57632-90-3; **28c** hydrochloride, 56969-35-8; **28d,** 68013-42-3; **28d** hydrochloride, 56969-36-9; **28e,** 68013-43-4; **28e** hydrochloride, 56969-37-0; **28f,** 68013-44-5; **28f** hydrochloride, 56969-38-1; **28g,** 68013-45-6; **28g** hydrochloride, 56969-39-2; **29,** 63354-18-7; **29** hydrochloride, 60929-11-5; **30a,** 68024-69-1; **30b,** 68013-46-7; **30b** hydrochloride, 60929-09-1; **31a,** 68013-47-8; **31b,** 60929-10-4; **32a,** 68013-48-9; **32a** hydrochloride, 60726-56-9; **32b,** 60726-57-0; **32b** dihydrochloride, 68013-49-0; *tert*-butyl carbazate, 870-46-2; trifluoroacetic anhydride, 407-25-0; chloroacetic anhydride, 541-88-8; ethyl carbazate, 4114-31-2; thallous ethoxide, 20398-06-5; (dimethylamino)ethyl chloride, 107-99-3; 3-chloropropanol, 627-30-5; (dimethylamino)propyl chloride, 109-54-6; bromobenzene, 108-86-1; oxamic hydrazide, 515-96-8; diethyloxalate, 95-92-1; benzyl bromide, 28807-97-8; (diethylamino)ethyl chloride, 100-35-6; *N*-(2-chloroethyl)pyrrolidine, 5050-41-9; *N*-(2-chloroethyl)morpholine, 3240-94-6; pyrrolidine, 123-75-1; morpholine, 110-91-8; *N*-methylpiperazine, 109-01-3.

Supplementary Material Available: X-ray data for the methiodide of **20c** (both molecules) and the hydrobromide salt of **28c** (Figure 4) consisting of fractional atomic coordinates, temperature factors, bond distances, and bond angles (11 pages). Ordering information is given on any current masthead page.

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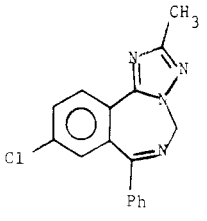
(24) The $\Delta F^{\ddagger}$ for the isomeric triazole **34** was even lower (Table IV).

(25) X is triazolo[5,1-*a*][2,4]benzodiazepine. An account of the synthesis and X-ray structure determination appears in a companion paper, this issue.



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Reactions of Azoles with Isocyanates at Elevated Temperature

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Received August 21, 1978

1*H*-1,2,4-Triazole, 1-methyl-1*H*-1,2,4-triazole, 4-methyl-4*H*-1,2,4-triazole, and benzothiazole react with aryl isocyanates in boiling nitrobenzene to form *N*-aryl heterocyclic *C*-carboxamides. Under the same conditions, pyrazole and benzotriazole yield their 1-carboxanilides, whereas benzoxazole is inert. Treatment of *N*-phenylimidazole-2-carboxamide (**6**), *N*-phenylimidazole-4(5)-carboxamide (**11**), and *N*-phenyl-1*H*-1,2,4-triazole-5-carboxamide (**1a**) with phenyl isocyanate leads to *N,N'*-diphenyl heterocyclic *C,N*-dicarboxamides. The *N*-carboxanilide group of these compounds is particularly reactive, and heat or reaction with nucleophilic reagents causes removal of the corresponding isocyanate unit.

Depending upon the conditions, imidazole reacts with isocyanates at either a nitrogen or a carbon atom of its ring. Thus, in the absence of solvent at 80 °C,[1] in tetrahydrofuran at the boiling point,[2] and in dichloromethane at room temperature[3] the products are N-substituted imidazole-1-carboxamides. In contrast, the reaction leads to N-substituted imidazole-2-carboxamides when run in boiling nitrobenzene or phenyl ether.[3] This temperature-controlled regiospecificity of the reaction is interesting and potentially useful, especially with regard to preparation of carbon-substituted imidazoles since very few acylation reactions are known to occur at ring carbon atoms of imidazole and other similar heterocycles.[4]

In this paper we wish to report on an extension of our earlier investigation[3] to other azole systems. Like imidazole, 1*H*-1,2,4-triazole and pyrazole have been known to react readily with isocyanates, under mild conditions to form N-substituted heterocyclic 1-carboxamides.[1,2] Our present results show that the reaction of 1*H*-1,2,4-triazole with an aryl isocyanate in boiling nitrobenzene leads to the corresponding *N*-aryl-1*H*-1,2,4-triazole-5-carboxamide (**1a–d**)[5] in analogy with the case of imidazole. In contrast, pyrazole still yields *N*-arylpyrazole-1-carboxamides when its reaction is run in boiling ni-

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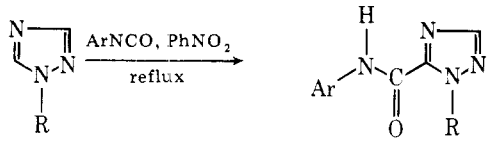
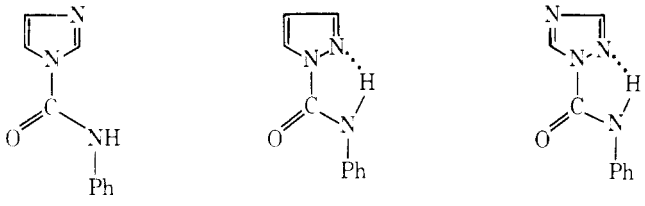


1a, R = H; Ar = Ph
b, R = H; Ar = 4-MeC_6H_4
c, R = H; Ar = 3-ClC_6H_4
d, R = H; Ar = 1-naphthyl
e, R = Me; Ar = Ph
f, R = Me; Ar = 4-MeC_6H_4
g, R = Me; Ar = 3-ClC_6H_4

trobenzene or phenyl ether, just as under much milder conditions.

Structures **1a–d** for the products of the high temperature reactions of 1*H*-1,2,4-triazole are supported by spectral (IR, NMR) as well as microanalytical data. In particular, the carbonyl stretching bands in the infrared spectra of the products appear at 1680 cm^{-1}, indicating that the side chain is attached to a ring carbon rather than a nitrogen atom.[2,3] In agreement with the lower reactivity of triazole toward electrophilic reagents,[6] these are slower reactions requiring longer periods of refluxing than the corresponding reactions of imidazole.

It is very likely that *N*-carboxanilides are rate controlled and reversibly formed, whereas *C*-carboxanilides are equilibrium controlled, irreversibly formed products of these reactions.[3] *N*-Phenylimidazole-1-carboxamide (**2**) is known to dissociate in solution to a considerable extent (16.1% at 20 °C and 36.7% at 45 °C, in $CHCl_3$) into imidazole and phenyl isocyanate.[7] An analogous dissociation has not been observed in the solutions of the corresponding pyrazole (**3**) and 1*H*-1,2,4-triazole (**4**) derivatives, although such compounds have

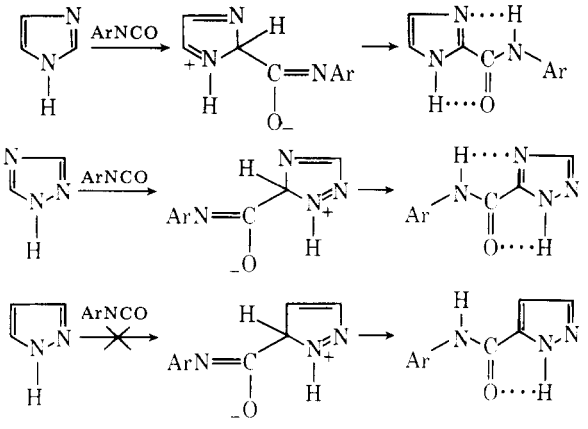


2 3 4

been reported to decompose into isocyanate and heterocycle upon stronger heating.[7,8] We have found that when 1-carboxanilides **3** and **4** are refluxed in nitrobenzene, some dissociation does occur. This is evidenced by the presence of a very weak (for **3**) and a stronger (for **4**) isocyanate band at 2250 cm^{-1} in the infrared spectra (taken in chloroform) of samples withdrawn from the hot reaction mixture. After 1 h of refluxing in nitrobenzene, the amount of free isocyanate relative to undissociated 1-carboxanilide is about three times larger for compound **4** than for **3**. After 26 h of refluxing, **4** is essentially completely isomerized into the C-substituted derivative **1a**, as indicated by the replacement of the *N*-carbonyl band (1750 cm^{-1}) by a *C*-carbonyl band (1680 cm^{-1}) in the infrared spectrum of the product. On the contrary, there is no carbonyl band attributable to a *C*-carboxanilide in the infrared spectrum of a solution of **3** in nitrobenzene which has been refluxed for 72 h. The dissociation of azole-1-carboxanilides in solution is believed to involve transfer of the amide proton to a ring nitrogen atom through intermolecular hydrogen bonds.[7,9] Consequently, the different extent of dissociation of **2**, **3**, and **4** may reflect corresponding differences in basic strength and in stabilization through intramolecular hydrogen bonding of these compounds.

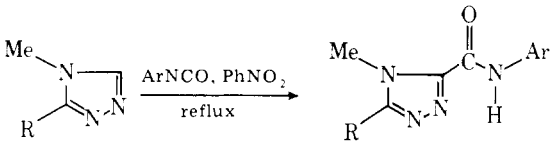
The difference in the behavior of the three azoles under study, with regard to formation of *C*-carboxanilides, may be rationalized qualitatively by considering concentration of reactants (free isocyanate and azole) and stability of the

Scheme I



presumed intermediate as rate-determining factors and relative stabilization by intramolecular hydrogen bonding of *C*- vs. *N*-carboxanilides as an equilibrium-affecting factor (Scheme I).

As observed earlier for 1-methylimidazole,[3] both 1-methyl-1*H*-1,2,4-triazole and 4-methyl-4*H*-1,2,4-triazole have been found to react with aryl isocyanates in boiling nitrobenzene to form ring carbon substituted products. Whereas the two ring carbon atoms of the latter heterocycle are equivalent and only one *C*-carboxanilide (**5a–c**) can be expected, two different products are in principle possible for the reactions of the former compound. The products actually isolated from these last reactions were assigned the structure of *N*-aryl-1-methyl-1*H*-1,2,4-triazole-5-carboxamide (**1e–g**) on the basis of analogy with the corresponding reactions of 1-methylimidazole,[3] the expected greater reactivity toward electrophiles of C-5 (α to electron-releasing pyrrolic nitrogen) than C-3 (α to electron-withdrawing pyridinic nitrogen) of the heterocycle, and NMR spectral data. The CH_3 resonance of 4-methyl-4*H*-1,2,4-triazole at δ 3.73 is shifted to δ 3.93 in its only possible *N*-phenyl-*C*-carboxamide (**5a**) as a result of the deshielding effect of the vicinal carbonyl group. In complete analogy, the CH_3 signal of 1-methyl-1*H*-1,2,4-triazole at δ 3.93 is shifted to δ 4.17 in the product of its reaction with phenyl isocyanate (**1e**). A carboxanilide group at C-3 of the triazole ring would be expected to have a smaller effect on the chemical shift of the CH_3 protons at N-1.[10a] Finally, reaction at C-5 of the heterocyclic ring is also indicated by the signal of the triazole ring proton of **1e** at δ 8.08. For 1-methyl-1*H*-1,2,4-triazole we have observed signals of δ 8.03 and 8.53, which correspond to the literature values for 3-CH (δ 7.95) and 5-CH (δ 8.47).[10b]



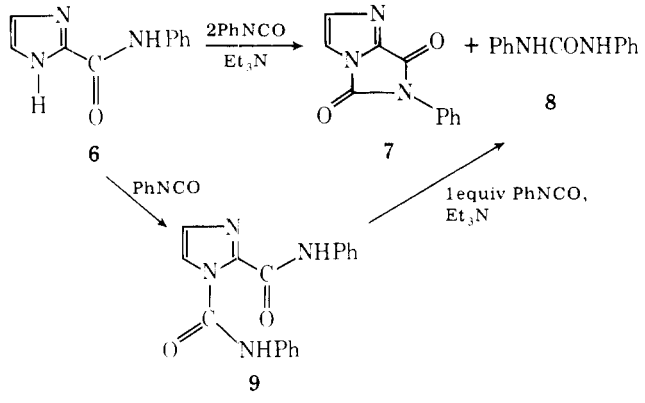
5a, R = H; Ar = Ph
b, R = H; Ar = 4-MeC_6H_4
c, R = H; Ar = 3-ClC_6H_4
d, R = 3-ClC_6H_4NHCO; Ar = 3-ClC_6H_4

It is interesting to note that 4-methyl-4*H*-1,2,4-triazole is much more reactive toward isocyanates than its 1-methyl-1*H* isomer. Under the same conditions, the reaction is spectroscopically (IR) complete for the former in a small fraction of the time required for the latter compound. Actually, unless special precautions are taken, the reaction of 4-methyl-4*H*-1,2,4-triazole with an aryl isocyanate leads to a mixture of the 3-carboxanilide and the 3,5-dicarboxanilide. For preparation of the monosubstituted product, the isocyanate should be added slowly to a boiling solution of an excess of 4-methyl-

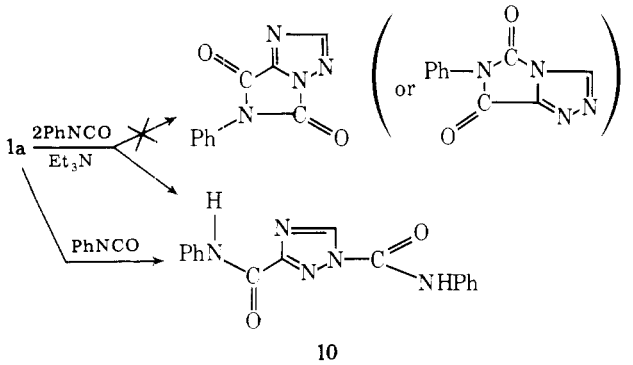
4*H*-1,2,4-triazole in nitrobenzene. The dicarboxanilide, on the other hand, is obtained by refluxing a nitrobenzene solution of the methyltriazole and 2 equiv of isocyanate. Another example of this remarkable ability of 4-substituted 4*H*-1,2,4-triazoles to undergo diacylation at ring carbon atoms is the formation of 3,5-diaroyl-4-phenyl-4*H*-1,2,4-triazoles when 4-phenyl-4*H*-1,2,4-triazole is heated with aroyl chlorides.[11]

In contrast to the behavior of methyl-1,2,4-triazoles, no reaction is observed when 1-methylpyrazole is refluxed with phenyl isocyanate in nitrobenzene. This could be attributed to the absence of stabilization by intramolecular hydrogen bonding in the expected product, *N*-phenyl-1-methylpyrazole-5-carboxamide, as opposed to its presence in the products of the corresponding reactions of the methyl-1,2,4-triazoles. Consistent with this argument is the observation that 1-methylpyrrole is also inert toward phenyl isocyanate, under the same conditions, even though its ring would be expected to be much more reactive toward electrophilic reagents than that of an *N*-methyltriazole.[6]

In view of the fact that a cyclization reaction occurs to form *N*-phenylimidazole-1,2-dicarboximide (**7**) and *N,N'*-diphenylurea (**8**) when *N*-phenylimidazole-2-carboxamide (**6**)



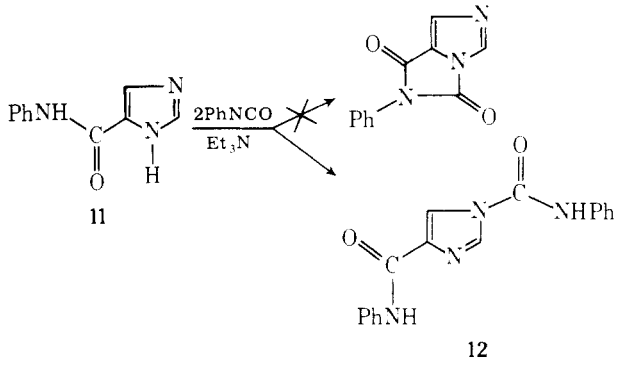
is heated with 2 equiv of phenyl isocyanate in the presence of triethylamine,[3] an analogous conversion was attempted using the triazole derivative **1a**. In this case, however, the reaction takes a different course and yields *N,N'*-diphenyl-1*H*-1,2,4-triazole-1,3-dicarboxamide (**10**). The same product is



obtained when **1a** is heated briefly (or allowed to stand at room temperature for several hours) with an excess of phenyl isocyanate in the absence of triethylamine. Structure **10** is consistent with the infrared spectrum of the product, which shows two carbonyl bands (1750, 1690 cm^{-1}), and its microanalytical data. It is further supported by the expected reactivity of the 1-carboxanilide group.[2] Although only a very weak isocyanate band can be seen in the infrared spectrum of a chloroform solution of **10**, this compound decomposes completely into **1a** and phenyl isocyanate when heated at 180–185 °C. Upon treatment with aqueous sodium hydroxide, **10** is hydrolyzed readily to yield **1a**. The fact that no significant amount of *N,N'*-diphenylurea is formed in this hydrolysis indicates direct nucleophilic attack at the 1-carbonyl group of **10** and precludes initial elimination of phenyl isocyanate.[8] Similarly, heating of **10** with aniline or isobutyl alcohol leads to **1a** together with *N,N'*-diphenylurea or isobutyl *N*-phenylcarbamate, respectively.

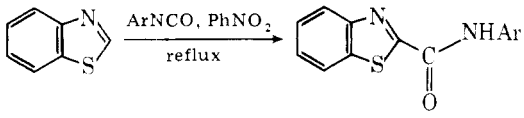
In the case of *N*-phenylimidazole-2-carboxamide (**6**), further reaction can only occur at one of the equivalent ring nitrogen atoms at positions 1 and 3. The vicinity of the two carboxanilide groups in the initial product (or intermediate) allows then cyclization to the *N*-phenyldicarboximide **7**, as for analogous derivatives of pyrrole and indole.[12] Indeed, when **6** is allowed to stand at room temperature (or heated briefly) with phenyl isocyanate, *N,N'*-diphenylimidazole-1,2-dicarboxamide (**9**) is formed. Although quite stable in the solid state, at room temperature, this compound dissociates into **6** and phenyl isocyanate partially when dissolved in chloroform and completely when heated at 116–118 °C. Treatment of **9** with aqueous alkali yields **6** together with a small amount of *N,N'*-diphenylurea, the latter product presumably resulting from hydrolysis of phenyl isocyanate formed by dissociation of **9**. The reactions of **9** with aniline or isobutyl alcohol proceed in complete analogy with those of **10**. As expected, treatment of **9** with 1 equiv of phenyl isocyanate in the presence of triethylamine yields the *N*-phenyldicarboximide **7** and *N,N'*-diphenylurea.

The results described earlier show that, unlike imidazole derivative **6**, *N*-phenyl-1*H*-1,2,4-triazole-5-carboxamide (**1a**) reacts with phenyl isocyanate not at a nitrogen atom flanking the existing carboxanilide group but at the sterically favored, further removed N-2 of the triazole ring, thus precluding cyclization to a dicarboximide. To test this interpretation of the difference in the behavior of **1a** and **6** toward phenyl isocyanate, an analogous reaction was attempted on *N*-phenylimidazole-4(5)-carboxamide (**11**)[13] in which, contrary to **6**, the two ring nitrogen atoms are not equivalent. When heated with phenyl isocyanate, with or without added triethylamine, **11**



reacts (like **1a**) at the sterically favored ring nitrogen atom farther from the carboxanilide group. Thus, no cyclization to a dicarboximide takes place and *N,N'*-diphenylimidazole-1,4-dicarboxamide (**12**) is formed as product.[14] Although this compound is thermally more stable than the analogous **9** and **10**, its 1-carboxanilide group is again reactive and easily removed by treatment with nucleophilic reagents such as aqueous alkali, aniline, and isobutyl alcohol.

The known formation of *N*-phenylbenzimidazole-2-carboxamide upon refluxing of a solution of benzimidazole and phenyl isocyanate in nitrobenzene[15] prompted us to investigate analogous reactivity of benzo derivatives of other azoles. We have found that benzothiazole reacts smoothly with aryl isocyanates in boiling nitrobenzene to form *N*-arylbenzothiazole-2-carboxamides (**13a–d**). Under the same conditions, benzoxazole is inert toward phenyl isocyanate, whereas benzotriazole yields its 1-carboxanilide.[1,16]



13a, Ar = Ph
b, Ar = 4-MeC_6H_4
c, Ar = 3-ClC_6H_4
d, Ar = 1-naphthyl

Experimental Section[17]

Preparation of Compounds 1a–d (Table I). A solution of 0.10 mol of 1*H*-1,2,4-triazole and 0.10 mol of isocyanate in 25 mL of nitrobenzene was refluxed for the period of time indicated in Table I. After the reaction mixture had been chilled and diluted with CCl_4, the precipitate was collected by filtration and washed with CCl_4. The solid product was then treated with 250 mL of 10% aqueous NaOH, and the resulting mixture was filtered to separate a small amount of insoluble material (largely *N,N'*-diphenylurea). Following neutralization of the filtrate by addition of hydrochloric acid, the precipitated product was collected by filtration and washed with water.

***N*-Phenylpyrazole-1-carboxamide (3). A.** A solution of 5.9 g (0.050 mol) of PhNCO in 10 mL of CH_2Cl_2 was added in portions to 3.4 g (0.050 mol) of pyrazole dissolved in 20 mL of CH_2Cl_2. The resulting solution was evaporated to dryness under reduced pressure, and the residue was washed with a small volume of cold petroleum ether (bp 63–75 °C) to yield 8.9 g (96%) of **3**, mp 69–71 °C (lit.[18] mp 73 °C).

B. A solution of 5.9 g (0.050 mol) of PhNCO and 3.4 g (0.050 mol) of pyrazole in 15 mL of $PhNO_2$ was refluxed for 42 h. Following removal of the bulk of $PhNO_2$ by distillation under reduced pressure, the residue was treated with petroleum ether (bp 63–75 °C) and chilled to give 7.2 g (77%) of **3**, mp 68–71 °C.

Isomerization of *N*-Phenyl-1*H*-1,2,4-triazole-1-carboxamide (4) into *N*-Phenyl-1*H*-1,2,4-triazole-5-carboxamide (1a). A mixture of 13.0 g of **4**[2] and 30 mL of nitrobenzene was refluxed for 26 h and then worked up as described before. There was obtained 8.0 g (62%) of **1a**, mp 220–222 °C.

Preparation of Compounds 1e–g (Table I). A solution of 0.10 mol of 1-methyl-1*H*-1,2,4-triazole[19] and 0.10 mol of isocyanate in 20 mL of nitrobenzene was refluxed for the period of time indicated in Table I. After the reaction mixture had been chilled, addition of petroleum ether (bp 63–75 °C) induced crystallization of the product, which was collected by filtration and washed with the same solvent.

Preparation of Compounds 5a–c (Table II). A solution of 0.050 mol of isocyanate in 20 mL of $PhNO_2$ was added dropwise, over 25–30 min, to a refluxing solution of 0.10 mol of 4-methyl-4*H*-1,2,4-triazole[20] in 20 mL of $PhNO_2$. The reaction mixture was refluxed for the additional period of time indicated in Table II and then chilled and diluted initially with CCl_4 and further with petroleum ether (bp 63–75 °C). The solid product, collected by filtration and washed with petroleum ether, was allowed to dry and then was washed with cold water to remove the excess of 4-methyl-4*H*-1,2,4-triazole.

***N,N'*-Bis(3-chlorophenyl)-4-methyl-4*H*-1,2,4-triazole-3,5-dicarboxamide (5d).** After addition of 4.15 g (0.050 mol) of 4-methyl-4*H*-1,2,4-triazole[20] to a solution of 15.3 g (0.10 mol) of 3-chlorophenyl isocyanate in 25 mL of $PhNO_2$, the mixture was brought quickly to boiling and was refluxed for 31 h. Chilling of the reaction mixture and dilution with petroleum ether (bp 63–75 °C) followed by filtration and washing of the precipitate with the same solvent yielded 15.0 g of crude product, mp 193–205 °C. This material was washed with ethanol to give 10.0 g (51%) of **5d**, mp 222–224 °C. An analytically pure sample was obtained by recrystallization from 1-propanol in the form of colorless crystals: mp 223.5–224.5 °C; IR 3370 (N–H), 1700 (C=O) cm^{-1}; NMR δ 11.13 (s, 2, NH), 8.10–7.10 (m, 8, aromatic), 4.17 (s, 3, CH_3). Anal. Calcd for $C_{17}H_{13}Cl_2N_5O_2$: C, 52.32; H, 3.36; N, 17.95. Found: C, 52.35; H, 3.29; N, 17.79.

***N,N'*-Diphenyl-1*H*-1,2,4-triazole-1,3-dicarboxamide (10). A.** A mixture of 1.90 g (0.010 mol) of **1a**, 2.38 g (0.020 mol) of PhNCO, and 5 mL of Et_3N was heated on a steam bath for 1 h and then cooled and treated with petroleum ether (bp 63–75 °C). Filtration, followed by washing of the precipitate with petroleum ether, yielded 3.10 g (100%) of **10**, which melted partially at 176–180 °C, resolidified, and melted completely at 217–220 °C.

B. A mixture of 2.0 g of **1a** and 20 mL of PhNCO was heated briefly on a Bunsen flame to obtain a solution, which was allowed to cool. Workup as before yielded 3.2 g (97%) of **10**, melting partially at 180–185 °C and completely at 215–220 °C.

C. A mixture of 1.0 g of **1a** and 10 mL of PhNCO was allowed to stand at room temperature for 24 h. Workup as before yielded 1.6 g (97%) of **10**, melting partially at 187–200 °C and completely at 223–225 °C. An analytical sample of **10** was obtained by recrystallization from MeCN in the form of colorless crystals: mp 180–185 °C[21] (partial melting followed by resolidifcation), 225–227 °C; IR 3350, 3330 (N–H), 1750, 1690 (C=O) cm^{-1}.[22] Anal. Calcd for $C_{16}H_{13}N_5O_2$: C, 62.54; H, 4.26; N, 22.79. Found: C, 62.37; H, 4.14; N, 22.99.

Thermal Decomposition of 10. A glass tube connected to an aspirator was inserted into the opening of a 10-mL flask which contained 0.30 g of **10** and was immersed into an oil bath kept at 200–210 °C. After 8–10 min, there was obtained 0.15 g of **1a**, mp 227–228 °C. When this decomposition was run without removal of vapor, the liquid that condensed on the upper walls of the flask was identified as phenyl isocyanate.

Hydrolysis of 10. A mixture of 0.50 g of **10** and 5 mL of 10% aqueous NaOH was swirled on a steam bath to effect dissolution. Addition of dilute hydrochloric acid to the chilled solution until it became weakly acidic caused evolution of CO_2 and precipitation of 0.30 g of **1a**, mp 226–228 °C.

Reaction of 10 with Aniline. A mixture of 0.50 g of **10** and 3 mL of $PhNH_2$ was heated briefly on a Bunsen flame to obtain a solution, which was cooled and diluted with CCl_4 to precipitate a solid. This was washed with CCl_4, dried, and then extracted with three 5-mL portions of 10% aqueous NaOH. The residue was 0.30 g of *N,N'*-diphenylurea, mp 232–233 °C (lit.[23a] mp 238 and 240 °C). Neutralization of the combined alkaline extracts yielded 0.25 g of **1a**, mp 225–226 °C.

Reaction of 10 with Isobutyl Alcohol. A mixture of 0.50 g of **10** and 15 mL of *i*-BuOH was boiled momentarily, and the resulting solution was cooled, diluted with EtOH, and filtered to give 0.25 g of **1a**, mp 223–224 °C. Removal of the solvents from the filtrate left a residue which was recrystallized from aqueous ethanol to yield 0.25 g of isobutyl *N*-phenylcarbamate, mp 85–87 °C (lit.[23b] mp 86 °C).

***N,N'*-Diphenylimidazole-1,2-dicarboxamide (9). A.** A mixture of 2.20 g of **6** and 20 mL of PhNCO was heated briefly on a hot plate to effect dissolution. The resulting solution was cooled and diluted with petroleum ether (bp 63–75 °C) to yield 3.10 g (86%) of **9**, which melted partially at 115–118 °C, resolidified, and then melted completely at 210–212 °C.

B. A mixture of 1.90 g of **6** and 12 mL of PhNCO was allowed to stand at room temperature for 40 h. Workup as before yielded 2.50 g (81%) of **9**, melting partially at 115–117 °C and completely at 210–212 °C. An analytical sample of **9** was obtained by recrystallization from petroleum ether (bp 63–75 °C) as colorless crystals: mp 116–118 °C (partial melting followed by resolidification),[21] 215–217 °C; IR 3360, 3330 (N–H), 1730, 1630 (C=O) cm^{-1}.[22] Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29. Found: C, 66.71; H, 4.45; N, 18.37.

Thermal decomposition of 9 was carried out as described for **10**, except that the oil bath was kept at 150–160 °C. From 0.40 g of **9** there was obtained 0.20 g of **6**, mp 216–218 °C (lit.[3] mp 218–219 °C).

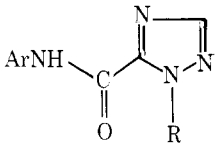
Hydrolysis of 9. When a mixture of 0.50 g of **9** and 5 mL of 10% aqueous NaOH had been swirled briefly on a steam bath, there resulted a solution and a small amount of oily material which later solidified. Chilling followed by filtration yielded a small amount of *N,N'*-diphenylurea and a solution, which was acidified with dilute hydrochloric acid (evolution of CO_2) and then made barely alkaline by addition of aqueous NH_3. The precipitate was recrystallized from *n*-PrOH to give 0.20 g of **6**, mp 216–218 °C.

Reaction of 9 with Aniline. Brief heating on a steam bath of 0.50 g of **9** with 3 mL of $PhNH_2$ yielded a pasty material which was cooled and mixed with CCl_4. The precipitated solid was collected by filtration, washed with CCl_4, and then extracted with three 25-mL portions of $CHCl_3$. The residue was 0.35 g of *N,N'*-diphenylurea, mp 210–230 °C raised to 237–239 °C by recrystallization from EtOH. Evaporation of the chloroform solution left 0.25 g of impure **6**, mp 204–208 °C, which was recrystallized from *n*-PrOH to give crystals melting at 216–218 °C.

Reaction of 9 with Isobutyl Alcohol. A mixture of 0.50 g of **9** and 5 mL of *i*-BuOH was heated on a steam bath for 5 min, and the resulting solution was evaporated to dryness under reduced pressure. Extraction of the residue with three 5-mL portions of 10% aqueous NaOH left an insoluble material, recrystallization of which from petroleum ether (bp 35–60 °C) gave 0.20 g of isobutyl *N*-phenylcarbamate, mp 84–86 °C. Neutralization of the alkaline extract with hydrochloric acid yielded 0.25 g of **6**, mp 215–217 °C.

Reaction of 9 with PhNCO in the Presence of Et_3N. A mixture of 2.5 g (8.2 mmol) of **9**, 1.0 g (8.2 mmol) of PhNCO, and 3 mL of Et_3N was heated on a steam bath for 17 h. After the reaction mixture had been cooled and washed with petroleum ether (bp 63–75 °C), it was extracted with five 10-mL portions of $CHCl_3$. The insoluble material was 1.6 g of impure *N,N'*-diphenylurea, mp 203–220 °C, which was

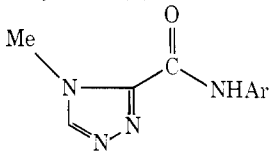
Table I.[a] ***N*-Aryl-1*H*-1,2,4-triazole-5-carboxamides (1a–g)**



compd	R	Ar	reaction time, h	yield,[b] %	mp, °C	IR (C=O), cm^{-1}	NMR, δ
1a	H	Ph	26	62	230–231.5[c]	1680	14.47 (s, 1, ring NH), 10. 27 (s, 1, amide NH), 8.35 (s, 1, triazole 3-CH), 7.77–7.57 (m, 2, aromatic), 7.27–6.93 (m, 3, aromatic)
1b	H	4-MeC_6H_4	52	52	267.5–269.5[d]	1680	10.42 (s, 1, amide NH), 8.62 (s, 1, triazole 3-CH), 7.85–7.70 (m, 2, aromatic), 7.23–7.08 (m, 2, aromatic), 2.27 (s, 3, CH_3)
1c	H	3-ClC_6H_4	22	79	254–255[e]	1680	10.68 (s, 1, amide NH), 8.65 (s, 1, triazole 3-CH), 8.05–7.07 (m, 4, aromatic)
1d	H	1-naphthyl	50	44	286–287 dec[c]	1680	10.57 (s, 1, amide NH), 8.63 (s, 1, triazole 3-CH), 8.05–7.38 (m, 7, aromatic)
1e	Me	Ph	26	46	84.5–86[c]	1690	10.63 (s, 1, NH), 8.08 (s, 1, triazole 3-CH), 7.92–7.75 (m, 2, aromatic), 7.50–7.08 (m, 3, aromatic), 4.17 (s, 3, CH_3)
1f	Me	4-MeC_6H_4	42	43	136.5–138.5[c]	1690	10.62 (s, 1, NH), 8.22 (s, 1, triazole 3-CH), 7.92–7.78 (m, 2, aromatic), 7.30–7.17 (m, 2, aromatic), 4.23 (s, 3, NCH_3), 2.28 (s, 3, CCH_3)
1g	Me	3-ClC_6H_4	25	77	143–144[f]	1690	10.88 (s, 1, NH), 8.13 (s, 1, triazole 3-CH), 8.07–7.08 (m, 4, aromatic), 4.20 (s, 3, CH_3)

[a] Satisfactory analytical data (±0.30% for C, H, N) were submitted for all new compounds listed in this table. [b] Product with melting point lower than that of the analytically pure compound by not more than 10 °C. [c] Recrystallized from EtOH. [d] Recrystallized from *n*-BuOH. [e] Recrystallized from EtOH–petroleum ether (bp 63–75 °C). [f] Recrystallized from *n*-PrOH.

Table II.[a] ***N*-Aryl-4-methyl-4*H*-1,2,4-triazole-3-carboxamides (5a–c)**



compd	Ar	reaction time, h	yield,[b] %	mp, °C[c]	IR (C=O), cm^{-1}	NMR, δ
5a	Ph	1	84	160.5–162	1670	10.80 (s, 1, NH), 8.70 (s, 1, triazole 5-CH), 7.93–7.77 (m, 2, aromatic), 7.50–7.05 (m, 3, aromatic), 3.93 (s, 3, CH_3)
5b	4-MeC_6H_4	1.5	88	206.5–208	1690	10.75 (s, 1, NH), 8.70 (s, 1, triazole 5-CH), 7.82–7.67 (m, 2, aromatic), 7.22–7.08 (m, 2, aromatic), 3.97 (s, 3, NCH_3), 2.30 (s, 3, CCH_3)
5c	3-ClC_6H_4	0.5	90	168–170	1690, 1680	10.97 (s, 1, NH), 8.68 (s, 1, triazole 5-CH), 8.07–7.07 (m, 4, aromatic), 3.95 (s, 3, CH_3)

[a] Satisfactory analytical data (±0.30% for C, H, N) were submitted for all new compounds listed in this table. [b] Product with melting point lower than that of the analytically pure compound by not more than 10 °C. [c] Recrystallization from EtOH.

purified by recrystallization from EtOH, mp 236–238 °C. Evaporation of the chloroform solution left a residue which was recrystallized from CCl_4–$CHCl_3$ (3:1) to give 0.6 g of **7**,[24] mp 170–172 °C (lit.[3] mp 179.5–180 °C).

***N,N'*-Diphenylimidazole-1,4-dicarboxamide (12). A.** An exothermic reaction took place when 1 mL of Et_3N was added to an intimate mixture of 0.93 g (0.0050 mol) of **11**[13] and 1.19 g (0.010 mol) of PhNCO. The resulting mixture was heated on a steam bath for 3 h and then cooled and mixed with petroleum ether (bp 63–75 °C). Filtration and washing of the precipitate with petroleum ether gave a solid which was extracted with six 25-mL portions of chloroform. The remaining insoluble material was 1.40 g (92%) of **12**, mp 212–217 °C. The IR spectrum of the chloroform extract was identical with that of authentic triphenyl isocyanurate.

B. Brief heating on a Bunsen flame of a mixture of 0.93 g of **11** and 5 mL of PhNCO gave a thick pasty material which was cooled, mixed with petroleum ether (bp 63–75 °C), and filtered to yield 1.35 g (88%) of **12**, mp 219–221 °C dec. An analytical sample of **12** was obtained by recrystallization from trichloroethane as colorless crystals: mp 223.5–225.5 °C dec; IR 3330 (N–H), 1730, 1650 (C=O) cm^{-1}.[22] Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29. Found: C, 66.54; H, 4.45; H, 18.51.

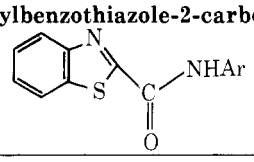
Thermal decomposition of 12 was carried out as described for **10**, except that the oil bath was kept at 230–240 °C. From 0.30 g of **12**, there was obtained 0.15 g of **11**, mp 223–226 °C (lit.[13] mp 227–228 °C).

Hydrolysis of 12. A mixture of 0.50 g of **12** and 5 mL of 10% aqueous NaOH was heated briefly on a steam bath to effect dissolution. Neutralization of the resulting solution with dilute hydrochloric acid followed by filtration yielded 0.30 g of **11**, mp 222–224 °C.

Reaction of 12 with Aniline. A mixture of 0.50 g of **12** and 5 mL of $PhNH_2$ was brought to the boiling point and then was cooled, diluted with CCl_4, and filtered to separate the precipitate, which was subsequently extracted with three 5-mL portions of 10% aqueous NaOH. The insoluble material was 0.30 g of *N,N'*-diphenylurea, mp 225–227 °C raised to 236–238 °C by recrystallization from EtOH. Neutralization of the extract with dilute hydrochloric acid caused precipitation of 0.20 g of **11**, mp 223–226 °C.

Reaction of 12 with Isobutyl Alcohol. A mixture of 0.50 g of **12** and 10 mL of *i*-BuOH was boiled for 2–3 min, and the resulting so-

Table III.[a] ***N*-Arylbenzothiazole-2-carboxamides (13a–d)**



compd	Ar	reaction time, h	yield,[b] %	mp, °C[c]	IR (C=O), cm^{-1}	NMR, δ
13a	Ph	26	64	157–158.5[c,d]	1670	10.93 (s, 1, NH), 8.13–7.00 (m, 9, aromatic)
13b	4-MeC_6H_4	26	56	146–148[c]	1670	10.95 (s, 1, NH), 8.30–8.13 (m, 2, aromatic), 7.87–7.53 (m, 4, aromatic), 7.25–7.10 (m, 2, aromatic), 2.30 (s, 3, CH_3)
13c	3-ClC_6H_4	8	67	142–143[c]	1680	11.28 (s, 1, NH), 8.33–7.13 (m, 8, aromatic)
13d	1-naphthyl	20	51	211–212[e]	1670	11.50 (s, 1, NH), 8.73–7.73 (m, 11, aromatic)

[a] Satisfactory analytical data (±0.30% for C, H, N) were reported for all new compounds listed in this table. [b] Product with melting point lower than that of the analytically pure compound by not more than 10 °C. [c] Recrystallized from EtOH. [d] Literature mp 157–158 °C [K. Zahn, *Chem. Ber.*, **56**, 578 (1923)]. [e] Recrystallized from *n*-BuOH.

lution was evaporated to dryness under reduced pressure. Extraction of the residue with three 5-mL portions of 10% aqueous NaOH left 0.30 g of isobutyl *N*-phenylcarbamate, mp 78–82 °C raised to 84–86 °C by recrystallization from aqueous EtOH. The alkaline extract was neutralized with hydrochloric acid to yield 0.20 g of **11**, mp 218–222 °C raised to 223–225 °C by recrystallization from water.

Preparation of Compounds 13a–d (Table III). A mixture of 0.10 mol of benzothiazole, 0.10 mol of isocyanate, and 30 mL of $PhNO_2$ was refluxed for the length of time indicated in Table III. Isolation of product was effected by dilution of the chilled reaction mixture with petroleum ether (bp 63–75 °C), filtration, and repeated washing of the precipitate with the same solvent.

1-Formyl-4-methyl-3-thiosemicarbazide. A mixture of 95 g of 4-methyl-3-thiosemicarbazide[25] and 200 mL of 88% HCOOH was heated on a steam bath for 45 min and then chilled and filtered. Washing of the precipitate with ice-cold Et_2O yielded 96 g (80%) of the title compound, mp 165–167 °C dec (lit.[25] mp 167–168 °C).

4-Methyl-4*H*-1,2,4-triazole-3-thiol. It was prepared from 1-formyl-4-methyl-3-thiosemicarbazide in 91% yield, mp 163–166 °C (lit.[20b] mp 168 °C), following the procedure for the preparation of 1,2,4-triazole-3(5)-thiol.[20c]

4-Methyl-4*H*-1,2,4-triazole. The procedure used to prepare 1*H*-1,2,4-triazole[20c] was followed up to the point of extraction of the product from its mixture with inorganic salts. The dried reaction mixture was successively refluxed, while being mechanically stirred, with twelve 200-mL portions of chloroform. The extracts, collected by decantation, were dried (Na_2CO_3) and evaporated to dryness under reduced pressure to yield the title compound. Starting with 115 g (1 mol) of 4-methyl-4*H*-1,2,4-triazole-3-thiol, there was obtained 70.7 g (85%) of 4-methyl-4*H*-1,2,4-triazole, mp 90–92 °C (lit.[20b] mp 90 °C).

Acknowledgment. Financial support from the Research Corporation, the Research Allocations Committee of the University of New Mexico, and the Department of Chemistry of the University of New Mexico is gratefully acknowledged.

Registry No.—**1a,** 68070-52-0; **1b,** 68070-53-1; **1c,** 68070-54-2; **1d,** 68070-55-3; **1e,** 68070-56-4; **1f,** 68070-57-5; **1g,** 68070-58-6; **3,** 27257-97-2; **4,** 68070-66-6; **5a,** 68070-59-7; **5b,** 68070-60-0; **5c,** 68070-61-1; **5d,** 68070-67-7; **6,** 63678-16-0; **7,** 63678-28-4; **9,** 68070-68-8; **10,** 68070-69-9; **11,** 13189-13-4; **12,** 68070-70-2; **13a,** 68070-62-2; **13b,** 68070-63-3; **13c,** 68070-64-4; **13d,** 68070-65-5; 1*H*-1,2,4-triazole-288-88-0; pyrazole, 288-13-1; 1-methyl-1*H*-1,2,4-triazole, 6080-21-1; aniline, 62-53-3; *N,N'*-diphenylurea, 102-07-08; isobutyl *N*-phenylcarbamate, 2291-80-7; benzothiazole, 95-16-9; 1-formyl-4-methyl-3-thiosemicarbazide, 58064-52-1; 4-methyl-3-thiosemicarbazide, 6610-29-3; 4-methyl-4*H*-1,2,4-triazole-3-thiol, 24854-43-1; 4-methyl-4*H*-1,2,4-triazole, 10570-40-8; phenyl isocyanate, 103-71-9; 4-methylphenyl isocyanate, 622-58-2; 3-chlorophenyl isocyanate, 2909-38-8; 1-naphthyl isocyanate, 86-84-0.

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(5) Formulation **1a–d,** which allows two intramolecular hydrogen bonds, is preferable to that of the tautomeric *N*-aryl-1*H*-1,2,4-triazole-3-carboxamide, in which only one such bond is possible. Representation of the product as the third possible tautomer, *N*-aryl-4*H*-1,2,4-triazole-3-carboxamide, is less desirable from the point of view of nomenclature.
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(21) The point and extent of decomposition vary somewhat with the rate of heating.
(22) When dissolved in Me_2SO, **9, 10,** and **12** partially dissociate into phenyl isocyanate and the corresponding monocarboxanilide. As a result, their NMR spectra are not useful for characterization.
(23) (a) "Handbook of Tables for Organic Compound Identification", Z. Rappoport, Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1974, p 245; (b) *ibid.*, p 80.
(24) The mother liquor was found to contain mainly triphenyl isocyanurate and **6**. Trimerization of the isocyanate seems to compete effectively with the main reaction, in this case, perhaps because of the inadequate distribution of the small volume of PhNCO over the solid **9.**
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