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Tricyanovinylation of Imidazole Derivatives with Tetracyanoethylene[1)]

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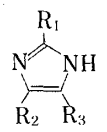
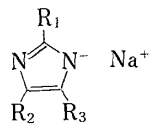
Imidazole, and 4(5)-methyl-, 4(5)-phenyl-, 4,5-diphenyl- and 2-methylimidazole were reacted with tetracyanoethylene (VI) in acetone or tetrahydrofuran at 20 °C. The major reaction products were found to be imidazolium 1,1,2,3,3-pentacyanopropenide derivatives. The minor reaction products were found to be 4(5)-tricyanovinylimidazole, 2,4(5)-bis(tricyanovinyl)imidazole, 4(5)-methyl-5(4)-tricyanovinylimidazole, 4(5)-methyl-2,5(4)-bis(tricyanovinyl)imidazole, 4(5)-phenyl-5(4)-tricyanovinylimidazole, 4,5-diphenyl-2-tricyanovinylimidazole and 2-methyl-4(5)-tricyanovinylimidazole.

Keywords——tetracyanoethylene; 4(5)-tricyanovinylimidazole; 2,4(5)-bis(tricyanovinyl)-imidazole; 4(5)-methyl-5(4)-tricyanovinylimidazole; 4(5)-methyl-2,5(4)-bis(tricyanovinyl)imidazole; 4(5)-phenyl-5(4)-tricyanovinylimidazole; 4,5-diphenyl-2-tricyanovinylimidazole; 2-methyl-4(5)-tricyanovinylimidazole

In our previous study[2)] on the reactions of imidazole (Ia), and 4(5)-methyl-(IIa), 4(5)-phenyl-(IIIa) and 4,5-diphenylimidazole (IVa) with tetracyanoethylene (VI) in dichloromethane (CH_2Cl_2) at room temperature, all of the reaction mixtures showed additional weak bands or shoulders in their ultraviolet (UV) spectra, besides the main absorption bands assignable to imidazolium 1,1,2,3,3-pentacyanopropenide (PCP) derivatives. These observations indicated that the above reactions produce not only imidazolium PCP derivatives but also some by-products. Recently, we reinvestigated the reactions of Ia—IVa and 2-methylimidazole (Va) with VI under different conditions and isolated the by-products. This paper describes the results (Fig. 1).





Ib: $R_1=R_3=H$, $R_2=C(CN)=C(CN)_2$
IIb: $R_1=H$, $R_2=CH_3$, $R_3=C(CN)=C(CN)_2$
IIIb: $R_1=H$, $R_2=C_6H_5$, $R_3=C(CN)=C(CN)_2$
IVb: $R_1=C(CN)=C(CN)_2$, $R_2=R_3=C_6H_5$
Vb: $R_1=CH_3$, $R_2=C(CN)=C(CN)_2$, $R_3=H$

Ic: $R_1=R_2=C(CN)=C(CN)_2$, $R_3=H$
IIc: $R_1=R_3=C(CN)=C(CN)_2$, $R_2=CH_3$

Fig. 1. Structures of Ib—Vb, and Ic and IIc

Results and Discussion

In preliminary experiments, it was observed that the UV absorption maxima of both imidazolium PCP derivatives and of the by-products did not shift significantly on changing the solvent from CH_2Cl_2 to EtOH, or acetone or tetrahydrofuran (THF). The by-products, however, were found to absorb much more strongly in acetone or THF than in CH_2Cl_2 or EtOH. All reactions of Ia—Va with VI, therefore, were carried out in acetone and THF (THF

only in the case of IVa, which is hardly soluble in acetone) at 20 °C for 3 h. Reaction products were separated by silica gel chromatography.

The molecular formula and melting point of the compound obtained from the first fraction of the reaction products of Ia coincided with those of 2,2,3,3-tetracyano-1,1-dimethylcyclopropane (VII).[3] Compound VII was also obtained from the first fractions of the reaction products of IIa, IIIa and Va. Compounds Ib—Vb obtained from the second (the first in the case of IVb) fractions of the reaction products of Ia—Va had the molecular formulae of mono-C_5N_3 derivatives of the respective imidazoles. The C_5N_3 group is considered to be the tricyanovinyl group ($-C(CN)=C(CN)_2$), because firstly this group must be derived from VI and secondly three peaks assignable to highly deshielded carbon were observed in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra of Ib—Vb. Every one of Ib—Vb showed a band assignable to the NH group in their infrared (IR) absorption spectra. Therefore, the tricyanovinyl (TCV) substituent must be located at a carbon atom of the imidazole ring. Protons of two CH groups of Ib were shown to be in clearly different magnetic environments. This result indicates that Ib is 4(5)-tricyanovinylimidazole. If Ib is assumed to be 2-tricyanovinylimidazole, protons of its C(4)H and C(5)H groups are expected to be in practically equivalent magnetic environments. The methyl protons of IIb in acetone-d_6 were found to show signals at about 0.5 ppm lower field than those of IIa (2.28 ppm) in the proton nuclear magnetic resonance (^{1}H-NMR) spectra. Thus, the methyl protons of IIb must be exposed to a large diamagnetic anisotropic effect[4] of the TCV group. Therefore, IIb is concluded to be 4(5)-methyl-5(4)-tricyanovinylimidazole. Compound IIIb is either the 2- or 5(4)-TCV derivative of IIIa. In either case, the spatial relationship between the TCV group and the proton of either C(2)H or C[5(4)]H is almost identical. If IIIb is the 2-TCV derivative, the singlet peak observed at 8.28 ppm in the ^{1}H-NMR spectrum of IIIb in acetone-d_6 is too far down-field to be assignable to C[5(4)]H, because the signals of the C(2)H proton and C[5(4)]H proton of IIIa were found at 7.86 and 7.52 ppm in the same solvent, respectively. Therefore, IIIb is considered to be 4(5)-phenyl-5(4)-tricyanovinylimidazole. Compounds IVb and Vb are 4,5-diphenyl-2-tricyanovinylimidazole and 2-methyl-4(5)-tricyanovinylimidazole, respectively.

In the cases of Ia and IIa, the third fractions afforded reddish-black residues contaminated with imidazolium PCP derivatives, but an attempt to purify the products by recrystallization was unsuccessful. They were, therefore, fractionated by a combination of Amberlite IR-120B(H) column chromatography (to remove Ia or IIa) and silica gel column chromatography to yield reddish-black crystals, Ic and IIc, respectively. Compounds Ic and IIc were sodium salts of the bis-TCV derivatives of Ia and IIa, respectively. If Ic is sodium 4,5-bis(tricyanovinyl)imidazolide, it must have only seven magnetically different carbon atoms. However, at least ten peaks were observed in the ^{13}C-NMR spectrum of Ic in methanol-d_4. This result indicates that Ic is sodium 2,4(5)-bis(tricyanovinyl)imidazolide. Compound IIc is sodium 4(5)-methyl-2,5(4)-bis(tricyanovinyl)imidazolide. It is considered that imidazolium 2,4(5)-bis(tricyanovinyl)imidazolide and 4(5)-methylimidazolium 4(5)-methyl-2,5(4)-bis(tricyanovinyl)imidazolide present in the reaction mixtures of Ia and IIa with VI were converted to Ic and IIc, respectively, during the purification processes using Amberlite IR-120B(H) and silica gel chromatography.

In the cases of Ia—Va, the last fractions gave Id, IId, IIIc, IVc and Vc, respectively. They were shown to be the imidazolium PCP derivatives[2] by thin layer chromatography.

The UV absorption spectra of Ib—Vb measured in CH_2Cl_2 were found to have maxima at 365, 384, 475, 503 and 382 nm, respectively. These absorption maxima coincide well with the observed weak bands at 479 (IIIa) and 506 nm (IVa) or shoulders at about 380 (Ia), 380 (IIa) and 380 nm (Va) in the spectra of CH_2Cl_2 solutions of reaction mixtures of Ia—Va with VI.

Experimental

All melting points were determined on a Yanagimoto MP-500 apparatus and are uncorrected. The UV spectra were recorded with a Hitachi 200-20 spectrometer. The IR spectra were recorded with a JASCO DS-701G spectrometer. The ^{1}H-NMR and the ^{13}C-NMR spectra were measured with JNM PS-100 and JNM FX-100 spectrometers, respectively, using tetramethylsilane as an internal standard. The mass spectra (MS) were measured on a JMS DX300-JMS 2000H spectrometer.

Reaction Products of Imidazole (Ia) with Tetracyanoethylene (VI)——An acetone solution (50 ml) of 1.36 g (0.02 mol) of Ia and an acetone solution (50 ml) of 2.56 g (0.02 mol) of VI were mixed, and the mixture was kept standing at 20 °C for 3 h, then evaporated *in vacuo*. The residue (4.92 g) was dissolved in MeOH–$CHCl_3$ [1 : 9 (v/v)], which will be designated as solvent mixture A, and applied to a column of silica gel (350 g). The faintly yellow residue (0.26 g) obtained from the first fraction was recrystallized from $CHCl_3$ to afford 0.05 g of 2,2,3,3-tetracyano-1,1-dimethylcyclopropane (VII), colorless needles of mp 209—211 °C. *Anal.* Calcd for $C_9H_6N_4$: C, 63.52; H, 3.55; N, 32.93; Mol. wt., 170.17. Found: C, 63.59; H, 3.62; N, 32.93; Mol. wt., 170 (MS *m/e*, M^+). UV (EtOH): no absorption band at longer wavelength than 210 nm. IR (KBr): 2264 (C≡N) cm^{-1}. ^{1}H-NMR (acetone-d_6) δ: 1.82 (s, CH_3). ^{13}C-NMR (acetone-d_6) δ: 19.8 (q, CH_3), 28.0 (s, C(2), C(3)), 41.5 (s, C(1)), 110.5 (s, C≡N). The yellow residue (0.69 g) obtained from the second fraction was recrystallized from EtOH to afford 0.37 g of 4(5)-tricyanovinylimidazole (Ib), yellow needles of mp 260—270 °C (dec.). *Anal.* Calcd for $C_8H_3N_5$: C, 56.80; H, 1.79; N, 41.41; Mol. wt., 169.14. Found: C, 56.91; H, 1.84; N, 41.14; Mol. wt., 169 (MS *m/e*, M^+). UV $\lambda_{max}^{CH_2Cl_2}$ nm: 365; λ_{max}^{EtOH} nm (log ε): 273 (3.56), 368 (4.22); $\lambda_{max}^{acetone}$ nm (log ε): 366 (4.44); λ_{max}^{THF} nm (log ε): 276 (3.61), 367 (4.28). IR (KBr): 3295 (NH), 2260 (C≡N) cm^{-1}. ^{1}H-NMR (in acetone-d_6) δ: 8.07 (1H, s, C(2)H), 8.31 (1H, s, C[5(4)]H), 12.20 (1H, br, NH). ^{13}C-NMR (in acetone-d_6) δ: 85.2 (s, =C(C≡N)$_2$), 112.9 (s, C≡N), 113.7 (s, C≡N), 114.3 (s, C≡N), 129.0 (d, C[5(4)]H), 133.8 (s), 134.7 (s), 140.8 (d, C(2)H). The reddish-black residue (0.34 g) obtained from the third fraction was dissolved in MeOH, and the solution was passed through a column of Amberlite IR-120B (H). The eluate was evaporated *in vacuo*. The residue (0.19 g) was dissolved in EtOH–benzene (C_6H_6) [1 : 3 (v/v)], which will be designated as solvent mixture B, and applied to a column of silica gel (20 g). The residue obtained from the first fraction was recrystallized from MeOH–C_6H_6 [1 : 20 (v/v)] to afford 0.02 g of sodium 2,4(5)-bis(tricyanovinyl)imidazolide (Ic), reddish-black prisms of mp 210—215 °C. *Anal.* Calcd for $C_{13}HN_8Na$: C, 53.43; H, 0.34; N, 38.35. Found: C, 53.42; H, 0.44; N, 38.22. UV $\lambda_{max}^{CH_2Cl_2}$ nm: 532; λ_{max}^{EtOH} nm (log ε): 238 (3.91), 292 (3.86), 334 (3.69), 518 (4.58); $\lambda_{max}^{acetone}$ nm (log ε): 522 (4.72); λ_{max}^{THF} nm (log ε): 240 (3.96), 297 (3.91), 527 (4.72). IR (KBr): 2258 (C≡N) cm^{-1}. ^{1}H-NMR (in methanol-d_4) δ: 8.20 (1H, s, C[5(4)]H). ^{13}C-NMR (in methanol-d_4) δ: 81.2 (s, =C(C≡N)$_2$), 85.2 (s, =C(C≡N)$_2$), 113.3 (s, C≡N), 114.0 (s, C≡N), 114.6 (s, C≡N), 114.7 (s, C≡N), 133.0 (s), 142.0 (s), 147.0 (d, C[5(4)]H), 154.6 (s). The residue (2.47 g) obtained from the last fraction was imidazolium PCP (Id).

Reaction Products of 4(5)-Methylimidazole (IIa) with VI——An acetone solution (50 ml) of 1.64 g (0.02 mol) of IIa and an acetone solution (50 ml) of 2.56 g (0.02 mol) of VI were mixed, and the mixture was kept standing at 20 °C for 3 h then evaporated *in vacuo*. The residue (4.22 g) obtained was dissolved in solvent mixture A and applied to a column of silica gel (350 g). The first fraction gave 0.04 g of VII. The residue (1.31 g) obtained from the second fraction was recrystallized from EtOH to afford 0.83 g of 4(5)-methyl-5(4)-tricyanovinylimidazole (IIb), yellow needles of mp 236—240 °C (dec.). *Anal.* Calcd for $C_9H_5N_5$: C, 59.01; H, 2.75; N, 38.24; Mol. wt., 183.17. Found: C, 59.22; H, 2.83; N, 38.16; Mol. wt., 183 (MS *m/e*, M^+). UV $\lambda_{max}^{CH_2Cl_2}$ nm: 384; λ_{max}^{EtOH} nm (log ε): 279 (3.46), 388 (4.27); $\lambda_{max}^{acetone}$ nm (log ε): 387 (4.28); λ_{max}^{THF} nm (log ε): 282 (3.55), 384 (4.33). IR (KBr): 3233 (NH), 2258 (C≡N) cm^{-1}. ^{1}H-NMR (in acetone-d_6) δ: 2.73 (3H, s, CH_3), 6.94 (1H, br, NH), 7.89 (1H, s, C(2)H). ^{13}C-NMR (in acetone-d_6) δ: 11.9 (q, CH_3), 84.4 (s, =C(C≡N)$_2$), 113.2 (s, C≡N), 114.5 (s, C≡N), 114.7 (s, C≡N), 130.3 (s), 131.7 (s), 138.2 (d, C(2)H), 140.9 (s). The residue (0.45 g) obtained from the third fraction was dissolved in MeOH, and the solution was passed through a column of Amberlite IR-120B (H). The eluate was evaporated *in vacuo*. The residue (0.29 g) was dissolved in solvent mixture B and applied to a column of silica gel (30 g). The residue obtained from the first fraction was recrystallized from MeOH–C_6H_6 [1 : 20 (v/v)] to afford 0.23 g of sodium 4(5)-methyl-2,5(4)-bis(tricyanovinyl)imidazolide (IIc), reddish-black needles of mp 295—310 °C (dec.). *Anal.* Calcd for $C_{14}H_3N_8Na$: C, 54.91; H, 0.99; N, 36.59. Found: C, 54.94; H, 1.08; N, 36.45. UV $\lambda_{max}^{CH_2Cl_2}$ nm: 563; λ_{max}^{EtOH} nm (log ε): 241 (3.98), 308 (3.94), 552 (4.59); $\lambda_{max}^{acetone}$ nm (log ε): 552 (4.70); λ_{max}^{THF} nm (log ε): 245 (3.95), 314 (3.91), 558 (4.68). IR (KBr): 2260 (C≡N) cm^{-1}. ^{1}H-NMR (in methanol-d_4) δ: 2.60 (3H, s, CH_3). ^{13}C-NMR (in methanol-d_4) δ: 15.9 (q, CH_3), 81.0 (s, =C(C≡N)$_2$), 83.6 (s, =C(C≡N)$_2$), 113.4 (s, C≡N), 114.0 (s, C≡N), 114.8 (s, C≡N), 115.5 (s, C≡N), 130.3 (s), 131.9 (s), 139.4 (s), 152.6 (s), 158.7 (s). The residue (1.62 g) obtained from the last fraction was 4(5)-methylimidazolium PCP (IId).

Reaction Products of 4(5)-Phenylimidazole (IIIa) with VI——An acetone solution (50 ml) of 2.88 g (0.02 mol) of IIIa and an acetone solution (50 ml) of 2.56 g (0.02 mol) of VI were mixed, and the mixture was kept standing at 20 °C for 3 h then evaporated *in vacuo*. The residue (5.34 g) was taken up in 50 ml of solvent mixture A, and the insoluble material (1.46 g) was removed by filtration. The insoluble product was 4(5)-phenylimidazolium PCP (IIIc). The filtrate was diluted with solvent mixture A and applied to a column of silica gel (350 g). The first fraction gave 0.05 g of VII. The residue (0.50 g) obtained from the second fraction was recrystallized from C_6H_6 to afford 0.10 g of 4(5)-

phenyl-5(4)-tricyanovinylimidazole (IIIb), red needles of mp 223—227 °C (dec.). *Anal.* Calcd for $C_{14}H_7N_5$: C, 68.56; H, 2.88; N, 28.56; Mol. wt., 245.24. Found: C, 68.61; H, 2.91; N, 28.40; Mol. wt., 245 (MS *m/e*, M^+). UV $\lambda_{max}^{CH_2Cl_2}$ nm: 475; λ_{max}^{EtOH} nm (log ε): 268 (4.15), 316 (3.67), 496 (4.51); $\lambda_{max}^{acetone}$ nm (log ε): 467 (4.35); λ_{max}^{THF} nm (log ε): 255 (4.14), 315 (3.67), 468 (4.36). IR (KBr): 3166 (NH), 2268 (C≡N), 2247 (C≡N) cm^{-1}. ^{1}H-NMR (in acetone-d_6) δ: 7.3—8.1 (5H, m, arom. H), 8.28 (1H, s, C(2)H), 10.60 (1H, br, NH). ^{13}C-NMR (in acetone-d_6) δ: 86.6 (s, $=\underline{C}(C\equiv N)_2$), 112.8 (s, C≡N), 113. 4(s, C≡N), 113.8 (s, C≡N), 125.1 (d), 126.1 (s), 126.6 (d), 129.8 (d), 132.6 (s), 138.8 (s), 147.7 (s). The residue (2.13 g) obtained from the third fraction was 4(5)-phenylimidazolium PCP (IIIc).

Reaction Products of 4,5-Diphenylimidazole (IVa) with VI——A THF solution (200 ml) of 4.40 g (0.02 mol) of IVa and a THF solution (20 ml) of 2.56 g (0.02 mol) of VI were mixed, and the mixture was kept standing at 20 °C for 3 h then evaporated *in vacuo*. The residue (8.18 g) was dissolved in solvent mixture A and applied to a column of silica gel (350 g). The residue (1.56 g) obtained from the first fraction was recrystallized from C_6H_6 to afford 0.14 g of 4,5-diphenyl-2-tricyanovinylimidazole (IVb), reddish-purple plates of mp 258—261 °C (dec.). *Anal.* Calcd for $C_{20}H_{11}N_5$: C, 74.75; H, 3.45; N, 21.80; Mol. wt., 321.33. Found: C, 74.85; H, 3.53; N, 21.65; Mol. wt., 321 (MS *m/e*, M^+). UV $\lambda_{max}^{CH_2Cl_2}$ nm: 503; λ_{max}^{EtOH} nm (log ε): 291 (4.08), 511 (4.54); $\lambda_{max}^{acetone}$ nm (log ε): 489 (4.46); λ_{max}^{THF} nm (log ε): 284 (4.11), 491 (4.46). IR (KBr): 3245 (NH), 2246 (C≡N) cm^{-1}. ^{1}H-NMR (in acetone-d_6) δ: 7.3—7.7 (10H, m, arom. H). ^{13}C-NMR (in acetone-d_6) δ: 86.1 (s, $=\underline{C}(C\equiv N)_2$), 112.9 (s, C≡N), 113.3 (s, C≡N), 114.0 (s, C≡N), 128.8 (s), 129.3 (d), 129.5 (d), 130.1 (d), 130.9 (s), 131.5 (s), 138.2 (s). The residue (4.19 g) obtained from the second fraction was 4,5-diphenylimidazolium PCP (IVc).

Reaction Products of 2-Methylimidazole (Va) with VI——An acetone solution (50 ml) of 1.64 g (0.02 mol) of Va and an acetone solution (50 ml) of 2.56 g (0.02 mol) of VI were mixed, and the mixture was kept standing at 20 °C for 3 h then evaporated *in vacuo*. The residue (4.23 g) was dissolved in solvent mixture A and applied to a column of silica gel (350 g). The first fraction gave 0.04 g of VII. The residue (1.53 g) obtained from the second fraction was recrystallized from EtOH to afford 0.75 g of 2-methyl-4(5)-tricyanovinylimidazole (Vb), yellow prisms of mp 200—202 °C (dec.). *Anal.* Calcd for $C_9H_5N_5$: C, 59.01; H, 2.75; N, 38.24; Mol. wt., 183.17. Found: C, 59.25; H, 2.75; N, 38.21; Mol. wt., 183 (MS *m/e*, M^+). UV $\lambda_{max}^{CH_2Cl_2}$ nm: 382; λ_{max}^{EtOH} nm (log ε): 282 (3.60), 385 (4.25); $\lambda_{max}^{acetone}$ nm (log ε): 382 (4.29); λ_{max}^{THF} nm (log ε): 282 (3.65), 380 (4.29). IR (KBr): 3259 (NH), 2260 (C≡N), 2240 (C≡N) cm^{-1}. ^{1}H-NMR (in acetone-d_6) δ: 2.50 (3H, s, CH_3), 8.20 (1H, s, C[5(4)]H), 11.06 (1H, br, NH). ^{13}C-NMR (in acetone-d_6) δ: 14.2 (q, CH_3), 83.3 (s, $=\underline{C}(C\equiv N)_2$), 112.9 (s, C≡N), 113.8 (s, C≡N), 114.2 (s, C≡N), 130.0 (d, C[5(4)]H), 132.9 (s), 134.9 (s), 150.8 (s, C(2)). The residue (1.75 g) obtained from the third fraction was 2-methylimidazolium PCP (Vc).

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References

1) This paper is Part III of a series entitled "Interaction of Imidazole Derivatives with Electron-Acceptors," Part II, K. Kouno, C. Ogawa, Y. Shimomura, H. Yano and Y. Ueda, *Chem. Pharm. Bull.*, **29**, 301 (1981).
2) K. Kouno and Y. Ueda, *Chem. Pharm. Bull.*, **19**, 2278 (1971).
3) H. Hart and Y. C. Kim, *J. Org. Chem.*, **31**, 2784 (1966).
4) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed., Pergamon Press, Inc., Oxford, 1969, p. 93.