Medium-sized cyclophanes. Part 76.[1] Synthesis of *syn*-9-methoxy (1,4)naphthaleno[3.3]metacyclophanes and their charge-transfer complexes with tetracyanoethylene in CH_2Cl_2

Jian-yong Hu, Ryuji Ueno, Minoru Miyazaki and Takehiko Yamato*

Department of Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi 1, Saga-shi, Saga 840-8502, Japan

The charge-transfer band of *syn*-9-methoxy(1,4)naphthaleno[3.3]metacyclophanes with tetracyanoethylene in CH_2Cl_2 are observed in the range of 604–606 nm, which is arising from the exclusive formation on the naphthalene ring due to the expanded π-electron density as well as the steric hindrance of the inner methoxy group at 9-position.

Keywords: metacyclophanes, conformation, charge transfer band, through-space interaction

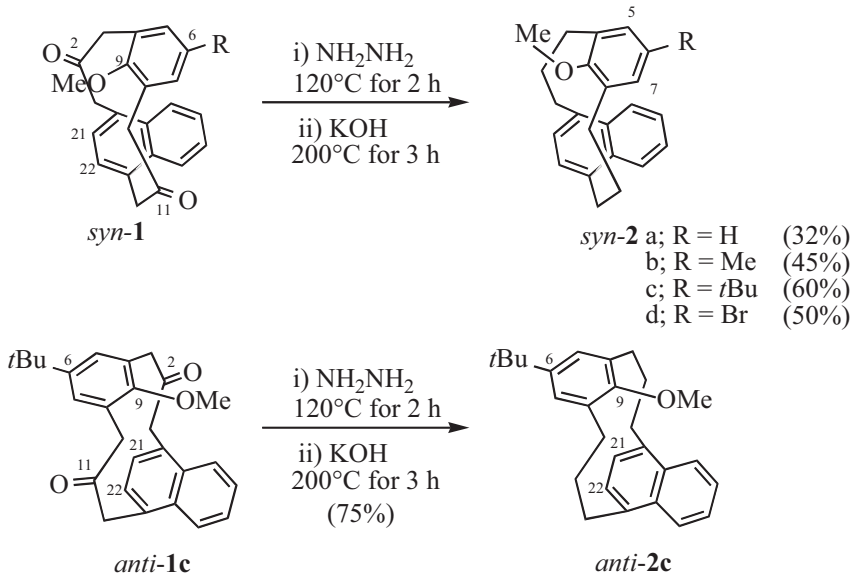
[3.3]MPCP (MPCP = metaparacyclophane) was first prepared by Shinmyozu and co-workers[2] using (*p*-tolylsulfonyl)methyl isocyanide (TosMIC) as the cyclisation reagent, followed by Wolff–Kishner reduction. The meta-bridged benzene ring of [3.3]MPCP has been shown to undergo conformational flipping[2,3] with a significantly lower energy barrier than that in [2.2]MPCP (*ca* 80 kJ mol^{-1}).[4] Recently, we have reported the synthesis of 9-substituted [3.3]MPCP-2,11-diones and conversion to the corresponding [3.3]MPCPs by Wolff–Kishner reduction,[5] and the different orientation for the acetylation was observed depending on the substituent at C (9) position.

On the other hand, we reported the preparation of 2,11-dithia (1,4)naphthaleno[3.3]MCPs (MCP = metacyclophane) and an internal substituent such as Me or OMe group is sufficient to allow the isolation of a discrete *syn* or *anti* isomer.[6] Thus, there is substantial interest that employing a naphthalene ring instead of a benzene ring of the para-bridged ring will provide good information about the π–π-interaction between the two stacking aromatic rings. Furthermore, the conformations of 9-substituted [3.3]MCPs having a naphthalene skeleton are so far not known in spite of the formation of two conformers, *i.e. syn*- and *anti*-conformers, being possible as in 2,11-dithia(1,4)naphthaleno[3.3]MCPs. Thus there is substantial interest in investigating the effects of substituents at positions 6 and 9 on the charge transfer complexes with tetracyanoethylene (TCNE). We report here on the synthesis and charge transfer complexation of series of *syn*-9-methoxy(1,4)naphthaleno[3.3]MCPs (*syn*-**2**) with TCNE.

Results and discussion

Recently, we have reported[6] the preparation of the series of *syn*- and *anti*-9-methoxy(1,4)naphthaleno[3.3]MCP-2,11-diones **1** by the stepwise cyclisation of TosMIC adduct of 4-substituted 2,6-bis(bromomethyl)anisoles with 1,4-bis(bromomethyl)naphthalene in dimethylformamide (DMF) with an excess of sodium hydride. The Wolff–Kishner reduction of *syn*- and *anti*-diketone **1c** afforded the desired *syn*- and *anti*-6-*tert*-butyl-9-methoxy(1,4)naphthaleno[3.3]MCP (**2c**) in 60 and 75% yields, respectively. No syn-anti-isomerisation was observed under the reaction conditions used (Scheme 1). In fact *syn*- and *anti*-**2c** are thermally stable and do not interconvert at 150°C in DMSO solution and at 400°C in the solid state. Similar results were obtained in the case of reduction of *syn*-**1a, 1b** and **1d** to afford the corresponding *syn*-**2a**, **2b** and **2d** in good yields.

The ^1H NMR spectrum (in $CDCl_3$) of *anti*-**2c** exhibits a singlet for the methoxy protons at an upfield shift δ 2.81 ppm from 4-*tert*-butyl-2,6-dimethylanisole (δ 3.83 ppm) due



Scheme 1

* Correspondent. E-mail: yamatot@cc.saga-u.ac.jp

to the ring current of the opposing naphthalene ring.[4,7] The same upfield shift of the inner naphthalene protons (H_{21}, H_{22}) was observed at δ_{MCP}[21,22] 6.24 ppm in *anti*-**2c** [$\Delta\delta$ = 0.93 ppm from 1,4-dimethylnaphthalene, δ_{DMN}[2,3] 7.17 ppm] due to the ring current effect by the opposing benzene ring. These observations strongly suggest that compound *anti*-**2c** adopts the *anti*-conformation. In contrast, the methoxy protons of *syn*-**2c** are observed at δ 3.27 ppm. Further, the aryl hydrogens can clearly be seen to be shielded at δ_{MCP}[5,7] 6.19 ppm by the adjacent naphthalene ring, a common consequence of a face-to-face aromatic ring.[4] Also the *tert*-butyl proton was observed at higher field, δ 0.91 ppm compared to that of the *anti*-**2c** at δ 1.34 ppm due to the strong shielding effect of the naphthalene ring. The above data show that *syn*-**2c** is the *syn*-conformer. Similarly, the assignments of structures for other *syn* conformers *syn*-**2a**, *syn*-**2b** and *syn*-**2d** were readily apparent from their ^{1}H NMR spectra.

The chemical shifts of the protons of the internal methoxy group at position 9 as well as the naphthalene and benzene rings of *syn*-**2a**–**d** and *anti*-**2c** and the differences (Δδ) in the chemical shifts of **2** from those of 5-substituted 2-methoxy-*m*-xylenes (MX) **3** and 1,4-dimethylnaphthalene **4** are also shown in Table 1.

The effect of the ring current of the opposite aromatic ring on the internal protons may be judged by the values of the shift differences (Δδ) since there is no ring current of the opposite aromatic ring in the 1,4-dimethylnaphthalene **4** and the corresponding 5-substituted 2-methoxy-*m*-xylenes (MX) **3**. The data of Table 1 show that the protons of the OMe group of the *anti*-conformer are clearly shifted upfield (Δδ = 1.20 ppm) by the strong ring current of the opposite naphthalene ring, unlike in the *syn*-conformer. In contrast, the methoxy protons of *syn*-**2a,** *syn*-**2b** and *syn*-**2d** are observed at δ 3.26–3.27 ppm. Further, the chemical shifts of the protons at positions 3 and 4 of the meta-substituted benzene ring ($H_{5,7}$) of *syn*-conformers are observed at a much higher field than those of conformer *anti*-**2c**, the values of the difference (Δδ) of *syn*-conformer being δ 1.06–1.17 ppm. Further the proton and methyl proton at position 6 in *syn*-**2a** and *syn*-**2b** were observed at upper field, δ 5.96 and 1.52 ppm (Δδ= 1.18 and 0.80 ppm, respectively) due to the strong shielding effect of naphthalene ring.

A solution of *syn*-6-*tert*-butyl-9-methoxy(1,4)naphthaleno [3.3]MCP (*syn*-**2c**) and TCNE in CH_2Cl_2 present a reddish brown colour and the charge-transfer band at 604 nm (log ε = 0.913) was observed in its UV spectrum. This absorption is due to the formation of 1 : 1 charge-transfer complex among the electron donor, [3.3]MCP and the electron acceptor, TCNE. The position of absorption maximum and the shape of absorption curve remain unchanged when a 4-12-fold excess of TCNE was added. The charge transfer band positions of other *syn*-9-methoxy(1,4)naphthaleno[3.3]MCPs (*syn*-**2a, 2b** and **2d**)-TCNE complexes are summarised in Table 2.

TCNE complexes have often been used in studies on the relative π-base strength of various methyl-substituted benzenes.[8] The π-basicity of the donor molecules increases with an increase in the number of substituted methyl groups and/or stacking benzene rings and an increase in the face-to-face overlapping between aromatic nuclei. In contrast to the cyclophanes having symmetric donor-sites, unsymmetric cyclophanes containing non-equivalent donor-sites such as 4-acetyl- and 4-methoxy[2.2]paracyclophanes[9] can be expected to form two isomeric one-to-one complexes with TCNE, *i.e.*, pseudo-configurational isomers.[10] An important factor for determining which isomeric compex is more predominant or exclusive is the magnitude of ionisation potentials of the constituent donor moieties. Similarly, two possible pseudo-configurational isomers **A** and **B** are also expected for the one-to-one complex of 9-methoxy(1,4)naphthaleno- [3.3]MCPs (*syn*-**2**) as shown in Fig. 1.

In studying the electronic spectra of *syn*-**2**-TCNE complexes, it is advantageous to examine that of the TCNE complex of [2.2]MPCP (**5**). In contrast to [2.2]MPCP (**5**), which exhibits the charge-transfer absorption band with TCNE at 486 nm (log ε = 2.415), a mixture of TCNE and 8,16-dimethoxy[2.2] MCP (**6**) exhibit no band in the visible region.[11] However, the charge transfer absorption band of the reference compound,

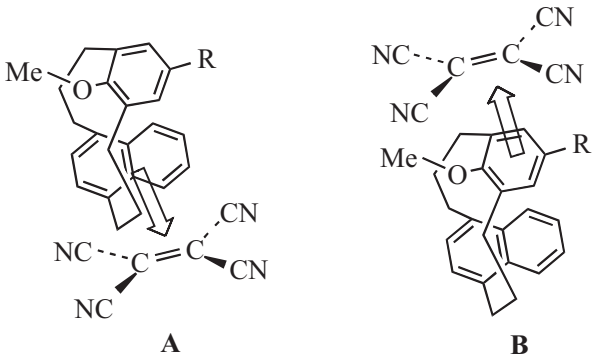


Fig. 1 Two possible charge transfer complexes of *syn*-(1,4) naphthaleno[2.2]metacyclophanes *syn*-**2** with TCNE.

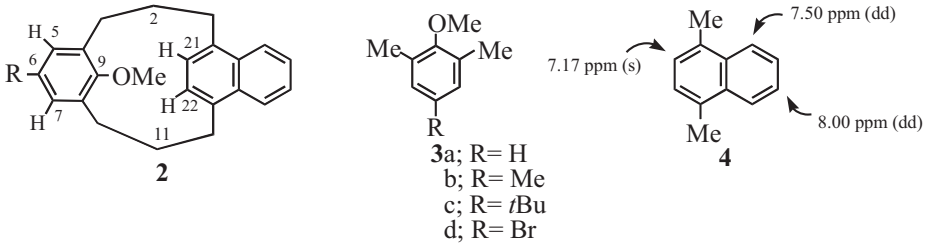


Table 1 Chemical shifts (δ) of the protons of the internal groups of *syn*- and *anti*-(1,4)naphthaleno[2.2]metacyclophanes **2**[a]

Compound	Methoxy protons δ_{OMe} ($\Delta\delta_{OMe}$[b])	Benzene protons $\delta_{H5,7}$ ($\Delta\delta_{H5,7}$[b])	Naphthalene protons $\delta_{H21,22}$ ($\Delta\delta_{H21,22}$[b])	R δ_R ($\Delta\delta_R$[b])
Syn-**2a**	3.26 (0.76)	6.25 (1.12)	7.11 (0.06)	5.96 (1.18)
Syn-**2b**	3.27 (0.75)	6.15 (1.06)	7.09 (0.08)	1.52 (0.80)
Syn-**2c**	3.27 (0.74)	6.19 (1.07)	7.12 (0.05)	0.91 (0.40)
Syn-**2d**	3.26 (0.76)	6.32 (1.17)	7.08 (0.09)	– –
Anti-**2c**	2.81 (1.20)	6.80 (0.46)	6.24 (0.93)	1.34 (-0.03)

[a]Determined in $CDCl_3$ by using $SiMe_4$ as a reference and expressed in ppm.
[b]$\Delta\delta$ = δ [MX] – δ [MCP].

Table 2 Charge transfer bands of π-π salts of *syn*-(1,4)naphthaleno[3.3]metacyclophane *syn*-**2a**–**2d** with TCNE in CH_2Cl_2[a]

Compounds	R	λCT (nm)	log ε
Syn-**2a**	H	604	1.381
Syn-**2b**	Me	604	1.072
Syn-**2c**	tBu	604	0.913
Syn-**2d**	Br	606	1.086

[a]The complexes were prepared in CH_2Cl_2 using equimolar quantities of substrate and TCNE at 25°C.

2,6-dimethylanisole (**3a**) with TCNE was observed at 455 nm (log ε = 1.287). Complexing with TCNE is considered to be difficult owing to steric hindrance of methoxy group at 8-position in the latter case in spite of the increased π-basicity of the benzene ring by the methoxy groups. Thus the observed CT-bands of *syn*-**2**-TCNE complexes are supposed to be attributed to the naphthalene-site complex, but not to the 9-methoxy substituted benzene-site one. Although the charge-transfer of **5**-TCNE complex exhibits an absorption peak at 486 nm, that of *syn*-**2a** is shifted to 604 nm. Such a red shift could be due to the naphthalene ring which tends to work as an expanded π-electron donor. Introduction of the electron-donating group such as methyl or *tert*-butyl group at 6-position does not cause a larger red shift for the CT-band of *syn*-**2b** and *syn*-**2c**, respectively, due to the increased transannular π-electron donation from the non-complexed *meta*-benzene ring to the complexed naphthalene ring. Similarly, the CT-band of *syn*-**2d** having the electron-withdrawing group such as bromine at 6-position was also observed at almost same wave length (606 nm) as that of *syn*-**2a** in spite of being certainly electron withdrawing by the over-all transannular effect of the uncomplexed ring. These findings strongly support the observed CT-bands of *syn*-9-methoxy(1,4)naphthaleno[3.3]MCPs (*syn*-**2**)-TCNE complexes should be attributed to the (1,4)naphthalene-site complex.

In conclusion, the present study indicates that the substituents at the 6-position do not effect the complexation of 9-methoxy(1,4)naphthaleno[3.3]MCPs (*syn*-**2**) with TCNE. Through space electronic interaction of the opposite uncomplexed benzene ring is negligible. The further studies on the charge transfer complexes of 9-substituted (1,4)naphthaleno[3.3]MCPs are now in progress.

Experimental

All melting points are uncorrected. ^{1}H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me_4Si as an internal reference. IR spectra were measured as KBr pellets on a Nippon Denshi JIR-AQ2OM spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-HX110A Ultrahigh Performance Mass Spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.

Materials

Preparation of *syn*- and *anti*-9-methoxy(1,4)naphthaleno[3.3]MCP-2,11-diones **1** was carried out as previously reported.[6] The TCNE was recrystallised twice from chlorobenzene and sublimed twice at 125°C (4 mmHg).

Wolff–Kishner reduction of **1**

Typical procedure: A mixture of *syn*-**1c** (800 mg g, 2 mmol), KOH (930 mg, 16.7 mmol), 100% hydrazine hydrate (1.9 cm^3, 38.2 mmol), and triethylene glycol (26 cm^3) was heated at 120°C for 2 h and then at 200°C for 3 h. The cooled mixture was poured into water (50 cm^3), acidified with diluted HCl, and extracted with CH_2Cl_2 (3 × 50 cm^3), washed with water (2 × 20 cm^3), dried with Na_2SO_4, and concentrated under reduced pressure. The residue was chromatographed on silica gel using hexane as eluents to give *syn*-**2c** (446 mg, 60%) as a colourless solid. Recrystallisation from methanol afforded *syn*-6-*tert*-butyl-9-methoxy(1,4)naphthaleno[3.3]metacyclophane (*syn*-**2c**) as *prisms*; m.p. 163–165°C; ν_{max}(KBr)/cm^{-1} 2949, 2856, 1479, 1360, 1247, 1021; δ_H($CDCl_3$) 0.91 (9H, s, *t*Bu), 2.11–2.56 (10H, s, $CH_2CH_2CH_2$), 3.42–3.51 (2H, m, $CH_2CH_2CH_2$), 3.27 (3H, s, O*Me*), 6.19 (2H, s, $H_{5,7}$), 7.12 (2H, s, $H_{21,22}$), 7.12–7.15 (2H, m, $H_{15,18}$), 7.59–7.63 (2H, m, $H_{16,17}$); *m/z* 372 (M^+) (Found C, 87.41; H, 8.41. $C_{27}H_{32}O$ (372.56) requires C, 87.05; H, 8.66%).

Compounds *anti*-**2c**, *syn*-**2a**, *syn*-**2b** and *syn*-**2d** were similarly prepared in 75, 32, 45, and 50% yields as shown in Scheme 1.

Anti-6-*tert*-Butyl-9-methoxy(1,4)naphthaleno[3.3]metacyclophane (*anti*-**2c**) was obtained as *prisms* (hexane); m.p. 175–178°C; ν_{max}(KBr)/cm^{-1} 2949, 2856, 1479, 1360, 1247, 1021; δ_H($CDCl_3$) 1.34 (9H, s, *t*Bu), 2.21–3.62 (10H, m, $CH_2CH_2CH_2$), 2.81 (3H, s, O*Me*), 3.37–3.47 (2H, m, $CH_2CH_2CH_2$), 6.24 (2H, s, $H_{21,22}$), 6.81 (2H, s, $H_{5,7}$), 7.40–7.43 (2H, m, $H_{15,18}$), 8.02–8.06 (2H, m, $H_{16,17}$); *m/z* 372 (M^+) (Found C, 87.35; H, 8.54. $C_{27}H_{32}O$ (372.56) requires C, 87.05; H, 8.66%).

Syn-9-Methoxy(1,4)naphthaleno[3.3]metacyclophane (*syn*-**2a**) was obtained as a colourless oil; δ_H($CDCl_3$) 2.21–2.41 (6H, m, $CH_2CH_2CH_2$), 2.60–2.76 (4H, m, $CH_2CH_2CH_2$), 3.23 (3H, s), 3.48–3.54 (2H, m, $CH_2CH_2CH_2$), 5.96 (1H, t, *J* = 5.4 Hz), 6.25 (2H, d, *J* = 5.4 Hz), 7.11–7.12 (4H, m), 7.58–7.62 (2H, m); *m/z* 316 (M^+) (Found C, 87.32; H, 7.53. $C_{23}H_{24}O$ (316.45) requires C, 87.3; H, 7.64%).

Syn-9-Methoxy-6-methyl(1,4)naphthaleno[3.3]metacyclophane (*syn*-**2b**) was obtained as *prisms* (hexane); m.p. 203–204°C; ν_{max}(KBr)/cm^{-1} 3102, 3009, 2871, 2847, 1517, 1501, 1477, 1419, 1394, 1286, 1169, 1035, 855, 820, 777; δ_H($CDCl_3$) 1.62 (3H, s), 2.23–2.77(10H, m, $CH_2CH_2CH_2$), 3.27 (3H, s, O*Me*), 3.48–3.55 (2H, m, $CH_2CH_2CH_2$), 6.15 (2H, s, $H_{5,7}$), 7.09 (2H, s, $H_{21,22}$), 7.18–7.21 (2H, m, $H_{15,18}$), 7.58–7.61 (2H, m, $H_{16,17}$); *m/z* 330 (M^+) (Found C, 87.28; H, 7.96. $C_{24}H_{26}O$ (330.47) requires C, 87.23; H, 7.93%).

Syn-6-Bromo-9-methoxy(1,4)naphthaleno[3.3]metacyclophane (*syn*-**2d**) was obtained as *prisms* (hexane); m.p. 211–212°C; ν_{max}(KBr)/cm^{-1} 3063, 3026, 2989, 2952, 2923, 2856, 2354, 2030, 1871, 1727, 1595, 1572, 1558, 1517, 1502, 1462, 1440, 1422, 1377, 1329, 1255, 1207, 1196, 1167, 1163, 1023, 854, 820, 772, 747 673; δ_H ($CDCl_3$) 2.22–2.41(4H, m, $CH_2CH_2CH_2$), 2.49–2.54 (4H, m, $CH_2CH_2CH_2$), 2.63–2.74 (2H, m, $CH_2CH_2CH_2$), 3.26 (3H, s, O*Me*), 3.48–3.55 (2H, m, $CH_2CH_2CH_2$), 6.32 (2H, s, $H_{5,7}$), 7.08 (2H, s, $H_{21,22}$), 7.30–7.33 (2H, m, $H_{15,18}$), 7.60–7.63 (2H, m, $H_{16,17}$); *m/z* 394, 396 (M^+) (Found C, 69.83; H, 5.83. $C_{23}H_{23}BrO$ (395.34) requires C, 69.88; H, 5.86%).

Received 23 May 2007; accepted 3 July 2007
Paper 07/4662 doi: 10.3184/030823407X228768

References

1 T. Saisyo, M. Shiino, T. Hironaka and T. Yamato, *J. Chem. Res.,* 2007, 141.
2 T. Shinmyozu, T. Inazu and T. Yoshino, *Mem. Fac. Sci., Kyushu Univ.*, 1985, Ser. C **15**, 79.
3 L. Ernst, *Progress in Nuclear Magnetic Resonance Spectroscopy*, 2000, **37**, 47.
4 (a) P.M. Keehn and S.M. Rosenfield (eds), *Cyclophanes*, Academic Press, New York, vols. 1&2, 1983; (b) F. Vögtle, *Cyclophane-Chemistry*, Wiley, Chichester, 1993.
5 T. Yamato, K. Noda and K. Tanaka, *J. Chem. Res. (S)*, 2002*,* 63.
6 T. Yamato, R. Okabe, T. Saisyo, S. Miyamoto and M. Mitazaki, *J. Chem. Res.*, 2006*,* 593.
7 (a) M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 4556; (b) M. Tashiro and T. Yamato, *J. Org. Chem.*, 1983, **48**, 1461; (c) T. Yamato, J. Matsumoto, S. Ide, K. Suehiro and M. Tashiro, *Chem. Ber.*, 1993, **126**, 447; (d) T. Yamato, K. Fujita and H. Tsuzuki, *J. Chem. Soc. Perkin Trans. 1*, 2001, 2089; (e) T. Yamato, K. Fujita, T. Abe and H. Tsuzuki, *New J. Chem*., 2001, **25**, 728; (f) M. Takeshita and T. Yamato, *Angew. Chem. Int. Ed*., 2002, **41**, 2156; (g) M. Takeshita and T. Yamato, *Chem. Lett.,* 2004, **33**, 844; (h) T. Yamato, S. Miyamoto, T. Hironaka and Y. Miura, *Org. Lett.*, 2005, **7**, 3.
8 R.E. Merrifield and W.D. Phillips, *J. Am. Chem. Soc.*, 1958, **80**, 2778.
9 (a) D.J. Cram and R.H. Bauer, *J. Am. Chem. Soc.*, 1959, **81**, 5971; (b) L.A. Singer and D.J. Cram, *J. Am. Chem. Soc.*, 1963, **85**, 1080; (c) M. Sheehan and D.J. Cram, *J. Am. Chem. Soc.*, 1969, **91**, 3553.
10 T. Kaneda and S. Misumi, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 3310.
11 T. Yamato, J. Matsumoto, N. Shinoda, S. Ide, M. Shigekuni and M. Tashiro, *J. Chem. Res. (S)*, 1994, 178.