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DEHYDROGENATIONS USING BENZOFUROXAN AS OXIDANT

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Abstract: 2-Arylsubstituted benzimidazoles, quinoxalines, in 3,5-position substituted 2,6-dimethylpyridines, and 1,4-bis(alkylamino)-9,10-anthracenediones are easily prepared under mild conditions by means of benzofuroxan as oxidant. Thus, the preparation of 2-arylbenzimidazoles succeeds in acetonitrile at 50°C in yields of 65 to 78 %.

As part of our general interest in synthetic applications of benzofuroxan 2[1,2] we have examined the use of this compound in dehydrogenations. Recently, it could be shown that benzofuroxan may act as an oxidizing agent. Thus, the oxidation of thiophenols succeeds with 2 in the presence of a base leading to disulfides and o-benzoquinone dioxime 4 (for further examples see ref.[3]).

This communication describes convenient routes to 2-arylsubstituted benzimidazoles 3 and quinoxalines 6, 2,6-dimethylpyridines 8 and 1,4-bis(alkylamino)-9,10-anthracenediones 10 by means of benzofuroxan as oxidant starting from 1, 5, 7, and 9, respectively (Scheme 1).

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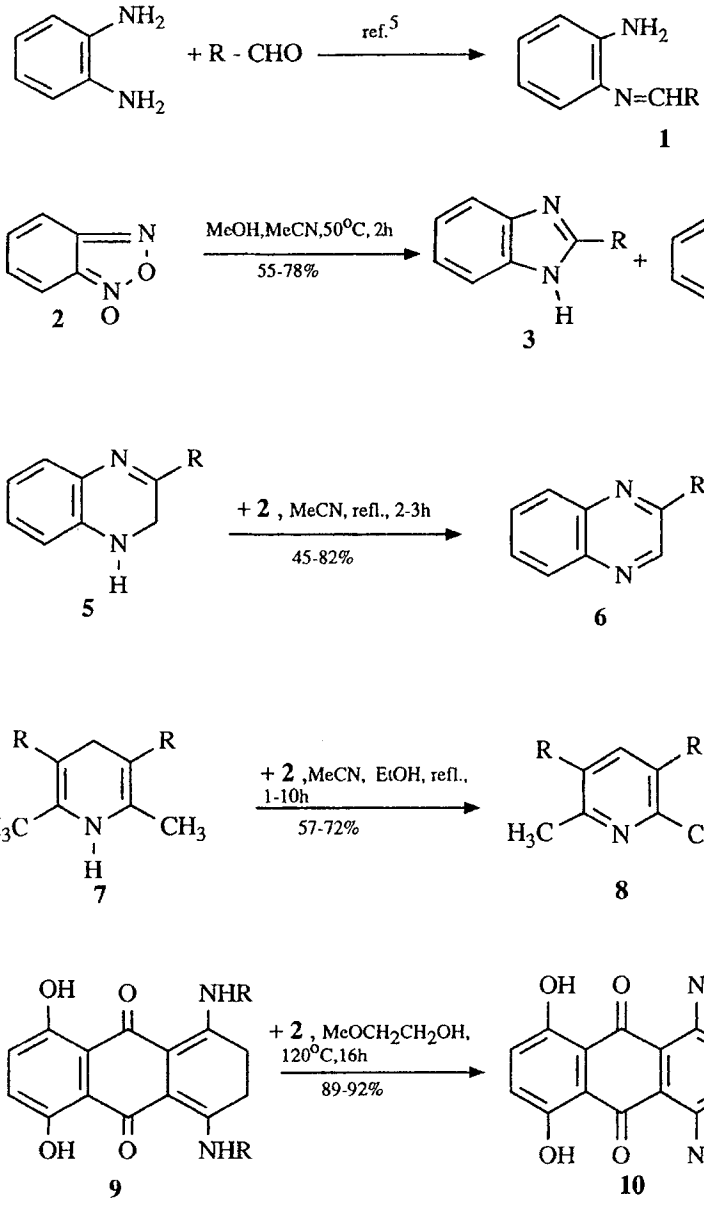
Scheme 1



Yadagiri and Lown[4] have reported the preparation of 2-arylbenzimidazoles from o-arylenediamines and aldehydes in the presence of nitrobenzene at 140-150°C for 24-36 h (cf. also ref.[5]). In this reaction the initially formed Schiff 's base 1 undergoes oxidative cyclization by nitrobenzene. Despite the usefulness of nitrobenzene as oxidant there are two main factors limiting its application: high reaction temperatures and long reaction times.

Now we have found that benzofuroxan 2 can be utilized for the convenient and efficient preparation of 3 . Yields of up to 78 % of isolated and purified 2-arylbenzimidazoles are obtained by heating the appropriate Schiff 's base 1 and equimolar amounts of 2 at 50°C for 2h (Table 1). The o-benzoquinone dioxime formed may be easily separated from the products 3 owing to its high solubility in water under alkaline conditions.

Moreover, dihydroquinoxalines such as 5 may be oxidized by 2. Thus, 6a is obtained in 82 % yield upon refluxing 5a in acetone for 5 min (cf. also ref.[10]). A further example is the oxidation of 3,5-disubstituted 2,6-dimethyl-1,4-dihydro-pyridines. Yields of up to 72 % are obtained by refluxing 7 for 1-10 h in a mixture of ethanol and acetonitrile (Table 2; for further oxidants cf. ref.[15]). Compounds 7 are not oxidized if they are substituted in 4-position.

For the oxidation of 9, comparative studies on the influence of the reaction temperature were performed. The results in Table 3 show that at 25°C only 26-43 % of 10 are formed after 16 h. Nearly complete conversion is achieved at 70°C for 9a and at 120°C for 9b, respectively. The

Table 1: 2-Substituted Benzimidazoles 3a - 3f and Quinoxalines 6a, 6b Prepared

Prod.	R	Yield[a] (%)	mp (°C) found (recryst.from)	reported
3a	$-C_6H_5$	70	295 ($EtOH/H_2O$)	288-289[6]
3b	$-C_6H_4$-4-$N(CH_3)_2$	70	249-250 (i-$PrOH/H_2O$)	286-287[7]
3c	$-C_6H_4$-4-OH	78	297-298 (i-$PrOH/H_2O$)	279[8]
3d	$-C_6H_4$-2-OH	75	247-248 (i-$PrOH/H_2O$)	240-241[9]
3e	$-C_6H_4$-3-NO_2	65	204-205 (i-$PrOH/H_2O$)	204[6]
3f	$-CH=CH-C_6H_5$	55	219-220 ($EtOH/H_2O$)	201-202[6]
6a	$-C_6H_4$-4-Br	82	137 (ethanol)	136-137[10]
6b	$-C_6H_5$	45	72-73 (cyclohexane)	76-77[10]

[a] Isolated and purified products. All compounds are characterized by IR and ^{1}H-NMR data.

formation of by-products (e.g. intramolecular cyclization products) may be suppressed using benzofuroxan as oxidant (for alternative oxidants see also ref.[16,17]).

Experimental

Benzofuroxan 2 was prepared by oxidative cyclization of 2-nitroaniline in an alkaline hypochlorite solution[18]. 3-Aryl-1,2-dihydro-quinoxalines

Table 2: 2,6-Dimethylpyridines 8a - 8d Prepared

Prod.	R	Yield (%)	Reaction Time (h)	mp (°C) found (recryst. from)	mp (°C) reported
8a	-CN	57	10	115-117 (cyclohexane)	112[11]
8b	-C(=O)-CH_3	62	1	64-68.5 (diethyl ether)	72[12]
8c	-C(=O)-O-C_2H_5	70	2	64-66 (cyclohexane)	72[13]
8d	-C(=O)-NH-C_6H_5	72	2	278-280	292-294[14]

Table 3: Influence of the Reaction Temperature on the Oxidation of 9a, 9b to 10a, 10b[a]

Substrate	R	Reaction Temp. (°C)	Conversion to 10 (%)
9a	-CH_2CH_2OH	25	43
		70	97
9b	n-Pr	25	26
		70	80
		120	92

[a] Reaction time: 16 h

5 were prepared according to ref.[10]. The 1,4-dihydropyridines 7 were synthesized according to standard procedures[15]. The dihydro-anthraquinones 9 were obtained from 1,4,5,8-tetrahydroxy-dihydro-9,10-anthracenedione as described in ref.[16,17].

2-Aryl (or Styryl)-1H-benzimidazoles 3

(General Procedure)

To a stirred solution of 1,2-phenylenediamine (5.4 g, 50 mmol) in 75 ml of methanol, 50 mmol of the appropriate aldehyde are added dropwise under N_2 and cooling with ice. Stirring is continued for 30 min at 0°C and for 1h at room temperature. Then benzofuroxan (6.8 g, 50 mmol), dissolved in acetonitrile (25 ml), is added dropwise, and stirring is continued for 2h at 50°C. The reaction is monitored by TLC (Silufol plates, toluene/acetone = 8:2, spraying with 1. $SnCl_2$ and 2. 4-dimethylaminobenzaldehyde).

The reaction mixture is cooled to 5°C, 10 % NaOH (10 ml) is added and the red solution is diluted with 400 ml of water. The precipitate is isolated by suction, washed with water, dried, and recrystallized (Table 1). The alkaline filtrate is acidified with acetic acid, the solid obtained is isolated, washed with ice-cold water, and dried. Yield: 4.5 g (65 %) of o-benzoquinone dioxime 4 (identified by comparison of IR spectra).

2-Arylquinoxalines 6

(General Procedure)

To a solution of 20 mmol of the appropriate 3-aryl-1,2-dihydroquinoxaline in acetone (80 ml) benzofuroxan (20 mmol) is added and refluxed for 5 min. The reaction is monitored by TLC. The reaction mixture is

cooled, filtered, the precipitate is washed with ice-cold acetone, and dried (Table 1).

3,5-Disubstituted 2,6-Dimethylpyridines 8

(General Procedure)

50 mmol of the appropriate 1,4-dihydropyridine 7 and benzofuroxan (6.8 g, 50 mmol), dissolved or suspended in a mixture of ethanol (100 ml) and acetonitrile (50 ml), are refluxed for several hours under stirring (Table 2). After cooling the mixture is diluted with 800 ml of water, th en treated with NaOH (50 %, 30 ml) to render it basic, cooled to 0°C, and the solid obtained is isolated by suction or may be extracted with diethyl ether. The compounds obtained were identified by comparison of IR spectra with those of authentic samples.

1,4-Bis(alkylamino)-5,8-dihydroxy-9,10-anthracenediones 10

(General Procedure)

A solution of 5 mmol of the appropriate dihydro-anthraquinone 9 in ethylene glycol monomethyl ether (150 ml) is purged with N_2 for 20 min. Then benzofuroxan (12 mmol) is added and the mixture is stirred at the temperature given in Table 3 for 16 h. The conversion rate is determined by TLC on Silufol plates (Kavalier) using the solvent system ethyl acetate/ethanol/ aq. NH_3 = 5:3:1. The compounds obtained were identified by comparison of IR spectra with those of authentic samples.

References

1. Niclas, H.-J. and Göhrmann, B., Synth. Commun. 1989, 19, 2141.
2. Niclas, H.-J., Göhrmann, B., and Gründemann, E., Synth. Commun. 1989, 19, 2789.

3. Alexenian, V., Haddadin, M. J., Issidorides, C. H., and Nazer, M. Z., Heterocycles 1981, 16, 391.

4. Yadagiri, B. and Lown, J. W., Synth. Commun. 1990, 20, 955.

5. Golser, L., in: Houben-Weyl, 4th ed., vol. IV/1b, Georg Thieme Verlag, Stuttgart, 1975, p. 967 and lit. cited therein.

6. Weidenhagen, R., Chem. Ber. 1936, 69, 2263.

7. Kiprianov, A. I. and Shrubovich, V. A., Zh. Obshch. Khim. 1959, 29, 1290.

8. Charlton, P. T Ialiphant, G. K., Oxley, P., and Peak, D. A., J. Chem. Soc. 1951, 485.

9. Mahesh, V. K., Maheswari, M., and Sharma, R., Can. J. Chem. 1985, 63, 632.

10. Figueras, J., J. Org. Chem. 1966, 31, 803.

11. Meyer, E. v., J. Prakt. Chem. 1908, 78, 509.

12. Scholtz, M., Chem. Ber. 1897, 30, 2295.

13. Griess, P. and Harrow, G., Chem. Ber. 1888, 21, 2740.

14. Dubur, G. Ya., Ogle, Z. Ya., and Uldrikis, Ya. R., Khim. Geterotsikl. Soedin. 1974, 1642; C. A. 82, 125248 m (1975).

15. Eisner, U. and Kuthan, J., Chem. Rev. 1972, 72, 1.

16. Bayer, O., in: Houben-Weyl, 4 th ed., vol. VII/3c, Georg Thieme Verlag, Stuttgart, 1979, p. 168, 592.

17. Murdock, K. C., Child, R. G., Fabio, P. F., Angier, R. B., Wallace, R. E., Durr, F. E., and Citarella, R. V., J. Med. Chem. 1979, 22, 1024.

18. Mallory, F. B., Org. Synthesis, 1957, 37, 1.

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