Mesoionic Compounds. XIV. Mesoionic Compounds of the Imidazole Series[1]

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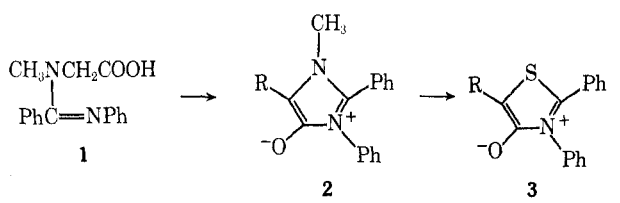
Received May 4, 1971

Reaction of *N*-methyl-*N*-(*N'*-phenylbenzimidoyl)aminoacetonitrile with dry HCl gave 4-amino-2,3-diphenyl-1-methylimidazolium chloride which, with acetic anhydride, followed by sodium bicarbonate, formed *anhydro*-4-acetimino-2,3-diphenyl-1-methylimidazolium hydroxide. This was also obtained from the reaction of acetyl chloride–benzene, followed by sodium bicarbonate, with the nitrile. An analogous series of 4-benzoylimino derivatives was also prepared. With warm, dilute potassium hydroxide solution, the nitrile gave 4-anilino-1-methyl-2-phenylimidazole which was also obtained from 4-amino-2,3-diphenyl-1-methylimidazolium chloride, through a Dimroth-type rearrangement. These exocyclic imino compounds showed very ready 1,3-dipolar reactivity with acetylenic and azo type dipolarophiles. With dimethyl acetylenedicarboxylate, the corresponding pyrrole was formed with possible extrusion of *N*-benzoyl-*N'*-phenylcarbodiimide from the initial cycloadduct.

Mesoionic derivatives of the imidazole ring system were first described[2] in 1959, though several ring-fused compounds containing the imidazole nucleus and now represented as mesoionic compounds were prepared earlier.[2,3] The monocyclic system, represented by *anhydro*-4-hydroxy-2,3-diphenyl-1-methylimidazolium hydroxide was prepared in the form of its 5-acetyl and 5-propionyl derivative (**2**, R = $COCH_3$ and COC_2H_5, respectively) by cyclization of *N*-(*N'*-phenylbenzimidoyl)glycine (**1**) with the appropriate acid anhydride. The action of acid or base had no effect on **2**, and it was remarkably stable in comparison with other mesoionic compounds. Representatives of this mesoionic ring system with an exocyclic sulfur atom are known and have been prepared from other mesoionic systems and phenyl isothiocyanate. Thus, *anhydro*-4-mercapto-1-methyl-2,3,5-triphenylimidazolium hydroxide was obtained[4] from anhydro-2,4-diphenyl-5-hydroxy-3-methyloxazolium hydroxide and phenyl isothiocyanate in xylene at 70°. Under similar conditions *anhydro*-2-aryl-5-hydroxy-3-methylthiazolium hydroxides also gave the corresponding *anhydro*-2-aryl-4-mercapto-1-methyl-3-phenylimidazolium hydroxides.[5]



Our studies in other mesoionic ring systems suggested that a study of the imidazole system would be of interest. Experience with other five-membered mesoionic systems indicated that the stability of **2** was due to the 5-acyl group which could quite effectively delocalize the exocyclic negative charge on the oxygen atom. We had found previously that, though *anhydro*-2,3-diphenyl-4-hydroxythiazolium hydroxide (**3**, R = H) was an extremely active substrate for nucleophiles and dipolarophiles, its 5-acyl derivative (**3**, R = $COCH_3$) was quite stable.[6] Thus the behavior of *anhydro*-4-hydroxy-2,3-diphenyl-1-methylimidazolium hydroxide (**2**, R = H) with acetylenic and olefinic dipolarophiles was of particular interest.

The most direct route to **2** (R = H) would be the acetic anhydride–triethylamine cyclization of *N*-(*N'*-phenylbenzimidoyl)glycine (**1**), analogous to the procedure used successfully for the synthesis of **3** (R = H). Attempts to prepare the acid **1** by condensation of sarcosine (or its ester) with *N*-phenylbenzimidoyl chloride were unsuccessful. An alternative route, the hydrolysis of *N*-methyl-*N*-(*N'*-phenylbenzimidoyl)-aminoacetonitrile (**4**), was employed in the original synthesis of **2** (R = $COCH_3$) and has recently been investigated by other workers with no success.[7] We have also found that the hydrolysis of **4** with 2% aqueous HCl[2] did not yield the acid **1** but gave *N*-methyl-*N*-(*N'*-phenylbenzimidoyl)acetamide hydrochloride (**5**), contaminated with benzanilide and sarcosine hydrochloride. Variations of these hydrolysis conditions did not appreciably alter the above results. However, when 20% HCl was used, the hydrochloride of the desired acid was obtained in small amounts in an impure state. This was converted into the sodium salt[2] which, with triethylamine (or pyridine) and acetic anhydride under a wide variety of conditions, always gave the acetyl derivative **2** (R = $COCH_3$). These results indicate that the unsubstituted mesoionic system **2** (R = H) is extremely susceptible to electrophilic attack and suggest a high-electron density at the 5 position of the nucleus. Recent MO calculations[7] show a considerably larger degree of negative charge associated with the C_4–C_5 atoms in **2** (R = H) compared with that in the sydnones.[8] The extremly facile acetylation is understandable in these terms. These calculations indicate, moreover, that mesoionic imidazoles should show considerable 1,3-dipolar reactivity though we found that the 5-acetyl compound (**2**, R = $COCH_3$) was completely unresponsive to a variety of dipolarophiles and heterocumulenes.

The best known[9] examples of mesoionic compounds with a negatively charged exocyclic nitrogen atom, either in the protonated form or with the negative charge delocalized to some extent over an acyl group

(1) (a) Support of this work by U. S. Public Health Service Research Grant CA 08495, National Cancer Institute, is gratefully acknowledged. (b) Part of this work has appeared in a preliminary communication: K. T. Potts, S. Husain, and S. Husain, *Chem. Commun.*, 1360 (1970).

(2) A. Lawson and D. H. Miles, *J. Chem. Soc.*, 2865 (1959).

(3) E. Besthorn and J. Ibel, *Ber.*, **37**, 1236 (1904); F. Knollpfieffer and K. Schneider, *Justus Leibigs Ann. Chem.*, **530**, 34 (1937); D. L. Hammick and A. M. Roe, *Chem. Ind. (London)*, 900 (1953).

(4) R. Huisgen, E. Funke, F. C. Schaefer, H. Gotthardt, and E. Brunn, *Tetrahedron Lett.*, 1809 (1967).

(5) K. T. Potts and D. N. Roy, *Chem. Commun.*, 1062 (1968).

(6) K. T. Potts, U. P. Singh, and E. Houghton, *ibid.*, 1128 (1969).

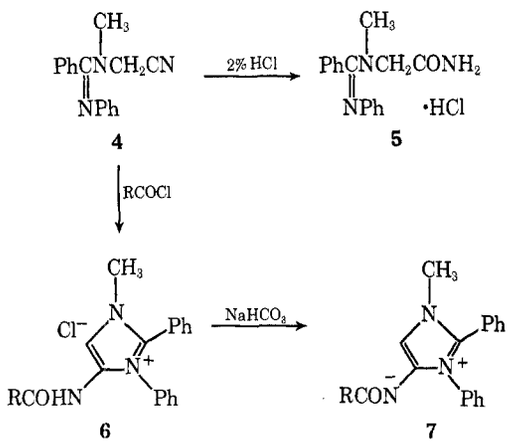
(7) E. B. Roche and D. W. Stansloski, *J. Heterocycl. Chem.*, **7**, 139 (1970).

(8) L. B. Kier, *J. Pharm. Sci.*, **55**, 807 (1966); E. B. Roche and L. B. Kier, *Tetrahedron*, **24**, 1673 (1968).

(9) H. Chosho, K. Ichimura, and M. Ohta, *Bull. Chem. Soc. Jap.*, **37**, 1670 (1964); M. Ohta and M. Sugiyama, *ibid.*, **38**, 598 (1965).

attached to the nitrogen atom, are the sydnone imines.[10] It was of importance, then, to prepare the corresponding imino derivatives of the imidazole system **7**, and the nitrile **4** was a suitable starting point for this synthesis.

Reaction of **4** with benzoyl chloride in dry benzene readily gave 4-*N*-benzamido-2,3-diphenyl-1-methylimidazolium chloride (**6**, R = Ph) which, when treated

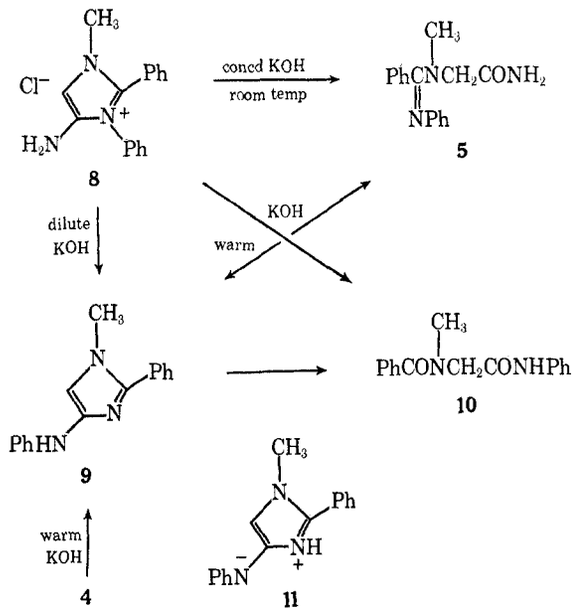


with aqueous sodium bicarbonate, formed *anhydro*-4-*N*-benzoylimino-2,3-diphenyl-1-methylimidazolium hydroxide (**7**, R = Ph). Analytical and spectral data, especially a carbonyl absorption at 1580 cm^{-1}, and a singlet proton resonance at τ 2.37 in the corresponding *N*-acetimino compound clearly indicated that cyclization had occurred as shown. In *N*-acylsydnone imines the carbonyl absorption was found[11] to be in the region 1667–1626 cm^{-1} and the corresponding ring proton resonated[11] between τ 2.00–2.37.

The corresponding *anhydro*-4-*N*-acetimino-2,3-diphenyl-1-methylimidazolium hydroxide (**7**, R = CH_3) was obtained similarly from **4** and acetyl chloride. Its spectral characteristics were consistent with those of the benzoyl derivative (see Experimental Section).

As anticipated, the action of dry hydrogen chloride on the nitrile **4** resulted in the formation of 4-amino-2,3-diphenyl-1-methylimidazolium chloride (**8**). The disappearance of the ν_{CN} 2250-cm^{-1} absorption of **4** and the presence of a ν_{NH_2} 3390-, 3250-cm^{-1} absorption, together with a singlet proton at τ 2.85, provided strong evidence for the assigned structure. Conversion of **8** into its picrate and perchlorate provided additional evidence for this structure. As **7** (R = CH_3) is the acetylated derivative of **8** minus the elements of HCl, it was possible to convert **8** into **7** (R = CH_3) by the action of acetic anhydride, followed by sodium bicarbonate. Similarly, treatment of **8** with benzoic anhydride followed by sodium bicarbonate gave **7** (R = Ph) in 71% yield. Additional evidence for the structure of the salt **8** was its behavior on mild treatment with aqueous potassium hydroxide solution. At room temperature over a short period of time, it was transformed into *N*-methyl-*N*-(N^1-phenylbenzimidoyl)acetamide (**5**).

A recent report[12] of the formation of *anhydro*-3-imino-4-methyl-5-phenyl-1,2,4-thiadiazolium hydroxide



from the action of Ag_2O on the corresponding hydroiodide is of particular interest in this area of imino derivatives of mesoionic compounds. This is the first instance in which the free base of such a compound has been isolated, and we were accordingly especially interested in studying the action of base on the compound **8**. On treatment with warm, dilute potassium hydroxide sulution, it was transformed into an isomeric product ($M \cdot^+$, *m/e* 249) with an infrared absorption band at 3275 cm^{-1}, indicative of an NH group. No carbonyl absorption was present and the nmr spectrum of the product indicated the presence of an NCH_3 group (τ 6.26), a sharp singlet at τ 3.07, aromatic absorptions at τ 2.99–2.42, and a single proton at τ 1.84 which rapidly exchanged with D_2O. This product was characterized further by conversion into its picrate and acetyl derivative which were not the same as the corresponding derivatives obtained from 4-amino-2,3-diphenyl-1-methylimidazolium chloride (**8**). This alkali-treatment product is best represented by structure **9**, 4-anilino-1-methyl-2-phenylimidazole, which could be formed by a Dimroth-type rearrangement from **8**. This is the first reported example of such a rearrangement in mesoionic-type systems,[13] though related interconversions of mesoionic ring systems, such as the imidazole → thiazole[4] and the 1,3,4-oxadiazole → 1,3,4-thiadiazole[14] ring system have been reported. The rearrangement product **9** was also formed by several other routes. Thus treatment of the nitrile **4** with warm potassium hydroxide solution, and also treatment of the amide **5** under similar conditions, gave **9**. It is most likely that the reaction of the nitrile **4** actually involved the intermediacy of the amide **5**. In another hydrolysis experiment, prolonged treatment of the salt **8** with aqueous potassium hydroxide over 3 days gave *N*-benzoyl-*N*-methylaminoacetanilide (**10**) which could only have arisen by hydrolysis of the rearrangement product **9** formed initially from **8**. As expected, treatment of **9** under similar conditions gave **10**.

(10) P. Brookes and J. Walker, *J. Chem. Soc.*, 4409 (1957); H. Kato, M. Hashimoto, and M. Ohta, *Nippon Kagaku Zasshi*, **78**, 707 (1957).

(11) H. U. Daeniker and J. Druey, *Helv. Chim. Acta*, **45**, 2441 (1962).

(12) J. Goerdeler and W. Roth, *Chem. Ber.*, **96**, 534 (1963).

(13) In a future communication, several other examples of Dimroth-type rearrangements [for a recent review see M. Wahren, *Z. Chem.*, **9**, 241 (1969)] in mesoionic systems will be described.

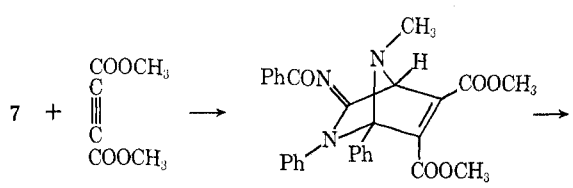
(14) A. R. McCarthy, W. D. Ollis, and C. A. Ramsden, *Chem. Commun.*, 499 (1968).

The acetyl product obtained from **9** and acetic anhydride is worthy of further comment. Mass spectral data ($M\cdot^+$, *m/e* 291) indicated that monoacetylation only had occurred and this was confirmed by nmr data. A sharp singlet at τ 7.49, coupled with the disappearance of the 5 H in **9** at τ 3.07 and an exchangeable proton at τ 0.13 (NH, a downfield shift of 1.71 ppm from the NH in **9**) suggested that C-acetylation had occurred. This is consistent with the known directive effects on electrophilic substitution of the imidazole nucleus.[15]

The above data are more consistent with the representation of this rearrangement product as **9** rather than as its tautomer **11**. However, in the oxazole series, analogous dipolar structures have been shown to be involved in the characteristic cycloadditions of azomethine ylides shown by Δ^2-oxazolin-5-ones.[16]

In cycloadditions utilizing mesoionic systems as 1,3 dipoles, small, stable molecules such as carbon dioxide[17] or carbon disulfide[18] are usually eliminated from the initial cycloadduct. We recently showed that *p*-tolyl isocyanate was readily lost from the initial cycloadduct formed from *anhydro*-4-hydroxy-1-methyl-3-*p*-tolyl-1,2,3-triazolium hydroxide and dimethyl acetylenedicarboxylate,[19] and we have now found that much larger fragments may be eliminated from primary cycloadducts.

Reaction of *anhydro*-4-benzoylimino-2,3-diphenyl-1-methylimidazolium hydroxide (**7**, R = Ph) with dimethyl acetylenedicarboxylate occurred over 10 min in refluxing benzene with the formation of dimethyl 1-methyl-2-phenylpyrrole-3,4-dicarboxylate (**13**) in 38% yield. By analogy with other 1,3-dipolar cycloadditions of this type, the reaction is regarded as involving an intermediate such as **12** from which *N*-benzoyl-*N'*-phenylcarbodiimide was eliminated. No trace of this product was detected, the only other compound isolated being benzanilide. The corresponding acetyl derivative of **7** (R = CH_3) also underwent ready reaction with the dipolarophile forming **13** in 45% yield.



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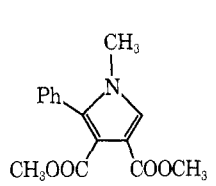

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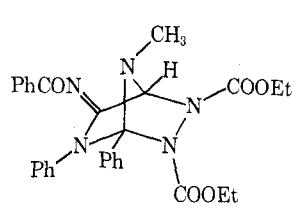

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With ethyl azodicarboxylate **7** (R = PH) formed a stable 1:1 adduct (85% yield) represented as **14** on the basis of analytical and spectral data. The nmr spectrum showed the presence of the two ester groups and the NCH_3 group. In this case, however, the bridgehead hydrogen at C_4 absorbed in the same region as the phenyl protons, no doubt due to the effect of the *N*-benzoylimino substituent at C_5. In the corresponding 1:1 adduct from *anhydro*-4-hydroxy-1-methyl-3-*p*-tolyl-1,2,3-triazolium hydroxide,[19] the analogous bridgehead proton was found at τ 0.18, though in the adduct from dimethyl acetylenedicarboxylate and *anhydro*-4-hydroxy-2-methylcinnolinium hydroxide[20] it occurred at τ 5.69. Ethyl azodicarboxylate also formed a 1:1 adduct with **7** (R = CH_3). Though the adduct was obtained crystalline, it was unstable and rapidly deteriorated.

Similarly dimethyl maleate formed a 1:1 adduct with **7** (R = Ph) which, on the basis of analytical data, is tentatively assigned a structure analogous to **14**. Spectral data were not sufficiently definitive to enable an unambiguous assignment of structure to be made.

Experimental Section[21]

Hydrolysis of *N*-Methyl-*N*-(*N'*-phenylbenzimidoyl)aminoacetonitrile (4). A. With 2% HCl.—The nitrile (2.5 g) was refluxed in 2% aqueous HCl (25 ml) for 45 min and, after cooling, the oily product which had solidified was removed by extraction with chloroform. It formed colorless needles, mp 164–165°, and was identified[22] as benzanilide (lit.[23] mp 163°): ν_{NH} 3350, ν_{CO} 1650 cm^{-1}. The aqueous phase was evaporated to dryness and dried thoroughly. The solid residue was then triturated with absolute ethanol and filtered giving sarcosine hydrochloride, 100 mg, mp 169° (lit.[24] mp 168–170°). The ethanol filtrate was diluted with an excess of anhydrous ether and cooled, and the resultant gummy solid was triturated with acetone whence it solidified. It crystallized from ethanol–ether as colorless shiny plates of *N*-methyl-*N*-(*N'*-phenylbenzimidoyl)acetamide hydrochloride (**5**): 0.8 g (28%); mp 192–193°; ir (KBr) 3210 (NH), 2850 ($\geq N^+-$), 1700 (CO), 1650 cm^{-1} (C=N); $\lambda_{max}^{CH_3OH}$ 225 nm (log ϵ 4.13), 197 (4.50); nmr (DMSO-d_6) τ 6.9 (s, 3, NCH_3), 5.25 (s, 2, CH_2), 2.53 (m, 10, aromatic).

Anal. Calcd for $C_{16}H_{18}ClN_3O$: C, 63.26; H, 5.93; N, 13.83. Found: C, 63.27; H, 5.97; N, 13.97.

The free base was obtained by the addition of sodium hydroxide to an aqueous solution of the hydrochloride and isolated by chloroform extraction. It crystallized from chloroform–petroleum ether (bp 60–80°) as colorless needles: mp 97–99°; ir (KBr) 3440, 3325 (NH), 1650 cm^{-1} (CO); $\lambda_{max}^{CH_3OH}$ 223 nm (log ϵ 4.07), 197 (4.46); nmr ($CDCl_3$) τ 6.95 (s, 3, NCH_3), 5.79 (broad s, 2, CH_2), 5.02 (broad s, 2, NH_2), 2.93 (m, 10, aromatic); $M\cdot^+$ *m/e* (rel intensity) 267 (39).

Anal. Calcd for $C_{16}H_{17}N_3O$: C, 71.88; H, 6.41; N, 15.72. Found: C, 72.02; H, 6.44; N, 15.83.

B. With 20% HCl.—The nitrile (2.5 g) in 20% aqueous HCl (25 ml) was refluxed for 45 min. On cooling, shiny plates (0.4 g) of benzoic acid, mp 122°, separated from the hydrolysis mixture. The filtrate was evaporated to dryness, water added, and the evaporation repeated. Absolute ethanol was then added and all traces of water were removed by several evaporations with absolute ethanol. The residue was treated with a further quantity of ethanol and the undissolved material, shown to be ammonium chloride, separated. Concentration of the ethanol solution and

(15) E. S. Schipper and A. R. Day in "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., Wiley, New York, N. Y., 1957, pp 199–203.

(16) H. Gotthardt, R. Huisgen, and H. O. Bayer, *J. Amer. Chem. Soc.*, **93**, 4340 (1970), and references cited therein; G. Kille and J. P. Fleury, *Bull. Soc. Chim. Fr.*, 4636 (1968); R. Huisgen, R. Grashey, and E. Steingruber, *Tetrahedron Lett.*, 1441 (1963).

(17) *E.g.*, R. Huisgen, H. Gotthardt, and R. Grashey, *Chem. Ber.*, **101**, 536 (1968).

(18) K. T. Potts and D. N. Roy, *Chem. Commun.*, 1061 (1968).

(19) K. T. Potts and S. Husain, *J. Org. Chem.*, **35**, 3451 (1970).

(20) D. E. Ames and B. Novitt, *J. Chem. Soc. C.*, 2355 (1969).

(21) All evaporations were carried out under reduced pressure using a Rotavap apparatus. Spectral characterizations were performed with the following instrumentation: ir and uv spectra, Perkin-Elmer Model 337 and Cary Model 14 spectrophotometers, respectively; nmr, Varian A-60 spectrometer; mass spectra, Hitachi Perkin-Elmer RMU-6E mass spectrometer (70 eV). Melting points were taken in capillaries and microanalyses were performed by Instranal Laboratories, Inc., Rensselaer, N. Y.

(22) Standards for product equivalency were superimposable infrared spectra, less than 2° depression in a mixture melting point, and identical R_f values on tlc.

(23) F. J. Sowa and J. A. Nieuwland, *J. Amer. Chem. Soc.*, **59**, 1202 (1937).

(24) L. Bauman, *J. Biol. Chem.*, **21**, 563 (1915).

cooling gave sarcosine hydrochloride which was removed. The ethanol filtrate was diluted with ether and the product which separated was triturated with acetone giving a dark solid material. This was dissolved in saturated sodium bicarbonate solution and yielded the impure sodium salt (*ca.* 0.5 g) of the acid 1 on evaporation to dryness.

Attempted Synthesis of *anhydro*-2,3-Diphenyl-4-hydroxy-1-methylimidazolium Hydroxide.—The acid hydrochloride prepared above, or the sodium salt of the acid, was treated, at 0° with acetic anhydride–triethylamine (3:1). Colorless needles (from benzene–petroleum ether) of *anhydro*-5-acetyl-2,3-diphenyl-4-hydroxyimidazolium hydroxide, mp 241–243° (lit.[2] mp 241–243°), were always obtained irrespective of the proportion and amount of acetic anhydride–triethylamine used: ir (KBr) 1690, 1625 cm^{-1} (CO); nmr ($CDCl_3$) τ 7.42 (s, 3, $COCH_3$), 6.05 (s, 3, NCH_3), 2.65 (m, 10, aromatic).

***anhydro*-4-Benzoylimino-2,3-diphenyl-1-methylimidazolium Hydroxide (7, R = Ph).**—The nitrile **4** (2.5 g), dry benzene (75 ml), and benzoyl chloride (1.5 g) were refluxed for 1 hr during which time the hydrochloride separated. After cooling, the solid material was treated with a 5% aqueous solution of sodium bicarbonate and a yellow product separated. It crystallized from chloroform–petroleum ether as shiny, yellow needles: 3.0 g (85%); mp 249–251°, with darkening at 230°; ir (KBr) 3170, 3040 (CH), 1580 (CO), 1540 cm^{-1} (C=N); $\lambda_{max}^{CH_3OH}$ 322 nm (log ϵ 3.92), 260 (3.98), 225 (4.31); $M^{\cdot+}$ *m/e* (rel intensity) 353 (42).

Anal. Calcd for $C_{23}H_{19}N_3O$: C, 78.16; H, 5.42; N, 11.89. Found: C, 78.00; H, 5.42; N, 11.82.

When the nitrile **4** (0.6 g) in dry benzene (10 ml) and acetyl chloride (0.2 g) were stirred at room temperature for 30 min and then warmed gently for an additional 30 min, the corresponding hydrochloride separated. Addition of 5% aqueous sodium bicarbonate solution to the hydrochloride and extraction of the resulting solution with chloroform finally gave a pale yellow product. ***anhydro*-4-Acetimino-2,3-diphenyl-1-methylimidazolium hydroxide (7, R = CH_3)** crystallized from methanol–benzene as pale yellow needles: 0.6 g (85%); mp 192–193°; ir (KBr) 3400 (H_2O), 3160, 3050 (CH), 1550 (CO), 1500 cm^{-1} (C=N); $\lambda_{max}^{CH_3OH}$ 257 nm (log ϵ 3.93); nmr (DMSO-d_6) τ 6.25 (s, 3, $COCH_3$), 6.37 (s, 3, NCH_3), 2.60 (s, 5, N_3-C_6H_5), 2.70 (s, 5, C_3-C_6H_5), 2.37 (s, 1, C_5-H); $M^{\cdot+}$ *m/e* (rel intensity) 291 (32).

Anal. Calcd for $C_{18}H_{17}N_3O \cdot {}^3/_4H_2O$: C, 70.85; H, 5.74; N, 13.78. Found: C, 70.76; H, 5.75; N, 13.67.

4-Amino-2,3-diphenyl-1-methylimidazolium Chloride (8).—Dry hydrogen chloride was passed into a solution of the nitrile **4** (5.0 g) in anhydrous ether (150 ml) at 0°. After saturation of the reaction mixture with hydrogen chloride the product was filtered and washed several times with anhydrous ether. Crystallization from ethanol–ether gave the above salt as colorless, hygroscopic needles: ir (KBr) 3390, 3250, 1650 cm^{-1} (NH_2); nmr (DMSO-d_6) τ 6.27 (s, 3, NCH_3), 2.85 (s, 1, C_5-H), 2.52 (s, 10, aromatic), 2.04 (s, 2, C_4-NH_2, exchanged with D_2O). It was characterized by conversion into its perchlorate by treatment of its aqueous solution with 70% perchloric acid. The perchlorate separated from ethanol–ether as colorless needles: mp 181–182°; ir (KBr) 3425, 3350, 1640 cm^{-1} (NH_2); $\lambda_{max}^{CH_3OH}$ 290 nm (log ϵ 3.83).

Anal. Calcd for $C_{16}H_{16}ClN_3O_4$: C, 54.93; H, 4.58; N, 12.01. Found: C, 55.00; H, 4.65; N, 12.27.

The picrate was obtained as yellow needles from ethanol: mp 143–144°; $\lambda_{max}^{CH_3OH}$ 355 nm (log ϵ 4.19), 303 (3.96).

Anal. Calcd for $C_{22}H_{18}N_6O_7$: C, 55.38; H, 3.78; N, 17.57. Found: C, 55.24; H, 3.75; N, 17.82.

Treatment of 4-Amino-2,3-diphenyl-1-methylimidazolium Chloride with Benzoic Anhydride.—The hydrochloride (3.0 g) and benzoic anhydride (5.0 g) were heated at 150° for 1 hr. The cooled reaction mixture was triturated with benzene and the solid product was collected. It was suspended in water and treated with 10% aqueous sodium bicarbonate whence a yellow product separated. It crystallized from chloroform–petroleum ether as yellow needles, 2.5 g (70%), mp 249–251°. This was identical with **7** (R = Ph). Use of acetic anhydride in the above reaction, except that the final product was isolated by chloroform extraction, gave **7** (R = CH_3) as yellow needles, mp 192–193° (68%).

Reaction of 4-Amino-2,3-diphenyl-1-methylimidazolium Chloride with Sodium Hydroxide. A. Formation of 4-Anilino-1-methyl-2-phenylimidazole (9).—The above chloride (2.0 g) in methanol (15 ml) and KOH (1.5 g) in water (50 ml) were warmed on the steam bath for 3 hr, keeping the reaction volume constant by the addition of water. The product, which started to separate after 30 min, was collected from the cooled reaction mixture and recrystallized from benzene–petroleum ether. It separated as colorless needles: 0.8 g (46%); mp 182–184°; ir (KBr) 3280 (NH), 1620 (C=N), 1580 cm^{-1} (C=C); $\lambda_{max}^{CH_3OH}$ 265 nm (log ϵ 4.00), 232 (3.89), 203 (4.33); nmr (DMSO-d_6) τ 6.26 (s, 3, NCH_3), 3.07 (s, 1, C_5-H), 2.99–2.42 (m, 10, aromatic), 1.84 (s, 1, NH, exchanged with D_2O); $M^{\cdot+}$ *m/e* (rel intensity) 249 (100).

Anal. Calcd for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.86. Found: C, 76.66; H, 5.95; N, 16.82.

Using this same reaction procedure, the nitrile **4** and the amide **5** were converted into **9**. The picrate crystallized from ethanol as yellow needles, mp 210–213°.

B. Formation of *N*-Methyl-*N*-(*N'*-phenylbenzimidoyl)acetamide (5).—The above chloride (1.7 g) in water (40 ml) and potassium hydroxide (2.5 g) in water (40 ml) were allowed to stand for 10 min. The oily product which separated was extracted into chloroform in the usual way. Crystallization from chloroform–petroleum ether afforded colorless needles of the amide **5**, 0.8 g, mp 97–99°.

C. Formation of *N*-Benzoyl-*N*-methylaminoacetanilide (10).—The hydrochloride (1.5 g) in water (10 ml) was stirred at room temperature for 3 days with aqueous potassium hydroxide (0.6 g) in water (30 ml). The crystalline product which separated crystallized from chloroform–petroleum ether as fine, colorless needles: 400 mg (51%); mp 165–166°; ir (KBr) 3300 (NH), 3150, 3100 (CH), 1710, 1650 cm^{-1} (CO); $\lambda_{max}^{CH_3OH}$ 242 nm (log ϵ 4.27); nmr ($CDCl_3$) τ 6.95 (s, 3, NCH_3), 5.62 (s, 2, CH_2), 2.65 (m, 10, aromatic), 0.88 (broad s, 1, NH, exchanged with D_2O); mass spectrum *m/e* (rel intensity) 176 (26), 105 (100), 77 (90).

Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.27; H, 5.92; N, 10.23.

5-Acetyl-4-anilino-1-methyl-2-phenylimidazole.—The 4-anilino compound **9** (400 mg) was heated at 100° with acetic anhydride (4 ml) for 3 hr. The reaction mixture was diluted with benzene and evaporated to dryness. This process was repeated using xylene until all traces of acetic anhydride were removed. The solid residue was dissolved in benzene and chromatographed on Florisil being eluted with chloroform–methanol (2%). It crystallized from benzene–petroleum ether as pale yellow silky needles: mp 149–150°; ir (KBr) 1600, 1625 (CO, C=N), 1580 cm^{-1} (C=C); $\lambda_{max}^{CH_3OH}$ 360 nm (log ϵ 4.24), 273 (4.39), 248 (sh, 4.18), 203 (4.40); nmr ($CDCl_3$) τ 7.49 (s, 3, $COCH_3$), 6.20 (s, 3, NCH_3), 2.92–2.50 (m, 10, aromatics), 0.13 (s, 1, NH, exchanged with D_2O); $M^{\cdot+}$ *m/e* (rel intensity) 291 (100).

Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.23; H, 5.84; N, 14.43. Found: C, 74.23; H, 5.89; N, 14.43.

Reaction of *anhydro*-4-*N*-Benzoylimino-2,3-diphenyl-1-methylimidazolium Hydroxide (7, R = Ph) with Dimethyl Acetylenedicarboxylate.—The 4-*N*-benzoylimino compound (0.7 g), dry benzene (25 ml), and the ester (0.3 g) were gently refluxed for 30 min. The reaction mixture was chromatographed on Florisil and, on elution with chloroform–methanol (98:2), a colorless crystalline product was obtained. This was found to be contaminated with benzanilide which was removed by sublimation *in vacuo* [150° (0.1 mm)]. Recrystallization of the residue from chloroform–petroleum ether afforded shiny, colorless plates of 1-methyl-2-phenylpyrrole-3,4-dicarboxylate: 0.21 g (38%); mp 117–118° (lit.[25] mp 117–118°); ir (KBr) 1710 cm^{-1} (CO); $\lambda_{max}^{CH_3OH}$ 262 nm (log ϵ 3.98), 215 (4.34); $M^{\cdot+}$ *m/e* (rel intensity) 273 (68).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 66.16; H, 5.56; N, 5.03.

Use of the corresponding 5-*N*-acetylimino compound in the above reaction resulted in formation of the pyrrole in 45% yield.

Reaction of 7 (R = Ph) with Ethyl Azodicarboxylate.—The *N*-benzoylimino compound (0.7 g) in benzene (25 ml) and ethyl azodicarboxylate (0.33 g) were warmed gently on the steam bath for 15 min. Evaporation of the benzene and trituration of the gummy residue with ether gave a finely crystalline product. It separated from chloroform–petroleum ether as shiny colorless plates: 0.9 g (85%); mp 187–189°; ir (KBr) 3055, 2980 (CH_3), 1750 cm^{-1} (CO); $\lambda_{max}^{CH_3OH}$ 295 nm (log ϵ 3.79), 260 (3.98), 220 (4.36); nmr ($CDCl_3$) τ 8.76 (t, 3, J = 7.0 Hz, CH_2CH_3), 8.71 (t, 3, J = 7.0 Hz, CH_2CH_3), 6.11 (s, 3, NCH_3), 5.80 (qt, 4, J = 7.0 Hz, CH_2CH_3), 2.66–2.0 (m, 16, aromatic and CH).

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Anal. Calcd for $C_{29}H_{20}N_5O_5$: C, 66.02; H, 5.54; N, 13.28. Found: C, 65.80: H, 5.53; N, 13.19.

Registry No.—**5**, 31446-92-1; **5** free base, 31446-93-2; **7** (R = Ph), 29985-00-0; **7** (R = Me), 31489-84-6; **8**, 31446-95-4; **8** perchlorate, 31446-96-5; **8** picrate, 31446-97-6; **9**, 31446-98-7; **9** picrate, 31446-99-8; **9** (5-acetyl), 31382-26-0; **10**, 31382-27-1; **13**, 19611-52-0; **14**, 31382-29-3.

Reactions of 3-Carboxyacryloylhydrazines and the Formation of Maleimides, Isomaleimides, and Pyridazinones

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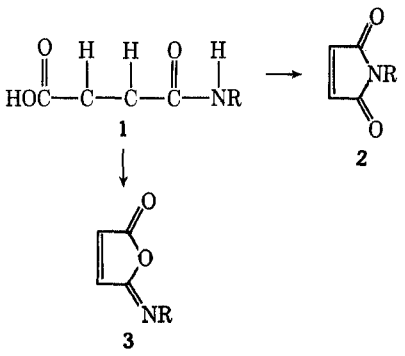
Received April 1, 1971

Some of the previous structure assignments for the reaction products arising from ring closure reactions of 3-carboxyacryloylhydrazines are in error. Criteria are presented for distinguishing between 3-carboxyacryloylhydrazines, isomaleimides, maleimides, and pyridazinones.

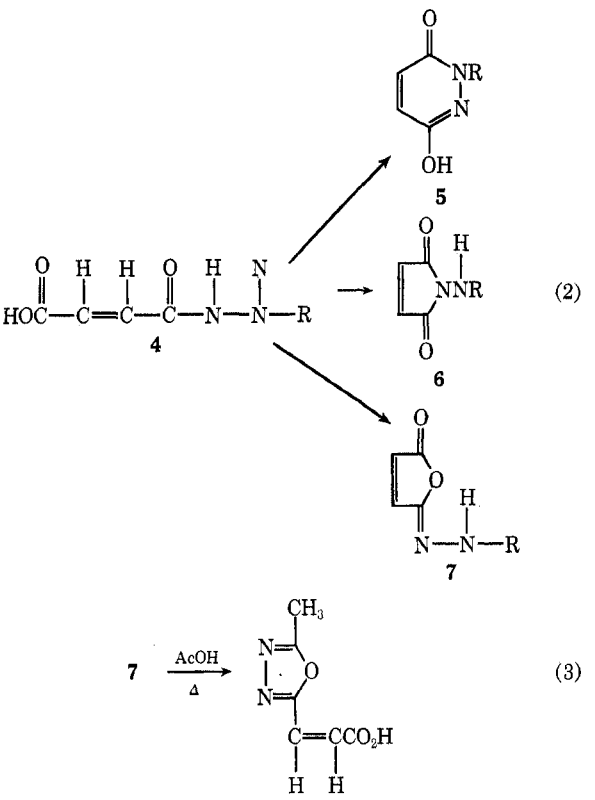
Recently, there has been a great deal of interest in the formation of N-substituted maleamic acid derivatives **1** and in their conversion to maleimides **2** and isomaleimides **3** upon dehydration[1-12] (eq 1).



(1)

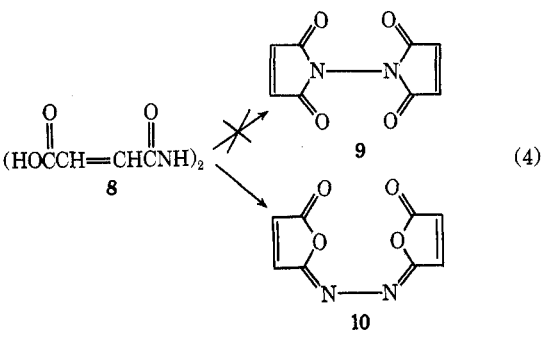
With substituted β-acryloylhydrazides **4** an additional ring closure to pyridazinones **5** may take place (eq 2). It also has been shown that **7** (R = $COCH_3$) rearranges in boiling acetic acid to a 1,3,4-oxadiazole[13-15] (eq 3).

Feuer and Rubinstein[1] suggested that the dehydration of substituted 3-carboxyacrylolylhydrazines **4** in thionyl chloride led to the corresponding substituted maleimides **6**. These structure assignments were based upon infrared absorption of the amide carbonyl group and elemental analysis. They also reported the formation of the bismaleimide **9** as the product of the dehydration of 1,2-bis(3-carboxyacryloyl)hydrazine (**8**) (eq 4).



(2)

(3)



(4)

Subsequently, Feuer and Asunskis[2] prepared what were thought to be various substituted aminomalei-

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