Triphenylphosphonium Phenylbenzoylmethylide (3g). A solution of 0.730 g (3.36 mmol) of **1a** and 1.52 g (3.33 mmol) of **3g** in 60 mL of dry benzene was refluxed for 20 h. The yellow solution turned blue gradually. After evaporation of the solvent in vacuo, the blue pasty residue was column chromatographed on silica gel with benzene–ethyl acetate (5:1) as eluent to give **14b** (25%), **10** (6%) and two unidentified blue pastes.

4,5-Diphenyl-2,3-di(*p*-toluenesulfonyl)-Δ^4-1,2,3-thiadiazoline (14b): Colorless fluffy needles (benzene), mp 183.5–183.7 °C; IR (nujol) 1600, 1590, 1555 (C=C), 1450, 1360, 1340, 1160 (SO_2), 1085 (SO_2), and 1060 cm^{-1}; MS *m/e* 379 (3) ($M^+ - Ts - N$), 258 (9) ($TsNCPh^+$), 238 (15) ($M^+ - 2\,Ts$), 224 (9) ($M^+ - 2\,Ts - N$), 155 (64) (Ts^+), 135 (23) ($PhCSN^+$), 121 (85) ($PhCS^+$), 103 (13) ($PhCN^+$), and 91 (100) ($CH_3C_6H_4^+$). Anal. Calcd for $C_{28}H_{24}N_2O_4S_3$ (548.7): C, 61.29; H, 4.41; N, 5.11; S, 17.53. Found: C, 61.38; H, 4.17; N, 5.12; S, 17.31. Mol wt 554 (VPO method in chloroform, cholesterol as calibration standard).

Supplementary Material Available. Tables III and IV containing mass spectral data for 4 and 5 will appear following this article in the microfilm edition of this journal. Ordering information is given on any current masthead page.

Registry No.—**1a,** 4104-47-6; **1b,** 13165-67-8; **3a,** 4756-25-6; **3b,** 7151-67-9; **3c,** 24764-32-7; **3d,** 63609-86-9; **3e,** 7293-75-6; **3f,** 63609-87-0; **3g,** 30416-76-3; **4a,** 63609-88-1; **4b,** 63609-89-2; **4c,** 63609-90-5; **4e,** 63609-91-6; **4f,** 63609-92-7; **5a,** 4440-32-8; **5c,** 63609-93-8; **5e,** 63609-94-9; *cis*-**5f,** 63609-95-0; *trans*-**5f,** 63609-96-1; **6,** 791-28-6; **8b,** 63609-97-2; **8c,** 63609-98-3; **8d,** 63609-99-4; **8f,** 63610-00-4; **9,** 63610-01-5; **12b,** 6967-03-9; **12d,** 63610-02-6; **12e,** 18374-46-4; **14b,** 63610-03-7; 2-benzoylfluorine, 15860-31-8; 9-bromo-2-benzoylfluorene, 63610-04-8; triphenylphosphine, 603-35-0; 2-benzoylfluorine-9-triphenylphosphonium bromide, 63626-33-5; 9-bromo-2-methoxyfluorene, 63610-05-9; 2-methoxyfluorene-9-triphenylphosphonium bromide, 7293-61-0.

References and Notes

(1) (a) G. Kresze and W. Wucherpfennig, *Angew. Chem., Int. Ed. Engl.*, **6** (2), 149 (1967). (b) G. Kresze, A. Maschke, R. Albrecht, K. Bederke, H. P. Patzschke, H. Smalla, and A. Trede, *ibid.*, **1** (2) 89 (1962).
(2) (a) Henri Ulrich, "Cycloaddition Reactions of Heterocumulenes", Academic Press, New York and London, 1967. (b) A. W. Johnson, "Ylid Chemistry" Academic Press, New York and London, 1966. (c) A. Senning, *Acta Chem. Scand.*, **18,** 1958 (1964). (d) A. Senning, *ibid.*, **19,** 1755 (1965).
(3) Reference 2b, page 226.
(4) Thione *S*-imides have recently been isolated by two different methods; one is the addition of nitrene to a thiocarbonyl compound and the other is a base-promoted 1,3-dehydrohalogenation of substituted sulfenamide. (a) S. Tamagaki and S. Oae, *Tetrahedron Lett.*, 1159 (1972). (b) S. Tamagaki, K. Sakaki, and S. Oae, *Bull. Chem. Soc. Jpn.*, **47** (12), 3084 (1974). (c) S. Holm, J. A. Boerma, N. H. Nilsson, and A. Senning, *Chem. Ber.*, **109,** 1069 (1976). (d) E. M. Burgess and H. R. Penton, Jr, *J. Org. Chem.*, **39** (19), 2885 (1974); *J. Am. Chem. Soc.*, **95** (1), 279 (1973).
(5) The IR and mass spectra of **8a** were identical with the data reported by A. Schönberg et al., *Chem. Ber.*, **102,** 2557 (1969).
(6) A similar change of the thione *S*-imides has been observed in the thermal decomposition of *S*-arylsulfonylimino-1,2-benzodithiol-3-thione; S. Tamagaki, K. Sakaki, and S. Oae, *Bull. Chem. Soc. Jpn.*, **46** (8), 2608 (1973).
(7) A. Tangerman, L. Thijs, A. P. Anker; and B. Zwanenburg, *J. Chem. Soc., Perkin Trans. 2,* 458 (1973).
(8) We were unable to separate the similar geometrical isomers which probably exist in the thione *S*-imides **4b, 4e,** and **4f.**
(9) B. Zwanenburg, L. Thijs, and A. Tangerman, *Tetrahedron,* **27** 1731 (1971).
(10) L. Horner and H. Oedinger, *Justus Liebigs Ann. Chem.*, 627, 142 (1959).
(11) W. A. Sheppard and J. Diekmann, *J. Am. Chem. Soc.*, **86,** 1891 (1964).
(12) (a) E. Bergmann, H. Hoffmann, and D. Winter, *Chem. Ber.*, **66,** 46 (1933). (b) E. D. Hughes and K. I. Kuriyan, *J. Chem. Soc.*, 1609 (1935).

Reactions of Imidazoles with Isocyanates at Elevated Temperature

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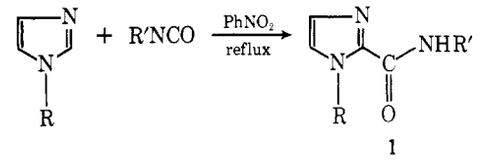
Imidazole and 1-methylimidazole react with isocyanates in boiling nitrobenzene or phenyl ether to form N-substituted imidazole-2-carboxamides in good yield. When 2-methylimidazole is used, the 4(5)-carboxanilide is obtained in low yield, but no corresponding product is isolated from the reaction involving 1,2-dimethylimidazole. Treatment of *N*-phenylimidazole-2-carboxamide with phenyl isocyanate and triethylamine results in formation of *N*-phenylimidazole-1,2-dicarboximide and *N,N'*-diphenylurea.

Imidazole is known to react with isocyanates under mild conditions to form N-substituted imidazole-1-carboxamides, which partially dissociate into their precursors upon melting, or in solution.[1] Under more drastic conditions, as in boiling nitrobenzene, 4,5-diarylimidazoles and their 1-alkyl derivatives were found to react with aryl isocyanates at the only available heterocyclic ring carbon atom to yield N-substituted imidazole-2-carboxamides.[2] Since the latter reactions are among very few known cases of imidazoles undergoing direct acylation at a ring carbon atom,[3] it was of interest to investigate analogous reactions of unsubstituted imidazole, where any one of three ring carbon atoms is in principle capable of reaction.

It has now been found that refluxing of a solution of equimolar amounts of imidazole and phenyl isocyanate in a high boiling solvent, such as nitrobenzene, *m*-nitrotoluene, or phenyl ether, yields *N*-phenylimidazole-2-carboxamide (**1a**) as the main product. There is considerable tar formation, but except for very small amounts of *N*-phenylimidazole-1-carboxamide (**2a**), *N,N'*-diphenylurea, and triphenyl isocyanurate, no other product has been detected. Structure **1a** is



1

a,	R = H, R' = Ph	f,	R = Me, R' = Ph
b,	R = H, R' = 4-MeC_6H_4	g,	R = Me, R' = 4-MeC_6H_4
c,	R = H, R' = 3-ClC_6H_4	h,	R = Me, R' = 3-ClC_6H_4
d,	R = H, R' = 1-naphthyl	i,	R = Me, R' = 1-naphthyl
e,	R = H, R' = *n*-Bu	j,	R = Me, R' = *n*-Bu

supported by spectral (IR, NMR) as well as microanalytical data. Appearance of the carbonyl stretching band at 1650 cm^{-1} in the infrared spectrum indicates attachment of the side chain to a ring carbon, rather than nitrogen atom.[2] On the other hand, spectra (IR, NMR) and depressed mixture melting point clearly establish the difference between this compound and the known, isomeric *N*-phenylimidazole-4(5)-carboxamide (**3**).[4]

In a similar manner, reaction of imidazole with *p*-tolyl, *m*-chlorophenyl, and 1-naphthyl isocyanate in boiling nitro-

Table I.[a] N-Substituted Imidazole-2-carboxamides (1a–j)

Compd	Registry no.	R	R′	Reaction time, h	Yield,[b] %	Mp (bp), °C	IR (C=O), cm^{-1}	NMR, δ
1a	63678-16-0	H	Ph	0.5	65[c,d]	218–219	1650	12.98 (s, 1, ring NH), 10.12 (s, 1, amide NH), 7.65–7.77 (m, 2), 6.90–7.28 (m, 5)
1b	63678-17-1	H	4-MeC_6H_4	1	50[e]	237–237.5	1650	12.87 (s, 1, ring NH), 9.97 (s, 1, amide NH), 7.53 (m, 2), 6.95 (m, 4), 2.23 (s, 3, CH_3)
1c	63678-18-2	H	3-ClC_6H_4	0.5	64[e]	208–209	1670	13.10 (s, 1, ring NH), 10.43 (s, 1, amide NH), 7.63–7.93 (m, 2), 6.90–7.33 (m, 4)
1d	63678-19-3	H	1-Naphthyl	1	61[e]	220–222	1670	13.05 (s, 1, ring NH), 10.22 (s, 1, amide NH), 7.07–7.85 (m, 9)
1e	63678-20-6	H	*n*-Bu	8	18[e]	188–190	1650	12.67 (s, 1, ring NH), 8.18 (m, 1, amide NH), 6.97 (s, 2, ring CH's), 3.20 (m, 2, CH_2–C_3H_7), 1.37 (m, 4, CH_2–CH_2CH_2–CH_3), 0.90 (m, 3, CH_3)
1f	35342-94-0	Me	Ph	5	82[e]	102–104[f]	1680	10.05 (s, 1, NH), 7.60–7.73 (m, 2), 6.77–7.27 (m, 5), 3.93 (s, 3, CH_3)
1g	63678-21-7	Me	4-MeC_6H_4	6	72[e]	102–103	1680	10.17 (s, 1, NH), 7.70 (m, 2), 7.37 (s, 1), 7.12 (m, 2), 7.07 (s, 1), 4.03 (s, 3, NCH_3), 2.30 (s, 3, CCH_3)
1h	63678-22-8	Me	3-ClC_6H_4	3	92[e]	120–122	1690	10.26 (s, 1, NH), 7.87 (m, 1), 7.55–7.67 (m, 1), 6.93–7.27 (m, 4), 3.93 (s, 3, CH_3)
1i	6314-34-7	Me	1-Naphthyl	4	67[e]	128–129	1690	10.45 (s, 1, NH), 7.40–8.08 (m, 8), 7.07 (s, 1), 4.00 (s, 1, CH_3)
1j	63678-23-9	Me	*n*-Bu	18	75[e]	(104 °C/1.5 Torr)	1670	8.40 (m, 1, NH), 7.32 (s, 1, ring CH), 6.97 (s, 1, ring CH), 3.98 (s, 3, NCH_3), 3.28 (m, 2, CH_2–C_3H_7), 1.40 (m, 4, CH_2–CH_2CH_2–CH_3), 0.90 (m, 3, C_3H_6–CH_3)

[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all new compounds listed in this table. [b] Crude or recrystallized (distilled) material with melting point (boiling point) lower than that of the pure compound by 1–10 °C. [c] Reaction run in Ph_2O. [d] Yields of 55 and 49% were obtained by running the reaction in $PhNO_2$ (2 h) and *m*-nitrotoluene (1 h), respectively. [e] Reaction run in $PhNO_2$. [f] Lit. mp 104–106 °C [F. H. Pinkerton and S. F. Thames, *J. Heterocycl. Chem.*, **9**, 67 (1972)].

benzene leads to the corresponding derivatives *N*-*p*-tolyl- (**1b**), *N*-*m*-chlorophenyl- (**1c**), and *N*-1-naphthylimidazole-2-carboxamide (**1d**). In all cases, the carbonyl stretching band appears at 1650–1670 cm^{-1} in the infrared spectrum of the product (Table I), whereas this band is found at 1730–1740 cm^{-1} in the spectra of the corresponding N-substituted imidazole-1-carboxamides (**2a–e**) (Table II).[1c,5] In contrast to the latter compounds, no sign of dissociation into imidazole and isocyanate is detected in solutions of **1a–e.** As further confirmation of the fact that the reaction under discussion occurs at position 2 of the imidazole ring, alkaline hydrolysis of **1c** followed by acidification has been found to give imidazole-2-carboxylic acid. Because of its simplicity, the latter two-step sequence compares favorably with the literature multistep synthesis of imidazole-2-carboxylic acid[6] and deserves consideration as a method of preparation of this compound, in spite of its low yield (26% from imidazole).

When position 2 of imidazole is occupied, the reaction with isocyanates at elevated temperature becomes difficult and its results are much less satisfactory. Thus, refluxing of 2-methylimidazole and phenyl isocyanate in nitrobenzene for 3 h or in phenyl ether for 2 h is accompanied by extensive tar formation and the expected product, *N*-phenyl-2-methylimidazole-4(5)-carboxamide (**5**), is obtained in quite low yield (13 and 17%, respectively).

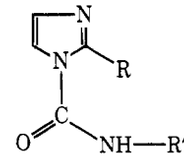
Analogous reactions of imidazole with alkyl isocyanates proceed much more slowly than those with aryl isocyanates. After a solution of imidazole and *n*-butyl isocyanate in nitrobenzene has been refluxed for 8 h, *N*-(*n*-butyl)imidazole-2-carboxamide (**1e**) is obtained in only 18% yield, while a much longer reaction time increases tar formation and yields a highly impure product.

Concerning the reaction pathway, it very likely involves typical competition between rate and equilibrium favored products, with faster but reversible formation of the 1-carboxanilide and slower but irreversible formation of the 2-carboxanilide.[7] Indeed, the IR spectrum ($CHCl_3$) of the reaction mixture for **1a,** at the beginning of the refluxing period in nitrobenzene, shows the isocyanate band at 2260 cm^{-1} and a carbonyl band at 1730 cm^{-1} (but no such band at 1650–1670 cm^{-1}), just like the spectrum of *N*-phenylimidazole-1-carboxamide (**2a**).[5,8] Furthermore, refluxing of a solution in nitrobenzene of independently prepared **2a** yields the 2-carboxanilide **1a** as the only isolated product and in essentially the same yield as the reaction of imidazole with phenyl isocyanate.

The relative reactivity of the isocyanates is reflected in isolation of the 2-carboxanilide in 64% yield after 0.5 h of boiling in nitrobenzene, in the case of *m*-chlorophenyl isocyanate; 50% yield after 1 h, in the case of *p*-tolyl isocyanate; and 18% yield after 8 h, in that of *n*-butyl isocyanate. These results contrast the observed decreasing tendency of imidazole-1-carboxanilides to dissociate in solution as the electrophilic character of the isocyanate increases.[9] They are consistent, however, with rate-determining electrophilic attack at position 2 of imidazole, since this would be expected to occur faster with stronger electrophilic character of the isocyanate.

The temperature at which the reaction is run has a crucial effect on its outcome. Although **2a** in solution partially dissociates into imidazole and phenyl isocyanate already at room temperature,[5,8] a much higher temperature is required for these two reagents to yield **1a.** Thus, 1-h refluxing in chlorobenzene (bp 132 °C) yields **2a** together with traces of **1a,** whereas in bromobenzene (bp 184 °C) roughly equal amounts of the two isomers are formed. In nitrobenzene (bp 210 °C) and phenyl ether (bp 259 °C) essentially only **1a** is obtained, but the yield is better after boiling for 0.5 h in the latter (65%), than after 2 h in the former solvent (55%). As the reaction temperature is raised, however, decomposition and tar for-

Table II.[a] N-Substituted Imidazole-1-carboxamides (2a–f)



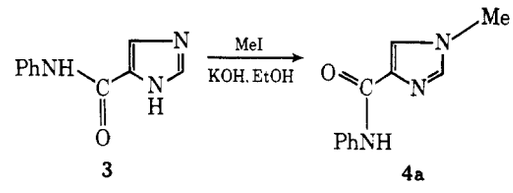
Compd	Registry no.	R	R′	Yield,[b] %	Mp, °C	IR (C=O), cm^{-1}	NMR, δ
2a	33876-94-7	H	Ph	98	115–116[c]	1730	10.27 (s, 1, NH), 8.40 (s, 1, imidazole 2-H), 7.10–7.80 (m, 7)
2b	63678-24-0	H	4-MeC$_6$H$_4$	95	145–147	1735	10.07 (s, 1, NH), 8.27 (s, 1, imidazole 2-H), 7.70 (m, 1, imidazole 5-H), 7.40 (m, 2), 7.03 (m, 3), 2.27 (s, 3, CH$_3$)
2c	33876-95-8	H	3-ClC$_6$H$_4$	98	136–137[d]	1730	8.43 (s, 1, imidazole 2-H), 7.10–7.80 (m, 6)
2d	63678-25-1	H	1-Naphthyl	99	109–111[e]	1730	8.35 (s, 1, imidazole 2-H), 7.0–8.0 (m, 9)
2e	63678-26-2	H	*n*-Bu	99	73–75	1730	8.43 (m, 1, NH), 8.22 (s, 1, imidazole 2-H), 7.65 (m, 1, imidazole 5-H), 7.02 (m, 1, imidazole 4-H), 3.30 (m, 2, CH$_2$C$_3$H$_7$), 1.50 (m, 4, CH$_2$–CH$_2$CH$_2$–CH$_3$), 0.97 (m, 3, CH$_3$)
2f	56023-08-6	Me	Ph	93	113–115	1730	10.32 (m, 1, NH), 6.75–7.53 (m, 7), 2.50 (s, 3, CH$_3$)

[a] Satisfactory analytical data (±0.3% for C, H, N) were reported for all new compounds listed in this table. [b] Crude product with melting point lower than that of the pure compound by 0–2 °C. [c] Lit. mp 114.5–115.5 °C (ref 1a). [d] Lit. mp 135 °C (ref 9). [e] Lit. mp 105–110 °C, resolidification, then 238–239 °C (ref 1a). An analytically pure sample could not be obtained in the present study because heating of **2d** in a recrystallization solvent would cause formation of an insoluble material, very likely the trimer of the isocyanate from partial dissociation of **2d**. Such behavior of analogous 1-naphthylureas is also reported in ref 1a.

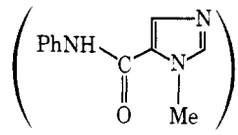
mation increase and the quality of the crude product deteriorates.

Although there can be no doubt that 1-carboxanilides are formed reversibly in the course of the reactions described so far, their intermediacy is not a condition for reaction to occur at position 2 of the imidazole ring. As observed earlier, isocyanates do react with 1-alkyl-4,5-diarylimidazoles at their only available ring carbon atom (C-2).[2] In the present study, 1-methylimidazole has been found to react smoothly with isocyanates in boiling nitrobenzene to give the corresponding N-substituted 1-methylimidazole-2-carboxamides (**1f–j**, Table I).[10] These reactions generally take place more slowly and require longer periods of refluxing, but their products are actually obtained in purer state and higher yield than for the corresponding reactions of imidazole itself. As expected, the reaction rate is higher, the more electrophilic the isocyanate. Monitoring of the reaction progress by the relative intensity of the bands at 2250–2270 cm^{-1} (N=C=O) and 1670–1690 cm^{-1} (C=O) in the IR spectrum ($CHCl_3$) of the reaction mixture shows the reaction to be practically complete after 1.5 h, for *m*-chlorophenyl isocyanate, but only after 3 h, for *p*-tolyl isocyanate. In both cases, a residual, weak isocyanate band decreases in intensity very slowly and persists even after 3 h for the former and 6 h for the latter reaction. Appearance of the carbonyl stretching band in the IR spectra of **1a–e** at a wavenumber lower by about 20–30 cm^{-1} than for the corresponding **1f–j** could be indicative of intramolecular hydrogen bonding between carbonyl oxygen and ring N–H in the former compounds, since such bonding is impossible for the *N*-methyl derivatives **1f–j**.

The structures of compounds **1f–j** are consistent with their IR and NMR spectra and are confirmed through the preparation of **1f** and **1h** by methylation of **1a** and **1c**, respectively. Analogous methylation of the 4(5)-carboxanilide **3** yields a methyl derivative for which two structures, **4a** and **4b**, are possible. Structure **4a**, which is favored by the possibility of intramolecular hydrogen bonding, as well as for steric reasons, appears likelier on the basis of spectroscopic data, also. In the NMR spectrum of **1f**, the signal of the methyl protons appears at δ 3.93. A compound of structure **4b** would be expected to give a methyl signal with chemical shift very nearly the same



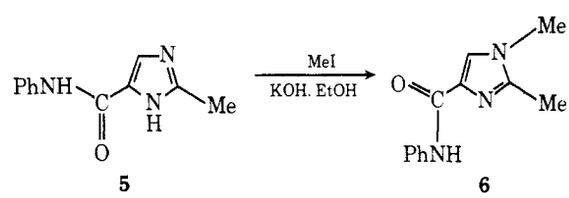
3 **4a**



4b

as that of **1f**, because of the same relative positions of methyl and carbonyl groups.[11] The NMR spectrum of the product of methylation of **3**, however, exhibits a methyl signal at δ 3.67, consistent with the larger distance between methyl and carbonyl in **4a**.[12]

A similar regioselectivity is observed in the methylation of *N*-phenyl-2-methylimidazole-4(5)carboxamide (**5**). The product, *N*-phenyl-1,2-dimethylimidazole-4-carboxamide (**6**),

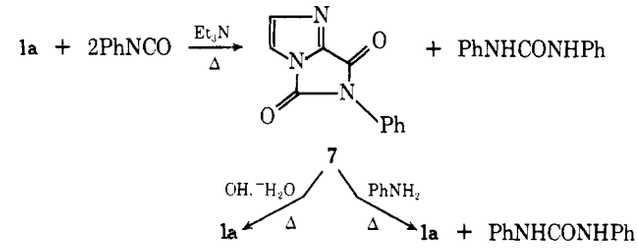


5 **6**

results from reaction at the sterically less-hindered ring nitrogen atom of **5**, as shown by the fact that the NMR signal of the 1-methyl protons appears at δ 3.54. The slight upfield shift, compared with **4a**, must be due to the second methyl group at position 2.[13] Unfortunately no carboxanilide could be isolated from the reaction of 1,2-dimethylimidazole and phenyl isocyanate in boiling nitrobenzene or phenyl ether for comparison with **6**. It seems that when both 1 and 2 positions of imidazole are occupied, the reaction with isocyanates becomes extremely difficult.[14]

In analogy with the behavior of *N*-phenylpyrrole-2-carboxamide[15] and *N*-phenylindole-2-carboxamide,[16] **1a** reacts

with 2 equiv of phenyl isocyanate, in the presence of triethylamine, to form *N*-phenylimidazole-1,2-dicarboximide (**7**)



and *N,N'*-diphenylurea. Similar hydantoin formation was observed when 4,5-disubstituted imidazoles had been boiled with an excess of phenyl isocyanate.[2] Structure **7** is supported by appearance of carbonyl bands at 1825 and 1750 cm^{-1} in the IR spectrum and signals at δ 7.33 (5 H) and 7.78 (2 H) in the NMR spectrum of the product. It is also consistent with the facile alkaline hydrolysis of this compound to **1a**, which results from nucleophilic attack on the 1-carbonyl. Traces of *N,N'*-diphenylurea found in the hydrolysis product indicate that, to a small extent, reaction also occurs at the 2-carbonyl, yielding phenyl isocyanate, which subsequently is hydrolyzed. As expected,[2,15,16] upon heating with aniline **7** undergoes ring opening to form **1a** together with *N,N'*-diphenylurea.

Experimental Section[17]

General Procedure for Compounds 1a–j (Table I). A solution of 0.10 mol of imidazole, or 1-methylimidazole, and 0.10 mol of isocyanate in 25–50 mL of solvent[18] was refluxed for the length of time indicated in Table I. The reaction mixture was then chilled, diluted with CCl_4, and filtered to yield a solid product, which was washed with CCl_4 until the washings became colorless.[19]

Hydrolysis of 1c to Imidazole-2-carboxylic Acid. A mixture of 4.0 g (0.018 mol) of **1c** and 50 mL of 10% aqueous NaOH was refluxed for 1.25 h and the resulting solution chilled and washed with ethyl ether. The aqueous solution was treated first with concentrated and then with dilute hydrochloric acid until it was barely alkaline to litmus. After filtration from a small amount of precipitate, the solution was evaporated to small volume under reduced pressure and the concentrate made weakly acidic with acetic acid. The gelatinous precipitate formed was collected and dissolved in a small amount of boiling water. Following filtration from some insoluble material, the solution was treated with a few drops of acetic acid and chilled to yield 0.80 g (40%) of imidazole-2-carboxylic acid: mp 163–164 °C dec (lit.[6] 163–164 °C dec); IR 1630 cm^{-1} (C=O); NMR (CF_3COOD) δ 7.53 (s, 2, CH), 11.55 (s, 2, NH, COOH).

***N*-Phenyl-1-methylimidazole-2-carboxamide (1f).** A solution of 1.9 g (0.010 mol) of **1a**, 0.75 g of KOH, and 3.0 g of MeI in 20 mL of ethanol was let stand in a stoppered flask for 24 h, then diluted with water. Chilling of the resulting mixture and filtration yielded 1.9 g of **1f**, mp 93.5–100 °C. Recrystallization from EtOH–H_2O (50:50) yielded the pure compound as colorless crystals, mp 101.5–103.5 °C, identical in all respects with the product of the reaction of 1-methylimidazole and phenyl isocyanate in boiling nitrobenzene.

***N*-(3-Chlorophenyl)-1-methylimidazole-2-carboxamide (1h).** As described for **1f**, from 2.1 g (0.0095 mol) of **1c**, 0.75 g of KOH, and 3.0 g of MeI, in 10 mL of EtOH, there was obtained 2.0 g (89%) of **1h**, mp 118.5–120.5 °C raised to 120.5–122 °C by recrystallization from EtOH–H_2O. This material was identical with the product of the reaction of 1-methylimidazole and *m*-chlorophenyl isocyanate in boiling nitrobenzene.

General Procedure for N-Substituted Imidazole-1-carboxamides (Table II). A solution of 0.050 mol of isocyanate in 10–15 mL of CH_2Cl_2 was added in small portions to 0.050 mol of imidazole dissolved in 25 mL of CH_2Cl_2. The resulting solution was let stand for 0.5–1 h, then evaporated to dryness under reduced pressure. Washing of the residue with petroleum ether (bp 35–60 °C) yielded the 1-carboxanilide essentially pure and in quantitative yield.

Rearrangement of *N*-Phenylimidazole-1-carboxamide (2a) into *N*-Phenylimidazole-2-carboxamide (1a). A mixture of 18.7 g (0.010 mol) of **2a** and 50 mL of nitrobenzene was refluxed for 2 h, then chilled, diluted with CCl_4, and filtered. The precipitate, washed with CCl_4, was 11.0 g (59%) of **1a**, mp 217–219 °C.

***N*-Phenyl-1-methylimidazole-4-carboxamide (4a).** As described for **1f**, from 1.9 g (0.10 mol) of **3**,[4] 0.75 g of KOH, and 3.0 g of MeI in 10 mL of ethanol, there was obtained 1.8 g (90%) of **4a**, mp 149–152 °C. Recrystallization, first from aqueous ethanol and then from EtOAc–petroleum ether (bp 60–75 °C), yielded the pure compound as colorless crystals: mp 152–153 °C; IR 3380 (N–H), 1670 cm^{-1} (C=O); NMR δ 3.67 (s, 3, CH_3), 6.77–7.30 (m, 3), 7.60–7.77 (m, 4), 9.57 (s, 1, NH).

Anal. Calcd for $C_{11}H_{11}N_3O$: C, 65.66; H, 5.51; N, 20.88. Found: C, 65.48; H, 5.49; N, 20.98.

***N*-Phenyl-2-methylimidazole-4(5)-carboxamide (5).** A solution of 8.2 g (0.10 mol) of 2-methylimidazole and 11.9 g (0.010 mol) of phenyl isocyanate in 100 mL of nitrobenzene was refluxed for 3 h, then chilled, diluted with ethyl ether, and extracted with dilute hydrochloric acid. After it had been washed with ethyl ether, the acidic extract was made alkaline with aqueous ammonia to give 6.5 g of a crude solid material, which was recrystallized from water. There was obtained 2.6 g (13%) of **5**, mp 203–219 °C, further recrystallization of which from EtOAc–petroleum ether (bp 60–75 °C) yielded the pure compound as colorless crystals: mp 203 °C (partial, followed by resolidification), 217.5–218.5 °C; IR 3380, 3150 (N–H), 1650 cm^{-1} (C=O); NMR δ 2.33 (s, 3, CH_3), 6.73–7.30 (m, 3), 7.53–7.73 (m, 3), 9.50 (s, 1, amide NH), 11.1–13.1 (broad, diffuse signal, 1, ring NH). A similar reaction in boiling phenyl ether (2 h) yielded 3.5 g (18%) of crude **5**, mp 195–200 °C.

***N*-Phenyl-1,2-dimethylimidazole-4-carboxamide (6).** A solution of 2.0 g (0.010 mol) of **5**, 0.75 g of KOH, and 3.1 g of MeI in 10 mL of EtOH was let stand in a stoppered flask for 67 h, then diluted with water. Chilling and filtration of the resulting mixture yielded 1.8 g (84%) of crude **6**, mp 153–156 °C. Recrystallization from benzene–petroleum ether (bp 60–75 °C) gave the pure compound as colorless crystals: mp 157–158.5 °C; IR 3370 (N–H), 1660 cm^{-1} (C=O); NMR δ 2.32 (s, 3, C–CH_3), 3.54 (s, 3, N–CH_3), 6.73–7.27 (m, 3), 7.53–7.73 (m, 3), 9.40 (s, 1, NH).

Anal. Calcd for $C_{12}H_{13}N_3O$: C, 66.96; H, 6.09; N, 19.52. Found: C, 67.14; H, 6.01; N, 19.47.

***N*-Phenylimidazole-1,2-dicarboximide (7).** A mixture of 3.8 g (0.020 mol) of **1a**, 4.8 g (0.040 mol) of phenyl isocyanate, and 5 mL of triethylamine was heated on a steam bath for 16 h. After it has been cooled and washed with petroleum ether (bp 60–75 °C), the solid product was extracted with 100 mL of boiling CCl_4–$CHCl_3$ (3:1). Chilling of the extract precipitated 1.15 g of **7**, mp 175–177 °C. The resulting filtrate was used for a second extraction of the remaining original product to obtain 0.85 g of **7**, mp 172–175 °C. A last repetition of this operation gave an additional 0.50 g of **7** (mp 161–166 °C), raising the total yield to 59%. Recrystallization from CCl_4–$CHCl_3$ (2:1) afforded the pure compound in the form of colorless crystals: mp 179.5–180 °C; IR 1825, 1750 cm^{-1} (C=O); NMR (CF_3COOD) δ 7.33 (m, 5), 7.78 (m, 2).

Anal. Calcd for $C_{11}H_7N_3O_2$: C, 61.97; H, 3.31; N, 19.71. Found: C, 62.09; H, 3.42; N, 19.86.

Hydrolysis of 7. A mixture of 0.30 g of **7** and 6 mL of 10% aqueous NaOH was swirled on a steam bath for about 3 min. Cooling of the resulting mixture followed by filtration yielded 0.02 g of insoluble material, mp 235–236 °C, identified as *N,N'*-diphenylurea. Acidification of the filtrate precipitated 0.13 g of **1a**, mp 216–217 °C. Recrystallization from *n*-PrOH raised this melting point to 218–219 °C.

Reaction of 7 with Aniline. A mixture of 0.50 g of **7** and 5 mL of aniline was boiled for 5 min, then cooled, and diluted with CCl_4. Filtration yielded 0.80 g of solid material, which was extracted with twelve 10-mL portions of $CHCl_3$. The insoluble residue was 0.38 g of *N,N'*-diphenylurea, mp 237–239 °C raised to 240–242 °C by recrystallization from EtOH. Evaporation of the chloroform extract yielded 0.38 g of crude **1a**, mp 206–208 °C. Recrystallization from *n*-PrOH raised the melting point of this product to 217–218 °C.

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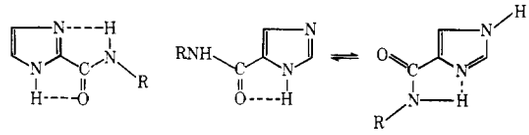
Registry No.—**3**, 13189-13-4; **4a**, 53629-38-2; **5**, 6286-11-9; **6**, 63678-27-3; **7**, 63678-28-4; R'NCO (R' = Ph), 103-71-9; R'NCO (R' = 4-MeC_6H_4), 622-58-2; R'NCO (R' = 3-ClC_6H_4), 2909-38-8; R'NCO (R' = 1-naphthyl), 86-84-0; R'NCO (R' = Bu), 111-36-4; imidazole, 288-32-4; 1-methylimidazole, 616-47-7; imidazole-2-carboxylic acid, 16042-25-4; 2-methylimidazole, 693-98-1; *N,N'*-diphenylurea, 102-07-8; aniline, 62-53-3.

References and Notes

(1) (a) R. A. Henry and W. M. Dehn, *J. Am. Chem. Soc.*, **71**, 2297 (1949); (b) K. Schlögl and H. Woidich, *Monatsh. Chem.*, **87**, 679 (1956); (c) H. A. Staab and W. Benz, *Justus Liebigs Ann. Chem.*, **648**, 72 (1961).
(2) R. Gompper, E. Hoyer, and H. Herlinger, *Chem. Ber.*, **92**, 550 (1959).
(3) (a) M. R. Grimmett, *Adv. Heterocycl. Chem.*, **12**, 179 (1970); (b) E. Regel and K. H. Buechel, German Patent 1 926 206, 1 956 711; *Chem. Abstr.*, **74**, 31754 f (1971), **75**, 49086 v (1971); (c) C. G. Begg, M. R. Grimmett, and Lee Yu-Man, *Aust. J. Chem.*, **26**, 415 (1973).
(4) R. G. Farguer and F. L. Pyman, *J. Chem. Soc.*, **115**, 217 (1919).
(5) J. Derkosch, K. Schlögl, and H. Woidich, *Monatsh. Chem.*, **88**, 35 (1957).
(6) R. G. Jones, *J. Am. Chem. Soc.*, **71**, 383 (1949).
(7) An analogous competition has been noted for Mannich reactions of imidazoles, which lead only to N-substitution, when run in acidic medium, but to both N- (reversibly) and C-substitution (irreversibly) in basic medium. However, with imidazole itself N-substitution still predominates after 24 h, in that case, and the relative reactivity of the heterocyclic ring positions is in the order 1 > 4,5 > 2 [F. B. Stocker, J. L. Kurtz, B. L. Gilman, and D. A. Forsyth, *J. Org. Chem.*, **35**, 883 (1970)]. The greater reactivity of position 2 in the present case may be related with the possible stabilization of the 2-carboxanilide by two intramolecular hydrogen bonds simultaneously, whereas only one such bond is possible for the 4(5) product.



(8) W. Otting and H. A. Staab, *Justus Liebigs Ann. Chem.*, **622**, 23 (1959).
(9) A. A. Zalikin, L. P. Nikitenkova, and Yu. A. Strepikheev, *J. Gen. Chem. USSR (Engl. Transl.)*, **41**, 1940 (1971).
(10) It is noteworthy that reaction of 1-methylimidazole with acid chlorides, in the presence of triethylamine, also results in acylation at the 2 position (ref 3b,c). Similarly, treatment of 1-methylimidazole with formaldehyde, at 160–170 °C, yields the 2-carbinol as product [P. C. Jocelyn, *J. Chem. Soc.*, 3305 (1957)].
(11) Cf. chemical shifts of methyl protons in 2-bromo-1-methylimidazole (δ 3.64) and 5-bromo-1-methylimidazole (δ 3.63) [G. B. Barlin and T. J. Batterham, *J. Chem. Soc. B*, 516 (1967)].
(12) Cf. chemical shifts of methyl protons in 1-methyl-4-nitroimidazole (δ 3.90) and 1-methyl-5-nitroimidazole (δ 4.05) (ref 11).
(13) Cf. chemical shifts of 1-methyl protons in 1-methylimidazole (δ 3.70) and 1,2-dimethylimidazole (δ 3.52) [(a) ref 11; (b) M. R. Grimmet, *Adv. Heterocycl. Chem.*, **12**, 148 (1970)].
(14) A reviewer pointed out the fact that 1,2-dimethylimidazole has been used effectively to catalyze di- and trimerization of isocyanates [R. Richter and H. Ulrich, *Synthesis*, 463 (1975)].
(15) E. P. Papadopoulos and H. S. Habiby, *J. Org. Chem.*, **31**, 327 (1966).
(16) E. P. Papadopoulos and S. B. Bedrosian, *J. Org. Chem.*, **33**, 4551 (1968).
(17) Melting points were determined in capillaries using a Thomas-Hoover UniMelt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 spectrophotometer using mineral oil mulls, unless otherwise indicated. NMR spectra were obtained on a Varian EM 360 spectrometer using solutions in hexadeuteriodimethyl sulfoxide (unless otherwise specified) and tetramethylsilane as internal standard. Identification of known compounds was accomplished by comparison of IR and NMR spectra, as well as determination of mixture melting points using authentic samples.
(18) In some cases, trimerization of the isocyanate was observed when it was added to the solution of 1-methylimidazole, but not when the order of addition was reversed.
(19) In the case of **1j**, the reaction mixture was fractionally distilled under reduced pressure to yield the product.

Photochemistry of 2,1-Benzisoxazolium (Anthranilium) Salts

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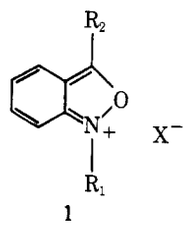
Photolysis of *N*-alkyl-2,1-benzisoxazolium perchlorates in aqueous solution results in the formation of 3-acyl- or 3-formyl-*p*-*N*-alkylaminophenols in excellent yields. Photolysis in methanol gives 3-acyl- or 3-formyl-*p*-*N*-alkylanisidines. Addition of inorganic salts to the aqueous solution leads to the introduction of the salt anion into the aromatic ring, giving 5-substituted 2-*N*-alkylaminobenzaldehydes, -acetophenones, or -benzophenones. However, photolysis of *N*-adamantyl-2,1-benzisoxazolium salts in aprotic solvents results in a ring expansion of the adamantyl moiety, yielding perhaps the first example of a stable 3-azahomoadamantyl carbenium ion.

Recent emphasis on the photochemistry of nitrogen heterocycles has prompted us to report our results on the photochemistry of N-alkylated, 2,1-benzisoxazolium salts (1).[1]

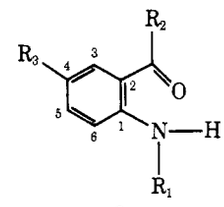


1

R_1 = Me, Et, *t*-Bu, 1-adamantyl
R_2 = H, Me, phenyl
X^- = ClO_4, FSO_3

While exploring the chemical reactivity of *N*-alkyl-3-methyl-2,1-benzisoxazolium perchlorates, we noticed that the salts acquired a dark-yellow to magenta color upon standing a few hours under normal fluorescent room light. The rate of color development as well as the hue was dependent upon both the N- and 3-substituents.[2] Since the photoreaction rate appeared to be rapid, we decided to investigate the solution photochemistry of **1** and determine the structure of the corresponding photoproducts.

Ultraviolet irradiation of an aqueous solution of **1a** (see Table I) with a 450-W Hanovia mercury lamp through a Pyrex filter quickly results in the rapid formation of a deep-yellow solution which upon basic workup yielded 82% of **2a** (see Table II). Similarly, irradiation in the presence of inorganic salts yielded photoproducts containing the inorganic anion substituted into the benzene ring of **2** instead of a hydroxyl group. Thus the addition of NaCl, NaBr, or KSCN to aqueous solutions of **1** results in the rapid formation of 4-substituted 2-acylanilines **2** (R_3 = Cl, Br, or SCN) as the major photoproducts.[3] Photolysis of **1** in methanol leads to the introduction



+ 10% ortho isomer

2

R_3 = Cl, Br, SCN, OH, OR