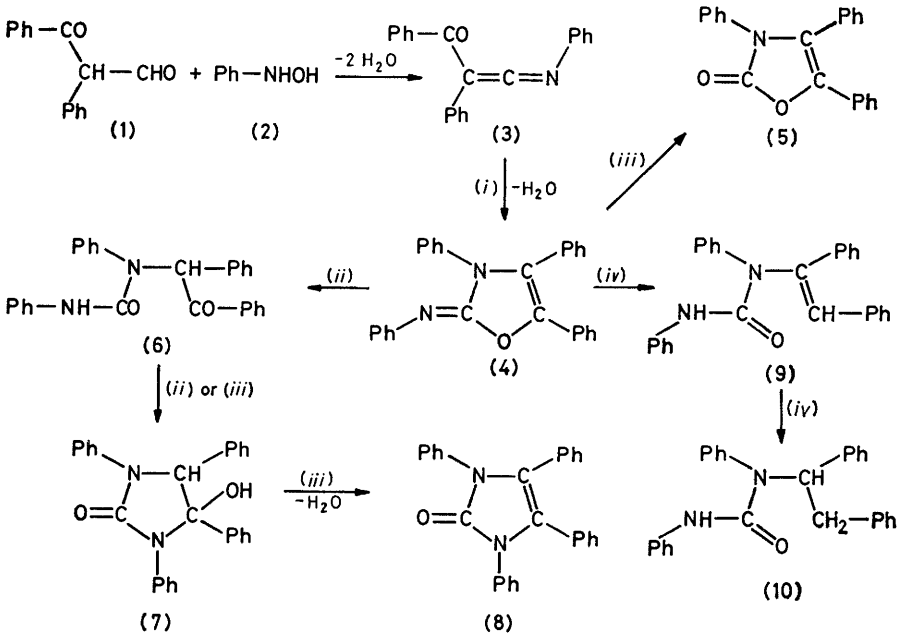
Ketenimines as Intermediates to Heterocycles. Part 2.[1] 2-Phenylimino-3,4,5-triphenyl-1,3-oxazoline

By **Francesco De Sarlo**, Centro di studio sulla chimica e la struttura dei composti eterociclici e loro applicazioni, C.N.R., Istituto di Chimica organica, Università di Firenze, Italy

The reaction product $C_{27}H_{20}N_2O$ from benzoylphenylacetaldehyde and *N*-phenylhydroxylamine has been identified as 2-phenylimino-3,4,5-triphenyloxazoline (4) on the basis of acid hydrolysis to 3,4,5-triphenyloxazolin-2-one (5), alkaline hydrolysis to *N*-desyl-*NN'*-diphenylurea (6), and catalytic hydrogenation to *N*-(1-phenylstyryl)-*NN'*-diphenylurea (9) and *N*-(1,2-diphenylethyl)-*NN'*-diphenylurea (10). A reaction mechanism is proposed, which accounts for the formation of the imino-oxazoline (4) by reaction of *N*-phenylhydroxylamine with the intermediate *C*-benzoyl-*CN*-diphenylketenimine (3).

ONE of the condensation products from benzoylphenylacetaldehyde (1) and *N*-phenylhydroxylamine (2), $C_{27}H_{20}N_2O$ (1 : 2 molar ratio of reagents),[1–3] has been shown to arise by reaction of *N*-phenylhydroxylamine with the intermediate *C*-benzoyl-*CN*-diphenylketenimine (3).[1] Assignment of the structure as 2-phenylimino-3,4,5-triphenyloxazoline (4) could not be made solely on spectroscopic data, and is based on its chemical behaviour.



SCHEME 1 (*i*) PhNHOH; (*ii*) OH^-; (*iii*) H_3O^+; (*iv*) H_2–Pd–C

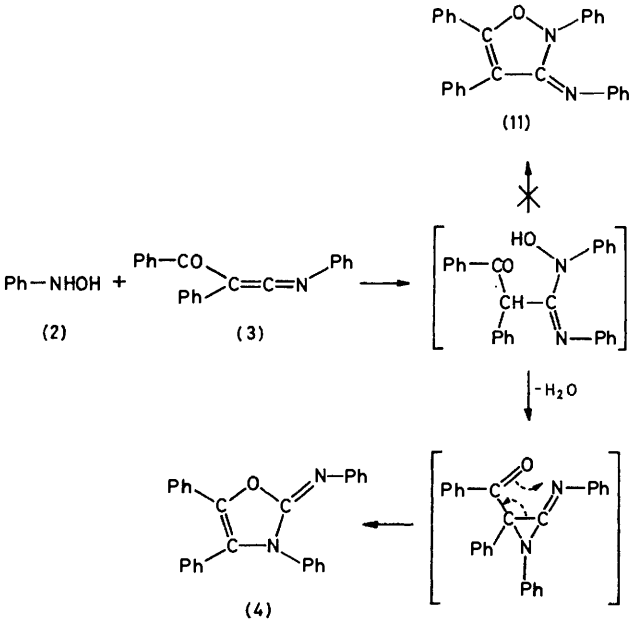
Thus compound (4) (*a*) is hydrolysed by acids to 3,4,5-triphenyloxazolin-2-one (5), as reported previously;[1] (*b*) gives, by alkaline treatment, a mixture of the known *N*-(α-benzoylbenzyl)-*NN'*-diphenylurea (6),[4] together with an isomer which is believed to be 5-hydroxy-1,3,4,5-tetraphenylimidazolidin-2-one (7); and (*c*) is converted, on mild catalytic hydrogenation, into *N*-(1-phenylstyryl)-*NN'*-diphenylurea (9) and *N*-(1,2-diphenylethyl)-*NN'*-diphenylurea (10).

The urea derivative (6), prepared as described,[4] is converted into the isomer (7) under the same conditions employed for the alkaline hydrolysis of the imine (4): both compounds (6) and (7) dehydrate, on acid treatment, to 1,3,4,5-tetraphenylimidazolin-2-one (8). However, the intermediate (7) dehydrates spontaneously even in neutral solution at room temperature: its ^1H n.m.r. spectrum (deuteriochloroform) has singlets at δ 4.25 and 5.22, the former being removed by deuterium exchange (hydroxy-proton); both signals disappear with time, as compound (7) is converted into the imidazolone (8) (t.l.c. control). The n.m.r. spectrum of the urea (6) in deuteriochloroform shows stable singlets at δ 2.68 (NH proton, exchangeable with D_2O) and at 5.37 (CH proton). Neither (6) nor (7) exhibit the u.v. absorption of the stilbene system, in agreement with the structures illustrated.

Two compounds are obtained in sequence by mild catalytic hydrogenation of the imine (4): the first of the two ($C_{27}H_{22}N_2O$) is a reduction intermediate, since it is converted into the other by further hydrogenation, and can be isolated only if the reaction is stopped early, when most of the starting material (4) is still unreacted. The u.v. absorption, extending beyond 300 nm, the lack of

signals outside the aromatic region in the ^1H n.m.r. spectrum, and a strong absorption in the Raman spectrum at 1 623 cm^{-1}, ascribed to $\nu_{C=C}$, indicate the presence of a C=C bond. The presence of C=O and N–H bonds, indicated by the i.r. spectrum, agree with the compound being *N*-(1-phenylstyryl)-*NN'*-diphenylurea (9): its formation is explained by assuming that hydrogenation at the C=C bond of the imine (4) is followed by ring-opening, *via* a hydrogen-shift from C-4 to the exocyclic N atom.

The product of further hydrogenation, which spectroscopically shows N–H and C=O (i.r., Raman) but no C=C bonds (Raman, u.v.), is *N*-(1,2-diphenylethyl)-*NN'*-diphenylurea (10), as confirmed by its degradation to diphenylurea and (1,2-diphenylethyl)aniline and by an independent synthesis from (1,2-diphenylethyl)aniline and phenyl isocyanate. The ^1H n.m.r. spectrum of the urea derivative (10) in deuteriochloroform shows a



SCHEME 2

singlet at δ 5.83 (NH proton), a multiplet and a triplet at 3.28 and 6.28 respectively (ratio 2 : 1), ascribed to the ABX system of the CH_2–CH protons ($J_{AX} \approx J_{BX} = 8$ Hz). Decoupling by irradiating the signal at δ 6.28 simplifies the multiplet at 3.28 into a typical AB pattern, with $|J_{AB}|$ 14.5 Hz.

The structure of the product $C_{27}H_{20}N_2O$ having been firmly established as 2-phenylimino-3,4,5-triphenyloxazoline (4), its formation from *N*-phenylhydroxylamine (2) and *C*-benzoyl-*CN*-diphenylketenimine (3) requires explanation. Normal nucleophilic attack by *N*-phenylhydroxylamine on the electrophilic C atom of the ketenimine (3), followed by condensation with the carbonyl group, would lead to a stable product, *i.e.* 3-phenylimino-2,4,5-triphenylisoxazoline (11): on the other hand, rearrangement of the isoxazoline (11) to the oxazoline (4) cannot occur in the mild reaction conditions employed.[1,*] Therefore, we postulate that another unstable reaction intermediate with an aziridine ring is produced from the primary adduct: then the final product (4) is obtained *via* the electron shifts indicated (*cf.* the rearrangement of isoxazolin-3-ones to oxazolin-2-ones).[5] We have no evidence so far in support of the outlined reaction pathway: attempts to prepare the last reaction intermediate from the ketenimine (3) and phenyl azide failed.

* The oxazoline (4) is produced from the ketenimine (3) even in the dark at room temperature.

EXPERIMENTAL (*with Miss Carla Chisci*)

Melting points were measured on a Kofler apparatus. Other instruments used were: Perkin-Elmer 337 (i.r. spectra), R 32 (^1H n.m.r. spectra), and 270 spectrometers (mass spectra); Pye-Unicam SP 8—100 u.v. spectrophotometer; Cary 81 spectrometer equipped with an Ar^+ laser source with 4 880 Å exciting radiation (for Raman spectra).

2-Phenylimino-3,4,5-triphenyl-1,3-oxazoline (4) *and 3,4,5-Triphenyl-1,3-oxazolin-2-one* (5).—These were prepared as previously described.[1] The base peaks in the mass spectra are at *m/e* 180 ($[Ph–N=C–Ph]^+$) for compound (4) and at *m/e* 44 ($[CO_2]^+$) for compound (5).

Alkaline Hydrolysis of 2-Phenylimino-3,4,5-triphenyl-1,3-oxazoline (4), *N-(α-Benzoylbenzyl)-NN'-diphenylurea* (6), *and 1,3,4,5-Tetraphenyl-5-hydroxyimidazolidin-2-one* (7).—2-Phenylimino-3,4,5-triphenyl-1,3-oxazoline (4) (0.85 g) was refluxed for 5 d in 8% potassium hydroxide in ethanol (220 ml). Bubbling through carbon dioxide, filtering, and concentrating the solution *in vacuo* afforded a residue which was chromatographed on a silica gel column [tetrachloromethane–diethyl ether (1 : 1) as eluant]. After some unchanged starting material (4), the hydroxyimidazolidinone (7), the urea derivative (6), and some imidazolinone (8) were collected in sequence. On silica gel plates (Merck F_{254}, 0.25 mm), with the same eluant, the following R_F values were found: 0.53 (4), 0.46 (7), 0.40 (6), and 0.33 (8). The urea derivative (6) [$\lambda_{max.}$ (ethanol) 250 nm (log ε 4.27); $\lambda_{max.}$ (methylene chloride) 248 nm (4.28); $\nu_{max.}$ (Nujol mull) 3 410 (br) and 1 690 cm^{-1}; $\nu_{max.}$ (CCl_4, 0.1 mm cell path) 3 560 and 1 730 cm^{-1}] was found to be identical to a sample prepared according to the literature,[4] and was easily converted into the imidazolinone (8), as described.[4]

The hydroxyimidazolidinone (7) was crystallized from benzene and dried *in vacuo*, very diffuse m.p., 120—195 °C (Found: C, 80.0; H, 5.6; N, 6.95. $C_{27}H_{22}N_2O_2$ requires C, 79.8; H, 5.5; N, 6.9%); $\lambda_{max.}$ (ethanol) 255 nm (log ε 4.38); $\lambda_{max.}$ (chloroform) 256 nm (4.35). $\nu_{max.}$ (Nujol mull) 3 200—3 400 (br) and 1 690 cm^{-1}; $\nu_{max.}$ (chloroform) 3 550 and 1 715 cm^{-1}.

1,3,4,5-Tetraphenyl-5-hydroxyimidazolidin-2-one (7).—This was prepared by refluxing for 2 h the urea derivative (6) (1 g) in 10% ethanolic potassium hydroxide (40 ml), bubbling carbon dioxide through the solution, and then diluting with water. The precipitated product (7) was washed with water, dried, and recrystallized from benzene at room temperature. Dehydration of the hydroxyimidazolidinone (7) to the imidazolinone (8) occurs spontaneously during 2—3 d in carbon tetrachloride or chloroform: the process is slower in ethanol or acetone.

1,3,4,5-Tetraphenylimidazolin-2-one (8).—This can be prepared from the urea derivative (6),[4] or by refluxing a solution of the hydroxyimidazolidinone (7) in ethanol containing 10% concentrated hydrochloric acid. A refer-

ence sample of the imidazolinone (8) was prepared from benzoin and diphenylurea.[6]

Catalytic Hydrogenation of 2-*Phenylimino*-3,4,5-*triphenyl*-1,3-*oxazoline* (4).—(a) N-(1-*Phenylstyryl*)-NN′-*diphenylurea* (9). The imine (4) (1 g) dissolved in tetrahydrofuran (30 ml) was hydrogenated at atmospheric pressure and room temperature with 10% palladium–carbon for 4.5 h. The filtered solution was concentrated *in vacuo* and the residue treated with methanol in order to separate most of the unchanged material. The solvent was removed from the filtered solution and the residue chromatographed on a silica gel column [light petroleum–benzene–acetone (6 : 2 : 1) as eluant] to give the urea derivative (9), m.p. 152—153 °C (from n-hexane), which is very soluble in the common organic solvents (Found: C, 82.7; H, 5.8; N, 7.5. $C_{27}H_{22}N_2O$ requires C, 83.05; H, 5.7; N, 7.2%); $\lambda_{max.}$ (methanol) 230 (log ε, 4.09), 264 (4.26), and 312 nm (3.92); i.r., $\nu_{max.}$ (carbon tetrachloride) 3 420 and 1 695 cm^{-1}; $\nu_{max.}$ (KBr pellet) 3 300 and 1 672 cm^{-1}; Raman (solid sample) 1 674 and 1 623 cm^{-1}; δ_H 6.7—7.75(m); *m/e* 390 (M^+, 33%), 271 {[Ph–NH–C(Ph)=CH–Ph]$^+$, 100%}; other fragments (>20%) at 272, 270, 180, 178, 168, 167, 165, 119, 104, 91, and 77.

T.l.c. (Kieselgel Merck F_{254}, 0.25 mm, same eluant as for the column) gave the following R_F values: 0.38 (4); 0.35 (10); and 0.24 (9).

(b) N-(1,2-*Diphenylethyl*)-NN′-*diphenylurea* (10). This was obtained by hydrogenating the imine (4) for 3 d as in (a), m.p. 108—109 °C (from methanol), yield 73% (Found: C, 82.2; H, 6.3; N, 6.9. $C_{27}H_{24}N_2O$ requires C, 82.6; H, 6.2; N, 7.1%), $\lambda_{max.}$ (methanol) 239 nm (log ε 4.31), $\nu_{max.}$ (carbon tetrachloride): 3 440 and 1 680 cm^{-1}; $\nu_{max.}$ (KBr pellet): 3 430 and 1 675 cm^{-1}; Raman (solid): 1 674 cm^{-1}, *m/e* base peak at 182; other fragments at 300 (23%), 119 (13%), 104 (14%), 93 (8%), 91 (11%), and 77 (25%); metastable peaks at *m** 110 and 59.5.

The intermediate (9) can be converted into the urea derivative (10) by further hydrogenation in the same conditions.

Reactions of N-(1,2-*Diphenylethyl*)-NN′-*diphenylurea* (10) *with Acids and Bases*.—The urea derivative (10) was refluxed in ethanol containing concentrated hydrochloric acid. From the neutralized solution, after removal of the solvent, (1,2-diphenylethyl)aniline, m.p. 56 °C (from ethanol),[7] and diphenylurea were isolated. Refluxing the urea derivative (10) with a solution of potassium hydroxide in ethanol gave (1,2-diphenylethyl)aniline. An authentic sample of (1,2-*diphenylethyl*)*aniline* was prepared from benzylideneaniline and benzylmagnesium chloride, according to the literature procedure.[7]

Synthesis of N-(1,2-*Diphenylethyl*)-NN′-*diphenylurea* (10).—Phenyl isocyanate (3.5 ml, stoicheiometric requirement 2.2 ml) was added to a solution of (1,2-diphenylethyl)-aniline (5.5 g) in light petroleum (100 ml), and the mixture gently refluxed for 4 h. After removal of the solvent, hot methanol was added and the product crystallized out on cooling, m.p. 106—109 °C (6.5 g, 82%).

[9/453 *Received*, 20*th March*, 1979]

REFERENCES

[1] Part 1: F. De Sarlo and G. Renzi, *J.C.S. Perkin I*, 1978, 1113.
[2] H. Rupe and R. Wittwer, *Helv. Chim. Acta*, 1922, **5**, 205.
[3] D. J. Woodman, N. Tontapanish, and J. V. Van Ornum, *J. Org. Chem.*, 1971, **36**, 1685.
[4] S. A. Brazier and H. McCombie, *J. Chem. Soc.*, 1912, **101**, 2352.
[5] A. R. Gagneux and R. Göschke, *Tetrahedron Letters*, 1966, 5451.
[6] H. Biltz, *Annalen*, 1909, **368**, 219.
[7] M. Busch and A. Rinck, *Ber.*, 1905, **38**, 1766.