Oxidation of Triarylimidazoles. Structures of the Photochromic and Piezochromic Dimers of Triarylimidazyl Radicals[1]

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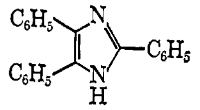
Abstract: Two dimers of the 2,4,5-triphenylimidazyl radical have been prepared and characterized. One compound, an isoimidazylisoimidazole (**3**), is photochromic and thermochromic. The isomeric compound, a bisisoimidazole (**2**), is a piezochromic solid which rapidly dissociates to triphenylimidazyl radicals in solution. Interconversions of **2** and **3** have been carried out and indicate that **3** is more stable than **2**, both in solution and in the solid state. Various substituted triarylimidazoles have been converted to dimers with analogous photo- and piezochromic properties.

A large number of organic materials of various structural classes change color when irradiated with ultraviolet or visible light.[2] These materials are termed photochromic if in the dark or upon exposure to light of a different wavelength the colored species revert to their original forms. Similarly, piezochromic compounds[3] and many thermochromic compounds are known.[4] This report describes syntheses, structural studies, and interconversions of oxidation products of 2,4,5-triarylimidazoles which show photo-, thermo-, and piezochromic properties.

Oxidation of the parent compound, lophine (2,4,5-triphenylimidazole, (**1**), in a solution of potassium hydroxide and ethanol with a dilute aqueous potassium ferricyanide solution at 5° produces a light violet solid (**2**). In the solid state **2** has a very weak esr signal which is enhanced only slightly by irradiation. No change in color is noted during the irradiation. Application of a shearing force by exerting a moderate pressure or dissolution of **2** in most organic solvents produces an intense violet color and a strong esr signal. On standing, the color of the solution rapidly lightens and the esr signal decreases. Evaporation of the solvent and recrystallization from benzene–hexane yields a pale yellow photochromic solid (**3**) which has been described previously.[5] Compound **3** is identical by mixture melting point determination and comparison of infrared spectra with the product obtained from the oxidation of **1** with lead dioxide.[6] The colored species which appears during these reactions has esr and visible spectra which are identical with spectra of the 2,4,5-triphenylimidazyl radical (**4**).[5c]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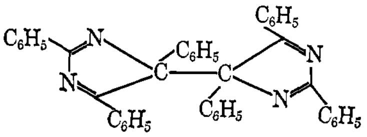
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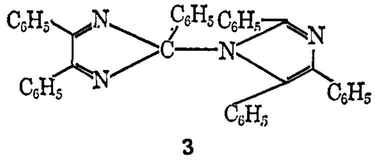
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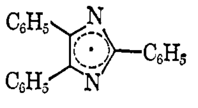
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The structures which are depicted for **2** and **3** in this report differ from the structure proposed previously[7] and are based on the chemical and spectral studies which are described below. Elemental analyses of both compounds are consistent with dimers of **4**, *i.e.*, $C_{42}H_{30}N_4$.[8] The infrared spectra of **2** and **3** differ significantly yet display many similar features (Figure 1).

Compound **3** is converted to **1** quantitatively with lithium aluminum hydride and in approximately 50% yield with either acetic acid or hydrogen chloride. The other products of the reactions with acids appear to be relatively unstable acetoxy- and chlorotriarylimidazoles. Compound **2** is reduced to **1** in 96% yield with lithium aluminum hydride. Thus, there do not seem to be any skeletal rearrangements in the oxidation of **1** to **2** and **3**. These results, with the evidence that (a) **3** is in thermal equilibrium with **4**, (b) **3** can be converted to **4** photolytically, and (c) **2** dissociates to **4** in solution, suggest the triphenylimidazyl moieties are linked by bonds between the imidazole rings. Coupling of one triphenylimidazyl group by a bond between one of its phenyl groups and either a phenyl

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[1] Presented in part at the 144th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1963, p 55M.

[2] R. H. Brown and W. G. Shaw, *Rev. Pure Appl. Chem.*, **11**, 1 (1961); R. Exelby and R. Grinter, *Chem. Rev.*, **65**, 247 (1965).

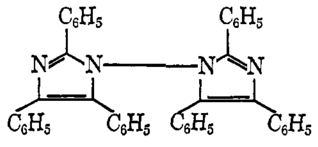
[3] Materials which become colored when shearing forces or pressure are applied; see A. Schönberg, *et al.*, *J. Am. Chem. Soc.*, **80**, 6312 (1958); *J. Chem. Soc.*, 442 (1946).

[4] J. H. Day, *Chem. Rev.*, **62**, 65 (1962).

[5] (a) T. Hayashi and K. Maeda, *Bull. Chem. Soc. Japan*, **33**, 565 (1960); (b) *ibid.*, **35**, 2057 (1962); (c) T. Hayashi, K. Maeda, S. Shida, and K. Nakada, *J. Chem. Phys.*, **32**, 1568 (1960).

[6] H. Zimmermann, H. Baumgärtel, and F. Bakke, *Angew. Chem.*, **73**, 808 (1961); H. Baumgärtel and H. Zimmermann, *Z. Naturforsch.*, **18b**, 406 (1963).

[7] Both Hayashi and Maeda,[5b] and Zimmermann, *et al.*,[6] proposed a hydrazine-type structure for **3**. No structural evidence other than elemental analysis, molecular weight, a negative Zerewitinoff test, and the thermal equilibrium between the dimer and the radical **4** was presented. Isomeric structures were not considered.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[8] Molecular weights of **3** were obtained in benzene by isothermal distillation at 25° in the dark (554), and ebullioscopic measurement (552). Hayashi and Maeda reported a value of 295[5a] and later suggested that **3** was dimeric.[5b] The immediate dissociation of **2** in solution prevented a direct molecular weight determination. The formula $C_{21}H_{15}N$ for **2** can be ruled out, however, since **2** in the solid state does not have an appreciable esr signal.

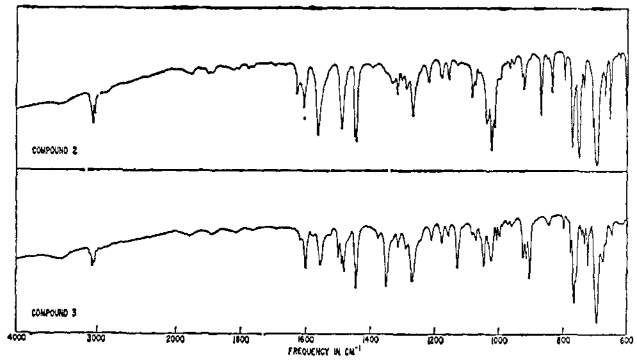
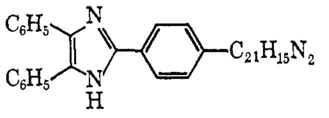


Figure 1.

or the imidazole ring of the other triphenylimidazyl moiety to form a structural unit such as **6** is unlikely. A product such as **6** would contain an NH group which would be detectable by a Zerewitinoff test[6,7] and would be expected to exhibit a broad absorption in the infrared spectrum at 2800 to 2400 cm^{-1} (see Figure 1). Also, compounds such as **6** would be expected to be too stable to exhibit thermochromism in solution at temperatures as low as 60° (*i.e.*, dissociate to **4**) and undergo rapid reduction to **1** with lithium aluminum hydride.



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Six dimer structures are possible when the imidazole rings are linked together *via* bonds between various combinations of the nitrogen atoms and the C_2 and C_4 carbon atoms. These structures can be differentiated by the characteristic infrared absorptions of arylimidazoles and arylisoimidazoles in the 1625- to 1475-cm^{-1} region.[9]

Compound **3** absorbs at 1616 (vw), 1600 (m), 1580 (vvw), 1554 (m), 1540 (vvw shoulder), 1520 (vvw), 1499 (m–w), 1487 (m–w), and 1480 (m) cm^{-1} in the 1625- to 1475-cm^{-1} region. The sharp, medium-weak band at 1499 cm^{-1} is strongly indicative of the presence of an imidzole ring (normally at 1498–1506 cm^{-1}). The band at 1616 cm^{-1} suggests the presence of an isoimidazole ring in addition to the imidazole ring. This is further supported by the absorption at 1554 cm^{-1}. This band lies close to the 2H-isoimidazole region (*i.e.*, 1548–1552 cm^{-1}) and indicates such a moiety in **3**. However, the extent of the frequency range of the 4H-isoimidazole absorption in the 1563-cm^{-1} region[10] has not been determined in detail. Thus, the presence of the 4H-isoimidazole ring cannot be excluded unequivocally by this criterion alone. Compound **2**, however, is shown to contain two isoimidazole rings and these rings absorb at 1562 cm^{-1}, *i.e.*, near the band for the 4H-isoimidazole ring. Thus it seems likely that the 1554-cm^{-1} band is due to the 2H-isoimidazole ring, and compound **3**, on this basis, is the N-2H-isoimidazylisoimidazole depicted in structure **3**.

The piezochromic material **2** absorbs in the region of C=C and C=N stretching vibrations at 1626 (w), 1605 (m), 1562 (s), and 1489 (s). No absorptions are present in the characteristic regions for the imidazole ring or the 2H-isoimidazole ring. The strong band at 1562 cm^{-1} in **2** is very near the frequency for the only strong band (at 1563 cm^{-1}) in 2,4,4,5-tetraphenyl-4H-isoimidazole in the 1575- to 1500-cm^{-1} region. The 1489-cm^{-1} band in **2** is due to the phenyl groups. The simplicity of the spectrum of **2** (compared to **3**; see Figure 1), especially in the region for characteristic heterocyclic and aromatic absorption from 1650 to 1400 cm^{-1}, also supports the possibility that both heterocyclic rings are the same and the molecule is symmetrical about the C_4–C_4 bond. The structure represented by formula **2** is the only one which accommodates the infrared spectrum closely.

The ultraviolet spectra of **2** and **3** cannot be used to unequivocally establish the dimer structures but are consistent with the proposed structures. The two chromophoric groups in each dimer molecule are isolated by quaternary carbon atoms (C_4 and C_4' in **2**; C_2 in **3**) as well as the obvious twisting of the rings from coplanarity. Without extensive conjugation between the heterocyclic rings the ultraviolet spectra of the dimers should approximate the sum of their two conjugated systems. Table I lists the spectral data for **2** and **3** and for several model compounds containing the various possible chromophores. The single absorption at 266 mμ for dimer **3** approximates the sum of the linear combinations of the absorptions for a 2H-isoimidazole ring and an N-substituted imidazole ring (*ca.* 270 mμ).

Table I. Ultraviolet Absorptions of Some Arylimidazoles and Arylisoimidazoles in 95% Ethanol

Compound	λ_{max}, mμ ($\epsilon \times 10^{-4}$)
2,4,5-Triphenylimidazole (**1**)	302 (2.65)
1-Ethyl-2,4,5-triphenylimidazole	276 (2.00)
2,2,4,5-Tetraphenyl-2H-isoimidazole	260 (1.24)
2,4,4,5-Tetraphenyl-4H-isoimidazole	246 (1.98) 257 (1.90) 269 (1.87)
Dimer **2**	268[a]
Dimer **3**	266 (2.80)

[a] Compound **2** is converted to the radical immediately after solution and absorbs strongly at 348 and 550 mμ. These bands rapidly disappear giving a spectrum identical with that of **3**. The value of λ_{max} was determined in a KBr disk and is corrected for the shift caused by solution in ethanol (11 ± 2 mμ for all compounds in this table).

The interconversions of the dimers and the colored triphenylimidazyl radicals in the equilibria presented below can account for the mechanism of photochromism and thermochromism in solution. The thermochromic reactions of the two dimers are represented by the equilibria between **2** and **4** and between **3** and **4**. In solution at room temperature **3** is the more stable

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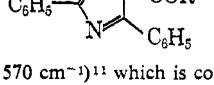
(9) D. M. White and J. Sonnenberg, *J. Org. Chem.*, **29**, 1926 (1964).

(10) In the case of peroxy-4H-isoimidazoles, this absorption occurs

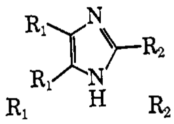


at a higher frequency (1570 cm^{-1})[11] which is consistent with the generally observed increase in frequency with electronegative substituents.[12]

(11) J. Sonnenberg and D. M. White, *J. Am. Chem. Soc.*, **86**, 5685 (1964).

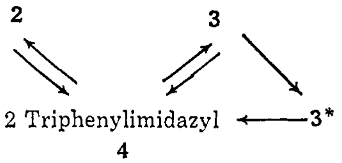
(12) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 390.

Table II. Physical Properties of Some Triarylimidazole Dimers

				Piezochromic dimer		Photochromic dimer	
R_1	R_2	Oxidizing agent[a]	Radical λ_{max}, mμ, in C_6H_6	Mp, °C	Infrared, cm^{-1}	Mp, °C	Infrared, cm^{-1}
C_6H_5	C_6H_5	$K_3Fe(CN)_6$	554	187.5–88.5	1562	202–202.5	1554, 1499
C_6H_5	*m*-ClC_6H_4	$K_3Fe(CN)_6$	561	129–131[c]	1546	165–167[c]	1552, 1501[f]
C_6H_5	*p*-ClC_6H_4	$K_3Fe(CN)_6$	568	195–200[c]	1550	203–205[c]	1559, 1500
C_6H_5	*o*-ClC_6H_4	$K_3Fe(CN)_6$	551[b]	*d*		115–120	1555, 1501
C_6H_5	2,4-$Cl_2C_6H_3$	PbO_2	560[b]			Glass	1554, 1502
C_6H_5	*o*-$CH_3OC_6H_4$	$K_3Fe(CN)_6$	605[b]	*d*		182–185	1555, 1502
C_6H_5	α-Naphthyl	$K_3Fe(CN)_6$	462[b]	*d*		150–165	1555, 1503
p-ClC_6H_4	*p*-ClC_6H_4	$K_3Fe(CN)_6$	583	105–15[e]	1561, 1549	209–210[e]	1553, 1497

[a] Reaction conditions are specified in the Experimental Section. [b] This value for the absorption maximum compares closely with the value reported by L. A. Cescon, South African Patent 633,627 (August 12, 1963). Satisfactory elemental analyses are reported by Cescon for the corresponding photochromic products. [c] *Anal.* Calcd for $C_{42}H_{28}N_4Cl_2$: C, 76.5; H, 4.3; N, 8.5. Found (for 129° dimer): C, 76.9; H, 4.0; N, 8.5. Found (for 165° dimer): C, 76.3; H, 4.5; N, 8.6. Found (for 195° dimer): C, 76.1; H, 4.3; N, 8.7. Found (for 203° dimer): C, 76.4; H, 4.4; N, 8.4. [d] The presence of a small amount of this isomer is indicated by weak piezochromism and low-temperature thermochromism of the reaction product. [e] *Anal.* Calcd for $C_{42}H_{24}N_4Cl_6$: C, 63.2; H, 3.0; N, 7.0. Found (for 105° dimer): C, 62.7; H, 3.2; N, 6.8. Found (for 209° dimer): C, 62.9; H, 3.1; N, 6.8. [f] Absorption bands also occur at 1568 and 1520 cm^{-1} but are much weaker than the characteristic 4H-isoimidazole absorption.[11]

dimer as evidenced by the thermolysis of **2** to **4** and the subsequent formation of **3**. The photochromic reaction of **3** in solution (and similarly in the solid state)



is represented by the formation of an excited dimeric species (**3***) which dissociates to produce the colored radicals. When **3** is photolyzed at −40° the resultant radicals dimerize to form **2** and possibly **3**. Since dimer **2** is only slightly dissociated at −40° and is not photochromic, a substantial buildup of **2** results. Thus, **3** under these conditions is converted to **2** by use of the higher energy intermediate **3***. When the solution of **2** is warmed to room temperature, the colored radical **4** is observed, then slowly fades to **3**.[13]

An alternate method of demonstrating the thermochromism of **2** is to dissolve **2** at room temperature and after several seconds cool the deeply colored clear solution to −40°. Within 20 sec the color fades to a light pink. Rewarming brings back the deep violet color and the cooling-heating cycle can be repeated. Similarly, the cycle can be carried out by initially dissolving **2** in cold solvent to give a light pink solution which becomes dark when warmed.

These interconversions indicate **2**, **3**, and **4** in solution are related energetically according to Figure 2.

Previous workers have studied the relationship between **3** and **4** and have reported values for the activation energies C and D of approximately 7 and 20 kcal/mole, respectively.[6,14] The effect of the equilibrium between **2** and **4**, however, was not considered. The potential energy of **2** in Figure 2 is placed below that of **4** because dimer **2** is only slightly dissociated to **4** at −40°. The fact that some of the radicals **4** are in equilibrium with **2** at −40° indicates that the levels of **2** and **4** are relatively close to each other. Activation energy B is very small since even at −40° **4** dimerizes rapidly to **2**. Due to the proximity of the energy levels of **2** and **4** activation energy A must be only slightly larger than B, and considerably less than the value of *ca.* 7 kcal for C. This is also evident from the observation that at 25° **2** dissociates to **4** in less than 1 sec while **4** dimerizes to **3** at a much slower rate (a half-life of several minutes for a 0.005 *M* solution of **4**).

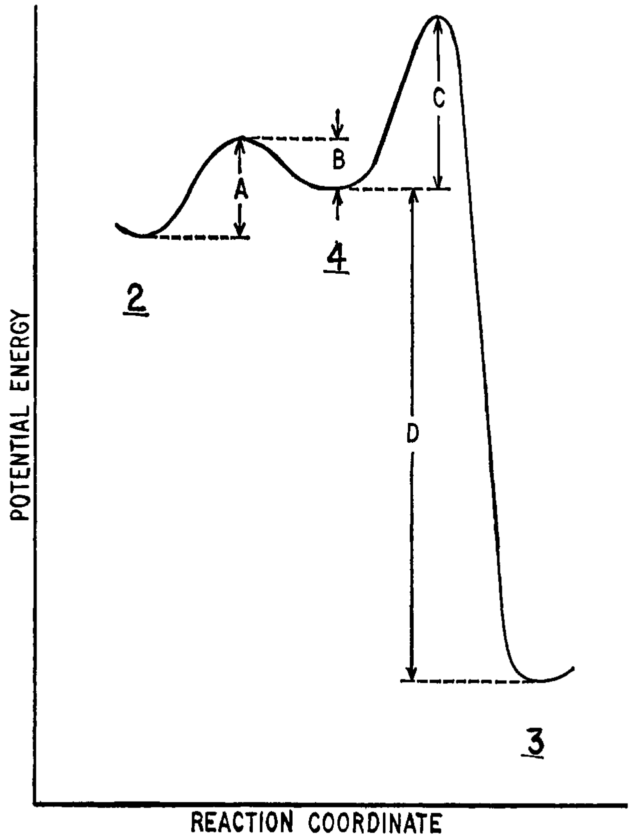


Figure 2.

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(13) The photolytic conversion of 3 to 2 at −40° explains the "low temperature energy storage phenomena" described by T. Hayashi and K. Maeda, *Bull. Chem. Soc. Japan*, **36**, 1052 (1963).

(14) T. Hayashi, K. Maeda, and M. Mounga, *ibid.*, **37**, 1563 (1964).

Dimer **2** appears to be stable in the solid state up to temperatures of approximately 100°; above this temperature it is isomerized to **3**. The enhanced stability of **2** in the solid state is probably due to stabilization by the crystal lattice. Mechanical rupture of the lattice causes homolysis of the weak C_4–C_4 bond and the color of the resultant radicals produces the piezochromic effect. Similarly, destruction of the lattice by solvents results in the rapid dissociation of the dimer at room temperature.

Substituted triarylimidazoles when oxidized in the same manner as lophine (**1**) also give rise to analogous dimers, exhibiting piezochromic and photochromic behavior.[15] In some cases the piezochromic compound is not formed in quantitative yield but only as a minor constituent along with the photochromic dimer and cannot be isolated in a pure state. The presence of small quantities of piezochromic material can be demonstrated, however, by direct observations of the piezochromism and by the immediate dissociation to the corresponding triarylimidazyl radicals when the solid is added to benzene in the dark. In Table II are listed the melting points and the characteristic infrared absorptions of the oxidation products of some triarylimidazoles and the wavelengths of the maximum absorptions in the visible spectra for the corresponding triarylimidazyl radicals.

The infrared spectra of the chloro-substituted piezochromic compounds in Table II indicate that the compounds are bisisoimidazyls. Two dimers ($R_1 = C_6H_5$, $R_2 =$ *m*-ClC_6H_4 or *p*-ClC_6H_4) appear to be symmetrical about the central C–C bond and contain only 2H-isoimidazole rings as in the case of compound **2**. In the remaining example ($R_1 = R_2 =$ *p*-ClC_6H_4) a mixed dimer linked *via* a C_2–C_4 bond, or a mixture of at least two of the possible C–C dimers, the C_2–C_2, C_4–C_4, and C_2–C_4, is indicated.

The infrared spectra of the photochromic products in Table II indicate that they are N-isoimidazylimidazoles. Most of the spectra suggest the isoimidazole ring is the 2H-isoimidazole isomer as in the case of compound **3**. The isoimidazole ring cannot be differentiated in the case of the photochromic product with $R_1 = C_6H_5$ and $R_2 =$ *p*-ClC_6H_4, since the characteristic absorption falls between that for the 2H and 4H isomers.

Experimental Section

Oxidation of 2,4,5-Triphenylimidazole. Preparation of 2. A cold 1% aqueous solution of potassium ferricyanide (450 ml) was added slowly to a solution of 2,4,5-triphenylimidazole (**1**, 1.0 g) dissolved in 95% ethanol (100 ml) containing potassium hydroxide (12.0 g). During addition the reaction mixture was maintained at 5 to 10° and vigorously stirred. A violet color appeared during the addition of the first equivalent of ferricyanide solution, but disappeared quickly while a precipitate formed. After the addition was completed (1.5 hr) the precipitate was collected by suction filtration, thoroughly washed with water, and dried. (The filtrate gave a strong, positive test for ferrocyanide ion.) The dried precipitate (0.92 g, mp 177–184°) was a light violet powder.

With the conditions described above but employing either an oxygen or a nitrogen atmosphere instead of air, similar results were obtained. In both cases a light violet precipitate was obtained in 100% yield in the nitrogen case (mp 182–183°) and in 97% yield in the oxygen case (mp 182–186°). The infrared spectra of the three products were identical. On long standing in the dark, the materials became completely white. Careful washing of the precipitate with 95% ethanol gave material **2** (mp 187.5–188.5°) with characteristic infrared absorption bands at 1020, 868, and 750 cm^{-1}.

Anal. Calcd for $C_{42}H_{30}N_4$: C, 85.40; H, 5.12; N, 9.49. Found: C, 85.1; H, 5.2; N, 9.5; Fe, 0.10.

When lophine was oxidized by ferricyanide with the procedure described above except at 25° and higher temperatures, a mixture of products was obtained. Under an oxygen stream at 25°, the major products were **2** and **3**. In addition, there were small amounts of at least two other products. Under a nitrogen atmosphere at 30°, 50% of the starting material was recovered. The remaining material was a complex mixture which was neither photochromic nor piezochromic.

Conversion of 2 to 3. Sample **2** was dissolved in benzene and produced a deep violet color which gradually faded. Filtration and evaporation of the filtrate gave a yellow oil which crystallized on addition of ethanol. The yellow, crystalline material (mp 193–194°) was recrystallized twice from benzene–heptane to give material **3** (mp 202–202.5°) with characteristic infrared absorption bands at 1350 and 904 cm^{-1}.

Anal. Calcd for $C_{42}H_{30}N_4$: C, 84.50; H, 5.12; N, 9.49; mol wt, 590. Found: C, 85.8; H, 5.3; N, 9.5; mol wt, 554.

The solution of **3** in benzene gave rise to a slightly yellow solution. On exposure to light or heat a violet color developed which gradually faded on removal from the light or heat source. This phenomenon remained reversible after many light–dark cycles.

Conversion of 2 to 1 with $LiAlH_4$. Compound **2** (600 mg) was added to a 0.5% solution of lithium aluminum hydride in ether (60 ml) at 25°. No color change or gas evolution was noted. After 30 min, 5 ml of ethanol was added slowly. A 25% sodium hydroxide solution (100 ml) was added and the ether was removed by evaporation. The residual solid was collected on a filter, washed with water, and dried to give 2,4,5-triphenylimidazole (598 mg, mp 276.5–277°, no depression when mixed with authentic **1**; the infrared spectrum was identical with that of **1**).

Conversion of 3 to 1 with $LiAlH_4$. The procedure described above was used with **3** (200 mg) partially dissolved in 20 ml of benzene and 20 ml of ether. The product consisted of **1** (193 mg) and **3** (14 mg).

Conversion of 3 to 1 with Acids. Compound **3** (93.2 mg) in 2 ml of chloroform was treated dropwise with 0.5 ml of acetic acid. The pale yellow solution was evaporated to an oily residue. Addition of 1 ml of ethanol induced crystallization. The solid was collected on a filter, washed with ethanol, and dried to yield 2,4,5-triphenylimidazole (**1**, 27 mg, mp 273–274; no depression when mixed with authentic **1**, mp 275–276°; the infrared spectrum was identical with that of **1**). The filtrate contained **1** (*ca.* 15 mg) and a liquid that did not crystallize (infrared absorption at 1615 cm^{-1}).

In a similar experiment using anhydrous hydrogen chloride in 40 ml of ether, **3** (22.0 mg) was converted to an ether-insoluble fraction, the hydrochloride of **1** (11.9 mg), and an ether-soluble product with an infrared spectrum identical with chlorolophine hydrochloride (prepared from chlorination of 2,4,5-triphenylimidazole).

Conversion of 2 to 1 with HCl. Compound **2** (223 mg) was added to 100 ml of anhydrous ether which had been saturated with hydrogen chloride. The mixture was stirred 20 min and filtered to yield a pale yellow solid (216 mg). The solid (208 mg) was washed thoroughly with 5% sodium carbonate solution (5 ml) and twice and with water to produce a white solid (172 mg). The solid was a mixture of **1** (*ca.* 100 mg) and a second component with an infrared absorption at 1680 cm^{-1}.

Conversion of 3 to 2. A solution of compound **3** (15 mg) in 15 ml of ether was cooled to −40° and irradiated with the focused beam of a 6.5-v, 2.75-amp microscope lamp. The clear, colorless solution rapidly developed a weak pink color which remained at the same intensity during the course of the irradiation. After 2 hr the irradiation was stopped. A small portion of the pink solution was warmed to 25° and immediately developed an intense red-violet color. Evaporation to dryness of the remainder at reduced pressure at −40° left a colorless, partially crystalline glass. A 1-mg portion in 0.5 ml of benzene immediately produced a red-violet color. When the material was warmed to room temperature, the glassy portion of the sample became red-violet and gradually solidified with a loss of the color. An infrared spectrum of the sample at 25° indicated compounds **2** and **3** to be present in the ratio of 1:3. The sample was piezochromic and when dissolved in benzene pro-

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(15) The alkaline ferricyanide oxidation of several monophenyl- and diphenylimidazoles gives rise to products which do not exhibit piezochromism or photochromism: J. Sonnenberg and D. M. White, unpublished work.

duced a moderately strong red-violet color. Thus, it appears that on warming to room temperature a large portion of compound **2** in the glass phase lacked the stabilization afforded by the crystal lattice and rearranged to **3** *via* dissociation to **4**. Thus the conversion to **2** at $-40°$ is probably greater than indicated by the infrared spectrum of the 25° crystallized product.

Thermochromism of 2. Compound **2** (5 mg) was added to 1 ml of chloroform at 25° and dissolved within 30 sec. The intensity of the red-violet color increased as rapidly as the solid dissolved. The colored solution was cooled rapidly to $-40°$ and the color diminished to a light pink within 20 sec (with the major decrease within the first 5 sec) and remained light pink on continued standing. On warming to 25° the solution rapidly restored the deep red-violet color and on recooling the color was diminished once again.

Piezochromism of 2. A solid sample of **2** was ground manually in a mortar with a pestle at 25°. The color of the solid changed from white to a deep purple. An identical change could be effected when the sample was ground under liquid nitrogen. Even the pressure of a typewriter key impinging on a sheet of paper impregnated with finely powdered **2** was sufficient to produce a dark color. The color disappeared after several days at 25°.

Oxidation of Other Imidazoles. The types of imidazoles and the methods of oxidation are presented in Table II. The procedure for oxidation with potassium ferricyanide and product isolation is identical with the procedure for the oxidation of lophine at 5° under oxygen. The imidazoles which were unreactive under these conditions were oxidized by an alternate method. The imidazole (0.01 mole) was heated with lead dioxide (30 g, Eimer and Amend, ACS grade) in 300 ml of benzene at reflux for 15 hr. After filtration the benzene solution was evaporated to dryness and the residue was recrystallized from ethanol and water. The product from this procedure was the photochromic dimer.

Esr Measurements. All measurements were made on a Varian V-4500 A EPR instrument at 25°. All of the spectra had the same band width, general shape, and no fine structure. The signal from **2** was very weak for the solid, very strong immediately after solution, and weak after the solution was stored in the dark for several minutes. The signal was strong after the solid was ground with a mortar and pestle and diminished on standing. The signal from sample **3** was very weak for the solid, weak when in solution, strong after irradiation of the solution, and weak after the irradiated solution was stored in the dark. In all cases the intensity of the signal was proportional to the color of the substrate.

Infrared Measurements. The infrared spectra were determined with a Beckman IR-7 spectrophotometer. Thoroughly dried, crystalline samples were analyzed in potassium bromide pellets with concentrations of approximately 6 mg/g of potassium bromide.

Ultraviolet Measurements. All measurements were made on a Cary 14 spectrophotometer using 95% ethanol as the solvent or KBr as a matrix. In Table I the spectral data obtained for several arylimidazoles and isoimidazoles are listed.

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Studies in Prebiotic Synthesis. I. Aminomalononitrile and 4-Amino-5-cyanoimidazole[1,2]

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Abstract: The syntheses of aminomalononitrile and 4-amino-5-cyanoimidazole are described. Acid anhydrides react with aminomalononitrile to yield oxazoles. Aminomalononitrile is converted to diaminomaleonitrile by cyanide and to 4-amino-5-cyanoimidazole by formamidine. Adenine results from the reaction of 4-amino-5-cyanoimidazole with formamidine. 4-Cyano-5-aminooxazole is converted to 7-aminooxazolo[5,4-*d*]pyrimidine on treatment with formamidine.

In pioneering experiments Miller[3] demonstrated that substantial quantities of amino acids are produced when an electric discharge is passed through a mixture of methane, ammonia, and water. Subsequently, he showed that these amino acids are formed following an initial condensation of hydrogen cyanide with aldehydes formed in the discharge.[4] When Oro showed that adenine is obtained on refluxing ammoniacal solutions of hydrogen cyanide it became clear that hydrogen cyanide might be a central compound in the prebiotic synthesis of nitrogen compounds.[5] More recently adenine has been obtained from cyanide in a variety of ways, and several pathways have been discussed.[5,6] We have attempted a detailed study of the steps involved in the hope that this might throw light on the prebiotic synthesis.

Adenine was formed in only 0.5% yield in Oro's experiment; most of the cyanide formed an intractable polymer. Therefore, we decided to attempt the synthesis of the most plausible intermediates, namely aminomalononitrile (I) and 4-amino-5-cyanoimidazole (II). In this way we hoped to study the key steps in adenine synthesis in a comparatively simple system. In the present paper we discuss the chemistry of these two key intermediates, without particular regard to their reactions under "prebiotic" conditions. In later

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[1] For a preliminary account of this work see J. P. Ferris and L. E. Orgel, *J. Am. Chem. Soc.*, **87**, 4976 (1965).

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[3] S. L. Miller, *J. Am. Chem. Soc.*, **77**, 2351 (1955).

[4] S. L. Miller, *Biochim. Biophys. Acta*, **23**, 480 (1957).

[5] J. Oro and A. P. Kimball, *Arch. Biochem. Biophys.*, **94**, 217 (1961); **96**, 293 (1962); J. Oro and J. S. Kamat, *Nature*, **190**, 442 (1961).

[6] J. Oro, *ibid.*, **197**, 971 (1963); C. U. Lowe, M. W. Rees, and R. Markham, *ibid.*, **199**, 219 (1963); C. Ponnamperuma, R. M. Lemmon, R. Mariner, and M. Calvin, *Proc. Natl. Acad. Sci. U. S.*, **49**, 737 (1963); R. M. Kliss and C. N. Matthews, *ibid.*, **48**, 1300 (1962); M. Calvin, "Chemical Evolution," University of Oregon Press, Eugene, Ore., 1961, p 24; C. Palm and M. Calvin, *J. Am. Chem. Soc.*, **84**, 2115 (1962); for recent reviews, see "The Origins of Prebiological Systems," S. W. Fox, Ed., Academic Press Inc., New York, N. Y., 1965, pp 137–172, 221–242.