 **1a**	 **2m**	12 h	Et_3N	50	 **3u**	80	92	C

Table 5 (*continued*)

Entry	1	2	*t*	b	*T* (°C)	Product 3	Yield (%)	*c*	W
6	 **1a**	 **2n**	2 h	N	50	 **3v**	100	100	A
7	 **1c**	 **2n**	25 min	N	rt	 **3x**[#]	95	95	D
8	 **1a**	 **2o**	2 h	N	50	 **3y**[#]	97	89	C
9	 **1a**	 **2p**	15 min	N	rt	 **3z**	98	100	A

b: base, N: not required.

[#] Other product was not isolated, c: conversion% of [**1**], W: workup process, A: product directly filtered, B: product filtered as ppt [**3**], C: product filtered and purified by column chromatography, D: water was evaporated or extracted with suitable solvent and purified by column chromatography using silica gel in hexane and ethyl acetate.

anti-neoplastic,[9] anti-trypanosomal,[10] anti-malarial,[11] anti-viral,[20] anti-platelet, anti-inflammatory, anti-allergic,[12] anti-bacterial, anti-fungal,[18–23] anti-proliferative, anti-tumor, cytotoxic, and anti-cancer activities.[13,19,24,25] They have also found widespread industrial applications in color chemistry, hair dyeing,[14] photostabilizers,[15] electrochemical fluorescent switching,[25] anion sensors, and colorimetric test for resin-bond amines.[26] The derivatives of benzoquinone have also been used in the synthesis of charge-transfer complexes, as anti-tumor, as HIV transcriptase inhibitor, in immunomodulation, as oxidative inhibitors, in stabilization of petroleum products, in protecting iron surface, as additives in rubber, to inhibit polymerization in gasoline and lubricating oil, as cocatalysts to improve stereoselectivity.[27]

Further work is in progress to explore the 'on water' phenomenon for industrial applications and study of substituted quinones with other nucleophiles.

Acknowledgment

H.K.M. acknowledges UGC, New Delhi, India for Senior Research Fellowship.

References and notes

1. Herrerias, C. I.; Xiaoquan, Y.; Li, Z.; Li, C.-J. *Chem. Rev.* **2007**, *107*, 2546.
2. Feng, C.-G.; Wang, Z.-Q.; Shao, C.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2008**, *10*, 4101.
3. Yang, J.; Breslow, R. *Angew. Chem., Int. Ed.* **2000**, *39*, 2692.
4. Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2005**, *44*, 3275.
5. Dambacher, J.; Zhao, W.; El-Batta, A.; Anness, R.; Jiang, C.; Bergdahl, M. *Tetrahedron Lett.* **2005**, *46*, 4473.
6. Hamada, T.; Manabe, K.; Kobayashi, S. *J. Am. Chem. Soc.* **2004**, *126*, 7768.
7. Yanai, H.; Saito, A.; Taguchi, T. *Tetrahedron* **2005**, *61*, 7087.
8. (a) Moore, W. H. *Chem. Soc. Rev.* **1973**, *2*, 415; (b) Sartori, M. F. *Chem. Rev.* **1963**, *63*, 279; (c) Shishkina, R. P.; Berezhnaya, V. N.; Russ, V. N. *Chem. Rev.* **1994**, *63*, 139; (d) Aguilar-Martinez, M.; Macias-Ruvalcaba, N. A.; Bautista-Martinez, J. A.; Gomez, M.; Gonzalez, F. J.; Gonzalez, I. *Curr. Org. Chem.* **2004**, *8*, 1721.
9. (a) Giorgi-Renault, S.; Renault, J.; Gebel-Servaltes, P.; Baron, M.; Paolett, C.; Cros, S.; Bissery, M. C.; Lavelte, F.; Atassi, G. *J. Med. Chem.* **1991**, *34*, 38; (b) Lin, T. S.; Xu, S. P.; Zhu, L. Y.; Cosby, L. A.; Sartorell, A. C. *J. Med. Chem.* **1989**, *32*, 1467.
10. Salman-Chemin, L.; Buisine, E.; Yardley, V.; Kohler, S.; Debreu, M. A.; Landry, V.; Sergheraert, C.; Croft, S. L.; Krauth-Siegel, R. L.; David-Charvet, E. *J. Med. Chem.* **2001**, *44*, 548.
11. dos Santos, E. V. M.; Carneiro, J. W. de M.; Ferrira, V. F. *Bioorg. Med. Chem.* **2004**, *12*, 87.
12. Lien, J.-C.; Huang, L.-J.; Wang, J.-P.; Teng, C.-M.; Lee, K.-H.; Kuo, S.-C. *Bioorg. Med. Chem.* **1997**, *5*, 2111.
13. (a) Johnson, M. G.; Kiyokawa, H.; Tani, S.; Koyama, J.; Morris-Natschke, S. L.; Mauger, A.; Bowers-Daines, M. M.; Langer, B. C.; Lee, K.-H. *Bioorg. Med. Chem.* **1997**, *5*, 1469; (b) Miguel del Corral, J. M.; Castro, M. A.; Gordaliza, M.; Martin, M. L.; Gamito, A. M.; Cuevas, C.; Feliciano, A. S. *Bioorg. Med. Chem.* **2006**, *14*, 2816.
14. (a) Takagi, K.; Matsuoka, M.; Hamano, K.; Kitao, T. *Dyes Pigments* **1984**, *5*, 241; (b) Matsuoka, M.; Takagi, K.; Obasyashi, H.; Wakasugi, K.; Kitao, T. *J. Soc. Dyers Colour* **1983**, *99*, 257; (c) Kikuchi, M.; Komatsu, K.; Nakano, M. *Dyes Pigments* **1990**, *52*, 107.

15. (a) Escolastico, C.; Santa Maria, M. D.; Claramunt, R. M.; Jimeno, M. L.; Alkorta, I.; Foces-Foces, C.; Cano, F. H.; Elguero, J. *Tetrahedron* **1994**, *50*, 12489; (b) Catalan, J.; Febero, F.; Guijarro, M. S.; Claramunt, R. M.; Santa Maria, M. D.; Foces-Foces, M.; Cano, F. H.; Elguero, J.; Sastre, R. *J. Am. Chem. Soc.* **1990**, *112*, 747.
16. Tandon, V. K.; Chhor, R. B.; Singh, R. V.; Rai, S.; Yadav, D. B. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1079–1083.
17. Tandon, V. K.; Singh, R. V.; Yadav, D. B. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 2901.
18. Tandon, V. K.; Yadav, D. B.; Chaturvedi, A. K.; Shukla, P. K. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3288.
19. Tandon, V. K.; Yadav, D. B.; Singh, R. V.; Vaish, M.; Chaturvedi, A. K.; Shukla, P. K. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3463.
20. Tandon, V. K.; Yadav, D. B.; Singh, R. V.; Chaturvedi, A. K.; Shukla, P. K. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 5324.
21. Tandon, V. K.; Maurya, H. K.; Yadav, D. B.; Tripathi, A.; Kumar, B. M.; Shukla, P. K. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5883.
22. Tandon, V. K.; Yadave, D. B.; Maurya, H. K.; Chaturvedi, A. K.; Shukla, P. K. *Bioorg. Med. Chem.* **2006**, *14*, 6120.
23. Tandon, V. K.; Maurya, H. K.; Tripathi, A.; Shiva Keshva, B.; Shukla, P. K.; Srivastava, P.; Panda, D. *Eur. J. Med. Chem.* **2009**, *44*, 1086.
24. Tandon, V. K.; Maurya, H. K. *Heterocycles* **2008**, *76*, 1007.
25. (a) Illos, R. A.; Harlev, E.; Bittner, S. *Tetrahedron Lett.* **2005**, *46*, 8427; (b) Sutovsky, Y.; Likhtenshtein, G. I.; Bittner, S. *Tetrahedron* **2003**, *59*, 2939.
26. (a) Anzenbacher, P.; Palacios, M. A.; Jursikova, K.; Marquez, M. *Org. Lett.* **2005**, *7*, 5027; (b) Blackburn, C. *Tetrahedron Lett.* **2005**, *46*, 1405.
27. Katritzky, A. R.; Fedoseyenko, D.; Mohapatra, P. P.; Steel, P. J. *Synthesis* **2008**, *5*, 0777 and references cited therein.
28. (a) Knapp, V.; Schmidt, S. *Ann.* **1881**, *210*, 189; (a) Plogemann, A. *Ber.* **1883**, *15*, 48.
29. Yerushalmi, S.; Lemcoff, G.; Bittner, S. *Synthesis* **2007**, *2*, 239.
30. (a) Orden, M.; Teresa, M.; Sun, H.; Chamudis, S. T.; Moya, A. C.; Rodriguez, F. B.; Ocana, M.; Victoria, M. *PCT Int. Appl.*, 2007, WO 2007026041.; (b) Kallmayer, H.-J.; Thierfelder, B. *Pharmazie* **2003**, *58*, 104; (c) Huang, S.-T.; Kuo, H.-S.; Hsiao, C.-L.; Lin, Y.-L. *Bioorg. Med. Chem.* **2002**, *10*, 1947; (d) Brun, M.-P.; Braud, E.; Angotti, D.; Mondésert, O.; Quaranta, M.; Montes, M.; Miteva, M.; Gresh, N.; Ducommun, B.; Garbay, C. *Bioorg. Med. Chem.* **2005**, *13*, 4871; (e) Padia, J. K.; O'Brien, S.; Lu, J. Pikul, S. *PCT Int. Appl.*, 2005, 77, WO 2005013903.; (f) Aly, A. A.; Hassan, A. A.; Mohamrd, N. K.; Mourad, A.-F. F. *Pharmazie* **1997**, *52*, 282; (g) Wang, X.-L.; Zheng, X.-F.; Reiner, J. *Synlett* **2006**, *6*, 942.
31. Sarhana, E.-W. A. O.; El-Dean, A. M. K.; Abdel-Monem, M. I. *Monatshefte fuer Chemie* **1998**, *129*, 205.
32. Bhattacharya, S. *Molecules* **2000**, *5*, M160.
33. Wang, X. L.; Zheng, X. F.; Wang, L.; Reiner, J.; Xie, W. L.; Chang, J. B. *Synthesis* **2007**, *7*, 0989.
34. Dallinger, D.; Kappe, C. O. *Chem. Rev.* **2007**, *107*, 2563.
35. *Representative procedure for the synthesis*: Suspension of quinone **1** (0.5 mmol) in water (3 mL) and amines, hydrazines, amino acids, or thiols (solid, 0.5 mmol or liquid, 0.6 mmol) **2** was smoothly stirred at room temp. or 50 °C for 10 min to 12 h. and workup as shown in Table 3 and Table 5. Column chromatography (if required) of the reaction mixture (hexane/EtOAc 50:1→15:1) gave **3** as orange or red solid.
36. (a) Döpp, D.; Gomaa, M. A.-M.; Henkel, G.; El-Din, A. M. N. *J. Heterocycl. Chem.* **1995**, *32*, 603; (b) Nagami, T.; Yoshihara, K.; Nagakura, S. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 122; (c) Dwivedi, P. C.; Agarwal, R. *Indian J. Chem.* **1985**, *24A*, 100.