Recrystallization from EtOH gave 0.3 g. of white crystals, m.p. 243~245°, which was identified with the authentic sample (m.p. 245°) by IR spectral comparison and by mixed melting point determination.

7) **Heating of 3-Phenacylideneoxindole Hydrazone in Acetic Acid**——A solution of 0.5 g. of 3-phenacylideneoxindole in 5 ml. of AcOH was heated on a boiling water bath for 3.5 hr. The solvent was removed *in vacuo*, and the resulting oily materials was dissolved into $CHCl_3$. The $CHCl_3$ solution was washed with 3% Na_2CO_3 solution, H_2O, and dried. The $CHCl_3$ residue was crystallized by addition of benzene and on standing at room temperature overnight. The crystals was collected by filtration, recrystallized from AcOEt to give 0.32 g. of colorless crystals, m.p. 230°. *Anal.* Calcd. for $C_{18}H_{15}O_2N_3$: C. 70.80; H, 4.95; N, 13.76. Found : C, 70.88; H, 5.05; N, 13.59.

This compound corresponds to 3-phenacylideneoxindole hydrazone monoacetate.

8) **Tosylhydrazone of 3-Phenacyloxindole (VII)**——To a solution of 1.25 g. of I in 20 ml. of EtOH were added 0.9 g. of tosylhydrazine (m.p. 113°) and ca. 10 mg. of tosylchloride as catalyst. The solution was refluxed for 2 hr. The solvent was removed under reduced pressure and resulting solid was filtered and washed with H_2O. Recrystallization from MeOH afforded 1.3 g. (62%) of colorless prisms, m.p. 194° (decomp.). *Anal.* Calcd. for $C_{23}H_{21}O_3N_3S$: C, 65.86; H, 5.05; N, 10.02. Found; C, 66.22; H, 5.20; N, 10.13.

9) **Reaction of VII with Acetic Acid**——A solution of 1.0 g. of Ⅶ in 6 ml. of AcOH was refluxed for 6 hr. and then evaporated to dryness. To the residue was added 10 ml. of H_2O and basified with 10% Na_2CO_3. The resulting precipitate was collected by filtration and recrystallized from EtOH to give colorless needles, m.p. 172~174° (0.5 g.), which was identical with an authentic sample (I).

10) **Reaction of VII with Polyphosphoric Acid**——A mixture of 0.5 g. of Ⅶ and 5.0 g. of polyphosphoric acid was heated on a boiling water bath for 3 hr. After cooling, the reaction mixture was poured into crushed ice. The resulting precipitate was collected by filtration and washed with H_2O, Et_2O sufficiently. Recrystallization from EtOH yielded 0.2 g. of slightly yellow crystals, m.p. 241~245°. This was identified with authentic sample (Ⅲ) by admixture, and IR spectral comparison.

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Summary

Several 3-phenyl-9*H*-pyridazino[3,4-*b*]indoles were prepared by heating 3-phenacyloxindoles and hydrazine hydrate in acetic acid solution.

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154. Kunio Nakagawa, Hiroshi Onoue, and Jitsuo Sugita : Oxidation with Nickel Peroxide. IV.*1 The Preparation of Benzoxazoles from Schiff's Bases.

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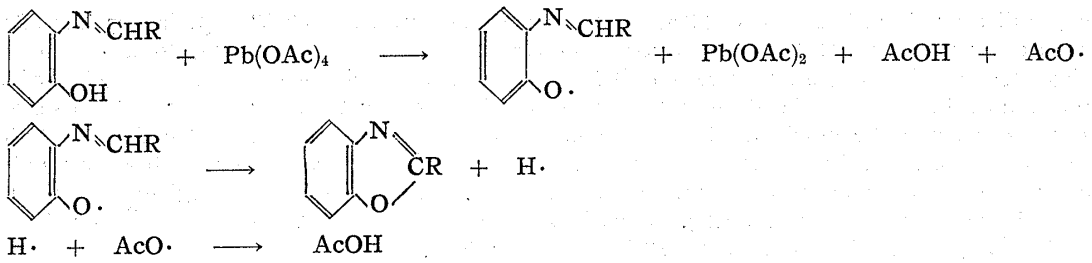
Stephens and Bower reported[1] that the various kinds of Schiff's bases prepared from substituted *o*-aminophenols and benzaldehydes readily underwent dehydrogenation by lead tetraacetate in benzene or acetic acid and caused ring closure to form 2-phenylbenzoxazole derivatives. He proposed that the ring closure of Schiff's bases by lead tetraacetate proceeds by a free radical mechanism described as follow.

*1 Part I: J. Org. Chem., **27**, 1597 (1962); Part II: This Bulletin, **11**, 296 (1963); Part III: *Ibid.*, **12**, 403 (1964).

*2 Fukushima-ku, Osaka (中川国夫，尾上 弘，杉田実男).

1) F. F. Stephens, J. D. Bower : J. Chem. Soc., **1949**, 2971; **1950**, 1722.



This mechanism suggested to us that a hydroxyl radical might play the same role to that of the acetoxy radical in these kinds of reaction.

TABLE I. Benzoxazoles from Schiff's Bases

Benzoxazole[a]	Reaction Temp. (°C)	Conditions (hr.)	m.p.[b] (°C)	Yield (%)	Color
2-Phenyl	15	1	102~103	72.0	white
2-(*o*-Nitrophenyl)[f]	15	1	104~105	60.6	pale yellow
2-(*m*-Nitrophenyl)	15	1	211.5~212	76.6	white
2-(*p*-Nitrophenyl)	15	1	268~269	72.7	pale yellow
2-(*p*-Cyanophenyl)[g]	15	1	207~208	69.3	white
2-(*p*-Dimethylaminophenyl)	15	1	181.5~183.5	65.7	〃
2-(*p*-Methylphenyl)	15	1	115.5~116	72.8	〃
2-(*p*-Methoxyphenyl)	15	1	100~101	72.4	〃
2-(*o*-Hydroxyphenyl)	15	1	122~123	19.6	〃
〃	0[c]	1	122~123	23.0	〃
2-(*p*-Chlorophenyl)	15	1	150~151	71.4	〃
2-Phenyl-5-nitro	60	1	171.5~172.5	71.8	〃
2-(*p*-Nitrophenyl)-5-nitro	75	1	258~259	73.0	pale yellow
2-(*p*-Methoxyphenyl)-5-nitro[h]	50	1	184~186	72.7	yellow
2-(*p*-Chlorophenyl)-5-nitro[i]	50	1	218~219	65.2	white
2-(*p*-Cyanophenyl)-6-nitro	70	1	210~211	66.2	〃
2-(*p*-Nitrophenyl)-6-nitro	70	1	219.5~220.5	77.9	pale yellow
2-(*p*-Nitrophenyl)-5-chloro[j]	50	1	242~243.5	63.9	〃
2-Phenyl-5-chloro	15	1	103.5~105	70.0	white
2-(*p*-Methoxyphenyl)-5-chloro[k]	15	1	150.5~152.5	62.0	〃
2-(*p*-Chlorophenyl)-5-chloro[l]	0[c]	1	192~193	73.6	〃
2-(*p*-Nitrophenyl)-5-methyl	60	0.5	211~211.5	76.3	yellow
2-(*p*-Chlorophenyl)-6-chloro	15	1	146.5~147	47.5	white
2-Styryl	−5~−10[c]	1	80~81.5	61.0	〃
2,2′-(*p*-Phenylene)dibenzoxazole	15	1.5	339~341[e]	83.5	〃
2-Furyl[d]	15	1	86~86.5	28.3	〃

a) All analytical values were in good accord with the molecular formula.
b) Melting points were corrected by standard substances.
c) Oxidation was carried out in Et_2O.
d) Product was obtained from the oxidation of a mixture of *o*-aminophenol and furfral.
e) Melting point was not corrected.
f~*l*) These substances have not been reported in literature.
Analytical values were as follows.

	Found				Calcd.			
	C	H	N	Cl	C	H	N	Cl
f)	64.99	3.36	11.66	—	65.05	3.41	11.41	—
g)	76.34	3.66	12.72	—	76.64	3.80	12.63	—
h)	62.21	3.74	10.37	—	62.45	3.81	10.42	—
i)	56.84	2.57	10.20	12.91	57.10	2.66	10.39	12.81
j)	56.84	2.57	10.20	12.91	57.28	2.78	10.45	12.89
k)	64.74	3.89	5.39	13.73	64.99	3.91	5.33	13.95
l)	59.12	2.68	5.30	26.84	59.36	2.72	5.29	26.48

m) The compounds, which was not given an analytical value above, are already known concerning their authentic preparative method and their properties, for example, see F.F. Stephens, J.D. Bower: J. Chem. Soc., **1949**, 2972; *Ibid.*, **1950**, 1725.

In the previous paper,[2] we reported that nickel peroxide capable of generating a hydroxyl radical in an aprotic solvent was much more convenient reagent than lead tetraacetate for oxidative spilitting of some α-glycols. The mechanism of the α-glycol spilitting with lead tetraacetate was suggested by Waters[3] due to dehydrogenation by an acetoxy free radical.

From the consideration of this analogous behaviour of nickel peroxide and lead tetraacetate, we studied an application of nickel peroxide for the above oxazole formation.

Solid nickel peroxide[4] was prepared by the treatment of an aqueous solution of nickel sulfate with sodium hypochlorite in an alkaline solution as described in Part 1. Its quantity used in stoichiometric oxidation was calculated on the basis of the active oxygen content determined by iodometry.

The various kinds of Schiff's bases containing a variety of substituents in the benzene-ring, *e.g.*, chloro, nitro, cyano, and methoxy, were prepared from corresponding substituted *o*-aminophenols and benzaldehydes in ethanol by the method described in the general procedure.

Oxidation of the Schiff's bases was carried out as follow. The calculated amount of nickel peroxide was added gradually by stirring to a solution or suspension of the Schiff's base in benzene or ether at room temperature. The stirring was continued at room temperature or higher temperature in some cases, until the colour of the nickel peroxide was turned to gray (taking 10 minutes or an hour). After removal of nickel peroxide, the filtrate was concentrated and dissolved in a mixture of benzene and hexane.

Purification of the product was easily enough to be effected by merely filtering the solution through a glass tube containing a proper quantity of alumina. The product of oxidation was obtained in almost pure state by evaporation of the solvent. The yields from Schiff's bases were similar to that of the oxidation using lead tetraacetate.

Therefore, the oxidation with nickel peroxide is a much convenient and economical method because the work-up procedure is very simple and the oxidant can be stored at room temperature without a drop of activity for a long time and the oxidant recovered after the oxidation reaction can be renewed with alkaline hypochlorite solution.

Experimental

Preparation of Schiff's Bases——The Schiff's bases were prepared by the general method described for *o*-(*p*-nitrobenzylideneamino)phenol.

Preparation of *o*-(*p*-Nitrobenzylideneamino)phenol——*o*-Aminophenol (5.5 g.) in EtOH (30 ml.) was added to a solution of *p*-nitrobenzaldehyde (7.1 g.) in boiling EtOH (20 ml.). The mixture was boiled for 15 min. and cooled, and the product (10.5 g.) was obtained by filtration. Recrystallisation from EtOH gave yellow needles, m.p. 160.5~161° of the Schiff's base.

Determination of Available Oxygen of Nickel Peroxide——Available oxygen-content in nickel peroxide was determined by iodometry as shown in Part I. It contained after washing and drying at roon temperature about 3.5 mg.-atom active oxygen per gram.

Preparation of Benzoxazoles——Unless otherwise stated, the benzoxazoles detailed in Table I were obtained by the general method described in a following preparation of 2-(*m*-nitrophenyl)benzoxazole.

Preparation of 2-(*m*-Nitrophenyl)benzoxazole——To a suspension of *o*-(*m*-nitrobenzylideneamino)-phenol (2.423 g.) in benzene (50 ml.), 3.61 g. of nickel peroxide (1.1 times as much as the theoretical amount) was added gradually under stirring on a magnetic stirrer, and the heterogenous solution was allowed to react at 15° for 1 hr. The reaction mixture was filtered through a glass filter, nickel peroxide was washed with benzene, and the filtrate was concentrated to remove the solvent. After dissolving in a mixture of benzene and hexane (1:1), the mixture was chromatographed on alumina (40 g.).

2) Part Ⅲ: This Bulletin, **12**, 403 (1964).
3) W. A. Waters: Trans. Faraday Soc., 42, 184 (1946).
4) Nickel peroxide is a name expediently applied to designate the higher oxide of nickel which is formed by the reaction described in Part I.

2-(*m*-Nitrophenyl)benzoxazole was obtained from the first elute fraction by removal of the solvent (1.84 g., m.p. 211.5~212°).

Summary

Nickel peroxide, readily obtainable by the treatment of an aqueous solution of nickel sulfate with sodium hypochlorite in an alkaline solution, was shown to be a useful oxidizing agent for a preparation of substituted 2-phenylbenzoxazoles from the corresponding Schiff's bases in benzene or ether.

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155. Masahiro Nakadate, Chikako Matsuyama, and Michiya Kimura : Fundamental Studies on Clinical Chemistry. VII.*1 Janovsky Reaction of Polynitrodiphenyl Compounds.

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Since Janovsky[1] found that *m*-dinitrobenzene produced a color with acetone in the presence of alkali, the reactions of various nitrobenzene derivatives with active methylene compounds have been studied by many groups of workers. *m*-Dinitrobenzene,[2] 3,5-dinitrobenzoic acid,[3] 1,3,5-trinitrobenzene,[4] picric acid,[5] 2,2',4,4'-tetranitrobiphenyl[6] and some other *m*-dinitrobenzene derivatives have been employed for the chemical analysis of different kinds of active methylene compound. These methods, however, still have some defects in the following respects : (1) instability of coloration,[2] (2) interferences by some non-active methylene compounds,[7] (3) larger blank values of reagents in the cases of some polynitrobenzene derivatives, and (4) similar absorption spectra for the different active methylene compounds.[8] Moreover, sensitive methods have been required for micro amount of samples such as those from biological origins.

The present paper describes the studies on the polynitrodiphenyl derivatives which have been expected to give sensitive, stable and bathochromic coloration on the basis of preceding studies in this laboratory. Fifteen polynitrodiphenyl compounds such as 4,4'-dinitro-, 2,4-dinitro, 2,2',4,4'-tetranitro-derivatives of biphenyl, diphenylmethane, diphenyl ether, diphenyl sulfide, diphenylsulfone, and stilbene were examined in anticipation of bathochromic light absorption in their color reactions with active methylene

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*1 Part Ⅵ : Steroids, **4**, 255 (1964).

*2 Kita-12-Jo, Nishi-5-Chome, Sapporo (中舘正弘, 松山智郁子, 木村道也).

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