Bull. Chem. Soc. Jpn., ***66****, 1235—1238(1993)*

The Reaction of 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone with Benzofurans and Indoles

Kiyoshi TANEMURA,* Tsuneo SUZUKI, and Takaaki HORAGUCHI[†]
School of Dentistry at Niigata, The Nippon Dental University, Hamaura-cho 1-8, Niigata 951
[†]Department of Chemistry, Faculty of Science, Niigata University, Ikarashi, Niigata 950-21

(Received October 22, 1992)

The reaction of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) with 6-methoxy-3-methylbenzofuran gave carbon–oxygen adduct. The reaction in less polar solvents such as benzene and CH_2Cl_2 proceeds faster than that in more polar solvents such as THF and dioxane. In contrast, the reaction of DDQ with indoles gave carbon–carbon adducts. This reaction proceeds rapidly with increasing solvent polarity.

2,3-Dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) is known to form charge-transfer (CT) complex with many aromatic hydrocarbons, heterocycles, and olefins.$^{1,2)}$ Among them, some compounds afford substitution products with DDQ via CT complex. For instance, Becker$^{3)}$ isolated carbon–oxygen adduct **1** in the reaction of DDQ with 2,6-dichlorophenol. Bhattacharya and co-workers$^{4)}$ have reported that carbon–oxygen adduct **2** and carbon–carbon adduct **3** were produced by the reaction of DDQ with (trimethylsiloxy) cyclohexene and that relative yield of **3** increased with increasing solvent polarity (Chart 1). Carbon–carbon adducts were often isolated in the reaction of quinones.$^{5)}$ In this paper, we wish to report that DDQ reacts with 6-methoxy-3-methylbenzofuran (**6**) to give carbon–oxygen adduct **12**, while DDQ reacts with indoles **14**—**18**, which are heterocyclic analogs of benzofuran, to yield carbon–carbon adducts **19**—**23**, respectively. Solvent effects of these reactions were investigated.

Results and Discussion

First, the reactions of DDQ with benzofurans were examined. DDQ formed CT complex with benzofurans$^{1)}$ and λ_{max} of CT band in dioxane is shown in Table 1. For the series of benzofurans, λ_{max} is progressively red-shifted as electron-donative nature of benzofurans increases.$^{6,7)}$ 6-Methoxy-3-methylbenzofuran (**6**) has an absorption maximum at 715 nm, which is the longest wavelength among these benzofurans. In benzene, compound **6** immediately formed intensely green-colored CT complex with DDQ, transformed to carbon–oxygen adduct **12** within 5 min at room temperature. Solvent effects of the formation of the adduct were examined and the results are summarized in Table 2. Conversion of **6** to **12** was calculated by monitoring the absorbance at 715 nm of CT band. The reaction is very fast in less polar solvents such as benzene and CH_2Cl_2, although the reaction is less clean in CH_2Cl_2. In more polar solvents such as THF and dioxane, the reaction is more slowly. In $MeNO_2$ and MeCN, only polymeric materials were obtained. In MeOH, the reaction is very fast and the methanol adduct **13** was formed quantitatively. Compound **13** was obtained as a single diastereomer, but stereochemistry is unknown. Thus, the formation of **12** is preferred in less polar solvents (Chart 2).

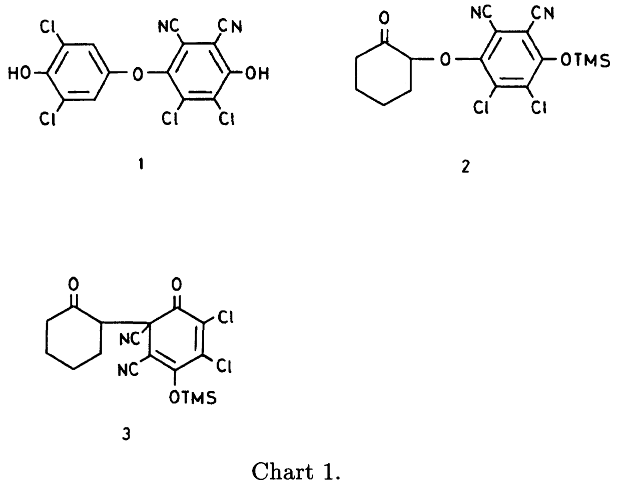
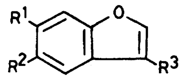


Chart 1.

The formation of the products **12** and **13** is explained by a single electron-transfer (SET) mechanism between DDQ and benzofuran **6** as shown in Scheme 1. Many examples are known affording carbon–oxygen adduct via an SET mechanism in photochemical$^{8)}$ or thermal$^{9)}$ reactions of quinones. In less polar solvents, coupling of the geminate radical ion pair in the solvent cage is favored. In more polar solvents, which encourage the radical ion pair to escape from the solvent cage, the radical coupling is suppressed.$^{10-12)}$ When the reaction was carried out in MeOH, benzofuran cation radical was immediately trapped by MeOH before escape from the solvent cage and hence the reaction was accelerated.$^{13)}$

Next, the reactions of DDQ with some indole derivatives were explored. Bergman and co-workers$^{14)}$ have investigated the reaction of DDQ with indole (**14**) in a few solvents, i.e., CH_2Cl_2, dioxane, and MeOH. They reported that dark-blue crystals of a stable CT complex were precipitated by the reaction of DDQ with indole (**14**) in CH_2Cl_2 at room temperature and carbon–carbon adduct **19** was produced in quantitative yield in dioxane or MeOH.$^{14)}$ In order to compare with the case of benzofuran **6**, we examined this reaction in a variety of solvents and the results are summarized in Table 3. In all the solvents except for CH_2Cl_2, carbon–carbon adduct **19** was produced and the formation of the

Table 1. Absorption Maxima of the CT Complex between DDQ and Benzofurans in Dioxane

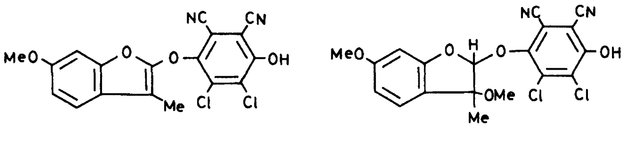


Benzofuran	R^1	R^2	R^3	λ_{max} of CT complex/nm
4	Cl	H	Me	500
5	Me	H	Me	625
6	MeO	H	Me	715
7	H	Cl	Me	510
8	H	Me	Me	550
9	H	MeO	Me	605
10	H	H	H	510
11	MeO	H	H	675

Table 2. Reactions of DDQ with 6-Methoxy-3-methylbenzofuran (**6**) in Various Solvents[a)]

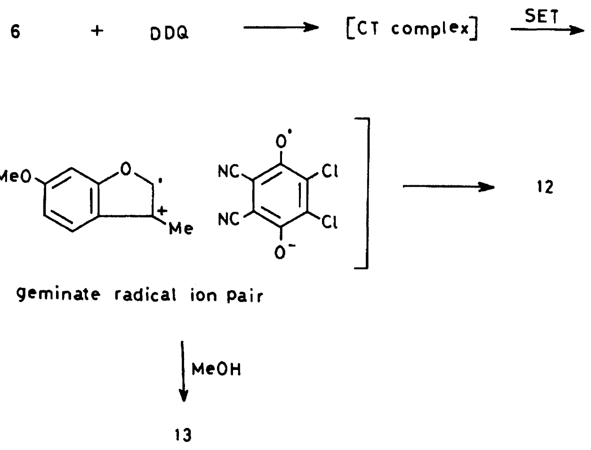
Entry	Solvent	Conv.[b)] /%
1	CH_2Cl_2	100
2	Benzene	90
3	THF	37
4	Dioxane	2
5	$MeNO_2$	100[c)]
6	MeCN	100[c)]
7	MeOH	100[d)]

a) Reaction conditions; **6** 1 mmol, DDQ 1.05 mmol, reaction time 15 min. b) Conversion was calculated by monitoring the absorbance at 715 nm of CT band. c) Polymeric materials were obtained. d) **13** was obtained in 99% yield.



12 13

Chart 2.



Scheme 1.

Table 3. Reactions of DDQ with Indole (**14**) in Various Solvents[a)]

Entry	Solvent	Conv.[b)] /%
1	CH_2Cl_2	—[c)]
2	Benzene	3
3	THF	9
4	Dioxane	8
5	CH_3NO_2	62
6	CH_3CN	72
7	MeOH	100

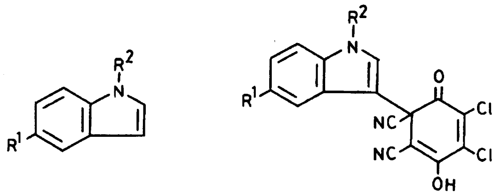
a) Reaction conditions; **14** 1 mmol, DDQ 1.05 mmol, reaction time 60 min. b) Conversion was calculated by monitoring the absorbance at 592 nm of CT band. c) The dark-blue precipitate of CT complex was yielded.

adduct proceeded rapidly with increasing solvent polarity. It is noteworthy that compound **19** was yielded in MeOH and that methanol adduct corresponding to **13** was not found.

The other indole derivatives **15**—**18** afforded carbon–carbon adducts **20**—**23** in dioxane, respectively. As substituent on benzene ring is more electron-donative, the reaction proceeded more rapidly as shown in Fig. 1. The reaction of 2-methylindole,[14)] 3-methylindole, or 5-methoxy-2-methylindole with DDQ in various solvents afforded only polymeric materials.

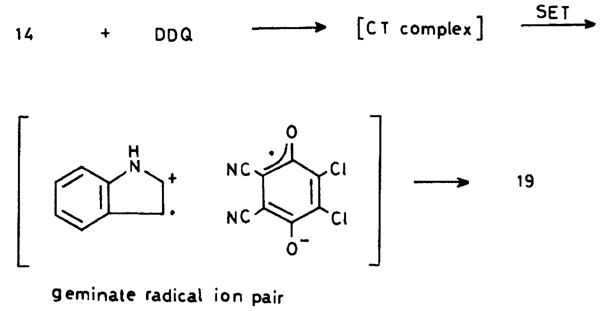
Carbon–carbon adduct **19** is considered to be formed by a nucleophilic attack of indole on DDQ.[15,16)] However, an SET mechanism between indole and DDQ shown in Scheme 2 cannot be ruled out. Carbon–carbon adducts are often produced via an SET mechanism. The formation of compound **3** was explained by an SET mechanism.[4)] A large difference of the solvent effects of the reactions of indole with DDQ toward that of benzofuran **6** suggests that carbon–carbon adduct **19** is formed by a different mechanism from that of the formation of carbon–oxygen adduct **12**. No incorporation of the solvent upon using MeOH also suggests a different mechanism.

In conclusion, the reaction of DDQ with 6-methoxy-3-methylbenzofuran (**6**) gave carbon–oxygen adduct **12**, while the reaction of DDQ with indoles **14**—**18** gave carbon–carbon adducts **19**—**23**. It is interesting to note



	R¹	R²		Time	Yield
14	H	H	19 (	24 h	98%)
15	Cl	H	20 (	120 h	95%)
16	Br	H	21 (	120 h	100%)
17	OMe	H	22 (	2 h	100%)
18	H	Me	23 (	24 h	100%)

Fig. 1.



Scheme 2.

that benzofuran **6** and indoles **14**—**18** afford the different type of adducts.

Experimental

All melting points are uncorrected. Column chromatography was performed on silica gel (Wakogel C-200). CH_2Cl_2, C_6H_6, and MeCN were distilled over P_2O_5. THF and dioxane were refluxed with sodium for 1 d and distilled. MeOH was dried by Molecular Sieves 4A and distilled. DDQ was recrystallized from benzene–hexane. IR spectra were determined on JASCO IRA-2 or Hitachi I-3000 spectrophotometer. ^1H and ^{13}C NMR spectra were determined on a JEOL JNM-FX 90Q or Hitachi R-24B spectrometer, using Me_4Si as the internal standard.

Reaction of 6-Methoxy-3-methylbenzofuran (6) with DDQ in Benzene. A solution of DDQ (294 mg, 1.29 mmol) in dry benzene (15 ml) was added to a solution of **6** (200 mg, 1.23 mmol) in dry benzene (15 ml) at room temperature under nitrogen. After stirring for 15 min, the mixture was evaporated. The residue was chromatographed and eluted with benzene–acetone (1 : 4) to give **12** (466 mg, 97%) as yellow needles; mp 197—198°C (from acetone); IR (KBr) 3260 (broad, OH) and 2240 cm^{-1} (CN); ^1H NMR (CD_3SOCD_3) δ=2.14 (3H, s, 3′-Me), 3.78 (3H, s, OMe), 6.88 (1H, dd, J=9 and 2 Hz, ArH), 7.07 (1H, d, J=2 Hz, ArH), 7.40 (1H, d, J=9 Hz, ArH), and 7.73 (1H, br s, OH); ^{13}C NMR (CD_3SOCD_3) δ=6.2 (q), 55.6 (q), 93.0 (s), 96.2 (d), 102.6 (s), 108.1 (s), 111.7 (d), 111.8 (s), 113.1 (s), 119.5 (d), 122.4 (s), 129.7 (s), 132.7 (s), 145.2 (s), 149.0 (s), 152.0 (s), 156.2 (s), and 157.3 (s). Found: C, 55.25; H, 2.79%. Calcd for $C_{18}H_{10}N_2O_4Cl_2$: C, 55.53; H, 2.59%.

Reaction of 6 with DDQ in Methanol. A solution of DDQ (294 mg, 1.29 mmol) in dry methanol (15 ml) was added to a solution of **6** (200 mg, 1.23 mmol) in dry methanol (15 ml) at room temperature under nitrogen. After stirring for 15 min, the mixture was evaporated at 0°C to give **13** (554 mg, 99%) as colorless needles (containing methanol of crystallization). The analytical sample was recrystallized from methanol carefully. This compound was converted into **12** on heating above mp. Mp 91—93°C (decomp); IR (KBr) 3470 (broad, OH) and 2250 cm^{-1} (CN); ^1H NMR (CD_3COCD_3) δ=1.80 (3H, s, 3′-Me), 3.10 (3H, s, 3′-OMe), 3.81 (3H, s, 6′-OMe), 5.72 (1H, br s, OH), 5.97 (1H, s, 2′-H), 6.56—6.79 (2H, m, ArH), and 7.35 (1H, dd, J=8 and 1 Hz, ArH); ^{13}C NMR (CD_3COCD_3) δ=17.7 (q), 50.8 (q), 56.0 (q), 85.6 (s), 98.7 (d), 103.5 (s), 109.0 (d), 111.9 (s), 112.6 (s), 113.1 (s), 113.7 (d), 120.1 (s), 125.8 (d), 129.2 (s), 135.6 (s), 148.9 (s), 155.4 (s), 161.3 (s), and 163.5 (s). Found: C, 52.93; H, 4.26%. Calcd for $C_{19}H_{14}N_2O_5Cl_2 \cdot CH_3OH$: C, 53.00; H, 4.00%.

Indole–DDQ CT Complex.[14] A solution of DDQ (119 mg, 0.52 mmol) in dry dichloromethane (6.1 ml) was added to a solution of indole (**14**) (59 mg, 0.50 mmol) in dry dichloromethane (6.1 ml) at room temperature under nitrogen. The solution was stirred for 15 min. The dark blue crystals formed were collected by filtration to give the CT complex (169 mg, 98%). The complex was recrystallized from dichloromethane. Mp 220—230°C (decomp); IR (KBr) 3412 (NH), 2232 (CN), and 1680 cm^{-1} (CO).

Reaction of Indole (14) with DDQ in Dioxane. A solution of DDQ (477 mg, 2.10 mmol) in dry dioxane (22 ml) was added to a solution of **14** (234 mg, 2.00 mmol) in dry dioxane (22 ml) at room temperature under nitrogen. After 24 h, the solvent was removed under reduced pressure to give **19** (847 mg, 98%) as orange-red prisms (containing dioxane of crystallization). The analytical sample was recrystallized from ether–hexane. Mp 130—133°C (lit,[14] 130—135°C); IR (KBr) 3424 (NH), 3115 (broad, OH), 2224 (CN), and 1700 cm^{-1} (CO); ^1H NMR (CD_3COCD_3) δ=7.10—7.94 (5H, m, ArH), 8.12 (1H, br s, OH), and 10.70 (1H, br s, NH); ^{13}C NMR (CD_3COCD_3) δ=51.8 (s), 105.2 (s), 113.3 (d), 114.7 (s), 115.6 (s), 120.0 (d), 121.4 (d), 122.2 (s), 123.7 (d), 124.4 (s), 125.1 (s), 125.5 (d), 138.3 (s), 143.8 (s), 156.0 (s), and 179.1 (s).

Spectral data and elemental analyses of C–C adducts **20**—**23** are as follows.

20; brown prisms, mp 129—132°C (decomp) (from ether–hexane); IR (KBr) 3440 (NH), 3184 (broad, OH), 2224 (CN), and 1714 cm^{-1} (CO); ^1H NMR (CD_3COCD_3) δ=6.01 (1H, br s, OH), 7.13—8.03 (4H, m, ArH), and 11.00 (1H, br s, NH). Found: C, 50.48; H, 1.85%. Calcd for $C_{16}H_6N_3O_2Cl_3$: C, 50.76; H, 1.60%.

21; brown prisms, mp 143—148°C (decomp) (from ether–hexane); IR (KBr) 3444 (NH), 3220 (broad, OH), 2224 (CN), and 1706 cm^{-1} (CO); ^1H NMR (CD_3COCD_3) δ=6.62 (1H, br s, OH), 7.24—8.27 (4H, m, ArH), and 10.98 (1H, br s, NH). Found: C, 45.69; H, 1.64%. Calcd for $C_{16}H_6N_3O_2Cl_2Br$: C, 45.43; H, 1.43%.

22; yellow prisms, mp 117—122°C (decomp) (from ether–hexane); IR (KBr) 3432 (NH), 3300 (broad, OH), 2224 (CN), and 1706 cm^{-1} (CO); ^1H NMR (CD_3COCD_3) δ=3.83 (3H, s, 5′-OMe), 5.69 (1H, br s, OH), 6.90 (1H, dd, J=9 and 2 Hz, ArH), 7.20—7.70 (3H, m, ArH), and 10.70 (1H, br s, NH). Found: C, 54.37; H, 2.60%. Calcd for $C_{17}H_9N_3O_3Cl_2$: C, 54.57; H, 2.42%.

23; orange-red prisms, mp 134—138°C (decomp) (from ether–hexane) (lit,[14] 130—135°C); IR 3220 (broad, OH), 2224 (CN), and 1710 cm^{-1} (CO); ^1H NMR (CD_3COCD_3) δ=3.79 (3H, s, 1′-Me), 6.20 (1H, br s, OH), and 7.10—8.00 (5H, m, ArH).

The authors thank Mr. Yoshiaki Matsuda for the elemental analyses.

References

1) J. P. Canselier, S. Domenech, S. Stankovsky, and S. Gautier, *Can. J. Chem.*, **60**, 862 (1982).

2) K. Kozawa, T. Hoshizaki, and T. Uchida, *Bull. Chem. Soc. Jpn.*, **64**, 2039 (1991).

3) H. D. Becker, *J. Org. Chem.*, **34**, 1203 (1969).

4) A. Bhattacharya, L. M. DiMichele, U. H. Dolling, and E. J. J. Grabowski, *J. Org. Chem.*, **54**, 6118 (1989); A. Bhattacharya, L. M. DiMichele, U. H. Dolling, A. W. Douglas, and E. J. J. Grabowski, *J. Am. Chem. Soc.*, **110**, 3318 (1988).

5) A. A. Kutyrev, *Tetrahedron*, **47**, 8043 (1991).

6) S. H. Hastings, J. L. Franklin, J. C. Schiller, and F. A. Matsen, *J. Am. Chem. Soc.*, **75**, 2900 (1953).

7) S. P. McGlynn and J. D. Boggus, *J. Am. Chem. Soc.*, **80**, 5096 (1958).

8) K. A. Schnapp, R. M. Wilson, D. M. Ho, R. A. Caldwell, and D. Creed, *J. Am. Chem. Soc.*, **112**, 3700 (1990).

9) H. D. Becker, *J. Org. Chem.*, **30**, 982 (1965).

10) W. Adam and E. G. Nunez, *Tetrahedron*, **23**, 3773 (1991).

11) H. Kobashi, S. Okabe, Y. Ohsugi, and H. Shizuka, *Bull. Chem. Soc. Jpn.*, **63**, 2173 (1990).

12) T. Miyashi, M. Kamata, and T. Mukai, *J. Am. Chem. Soc.*, **108**, 2755 (1986).

13) R. A. Neunteufel and D. R. Arnold, *J. Am. Chem. Soc.*, **95**, 4080 (1973); D. R. Arnold and A. J. Maroulis, *J. Am. Chem. Soc.*, **98**, 5931 (1976).

14) J. Bergman, R. Carlsson, and S. Misztal, *Acta Chem. Scand., Ser. B*, **30**, 853 (1976).

15) D. W. Cameron, P. J. Chalmers, and G. I. Feutrill, *Tetrahedron Lett.*, **25**, 6031 (1984).

16) F. P. Plá, J. Palou, R. Valero, C. D. Hall, and P. Speers, *J. Chem. Soc., Perkin Trans. 2*, **1991**, 1925.

17) C. T. Wigal, *J. Org. Chem.*, **56**, 3759 (1991).