Pergamon

Tetrahedron Vol. 51, No. 20, pp. 5813-5818, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00252-9

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, a Mild Catalyst for the Formation of Carbon-Nitrogen Bonds

Jean Jacques Vanden Eynde,* Florence Delfosse, Pascal Lor, and Yves Van Haverbeke

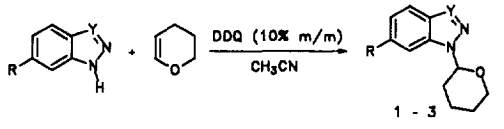
University of Mons-Hainaut, Organic Chemistry Department
20 Place du Parc, B - 7000 Mons, Belgium

Abstract: 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) catalyzes the preparation of N-tetrahydropyranylbenzazoles, 2-substituted 1,3-diphenylimidazolidines, and N-(arylmethylene)benzene-1,2-diamines. In the latter case, use of one equivalent of DDQ provides a novel one-pot method for the synthesis of 1*H*-benzimidazoles.

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), whose first synthesis has been described by Thiele and Gunther[1] in 1906, is well known for its high oxidation potential[2] and it is largely used for dehydrogenation reactions.[2,3] DDQ was also found to be an excellent reagent to cleave methoxybenzyl ethers[4] and an efficient catalyst for the alcoholysis of epoxydes[5] as well as for the hydrolysis of acetals.[6,7] Beside these latter examples in which DDQ is used to break carbon-oxygen bonds, recent papers report that DDQ acts as a Lewis acid catalyst for the formation of carbon-oxygen bonds and, more particularly, for the tetrahydropyranylation of alcohols,[8] the glycosidation of glycals,[9] and the isopropylidenation of carbohydrates.[10]

We now wish to present our results regarding the possibility of using DDQ to promote the formation of carbon-nitrogen bonds.

Thus, as DDQ catalyzes the formation of tetrahydropyranyl ethers[8] (from 3,4-dihydro-2*H*-pyran and alcohols), it was tempting to test its activity as a catalyst for the tetrahydropyranylation of benzazoles, a key step in the synthesis of 2-substituted tetrahydropyrans.[11-13] We found that 3,4-dihydro-2*H*-pyran readily reacts with 1*H*-benzotriazole, 1*H*-indazole, and 6-nitro-1*H*-indazole in acetonitrile in the presence of a catalytic amount of DDQ (Fig. 1). The reactions were monitored by ^{1}H NMR spectroscopy (intensity of the **H**-C(6) in dihydropyran). In this way, we observed that they were complete (yields higher than 90 %) within two hours, at room temperature, from 1*H*-benzotriazole and within one hour, at reflux, from the 1*H*-indazole derivatives.

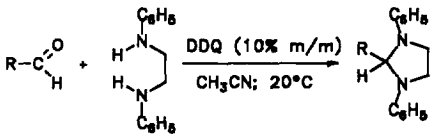


1: Y = N; R = H
2: Y = CH; R = H
3: Y = CH; R = NO_2

Fig. 1. Preparation of 1-Tetrahydropyranyl-1*H*-benzazoles Catalyzed by DDQ

1,3-Dioxolanes are probably the most commonly encountered type of acetals that can be prepared to protect aldehyde functions. [14] By analogy, we examined (Table 1) the syntheses of 2-substituted 1,3-diphenylimidazolidines [15-17] from aldehydes and N,N'-diphenylethylenediamine. We performed the reactions in acetonitrile at room temperature and we followed their evolution by ^1H NMR spectroscopy too (intensity of the aldehyde proton). The results gathered in Table 1 clearly indicate that DDQ can promote the formation of diazolidines, especially when starting from an aromatic or heteroaromatic aldehyde.

Table 1. Preparation of 2-Substituted 1,3-Diphenylimidazolidines



4 - 11

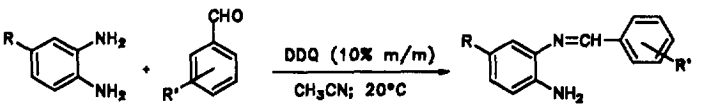
	R	Without catalyst Yield (%)	after (h)	In the presence of DDQ Yield (%)	after (h)
4	C_2H_5	70	6	85	0.25
5	C_3H_7	40	24	85	0.25
6	$(CH_3)_2CH$	30	24	90	0.25
7	C_6H_5	<5	24	85	7
8	4-(NO_2)-C_6H_4	10	24	90	6
9	4-(CH_3O)-C_6H_4	10	24	95	6
10	2-Cl-C_6H_4	<5	24	85	3
11	2-Furyl	<5	24	90	7

Similar enhancements have been noticed for the preparation of imines from benzene-1,2-diamines and aldehydes (Table 2). For example, in acetonitrile at room temperature, the reaction between benzene-1,2-diamine and 3-nitrobenzaldehyde requires more than 24 hours in the absence of catalyst whereas complete conversion is achieved within less than 1 hour in the presence of a small amount (10 % m/m) of DDQ. In addition, the expected regioselectivity [18] of the syntheses (that is governed by the nature of the substituent R on the ring of the starting benzene-1,2-diamine) is not altered by the action of the quinone. This is illustrated by the formation of **15** (Table 2) from 4-nitrobenzene-1,2-diamine.

Imines derived from benzene-1,2-diamines and aldehydes afford 1*H*-benzimidazoles [19,20] by oxidation of their corresponding ring tautomers (see Table 3). Therefore, we reasoned that performing the reactions described in Table 2 with one equivalent of DDQ (in place of a catalytic amount) could provide a simple one-pot route to 1*H*-benzimidazoles. That assumption agrees with the experiment: 2-(3-nitrophenyl)-1*H*-benzimidazole (**16**) was prepared in 80 % yield by reacting equimolar amounts of benzene-1,2-diamine, 3-

nitrobenzaldehyde, and DDQ in acetonitrile at room temperature (2 hours). The procedure appeared to be of general applicability as we could extend it from substituted benzene-1,2-diamines and other aromatic or heteroaromatic aldehydes[21-28] as depicted in Table 3.

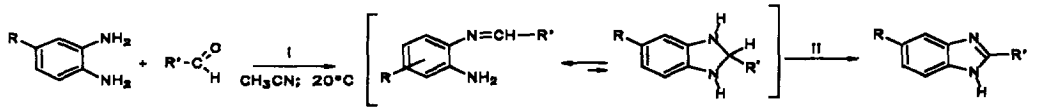
Table 2. Preparation of N-(Arylmethylene)benzene-1,2-diamines Catalyzed by DDQ



12 - 15

	R	R'	t (h)	Yield (%)		R	R'	t (h)	Yield (%)
12	H	3-NO_2	1	80	**14**	H	4-CN	2	80
13	H	4-NO_2	24	90	**15**	NO_2	4-NO_2	24	95

Table 3. Preparation of 2-Substituted 1*H*-benzimidazoles in the Presence of DDQ



16 - 24

	R	R'	t (h)	Yield (%)		R	R'	t (h)	Yield (%)
16	H	3-(NO_2)-C_6H_4	2	80	**21**	NO_2	C_6H_5	2	85
17	H	4-(NO_2)-C_6H_4	24	95	**22**	NO_2	4-Cl-C_6H_4	24	70
18	H	4-(CN)-C_6H_4	3	80	**23**	Cl	4-Cl-C_6H_4	24	95
19	H	C_6H_5	6	90	**24**	CH_3	4-(CH_3)-C_6H_4	2	90
20	H	2-Thienyl	24	85					

i: catalytic amount of DDQ required; ii: one equivalent of DDQ required

In conclusion, our results demonstrate that DDQ can be employed in the place of other (Lewis) acids to promote the formation of carbon-nitrogen bonds under very mild conditions and suggest that the quinone could be advantageously involved in the synthesis of derivatives containing various acid sensitive functionalities. Especially useful is the exploitation of both the catalytic activity and the dehydrogenating properties of DDQ: such a methodology enables the preparation of 1*H*-benzimidazoles, from benzene-1,2-diamines and aldehydes, without the necessity of isolating the intermediate imines. This constitutes a novel one-pot procedure for preparing benzimidazole derivatives that are known as herbicides, fungicides, and drugs used in human as well as in veterinary medicine.[20,29,30]

EXPERIMENTAL

All compounds have been described in the literature and were identified on the basis of their spectral data and, eventually, their melting points.

Preparation of the Tetrahydropyranylbenzazoles **1 - 3**

A mixture of the benzazole (10 mmol), 3,4-dihydro-2*H*-pyran (0.9 mL; 10 mmol), and DDQ (0.23 g; 1 mmol) in acetonitrile (20 mL) at room temperature or under reflux was stirred for an appropriate period (see text). After evaporation of the solvent, the residue was purified by column chromatography (Al_2O_3 - CH_2Cl_2).

1[12] ^{1}H NMR ($CDCl_3$): 1.3-1.8 (c; 6H; $H^{3'}$-$H^{5'}$); 3.8-3.9 (c; 2H; $H^{6'}$); 5.8 (c; 1H; $H^{2'}$); 7.0-7.9 (c; 4H; Ar) ppm. Oil. See Ref. 12 for a discussion about the structure of **1**.

2[11] ^{1}H NMR ($CDCl_3$): 1.3-1.8 (c; 6H; $H^{3'}$-$H^{5'}$); 3.8-3.9 (c; 2H; $H^{6'}$); 5.7 (c; 1H; $H^{2'}$); 7.1-7.8 (c; 4H; H^4-H^7); 8.1 (s; 1H; H^3) ppm. Oil.

3[11] ^{1}H NMR ($CDCl_3$): 1.3-1.8 (c; 6H; $H^{3'}$-$H^{5'}$); 3.8-3.9 (c; 2H; $H^{6'}$); 5.8 (c; 1H; $H^{2'}$); 8.1 (c; 2H; H^3, H^4); 8.3 (c; 1H; H^5); 8.5 (c; 1H; H^7) ppm. M.p.: 108-110 °C.

Preparation of the 1,3-Diphenylimidazolidines **4 - 11**

A mixture of N,N'-diphenylethylenediamine (2.1 g: 10 mmol), the aldehyde, and DDQ (0.23 g; 1mmol) in acetonitrile (20 mL) at room temperature was stirred for an appropriate period (see Table 1). After evaporation of the solvent, the residue was purified by column chromatography (Al_2O_3 - CH_2Cl_2).

4[16] ^{1}H NMR ($CDCl_3$): 0.6 (t; 3H; CH_3); 1.7 (c; 2H; CH_3-$\mathbf{CH_2}$); 3.3-3.7 (c; 4H; H^3, H^4); 5.2 (t; 1H; H^2); 6.3-7.2 (c; 10H; Ar) ppm. M.p.: 110-112 °C.

5[16] ^{1}H NMR ($CDCl_3$): 0.5-1.3 (c; 5H; CH_3 and CH_2 of R); 1.8 [c; 2H; C(2)CH_2]; 3.3-3.7 (c; 4H; H^3, H^4); 5.2 (t; 1H; H^2); 6.3-7.2 (c; 10H; Ar) ppm. M.p.: 106-107 °C.

6[15] ^{1}H NMR ($CDCl_3$): 0.7 (d; 6H; CH_3); 2.0 [c; 1H; C(2)CH]; 3.3-3.7 (c; 4H; H^3, H^4); 5.1 (d; 1H; H^2); 6.3-7.2 (c; 10H; Ar) ppm. M.p.: 97-99 °C.

7[16] ^{1}H NMR ($CDCl_3$): 3.3-3.7 (c; 4H; H^3, H^4); 5.8 (s; 1H; H^2); 6.3-7.3 (c; 15H; Ar) ppm. M.p.: 137-138 °C.

8[17] ^{1}H NMR ($CDCl_3$): 3.3-3.7 (c; 4H; H^3, H^4); 6.1 (s; 1H; H^2); 6.3-7.2 (c; 10H; N-Ar); 7.7 (d; 2H; H^2 and H^6 of R); 8.2 (d; 2H; H^3 and H^5 of R) ppm. M.p.: 127-128 °C.

9[16] ^{1}H NMR ($CDCl_3$): 3.3-3.7 (c; 4H; H^3, H^4); 3.6 (s; 3H; OCH_3); 5.8 (s; 1H; H^2); 6.3-7.3 (c; 14H; Ar) ppm. M.p.: 164-165 °C.

10 [16] ^{1}H NMR ($CDCl_3$): 3.3-3.7 (c; 4H; H^3, H^4); 6.1 (s; 1H; H^2); 6.3-7.3 (c; 14H; Ar) ppm. M.p.: 128-129 °C.

11 [16] ^{1}H NMR ($CDCl_3$): 3.3-3.7 (c; 4H; H^3, H^4); 6.2 (s; 1H; H^2); 6.3-7.3 (c; 13H; Ar + Fur) ppm. M.p.: 135-137 °C.

Preparation of the N-(Arylmethylene)benzene-1,2-diamines **12 - 15**

A mixture of the benzene-1,2-diamine (10 mmol), the aldehyde (10 mmol), and DDQ (0.23 g; 1 mmol) in acetonitrile (25 mL) was stirred at room temperature for an appropriate period (see Table 2). After addition of water (20 mL), the precipitate was filtered and recrystallized from ethanol.

12 [18] ^{1}H NMR (DMSO-d_6): 5.1 (br; 2H; NH_2); 6.0-7.0 (c; 4H; $C_6H_4NH_2$); 7.2-8.5 (c; 4H; $C_6H_4NO_2$); 8.6 (s; 1H; N=CH) ppm. M.p.: 106-108 °C.

13 [31] ^{1}H NMR (DMSO-d_6): 5.1 (br; 2H; NH_2); 6.5-8.6 (c; 8H); 8.9 (s; 1H; N=CH) ppm. M.p.: 142-144 °C.

14 [18] ^{1}H NMR (DMSO-d_6): 5.6 (br; 2H; NH_2); 6.6-7.2 (c; 4H; $C_6H_4NH_2$); 7.9-8.4 (d,d; 4H; C_6H_4CN); 8.8 (s; 1H; N=CH) ppm. M.p.: 135-136 °C.

15 [18] ^{1}H NMR (DMSO-d_6): 6.2 (br; 2H; NH_2); 6.9 (d; 1H; H^3); 7.8-8.3 (c; 2H; H^4 and H^6); 8.4 (s; 4H; $C_6H_4NO_2$); 9.1 (s; 1H; N=CH) ppm. M.p.: > 300 °C.

Preparation of the 1H-benzimidazoles **16 - 24**

A mixture of the benzene-1,2-diamine (10 mmol), the aldehyde (10 mmol), and DDQ (2.27 g; 10 mmol) in acetonitrile (25 mL) was stirred at room temperature. After the appropriate period (see Table 3), the mixture was diluted with sodium hydroxide (0.5 M; 40 mL) and stirred at room temperature overnight. The precipitate was filtered and recrystallized from a mixture (1/1) of ethanol and water.

16 [21,22] ^{1}H NMR (DMSO-d_6): 5.3 (br; 1H; NH); 6.8-7.7 (c; 4H; H^4-H^7); 7.9-8.9 (c; 4H; 2-Ar) ppm. M.p.: 204-206 °C.

17 [23,24] ^{1}H NMR (DMSO-d_6): 6.7 (br; 1H; NH); 7.2-7.9 (c; 4H; H^4-H^7); 8.5 (s; 4H; 2-Ar) ppm. M.p.: 297-299 °C.

18 [18] ^{1}H NMR (DMSO-d_6): 5.5 (br; 1H; NH); 7.1-7.8 (c; 4H; H^4-H^7); 7.9-8.6 (d,d; 4H; 2-Ar) ppm. M.p.: 257-259 °C.

19 [24,25] ^{1}H NMR (DMSO-d_6): 6.0 (br; 1H; NH); 7.0-7.7 (c; 7H); 8.0-8.2 (c; 2H; H^2 and H^6 of R) ppm. M.p.: 286-289 °C.

20 [18] ^{1}H NMR (DMSO-d_6): 7.2-8.2 (c; 7H); 8.9 (br; 1H; NH) ppm. M.p.: 287-289 °C.

21 [22] ^{1}H NMR (DMSO-d_6): 6.9 (br; 1H; NH); 7.2-8.1 (c; 7H); 8.3 (s; 1H; H^4) ppm. M.p.: 207-208 °C.

22 [26] ^{1}H NMR (DMSO-d_6): 7.4-8.2 (c; 6H); 8.4 (s; 1H; H^4) 8.7 (br; 1H; NH) ppm. M.p.: 305-308 °C.

23 [27] ^{1}H NMR (DMSO-d_6): 6.5 (br; 1H; NH); 7.0-7.7 (c; 5H); 8.1-8.3 (c; 2H; H^2 and H^6 of R) ppm. M.p.: 225-227 °C.

24 [28] ^{1}H NMR (DMSO-d_6): 2.2 (s; 3H); 2.3 (s; 3H); 6.8 (br; 1H; NH); 7.0-8.0 (c; 7H) ppm. M.p.: 190-191 °C.

REFERENCES

1. Thiele, J.; Gunther, F. *Ann.*, **1906**, *349*, 45.
2. Walker, D.; Hiebert, J.D. *Chem. Rev.*, **1967**, *67*, 153-195.
3. Fu, P.P.; Harvey, R.G. *Chem. Rev.*, **1978**, *78*, 317-361.
4. Oikawa, Y.; Tanaka, T.; Horita, K.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.*, **1984**, *25*, 5393-5396.
5. Iranpoor, N.; Mohammadpour Baltock, I. *Tetrahedron Lett.*, **1990**, *31*, 735-738.
6. Tanemura, K.; Suzuki, T.; Horaguchi, T. *J. Chem. Soc., Chem. Commun.*, **1992**, 979-980.
7. Tanemura, K.; Suzuki, T.; Horaguchi, T. *Bull. Chem. Soc. Jpn.*, **1994**, *67*, 290-292.
8. Tanemura, K.; Horaguchi, T.; Suzuki, T. *Bull. Chem. Soc. Jpn.*, **1992**, *65*, 304-305.
9. Toshima, K.; Ishizuka, T.; Matsuo, G.; Nakata, M.; Kinoshita, M. *J. Chem. Soc., Chem. Commun.*, **1993**, 704-705.
10. Kjolberg, O.; Neumann, K. *Acta Chem. Scand.*, **1993**, *47*, 843-845.
11. Alonso, G.; Diez, C.; Garcia-Munoz, G.; De Las Heras, F.G.; Navarro, P. *J. Carbohydr. Nucleosides, Nucleotides*, **1976**, *3*, 157-167.
12. Katritzky, A. R.; Rachwal, S.; Rachwal, B. *J. Chem. Soc., Perkin Trans 1*, **1990**, 1717-1725.
13. Saladino, R.; Crestini, C.; Nicoletti, R. *Heterocycles*, **1994**, *38*, 567-573.
14. Greene, T.W.; Writs, P.G.N. "*Protective Groups in Organic Synthesis*" Ed. Wiley and Sons Inc., New York, **1991**.
15. Moos, M. *Ber*, **1887**, *20*, 734.
16. Wandelick, H.W.; Lochel, W. *Chem. Ber.*, **1953**, *86*, 1463-1466.
17. Robe, E.; Wanzlich, H.W. *Justus Liebigs Ann. Chem.*, **1975**, 195-200.
18. Stephens, F.F.; Bower, J.D. *J. Chem. Soc.* **1949**, 2971-2972.
19. Wright, J.B. *Chem. Rev.* **1951**, *48*, 397-541.
20. Preston, P.N. *Chem. Rev.* **1974**, *74*, 279-314.
21. Bapat, D.G.; Shirsat, M.V. *Indian J. Chem.*, **1965**, *3*, 81-83.
22. Sterba, V.; Arient, J.; Slosar, J. *Collect. Czech. Chem. Commun.*, **1965**, *31*, 1093-1100.
23. Stephens, F.F.; Bower, J.D. *J. Chem. Soc.*, **1950**, 1722-1726.
24. Ridley, H.F.; Spickett, R.G.; Timmis, G.M. *J. Heterocycl. Chem.*, **1965**, *2*, 453-456.
25. Von Auwers, K.; Von Meyenburg, F. *Ber.*, **1891**, *24*, 2386.
26. Sandera, G.; Isensee, R.W.; Joseph, L. *J. Am. Chem. Soc.*, **1954**, *76*, 5173.
27. Subba Rao, N.V.; Ratman, C.U. *Proc. Indian Acad. Sci.*, **1958**, *48A*, 256.
28. Hubner, H. *Ann.*, **1881**, *210*, 331.
29. Lavaca, M.; Abliami, S.; Perjessy, A.; Kralova, K.; Chovancova, J. *Chem. Papers*, **1993**, *47*, 393-400.
30. Fisher, H.-P.; Buser, H.-P.; Chemla, P.; Huxley, P.; Lutz, W.; Mirza, S.; Ramos Tombo, G.M.; Van Lommen, G.; Sipido, V. *Bull. Soc. Chim. Belg.*, **1994**, *103*, 565-581.
31. Hinsberg, H. Funcke, F. *Ber.*, **1894**, *27*, 2190.

(*Received in Belgium* 20 *December* 1994; *accepted* 7 *March* 1995)