[Chem. Pharm. Bull. 36(12)4986—4988(1988)]

Reactions of N-Substituted Pyrrole Derivatives and Related Compounds with 3,4,5,6-Tetrachloro-1,2-benzoquinone

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(Received May 16, 1988)

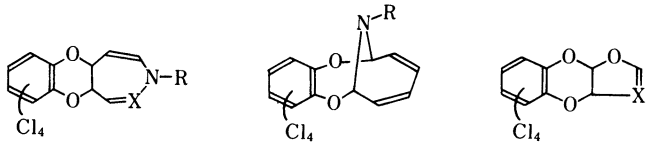
While furans and oxazoles give [4+2]-type cycloaddition products in the reactions with 3,4,5,6-tetrachloro-1,2-benzoquinone, 1-methyl-, 1-phenyl-, and 1-dimethylaminopyrrole and 1-methylindole afforded keto-enol-type substitution products under the same reaction conditions. The reaction of pyrroles proceeds *via* nucleophilic attack of the pyrroles on the *o*-quinoid ring. The difference in the reaction of pyrroles from that of the other heterocycles is considered to be attributable to the degree of aromaticity of these compounds.

Keywords——pyrrole derivative; 1-methylindole; 3,4,5,6-tetrachloro-1,2-benzoquinone; substitution reaction; aromaticity

Previously, the authors reported that azepine and diazepine derivatives reacted as olefinic compounds with 3,4,5,6-tetrachloro-1,2-benzoquinone (**4**) to give mainly the [4+2]- (**1**) and [4+6]-type (**2**) cycloaddition products.[1] The analogous type of reaction is known with oxygen-containing five membered aromatic heterocyclic compounds such as furan and oxazole derivatives, affording [4+2]-type addition products (**3**).[2] However, only a little is known about the reaction of five-membered heterocycles which do not contain an oxygen atom.[3] As a part of our research on the reactivities and the electronic nature of heterocyclic compounds, reactions of **4** with pyrrole derivatives were investigated.[1,3,4] Here the results are reported.

When 1-methylpyrrole (**5a**) was allowed to react with an equimolar amount of **4** in benzene at room temperature for 3 h, a keto-enol-type substitution product (**6a**) was afforded in 25% yield. Analogously, 1-phenylpyrrole (**5b**), 1-dimethylaminopyrrole (**5c**), and 1-methylindole (**7**) gave the same type of products **6b**, **6c**, and **8** in 32, 26, and 86% yields, respectively. The analogous reactions but using 1-methoxycarbonylpyrrole (**5d**), 1-methylpyrazole, 1-phenylpyrazole, and 1-methoxycarbonylpyrazole resulted in quantitative recovery of the starting materials, and the reaction using 1-methylimidazole afforded a polymeric product.

The substituted positions on the pyrrole moieties of the products were deduced on the basis of the nuclear magnetic resonance (NMR) spectral properties and confirmed by comparison of the properties with those of the analogous compounds.[5] The ketoenol form of the products is clearly demonstrated by the infrared (IR) spectra, which show two characteris-



1 : X=CH or N　　2　　3 : X=CH or N

Fig. 1

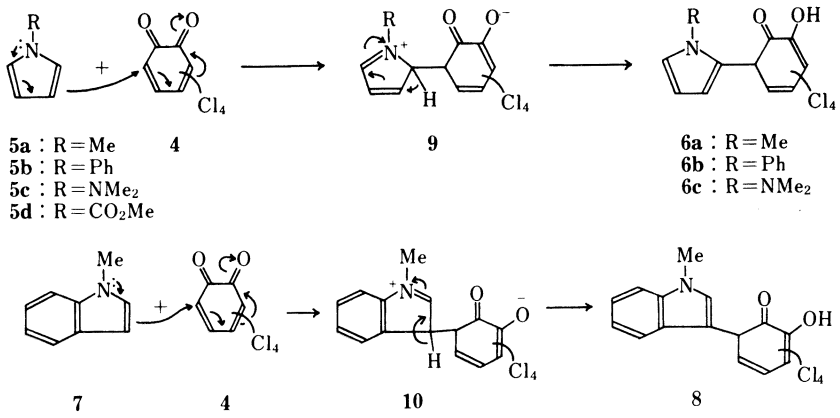


Fig. 2

tic carbonyl group and hydroxy group absorptions. The reaction point of the benzoquinone moiety is suggested by the ultraviolet (UV) spectrum of **6a** which has an absorption maximum at 340 nm, showing that **6a** contains a conjugated dienone moiety.

The reaction mechanism is proposed to be as follows. Nucleophilic attack of the pyrrole ring at the quinone moiety produces the ionic intermediates **9** or **10**, which afford the final products through hydrogen migration. The important contribution of the lone-pair electrons on the nitrogen atom is demonstrated by the fact that **5d**, which has an electron-attracting group on the nitrogen atom, does not react under these conditions.

There is an apparent difference between the reactions of **4** with pyrrole derivatives (**5**, **7**), azepines, diazepines, furans, and oxazoles. While pyrrole derivatives give substitution products, the others undergo [4 + 2]-type cycloaddition reactions. This difference is considered to be attributable to the degree of aromaticity of these compounds. Aromatic compounds are well known to give substitution products but scarcely afford cycloaddition products. Azepines and diazepines are olefinic compounds and, consequently, give addition products. Comparing pyrroles with furans and oxazoles, pyrroles are considered to be more aromatic because the nitrogen atom in pyrroles is less electronegative than the oxygen atom in furans and oxazoles. Therefore, more negative charge resides on the ring of pyrroles than furans and oxazoles. For this reason, pyrroles are believed to undergo substitution reaction with **4** and behave as aromatic compounds. On the other hand, furans and oxazoles, which are less aromatic than pyrroles, afford the cycloaddition products and behave as conjugated olefins.

Experimental

All melting points are uncorrected. NMR spectra were measured with Hitachi R 20B or Varian XL 200 spectrometers with tetramethylsilane as an internal standard. Mass spectra (MS) were measured with Hitachi M-52 or JMS DX 300 spectrometers. IR spectra were measured with a DS 701G spectrometer. Wako gel C 200 was used for column chromatography.

Reaction of 1-Methylpyrrole (5a) with 3,4,5,6-Tetrachloro-1,2-benzoquinone (4)——A mixture of **5a** (4.05 g, 50 mmol) and **4** (12.30 g, 50 mmol) in benzene (50 ml) was stirred at room temperature for 3 h. After evaporation of the solvent the residue was column-chromatographed on silica gel with benzene to give **6a** as yellow crystals (4.14 g, 25.3%). Recrystallization from benzene gave pure **6a**.

6a: mp 122—123 °C. *Anal.* Calcd for $C_{11}H_7Cl_4NO_2$: *m/z* 324.9230. Found: *m/z* 324.9250. MS *m/z* (rel. intensity): 327 (M^+, 50), 292 (32), 108 (100). UV (EtOH): 340 nm (log ε, 3.92). IR (KBr): 3400, 3030, 2950, 1697 cm^{-1}. NMR ($CDCl_3$) δ ppm: 3.74 (s, 3H), 3.96 (br s, 1H), 6.02 (m, 1H), 6.06 (m, 1H), 6.61 (m, 1H).

Reaction of 1-Phenylpyrrole (5b) with 3,4,5,6-Tetrachloro-1,2-benzoquinone (4)——A mixture of **5b** (0.50 g, 3.5 mmol) and **4** (2.58 g, 10.5 mmol) in benzene (26 ml) was stirred at room temperature for 18 h. The same treatment as above gave **6b** as yellow crystals (0.43 g, 31.5%), which were recrystallized from cyclohexane.

6b: mp 151—152 °C. *Anal.* Calcd for $C_{16}H_9Cl_4NO_2$: C, 49.39; H, 2.33; N, 3.60%. Found: C, 49.24; H, 2.19; N, 3.65%. MS *m/z* (rel. intensity): 389 (M^+, 10), 170 (100), 115 (20). UV (EtOH): 345 nm (log ε, 3.60). IR (KBr): 3440, 3030, 1683, 1598 cm^{-1}. NMR ($CDCl_3$) δ ppm: 3.60 (br s 1H), 6.24 (m, 1H), 6.64 (m, 1H), 6.72 (m, 1H), 7.1—7.5 (m 5H).

Reaction of 1-Dimethylaminopyrrole (5c) with 3,4,5,6-Tetrachloro-1,2-benzoquinone (4)——A mixture of **5c** (0.55 g, 5 mmol) and **4** (1.23 g, 5 mmol) in benzene (10 ml) was stirred at room temperature for 3 h. The same procedure as above gave **6c** as a brown oil (0.46 g, 25.8%).

6c: *Anal.* Calcd for $C_{12}H_{10}Cl_4N_2O_2$: *m/z* 353.9496. Found: *m/z* 353.9512. MS *m/z* (rel, intensity): 356 (M^+, 24), 354 (M^+, 23), 321 (72), 223 (100). IR (oil): 3420, 3030, 2980, 1715 cm^{-1}. NMR ($CDCl_3$) δ ppm: 2.69 (s, 3H), 2.76 (s, 3H), 5.20 (br s, 1H), 6.22 (m, 2H), 7.03 (m, 1H).

Reaction of 1-Methylindole (7) with 3,4,5,6-Tetrachloro-1,2-benzoquinone (4)——A mixture of **7** (0.65 g, 5 mmol) and **4** (1.23 g, 5 mmol) in benzene (10 ml) was stirred at room temperature for 1 h. The usual treatment gave **8** as yellow crystals (1.62 g, 86.2%), whcih were recrystallized from benzene.

8: mp 143 °C (dec). *Anal.* Calcd for $C_{15}H_9Cl_4NO_2$: *m/z* 374.9388. Found: *m/z* 374.9380. MS *m/z* (rel. intensity): 374 (M^+, 100), 343 (69), 304 (50). IR (KBr): 3300, 3050, 2930, 1705 cm^{-1}. NMR ($CDCl_3$) δ ppm: 3.45 (s, 3H), 3.90 (br s, 1H), 7.13 (s, 1H), 7.4—8.0, (m, 4H).

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