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Interaction of Imidazole Derivatives with Electron-Acceptor. I. Isolation of Imidazolium 1,1,2,3,3-Pentacyanopropenide Derivatives[1]

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A solution of imidazole in dichloromethane developed blue color immediately by an addition of a solution of tetracyanoethylene in the same solvent at the temperature of lower than 0°. The color turned to yellowish brown when the temperature of the mixture was allowed to rise to higher than 0°. A mixing of both solutions at room temperature produced yellowish brown solution, directly. The mixture separated reddish brown crystals when it was stand at room temperature for about 30 min. The absorption maxima at 400 and 418 mμ of the crystals were proved to be attributable to 1,1,2,3,3-pentacyanopropenide anion, and this absorption spectrum was shown to be almost identical with that of the reaction mixture mixed at room temperature. 4(5)-Methyl-, 4(5)-phenyl- and 4,5-diphenylimidazole gave similar results. The chemical structures of these crystals were clarified as imidazolium and substituted imidazolium 1,1,2,3,3-pentacyanopropenide from the results of elemental analyses, infrared spectra, nuclear magnetic spectra, titrations with sodium hydroxide solution, and from the detections of imidazole and imidazole derivatives on thin-layer chromatogram developed by a basic solvent.

The fact that the imidazole derivatives isolated from the color reaction mixtures of urea derivatives and α-dioxo-compounds develop visible color in acidic media,[3] and the fact that the imidazole skeleton is found in a variety of biochemically important compounds brought us much interests on the electronic structure of imidazole molecule.

Imidazole is expected to be an electron–donor, because it has π and lone pair electrons, and actually molecular complex formation was supposed in the initial steps of the substitution reactions of imidazole with I_2[4] or Br_2.[5] And the reports on the formation of molecular complexes of imidazole with $TiCl_4$[6] and pyromellitic anhydride[7] prompted us to investigate the interaction of imidazole derivatives with electron–acceptors such as tetracyanoethylene (TCNE), chloranil and others.

The present experiments on the interaction of imidazole derivatives with TCNE in dichloromethane at the temperature higher than 0° showed that the interaction is not the usual charge–transfer complex formation,[8] but the salt formation of imidazole with 1,1,2,3,3-pentacyanopropene. This paper deals with the isolation and the chemical structure of the salt.

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[1] The main part of this paper was read at the 90th Annual Meeting of the Pharmaceutical Society of Japan (Sapporo) on July 29, 1970.

[2] Location: *Katakasu, Fukuoka.*

[3] Y. Ueda, J. Uchida, J. Kuroki, K. Toyonaga, Y. Watanabe and T. Momose, *Chem. Pharm. Bull.* (Tokyo), **16**, 2442 (1968); K. Kouno and Y. Ueda, *ibid.*, **19**, 110 (1971).

[4] L. Schutte, P. Provókluit and E. Haringa, *Tetrahedron*, *Supplement* No. **7**, 1966, 295.

[5] P. Linda, *Tetrahedron*, **25**, 3297 (1969).

[6] A.D. Garnovskii, O.A. Osipov, V.T. Panyushkin and A.F. Pozharskii, *J. Gen. Chem. USSR* (Eng. Transl.), **36**, 1078 (1966).

[7] B.H.M. Kingston, J.J. Carey and W.B. Jellwig, *Anal. Chem.*, **41**, 86 (1969).

[8] After we reported our result (July, 1970)[1] Takahashi, *et al.* stated in their report (September, 1970)[9] that imidazole and TCNE formed a charge–transfer complex at room temperature, however, their conclusion is clearly incorrect.

[9] F. Takahashi and S. Otsuka, *Nippon Kagaku Zasshi*, **91**, 815 (1970).

Result and Discussion

A mixture of solution of imidazole and that of TCNE both in dichloromethane developed different color depending upon the temperature of the mixed solution. Namely, when the temperature was lower than 0°, it developed blue,[10] but when higher than 0°, it developed yellowish brown (Fig. 1), and when about 0°, blue color was observed for a moment and turned very rapidly yellowish brown *via* green. If the mixture developed yellowish brown color once, the blue color could not be recovered by all means. We assumed at first that the yellowish brown color was due to the molecular complex formation between two reactants, and the composition of the expected complex was spectroscopically analysed by either a continuous variation method or a mole-ratio method. However, during the experiments for this purpose we found that a reaction mixture in dichloromethane precipitated yellowish brown crystals in some cases— the necessary condition to precipitate crystals is under investigation[11]—. Therefore, a small amount (0.5%) of ethanol was added to the solvent in order to prevent the precipitation in succeeding experiments. The addition of ethanol resulted a little bathochromic shift of both absorption maxima of the color (Fig. 1).

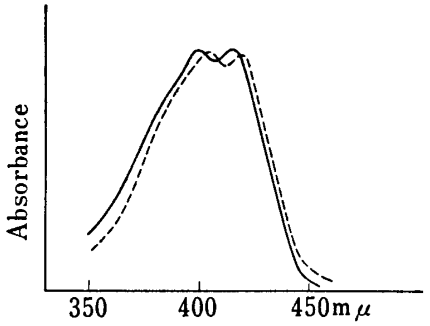

Fig. 1. Absorption Spectra of Reaction Mixture of Imidazole and TCNE

——: reaction mixture in CH_2Cl_2
------: reaction mixture in $EtOH-CH_2Cl_2$ (0.5: 99.5)

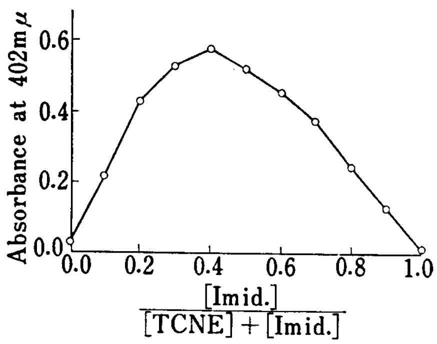

Fig 2. Continuous Variation Method

imidazole: 5×10^{-3}M TCNE: 5×10^{-3}M
solvent: $EtOH-CH_2Cl_2$ (0.5: 99.5)

The results did not give any unambiguous composition of the complex, but they suggested the color had the highest intensity when the ratio of imidazole to TCNE was roughly 2 to 1 (Fig. 2 and 3).

From the experiments mentioned above it is expected that the blue color may be more deeply concerned with the molecular complex formatoin. This is now under investigation.

On the other hand, as described hereinafter, the chemical structure of the crystals precipitated from the reaction mixture was proved to give an important information to the reactions of imidazole derivatives with TCNE at room temperature. Therefore, the authors wish to report the chemical structure of the crystals.

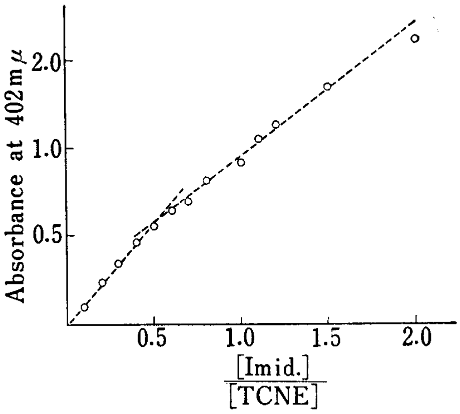

Fig. 3. Mole-ratio Method

TCNE (10^{-2}M): 2 ml
imidazole solutions: 8 ml
solvent: $EtOH-CH_2Cl_2$ (0.5: 99.5)

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[10] F. Takahashi, and S. Otsuka, did not refer the blue color.

[11] F. Takahashi, and S. Otsuka, stated in their report[9] that the mixture of [TCNE]>[Imidazole] in dichloromethane precipitated crystals.

A 5×10^{-4}M solution of imidazole in dichloromethane and an equal volume of 1×10^{-3}M solution of TCNE in the same solvent were mixed together at 0°. The reaction mixture developed immediately blue color and turned to brown color after a very short period, and after a while it precipitated reddish brown plates with fairly good yield.

4(5)-Methylimidazole, 4(5)-phenylimidazole and 4,5-diphenylimidazole gave the corresponding crystals by similar reactions with TCNE.

A reaction mixture in a mixed solvent of acetone and water[12] (10: 1) substituted for dichloromethane developed the same color as in dichloromethane, but did not precipitate any rcystals, and it left the same crystals after evaporation of the solvent.

Recrystallization of the precipitates from methanol–dichloromethane or acetone–dichloromethane afffoded pure crystals I (obtained from imidazole), II (from 4(5)-methylimidazole), III (from 4(5)-phenylimidazole) and IV (from 4,5-diphenylimidazole). Elemental analyses of them clarified that all of the crystals have the common elemental composition of (imidazole–derivative)+(C_8HN_5).

In spite of the remarkable difference of the substituent at 4(5) position of imidazole molecule all crystals have very similar color (yellow), and the main bands of their absorption spectra in visible region were at practically identical wave-length (Table I). Therefore, it may be reasonable to assume that the main bands can be attributed to the common part, C_8HN_5, of the molecules. This assumption received a strong support by the fact that the anion of an acid 1,1,2,3,3-pentacyanopropene (C_8HN_5), which was reported to be produced easily from TCNE in the presence of water and a base, showed strong absorption bands at 412 and 393 mμ.[9] Accordingly, I—IV are highly probable to be the imidazolium or substituted imidazolium salts of 1,1,2,3,3-pentacyanopropene (C_8HN_5).

TABLE I. Spectral Data of I—IV

		I	II	III	IV
UV	$\lambda_{max}^{CH_2Cl_2}$ mμ	400	400	399	399
		418	418	418	418
	$\lambda_{max}^{H_2O}$ mμ	396	396	396	396
		413	413	413	413
	λ_{max}^{EtOH} mμ (ε)	396 (2.49×10^4)	395 (2.02×10^4)	396 (2.01×10^4)	395 (2.23×10^4)
		415 (2.42×10^4)	415 (1.96×10^4)	414 (1.96×10^4)	414 (2.17×10^4)
IR	ν_{max}^{KBr} cm^{-1}				
	NH	3200	3200	3160	3220
	C≡N	2240	2230	2240	2230
NMR[a]	δppm (in $(CD_3)_2CO$)				
	N=CH–N	9.20(1H, s)[b]	9.02(1H, s)[b]	9.35 (1H, d, $J=1.7$ cps)	9.45 (1H, s)[b]
	C=CH	7.83(2H, s)[b]	7.49(1H, s, $J=1.2$ cps)[b]	8.18 (1H,d, $J=1.7$ cps)	—
	NH	11.88(2H, b) 3.93[c]	12.65(2H, b) 4.33[c]	— 3.92[c]	— 3.68[c]
	Arom. H	—	—	*ca.* 7.5—8.0 (5H, m)	7.54 (10H, *s*)
	C=C–CH_3	—	2.48(3H, d, $J=1.2$ cps)	—	—

a) Following abbreviation were used: s, singlet; d, doublet; m, multiplet; b, broad.
b) This signal was somewhat broad.
c) This signal obtained after exchanging by D_2O.

The infrared (IR) spectra of I—IV showed absorption bands at about 3200 and 2240 cm^{-1}, and which were assigned to ν_{NH} and $\nu_{C\equiv N}$, respectively. Nuclear magnetic resonance (NMR)

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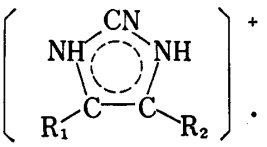
[12] W. J. Middleton, E. L. Little, D. D. Coffman, and V. A. Engelhardt, *J. Am. Chem. Soc.*, **80**, 2795 (1958).

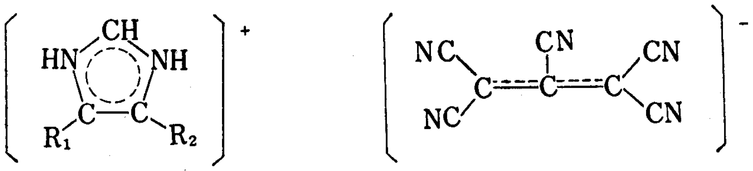
spectra of them determined in $(CD_3)_2CO$ proved that all compounds had one olefinic proton at C_2 position of imidazole ring, one olefinic proton at $C_{4(5)}$ position except IV, and two equivalent NH protons. Therefore, the chemical structure of the cation part of the molecule—not in the strict meaning of the word—, should be



The ionic structure of I—IV was also confirmed by following two experiments: (i) I—IV consumed equimolar sodium hydroxide when they were titrated, and (ii) two spots, one corresponded to the known 1,1,2,3,3-pentacyanopropenide anion[13] and the other corresponded to imidazole derivatives, were recognized on each thin-layer chromatogram of I—IV when developed with a basic solvent (Fig. 4).

Everyone of their mass spectra had a peak at *m/e* of the corresponding molecular weight. In general, the mass spectra of organic salts such as pyridinium 1,1,2,3,3-pentacyanopropenide had no parent peak. Therefore, this fact seemed to be a counterevidence of the ionic structures of I—IV. Although we have no adequate proof now, these peaks may be originated from the artifacts produced in the mass spectrometer.

Now, the chemical structures of I—IV could be elucidated as follows.



I: $R_1=R_2=H$
II: $R_1=CH_3$; $R_2=H$
III: $R_1=C_6H_5$; $R_2=H$
IV: $R_1=R_2=C_6H_5$

The fact that the visible absorption spectra of four reaction mixtures with TCNE in dichloromethane (Fig. 5) could be superimposed on the spectra of I—IV except the regions of a shoulder at about 380 mμ of the reaction mixture of imidazole, of a shoulder at about 465 mμ of 4(5)-methylimidazole, of a weak peak at 479 mμ of 4(5)-phenylimidazole and of a weak peak at 506 mμ of 4,5-diphenylimidazole means that the main interaction of imidazole derivatives with TCNE at room temperature does not terminate at the step of simple molecular complex formation, but it proceeds rapidly from the productions of an acid, 1,1,2,3,3-pentacyanopropene derived from TCNE, to its salt formation with imidazole derivatives.

According to Middleton, *et al.*[12] 1,1,2,3,3-pentacyanopropene is suposed to be produced by a basic hydrolysis of TCNE, however, our results showed that this acid was produced regardless of the presence of water. We consider that the absorption curves of the reaction mixture of imidazole with TCNE in acetone or acetonitrile reported by Takahashi, *et al.*[9] can be attributed to the spectrum of the anion $C_8N_5^-$. Dichloromethane employed in our work was purified twice by careful fractional distillations in a 40 cm Widmer column and discards of the initial boiling fraction, and it was thought to be practically dry. However, the amount of water in the solvent necessary to produce 1,1,2,3,3-pentacyanopropene in our experiments may be so small, equimolar with TCNE, that we cannot deny the possibility of the existence of a trace amount of water contaminated in dichloromethane. In the case of acetone and acetonitrile a trace amount of water might be much more difficult to remove. In respect of the mechanism of the formation of 1,1,2,3,3-pentacyanopropene from TCNE in dichloromethane we are still continuing our investigation.

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13) Pyridinium 1,1,2,3,3-pentacyanopropenide[12] was employed as a standard substance.

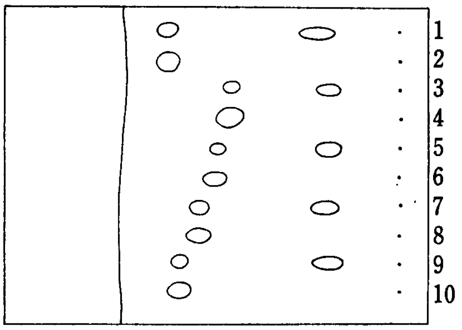

Fig. 4. TLC of I—IV, Pyridinium 1,1,2,3,3-Pentacyanopropenide and Reference Compounds

1: pyridinium 1,1,2,3,3-pentacyanopropenide
2: pyridine 3: I 4: imidazole 5: II
6: 4(5)-methylimidazole 7: III
8: 4(5)-phenylimidazole 9: IV
10: 4,5-diphenylimidazole

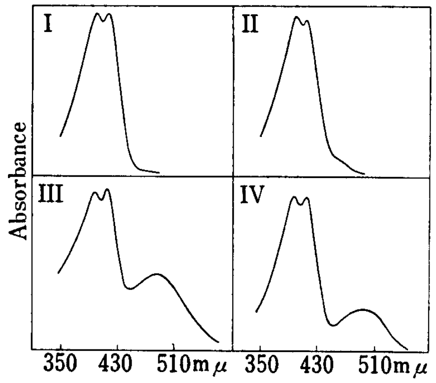

Fig. 5. Absorption Spectra of Reaction Mixtures

I : reaction mixture of imidazole and TCNE
II : reaction mixture of 4(5)-methylimidazole and TCNE
III : reaction mixture of 4(5)-phenylimidazole and TCNE
IV : reaction mixture of 4,5-diphenylimidazole and TCNE
solvent: CH_2Cl_2

Experimental[14]

Isolation of Imidazolium 1,1,2,3,3-Pentacyanopropenide——Imidazole (0.034 g; 0.0005 mole) and TCNE (0.128 g; 0.001 mole) were dissolved in each 50 ml of CH_2Cl_2 separately, and the solutions were cooled to 0°, then mixed together. The mixture developed blue for a moment and turned to brown [λ_{max}: *ca.* 380 (shoulder), 400 and 418 mμ]. The resulting solution was allowed to warm to the room temperature and kept for 30 min, the separated reddish brown plates were collected by filtration. Yield, 60 mg (51%). Recrystallization from CH_2Cl_2–CH_3OH afforded pure crystals of yellow plates of mp 201—202°. *Anal.* Calcd. for $C_{11}H_5N_7$: C, 56.17; H, 2.14; N, 41.69. Found: C, 56.26; H, 2.16; N, 41.42.

A cold (0°) solution of imidazole (0.068 g; 0.001 mole) in a mixture of 10 ml of acetone and 1 ml of H_2O were mixed with a cold (0°) solution of TCNE (0.256 g; 0.002 mole) in the same solvent mixture. The mixture developed blue color for a moment and turned to brown. After keeping it at room temperature for 30 min, the solvent was removed by distillation *in vacuo*. The reddish brown residue was recrystallized from CH_2Cl_2–CH_3OH to afford pure yellow plates of mp 201—202°. Yield, 50 mg (21%).

Isolation of 4(5)-Methylimidazolium 1,1,2,3,3-Pentacyanopropenide——A cold (0°) solution of 4(5)-methylimidazole (0.120 g; 0.0015 mole) in a mixture of 10 ml of acetone and 1 ml of H_2O were mixed with a cold (0°) solution of TCNE (0.380 g; 0.003 mole) in the same solvent mixture, the mixture developed blue color for a moment and turned to brown. After keeping it at room temperature for 30 min, the solvent was removed by distillation *in vacuo*. Recrystallization of the reddish brown residue from CH_2Cl_2–acetone afforded pure yellow needles of mp 155—157° (decomp.). Yield, about 200 mg (56%). *Anal.* Calcd. for $C_{12}H_7N_7$: C, 57.83; H, 2.83; N, 39.34. Found: C, 58.03; H, 2.78; N, 39.56. The reaction mixture in CH_2Cl_2 had visible absorption maxima at *ca.* 465 (shoulder), 401 and 419 mμ.

Isolation of 4(5)-Phenylimidazolium 1,1,2,3,3-Pentacyanopropenide——A cold (0°) solution of 4(5)-phenylimidazole (0.072 g; 0.0005 mole) in 25 ml of CH_2Cl_2 were mixed with a cold (0°) solution of TCNE (0.128 g; 0.001 mole) in 50 ml of CH_2Cl_2. The mixture developed blue color for a moment and turned to yellowish brown (λ_{max}: 400, 420 and 479 mμ). After keeping it at room temperature overnight, the separated reddish brown prisms were collected by filtration. Yield, 70 mg (45%). Recrystallization from CH_2Cl_2–CH_3OH afforded pure yellow needles of mp 227—228°. *Anal.* Calcd. for $C_{17}H_9N_7$: C, 65.59; H, 2.91; N, 31.50. Found: C, 65.65; H, 2.81; N, 31.48.

Isolation of 4,5-Diphenylimidazolium 1,1,2,3,3-Pentacyanopropenide——A cold (0°) solution of 4,5-diphenylimidazole (0.220 g; 0.001 mole) in 150 ml of CH_2Cl_2 were mixed with a cold (0°) solution of TCNE

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[14] All melting points were not corrected. All solvents were purified by repeated fractional distillations with dry equipment and out of contact with moist air. Spectra were measured by the following instruments: electronic absorption spectra by Shimadzu MPS-50L Spectrophotometer, infrared absorption spectra by Nihon-Bunko DS-301 Spectrophotometer equipped with NaCl prisms, nuclear magnetic resonance spectra by JNM C-60H Spectrometer at 60 MHz with TMS as the internal standard, and mass spectra by JMS-01SG Spectrometer.

(0.256 g; 0.002 mole) in 100 ml of CH_2Cl_2. The mixture developed blue color for a moment and turned to brown (λ_{max}: 400, 418 and 506 mμ). After keeping it at room temperature overnight, separated reddish brown prisms were collected by filtration. Yield, 30 mg (8%). Recrystallization from CH_2Cl_2–CH_3OH afforded pure orange yellow prisms of mp 231—232°. *Anal.* Calcd. for $C_{23}H_{13}N_7$: C, 71.31; H, 3.38; N, 25.31. Found: C, 71.14; H, 3.47; N, 25.24.

Thin-Layer Chromatography——Solutions of I—IV in CH_3OH were spotted on a silica gel (WAKOGEL B-5) plate (20 cm × 20 cm × 250 nm) activated at 115° for 1.5 hr, and developed with a clear mixture of 20 ml of CH_3OH and 80 ml of ammoniac $CHCl_3$—a mixture of 20 ml of conc. aq. NH_4OH and 100 ml of $CHCl_3$ were shaken vigorously and the under layer was employed after left to stand 2 min.

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