Aryliminodimagnesium Reagents. XVI.[1] Formation of *o*-Hydroxyazoarenes by Condensation with *o*-Hydroxynitroarenes. Favorable Role of *o*-Hydroxyl Group in the Reaction

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Hydroxy(HO)-azoxy- and -azoarenes were formed by condensation of $ArN(MgBr)_2$ with *o*-, *m*-, and *p*-HO-nitrobenzenes; nuclear substitution took place as a minor or a major pathway. *o*-HO-azobenzene was obtained in sufficiently high yield. Relative yields of the products varied according to the position of HO group and reaction conditions. The yield variation was explained by the effects of relative efficiency of single electron transfer, σ-complexation, and cooperation of reagent molecules.

o-Hydroxyazoarenes are useful chelating reagents,[2] and have usually been prepared by diazotization of appropriate phenols and naphthols.[3] This paper concerns exploration of an alternative procedure for preparing hydroxyazoarenes by condensation of N–Mg reagent, aryliminodimagnesium ($ArN(MgBr)_2$ derived from aniline, IDMg), with some hydroxy(HO)-substituted nitroarenes (Scheme 1).

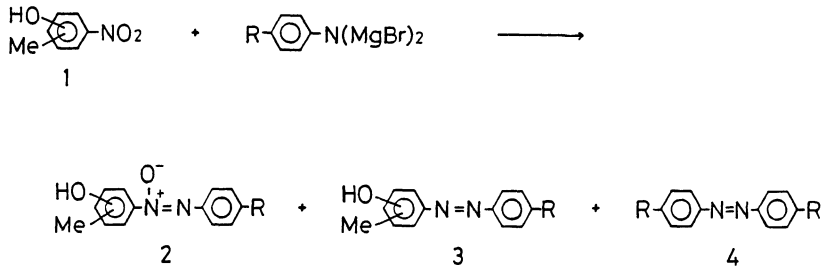
Grignard-type reagent has seldom been applied to HO-substituted substrate, although an example of conversion of 2-HO-5-Me-nitrobenzene (**1a**) into *o*-HO-azoxy- and -azobenzenes by use of *p*-MeC_6H_4-IDMg was reported.[4] A large molar excess of IDMg was used, because at least one mol of the reagent is consumed by exchange with HO-proton. Nevertheless, according to the general pathway,[5] *o*-HO-azoxy product (**2a**) is formed and deoxygenated by molar excess of reagent to give *o*-HO-azo product (**3a**). The alternative procedure using HO-substituted IDMg was impossible.[4]

In order to establish the grounds for synthetic application of IDMg reaction, the effect of HO group on the product distribution was examined using isomeric HO-nitrobenzenes and some related substrates. Condensation and nuclear substitution took place, and the product yields depended greatly on the position of HO group, electron-accepting and -donating abilities (EAA and EDA) of reactants (due to involvement of single electron transfer (SET)), and reaction conditions. Reasons for the variations in types and relative yields of products will be discussed.

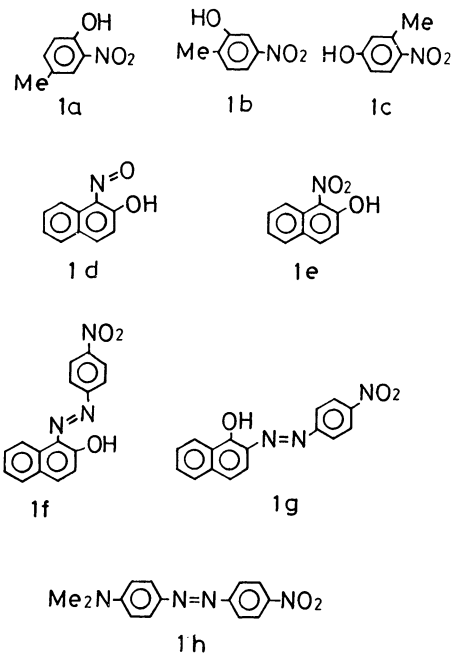
Results and Discussion

The distribution of major and minor products in IDMg reaction of **1a** was compared with that of the products from two positional isomers, 3-HO-4-Me- and 4-HO-2-Me-nitrobenzenes (**1b** and **1c**). The position of HO group of **1a**, **1b**, and **1c** to nitro groups is ortho, meta, and para, respectively. By typical treatments of **1a** with a small (1.9 or 2.0) and a large (8.0) molar excess of *p*-RC_6H_4-IDMg (R=Me, MeO, Cl) at 55 °C for 3 h, the HO-azoxy and HO-azo products (**2** and **3**), symmetrical azoarene (**4** formed via oxidative coupling of IDMg[5]), and nuclear substitution products (**5—10**) were obtained. The yields of products including those obtained from some related substrates (**1d—1h**) are given in Table 1 (Runs 1—18).

The results of Runs 1—6 using *p*-Me reagent and **1a—1c** were complicated, but reveal three noticeable features unexpected from the reported product distributions in IDMg reactions with ordinary nitroarenes.[5-9] First, nuclear substitution products were formed from **1a** and **1b** and not from **1c** (Run 1, 3, and 5). Second, independent of molar amount of reagent used, combined yield of **2** and **3** from **1a** (Runs 1 and 2) was



Scheme 1.



higher than that from **1b** and **1c** (Runs 3—6). Third, also independent of molar amount of IDMg, yield of **3a** was higher than that of **2a** (Runs 1 and 2). Reasons for the unexpected features, however, were explained on the basis of governing factors generally reported for reactions with C–Mg (Grignard) and N–Mg reagents; the relative SET efficiency as a major factor,[6] and σ-complexation[6] and cooperation of reagent molecules[7,8] as minor factors. Discussion will be described in the following sections.

Product Distribution and SET Efficiency. The "first feature" concerns relative SET efficiency estimated by the combination of EAA and EDA.[6] If the redox potentials of substrates cited in Table 1 are compared with the relative yields of **2** plus **3** with reference to those of substitution products (depending on molar amount of IDMg, vide infra), formation of **2** and **3** is favored with strong EAA's (small negative potentials of **1a**, **1b**, **1d**, and 1-nitro-2-naphthol (**1e**)) and not with weak EAA (large negative potential of **1c**). Strong EAA is explained by participation of *o*-quinonoid structure of **1a**, **1d**, and **1e** (Fig. 1). The similar substitution on aromatic ring having low π-electron density is observed in IDMg reactions of quinones without electron-repelling MeO group.[6,9] In contrast to **1c** having *p*-HO group, fairly strong EAA of **1b** due to the lack of electron-repelling resonance of *m*-HO group causes intramolecular successive substitution leading to novel phenazine-type products (**7** and **8**, see Experimental).

The product distribution in the reaction with **1a** is also affected by relative EDA of IDMg (MeO>Me>Cl,[6]

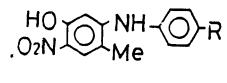
Table 1. Product Distribution in the Reaction of Hydroxynitroarenes with *p*-RC_6H_4-IDMg

Run No.	Substrate (Redn. Pot) (/V)	IDMg R	IDMg molar equiv.	Yield/%[a] 2	3	4	5	6	7	8	9	10	Recovery/%
1	**1a** (−1.080)	Me	1.9	14	33	6	27	—	—	—	—	—	0
2	**1a**	Me	8.0	7	57	19	0	—	—	—	—	—	0
3	**1b** (−1.308)	Me	1.9	13	18	1	—	0	12	0	—	—	37
4	**1b**	Me	8.0	35	7	12	—	0	0	0	—	—	0
5	**1c** (−1.634)	Me	1.9	0	6	2	—	—	—	—	—	—	30
6	**1c**	Me	8.0	3	22	19	—	—	—	—	—	—	0
7	**1a**	MeO	2.0	4	15	3	4	—	—	—	—	—	12
8	**1a**	MeO	8.0	3	43	0	0	—	—	—	—	—	0.6
9	**1a**	Cl	2.0	20	4	2	3	—	—	—	—	—	43
10	**1a**	Cl	8.0	43	17	11	0	—	—	—	—	—	0
11[b]	**1b**	Me	2.0	5	10	0	—	2	20	19	—	—	23
12[c]	**1b**	Me	1.0	0	0	2	—	0	0	0	—	—	93
13	**1d** (−0.898)	Me	3.0	—	5	0.7	—	—	—	—	59[d]	—	20
14	**1e** (−1.068)	Me	3.0	13	13	4	—	—	—	—	13[d]	—	18
15	**1e**	Me	8.0	2	16	13	—	—	—	—	19[d]	—	0
16	**1f** (−0.823)	Me	3.0	34	41	7	—	—	—	—	—	17[e]	0
17	**1g** (−0.870)	Me	3.0	36	44	7	—	—	—	—	—	11[e]	0
18	**1h** (−1.081)	Me	2.0	55	18	9	—	—	—	—	—	—	0

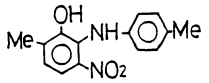
a) Yield based on the amount of substrate used. b) IDMg was added in reverse manner for 100 min and the mixture was heated at 55 °C for 3 h. c) IDMg was added in normal manner and the mixture was heated at 55 °C for 1 h. d) Nuclear substitution and replacement product was obtained as a mixture of tautomer (see Experimental). Product formed via replacement of hydroxynaphthylazo group (see text).

Runs 7—10). In comparison with the results of Runs 1 and 2, strong EDA of *p*-MeO reagent causes rapid deoxygenation leading to higher yield of **3** than **2** but to low overall yield due to self-decomposition of substrate via vigorous SET.[6] Weak EDA of *p*-Cl reagent leads sluggishly to fairly high combined yield of **2** and **3** (the yield of **2** was higher than that of **3**) and leaves a part of **1a** unreacted.

The effects of addition manner and molar ratio are remarkable. By comparison of the results of Runs 3 and 11, "normal addition" of *p*-Me reagent to solution of **1b** favors condensation slightly over substitution compared with "reverse addition." Further comparison of the results of Runs 1 and 2 (using **1a**) reveals that "normal addition" of substrate to large molar excess of IDMg favors condensation. The advantage of these conditions for the condensation with nitro group, due to "cooperation of reagent molecules essential for the pathway," was previously shown by the reaction of *p*-MeC$_6$H$_4$-IDMg with *o*-MeO- and *o*-halo-nitrobenzenes[7] and by that of IDMg having long-chain *p*-alkoxyl substituent.[8] An equimolar amount of *p*-Me reagent added even in "normal manner" to **1b** leads to almost complete recovery (Run 12); this indicates that HO-proton of substrate is precedently exchanged with reagent (vide infra) and the derived



5 (R=Me, MeO, Cl)



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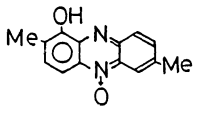

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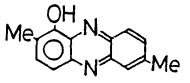

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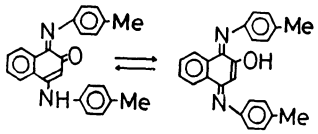

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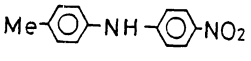
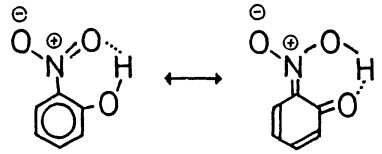


10

5a^R from **1a**; **6**, **7**, and **8** from **1b**;
9 (tautomer) from **1d** and **1e**; **10** from **1f** and **1g**.



ortho-Quinonoid Structure

Fig. 1. Quinonoid structure of *o*-hydroxynitrobenzene.

-OMgBr and -NHMgBr species form a stable complex which is incapable of SET.

Special Role of *o*-Hydroxyl Group. The "second feature" concerns good overall yeilds of four products from **1a** (**2**—**5**, over 80% yield, Runs 1 and 2) and a small amount of unidentified materials compared to the results of Runs 3—6. Though the clean reaction involving effective condensation of **1a** compared to **1b** and **1c** is appropriate for synthetic use of *o*-hydroxy-substituted nitroarenes, the cleanliness seems to contradict with **1a**'s strong EAA causing usually remarkable substitution or decomposition with much rapid SET.[6] The contradiction arises from special role of *o*-HO group, which is converted into "OMgBr acting as a center of IDMg aggregate in the proximity of nitro group" to facilitate the cooperation of IDMg molecules for condensation.[7,8] The aggregation of Grignard molecules in the presence of alkoxymagnesium species was reported.[10] The conversion of *o*-OH into OMgBr prior to SET is established by Run 12 (vide supra), and by the recovery (over 85%) of **1a** from an equimolar mixture with EtMgBr (having stronger EDA than IDMg[6]), which was added at −70 °C in 1 h. The mixture was gradually warmed up to room temperature, stirred at 55 °C for 1 h, and quenched with aqueous NH_4Cl.

It is likely that in the case of **1b** or **1c**, IDMg molecules are gathered by *m*- or *p*-OMgBr group apart from nitro group; condensation is thus retarded and strong EAA of **1b** will cause substitution. The *p*-HO and weak EAA of **1c** are unfavorable for both the pathways, and consequently result in self-decomposition even with mild SET. The steric repulsion caused by *o*-Me group of **1c** may be negligible (see poor combined product yield and recovery in Runs 5 and 6),[7] because the comparable result was obtained by the reverse addition of 8.0 mol of *p*-Me reagent to noncrowded 4-HO-nitrobenzene though the yields of **2**, **3**, and **4** were slightly improved by the normal addition.

Azoxyarene Precursor. Concerning the "third feature," the higher yield of **3a** than **2a** in spite of consumption of one of the two mol of IDMg used in Run 1 is noted. This fact seems to contradict to the usual tendency of yield variation,[5] i.e., the use of small molar excess of IDMg in the reaction with ordinary nitroarenes leads to a lower yield of **3** than **2**.[5] In order to examine the reason for the contradiction, two attempts were carried out: the one to test facile deoxygenation of **2a**, and the other to test facile condensation of *o*-HO-nitrosoarene[5] expected as an intermediate from deoxygenation of **1a**.

Both the two attempts were unsuccessful. First, treatment of pure **2a** (reduction peak potential: −1.438 V) at 55 °C with 5.0 mol of *p*-MeO reagent for 3 h,[5] caused sluggish deoxygenation leading to **3a** in 15% yield and 75% recovery of **2a**. Another attempt was

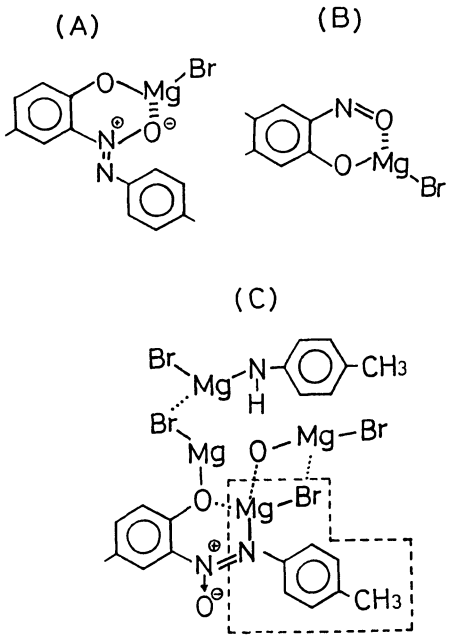


Fig. 2. Depiction of chelates formed in the IDMg reaction. (A): Formed from isolated **2a**. (B): Formed from **1d**. (C): Precursor of **2a** formed from **1a**. A fragment of IDMg is enclosed by broken line.

the treatment of 1-nitroso-2-naphthol (**1d**, reduction peak potential: 0.898 V) with 3.0 mol of *p*-Me reagent at 55 °C (Run 13, **1d** was used instead of nitrosophenol which is difficult to handle because of its high volatility). Yield of the expected 1-arylazo-2-naphthol was 5%, and a nuclear substitution product (cf. Run 14) was obtained in 59% yield. Poor results of the attempts (irrespective of the potential) using isolated **2a** and nitrosonaphthol are ascribed to the formation of Mg chelates (Fig. 2A, 2B): The azoxy and nitroso oxygen atoms incorporated in the chelates may be weakly reactive or almost inert toward IDMg.

As shown by the alternative chelate depicted in Fig. 2C, the "precursor of **2a** formed in the reaction mixture" must involve the ArN moiety of IDMg (enclosed by broken line). As discussed in the preceding section, the precursor 2C must be flanked further by an aggregate of N–Mg species around the OMgBr group. The azoxy oxygen of 2C, not incorporated in the chelate, will be easily attacked by IDMg aggregate and removed.

Reactions of Related Nitroarenes. The results obtained by use of some related nitroarenes (Runs 14—18) were explained similarly as the above discussion. The low overall yield from **1e** by use of both small and large molar excesses of *p*-Me reagent (Runs 14 and 15) is due to decomposition via SET caused by strong EAA. The nitro group of **1e** is sterically hindered by peri-hydrogen, and, at the expense of condensation products (**2e** and **3e**), gives tautomeric compound via substitution-replacement (**9**, the same as that obtained in Run 13, see Experimental). Two noncrowded hydroxy-substituted azonitroarenes (1-(4-NO_2-phenylazo)-2-naphthol and its 2,1-isomer (**1f** and **1g**)) condensed effectively with *p*-Me reagent (3.0 mol, Runs 16 and 17) giving azoxy-azo (**2f** and **2g**, 34—36%) and bis-azo (**3f** and **3g**, 41—44%) products. The slightly higher yield of **3** than **2** is ascribed to azo-OMgBr chelation (Fig. 3). The chelation will enhance the positive charge on azoxy nitrogen to facilitate the removal of oxygen,[5] and will also be responsible for the novel replacement of hydroxynaphthylazo groups leading to 4-Me-4′-NO_2-diphenylamine (**10**, 11—17%).

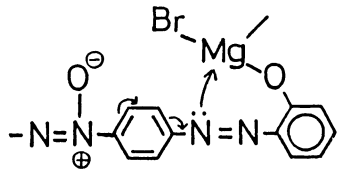


Fig. 3. Illustration of chelation effect on the deoxygenation and replacement in the reaction of **1f** and **1g**.

By comparison, 4-Me_2N-4′-nitroazobenzene (**1h** having no HO group) was treated with 2.0 mol of *p*-Me reagent (Run 18). In spite of strong EAA of **1h**, comparable to **1a** in isolated state, a moderate reaction took place leading to a good combined yield of azoxy-azo (**2h**, 55%) and bis-azo (**3h**, 18%) products. Lack of HO group may be at least partly responsible for the higher yield of **2h** than **3h**. The reaction must be moderated by stabilization of IDMg due to coordination of dimethylamino nitrogen to Mg atom, because the oxidation peak potential of *p*-Me reagent in the presence of equimolar amount of *N,N*-dimethylaniline is larger by ca. 200 mV than the potential in the absence.[5] A similar example of IDMg stabilization by interaction with a remote substituent of nitroarene was reported.[11]

Conclusion

The complicated results of IDMg reactions with HO-substituted nitroarenes were explained on the basis of governing factors and effects of various types of coordination[5–11] originating from strong affinity of Mg with O, Br, and N atoms of substrates. The moderate reactivity of IDMg[6] is responsible for observation of the coordination factors. Though the precise mechanism of condensation still remains to be studied, the grounds for synthetic use of *o*-HO-nitroarenes seem to be established.

Experimental

Procedures and Products. The nitrophenols and nitro- and nitrosonaphthols were commercially available. The isomeric (nitrophenylazo)naphthols were prepared from 1- and 2-naphthols by diazotization using 4-nitroaniline. The preparation of IDMg was previously described,[4] and most of its reactions were carried out under typical conditions at 55 °C for 3 h.

After quenching the reaction mixture with saturated

Table 2. Melting Points and ^{1}H NMR Data of Products

Product No.	Mp θ_m/°C	^{1}H NMR data/δ
2a^{Me}	109—109.5	11.94 (1H, s), 7.80—6.99 (7H, m), 2.42 (3H, s), 2.36 (3H, s)
2b^{Me}	163.5	8.12—7.21 (8H, m), 2.43 (3H, s), 2.33 (3H, s)
2c^{Me}	—[a]	8.12—6.82 (8H, m), 2.60 (3H, s), 2.34 (3H, s)
2a^{MeO}	95	11.91 (1H, s), 8.22—6.97 (7H, m), 3.81 (3H, s), 2.34 (3H, s)
2a^{Cl}	136—137	11.71 (1H, s), 8.09—7.00 (7H, m), 2.36 (3H, s)
2e	—[a]	10.91 (1H, s), 8.55—7.20 (10H, m), 2.39 (3H, s)
2f	244.5—245	16.30 (1H, s), 8.51 (1H, d), 8.43 and 7.77 (4H, ABq. J=8.8 Hz), 8.18 (1H, s), 8.15 (1H, s), 7.74—7.29 (6H, m), 6.79 (1H, d), 2.34 (3H, s)
2g	221—221.5	16.10 (1H, s), 8.42 (1H, s), 8.39 (1H, s), 8.15 (1H, d), 7.56—6.99 (9H, m), 7.69 (1H, s), 7.66 (1H, s), 2.43 (3H, s)
2h	198—199	8.41 and 6.77 (4H, ABq, J=9.3 Hz), 8.17 and 7.30 (4H, ABq, J=8.4 Hz), 7.96—7.90 (4H, m), 3.12 (6H, s), 2.43 (3H, s)
3f	222—222.5	16.41 (1H, s), 8.55 (1H, d), 8.06—7.32 (1sH, m), 6.82 (1H, d), 2.45 (3H, s)
3g	245—246	16.26 (1H, s), 8.43 (1H, d), 8.04—7.51 (11H, m), 7.34—6.87 (2H, m), 2.45 (3H, s)
5^{Me}	153 (sublimed)	11.18 (1H, s), 7.87 (1H, s), 7.23 and 7.13 (4H, ABq, J=8.3 Hz), 6.46 (1H, s), 6.06 (1H, s), 2.38 (3H, s), 2.24 (3H, s)
5^{MeO}	—[a]	11.20 (1H, s), 7.86 (1H, s), 7.15 and 6.97 (4H, ABq, J=2.4 Hz), 6.30 (1H, s), 6.01 (1H, s), 3.85 (3H, s), 2.24 (3H, s)
5^{Cl}	—[a]	7.87 (1H, s), 7.39 and 7.18 (4H, ABq, J=8.8 Hz), 6.50 (1H, s), 6.03 (1H, s), 2.25 (3H, s)
6	Oil	7.58—6.56 (5H, m), 5.78 (1H, s), 2.28 (3H, s), 2.19 (3H, s)
7	167 (sublimed)	8.42 (1H, s), 8.23 (1H, s), 8.03—7.49 (4H, m), 2.62 (3H, s), 2.47 (3H, s)
8	185 (sublimed)	8.22 (1H, s), 8.09—7.60 (5H, m), 2.63 (3H, s), 2.52 (3H, s)
9[b]	178	12.84 (1H, s), 8.90 (1H, d), 7.80—7.12 (13H, m), 2.36 (3H, s), 2.31 (3H, s)
10	138—139	8.11 and 6.85 (4H, ABq, J=2.2 Hz), 7.26—7.09 (4H, m), 6.27 (1H, broad s), 2.36 (3H, s)

a) Melting point was undetermined, because the product was not purified. b) One of the tautomers: the signal at δ 12.84 is assigned to HO-proton.

aqueous NH_4Cl, the products were separated by column and thin-layer chromatography on silica gel (Wako Gel C-200 and C-300). The elemental analyses of products gave satisfactory results. The melting points (uncorrected) and ^{1}H NMR data of **2a—2h**, **3f** and **3g**, **5**^{R}, and **6—10** are given in Table 2. The data for **3a—3e** and **4** are known.

The phenazine-type products (**7** and **8**) formed from **1b** (Runs 3 and 4) arise from substitution at 2-position (cf. **6**) followed by intramolecular attack of a nitrogen radical (derived from nitro group) at the *o*-position of anilino moiety, the precise mechanism being ambiguous. The two tautomeric products (**9**) formed from nitroso- and nitronaphthols (Runs 13—15) arise from substitution at 4-position followed by replacement of nitroso or nitro group; the physical data for the stable one having HO group is given in Table 2. The structure of **9** was confirmed by hydrolysis with aqueous hydrochloric acid to convert into 2-HO-1,4-naphthoquinone and 4-Me-aniline.

Reduction (redox) potentials of substrates were measured by the reported method[6] using bis(biphenyl)chromium(I) tetraphenylborate (BCTB) as an internal reference.

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References

1) Part XIV: See Ref. 7.

2) For example, G. Schetty, *Helv. Chim. Acta*, **52**, 1016 (1969); G. Schetty and E. Steiner, *ibid.*, **55**, 1509 (1972), and literatures cited therein.

3) H. Zollinger, "Color Chemistry," Verlagsgesellschaft, Weinheim (1987).

4) M. Ōkubo, M. Tokisada, and T. Gondo, *Nippon Kagaku Kaishi*, **1985**, 303.

5) M. Ōkubo, T. Takahashi, and K. Koga, *Bull. Chem. Soc. Jpn.*, **56**, 199 (1983); M. Ōkubo and K. Koga, *ibid.*, **56**, 203 (1983).

6) M. Ōkubo, T. Tsutsumi, and K. Matsuo, *Bull. Chem. Soc. Jpn.*, **60**, 2085 (1987); M. Ōkubo, T. Tsutsumi, A. Ichimura, and T. Kitagawa, *ibid.*, **57**, 2679 (1984).

7) M. Ōkubo, Y. Inatomi, N. Taniguchi, and K. Imamura, *Bull. Chem. Soc. Jpn.*, **61**, 3581 (1988).

8) M. Ōkubo, K. Matsuo, and A. Yamauchi, *Bull. Chem. Soc. Jpn.*, **62**, 915 (1989), and literatures cited therin.

9) M. Ōkubo and K. Matsuo, unpublished results.

10) A. D. Vreugdenhil and C. Blomberg, *Recl. Trav. Chim. Pays-Bas*, **84**, 38 (1965); H. O. House, R. A. Latham, and G. M. Whitesides, *J. Org. Chem.*, **32**, 3481 (1967); M. Ōkubo, *Bull. Chem. Soc. Jpn.*, **58**, 3108 (1985).

11) M. Ōkubo, K. Asao, and H. Hyakutake, *Bull. Chem. Soc. Jpn.*, **60**, 3781 (1987).