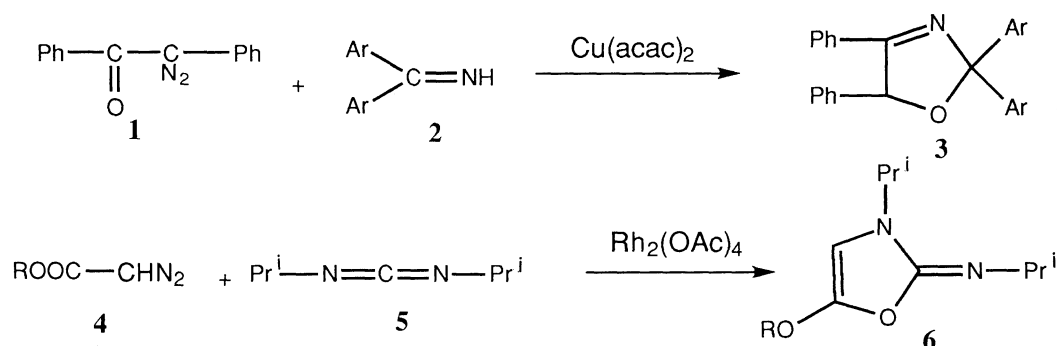


Formation and Reaction of Azomethine Ylide by the Reaction of $\text{Cu}(\text{acac})_2$ -ketocarbenoids with 1,1-Diphenylmethanimine

Toshikazu IBATA* and Girija Shankar SINGH
Institute of Chemistry, College of General Education,
Osaka University, Toyonaka, Osaka 560

The reaction of α -diazocarbonyl compounds with 1,1-diphenylmethanimine in the presence of $\text{Cu}(\text{acac})_2$ afforded the corresponding N-substituted imines in general together with pyrrolidine and 1,4,6-dioxazine derivatives (in the reaction of α -diazo-4-chloroacetophenone) and 1,1-diphenyl-2-(4-nitrobenzoyl)-ethylene (in the reaction of α -diazo-4-nitroacetophenone) through azomethine ylides.

Chemistry of carbenoids has been under extensive investigation in recent years to explore its synthetic potentiality in generation of ylides.¹⁾ Only a few examples are available in literature on the formation of azomethine ylide by the reactions of α -ketocarbenoids with compounds containing $\text{C}=\text{N}$ linkage followed by 1,5-cyclization. For example, azibenzil (**1**) reacts with 1,1-diarylmethanimines (**2**) in the presence of $\text{Cu}(\text{acac})_2$ to give 3-oxazolines (**3**),²⁾ and alkyl diazoacetates (**4**) react with diisopropylcarbodiimide (**5**) in the presence of $\text{Rh}_2(\text{OAc})_4$ to give 4-oxazolines (**6**).³⁾



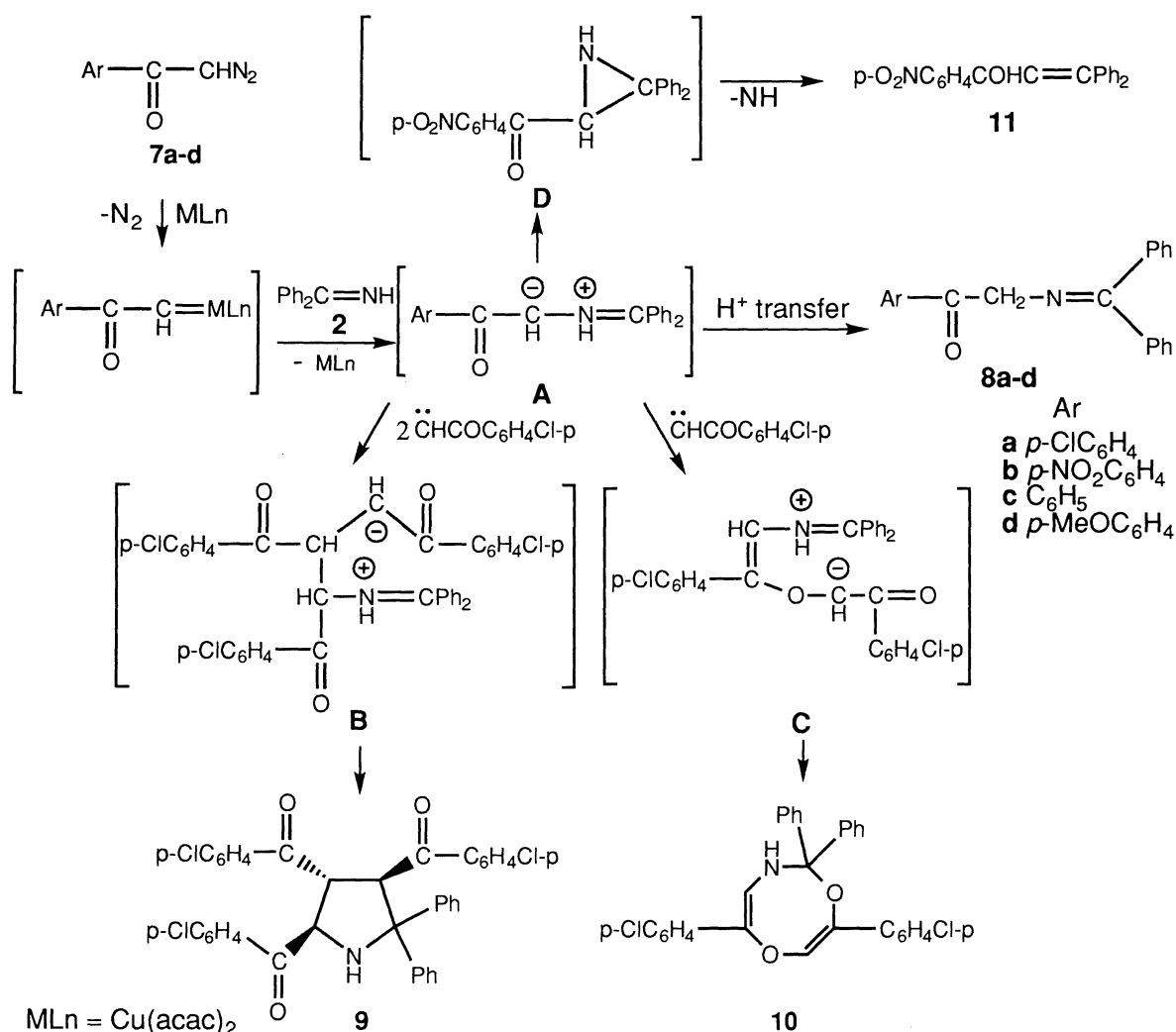
In continuation to our recent studies on the formation and reactions of nitrile ylides⁴⁾ and thiocarbonyl ylides⁵⁾, we now wish to report the reactions of α -diazocarbonyl compounds (**7**) with 1,1-diphenylmethanimine (**2**) in the presence of $\text{Cu}(\text{acac})_2$ leading to products through formal insertion of α -ketocarbenoids into the N-H bond of imine **2** and through the pathways other than the sole 1,5-

cyclization.^{2,3)} Although the insertion of benzoylphenyl carbene into an amine N-H bond has been proposed in the Cu(acac)₂-catalyzed reaction of azibenzil (**1**) with primary amines,⁶⁾ this is the first case of insertion of an α -ketocarbene into an imine N-H bond.

The reaction of α -diazo-4-chloroacetophenone (**7a**) with 1,1-diphenylmethanimine (**2**) in the presence of Cu(acac)₂ gave *N*-(4-chlorobenzoyl)methyl-1,1-diphenylmethanimine (**8a**, max. yield 28% in CH₂Cl₂ at reflux temperature), 2,2-diphenyl-3,4,5-tri(4-chlorobenzoyl)pyrrolidine (**9**, max. yield 21% in benzene at 55 °C) and 3,8-di(4-chlorophenyl)-5,5-diphenyl-1,4,6-dioxazocine (**10**, max. yield 14% in benzene at reflux temperature).^{7,8)} The *trans* orientation of *p*-chlorobenzoyl groups was deduced by the presence of singlet signals for methine protons of pyrrolidine ring in the ¹H NMR spectrum of **9**.⁹⁾ The main basis for assigning dioxazocine structure to **10** are the absence of carbonyl group in its IR and ¹³C NMR spectra and presence of fragment with *m/e* 139 (*p*-chlorobenzoyl) in the mass spectrum⁹⁾ which is similar to the reported fragmentation involving loss of aldehyde from 1,3,6-dioxazocin-2-ones.¹⁰⁾ The other fragments at 208 and 232 besides the molecular ion peak at 483 (M⁺-2) also supported the arrangement of atoms in the eight membered nucleus which is perhaps the first 1,4,6-dioxazocine derivative.

The plausible mechanistic route leading to the products is shown in Scheme 1. The formation of formal insertion product **8a** of α -ketocarbene into the N-H bond of imine **2** is explained by the proton transfer from azomethine ylide **A**. The formation of **9** and **10** can be explained by further attack of ketocarbenoids on ylide carbon and carbonyl oxygen of the azomethine ylide **A** to give the corresponding intermediates **B** and **C**, respectively, followed by cyclization. The similar intermediates like **A** and **B** have been reported in the reaction of benzoylphenyl carbenoid with 1,1-diarylmethanimines²⁾ and of sulfonium ylides.¹¹⁾ In the latter case, two carbenoids attack the sulfonium ylide to give a zwitterionic intermediate which cyclizes with extrusion of sulfide to afford a cyclopropane. Though the formation and 1,8-cyclization of the intermediate **C** leading to **10** is unprecedented, it appears to be quite logical if an extremely slow 1,5-cyclization of ylide **A** is assumed due to the creation of negative charge at oxygen like the case of reaction with azibenzil.²⁾ The decrease of yield of insertion product **8a** (12%) and formation of products **9** and **10** observed in the reaction in benzene suggest that transfer of proton from azomethine ylide **A** is slower in benzene than in CH₂Cl₂ providing sufficient time for further attack of the ketocarbenoid on azomethine ylide **A** to give **B** and **C**.

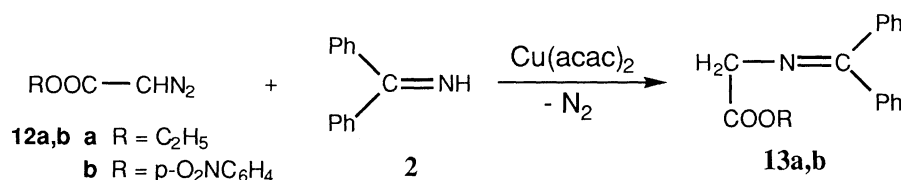
The reaction of α -diazo-4-nitroacetophenone (**7b**) with imine **2** led to *N*-(4-nitrobenzoyl)methyl-1,1-diphenylmethanimine (**8b**, max. yield 32% in CH₂Cl₂ at reflux temperature) through the same mechanism as in case of **8a** and 1,1-diphenyl-2-(4-nitrobenzoyl)ethylene (**11**, yield 11% in benzene at 55 °C). The olefin **11** is presumed to be formed by the decomposition of an aziridine (**D**) formed by the 1,3-cyclization of ylide **A**.



Scheme 1.

The reaction of α -diazoacetophenone (**7c**) and of α -diazo-4-methoxyacetophenone (**7d**) in CH_2Cl_2 at reflux temperature gave *N*-(benzoyl)methyl-1,1-diphenylmethanimine (**8c**, yield 19%) and *N*-(4-methoxybenzoyl)methyl-1,1-diphenylmethanimine (**8d**, yield 17%), respectively, as formal insertion products.

In case of diazoesters **12a,b**, insertion products **13a,b** were isolated only in about 4% yield (12 and 14%, respectively, as per ^1H NMR of the crude product mixtures) due to the sensitivity of **13** to moisture to undergo hydrolysis during work up. The occurrence of such hydrolysis is supported by the isolation of benzophenone in the reactions of **12a** and **12b** and isolation of 4-nitrophenol in the reaction of **12b**.



Further studies to get better insight into suitability of this method for generating azomethine ylides are in progress.

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- 7) General procedure: a solution of 1 mmol of **7** in 15 ml of C₆H₆ or CH₂Cl₂ was added dropwise to a stirring solution of 1 mmol of **2** and 1/10 mmol of Cu(acac)₂ in 15 ml of the same solvent at different temperatures under N₂ atmosphere. The products from the mixture were separated by silica gel column chromatography using hexane-ethyl acetate as an eluent.
- 8) The elemental analysis and spectral data of new compounds were satisfactory.
- 9) **9**. IR (KBr): 3403 (NH), 2923 and 1678 (C=O) cm⁻¹; ¹H NMR (CDCl₃, 270 MHz): δ 7.82-7.79 (d, 2H, arom.), 7.55-7.52 (m, 2H, arom.), 7.49-7.43 (m, 5H, arom.), 7.36 (s, 2H, two CH of pyrrolidine), 7.28-7.22 (m, 4H, arom.), 7.13-6.96 (m, 9H, arom.), 5.96 (s, 1H, CH) and 5.39 (s, 1H, NH, D₂O exchange); ¹³C NMR (CDCl₃, 126 MHz): δ 198.25, 189.54, 189.39, 154.15, 145.10, 140.77, 139.37, 138.95, 138.85, 137.37, 136.76, 134.91, 130.58, 129.47, 129.36, 129.07, 128.71, 128.67, 128.39, 128.33, 128.10, 127.79, 126.11, 115.74, 77.19, 75.95 and 58.81; MS (*m/e*): 635 (M⁺-2, 5) 619 (1), 496 (45, 635-ClC₆H₄CO), 456 (5, three ClC₆H₄COCH), 314 (10, two ClC₆H₄COCH), 165 (15), 139 (100, ClC₆H₄CO) and 111 (ClC₆H₄). Found: C, 69.37; H, 4.33; N, 2.25%. Calcd for C₃₇H₂₆NO₃Cl₃: C, 69.66; H, 3.95; N, 2.20%.
10. IR (KBr): 3439 (NH), 3065 (CH) and 1649 (CH=C) cm⁻¹; ¹H NMR (CDCl₃, 270 MHz): δ 8.12-8.04 (br, 1H, O-CH), 7.84-7.81 (d, 2H, arom.), 7.50-7.32 (m, 17H, arom. and NH) and 6.58 (s, 1H, CH); ¹³C NMR (CDCl₃, 126 MHz): δ 140.00 (br, C₂), 133.55 (br, C₇), 129.07 and 128.83 (s, C₃ and C₈), 126.15 (s, C₅), 133.04, 131.79 and 130.27 (s, three arom-C), 132.05 (brd, arom-CH), 128.96 (dt, ²J_{C-H}=6.55, *p*-C of Ph), 128.64 (two dd, ²J_{C-H}=4.88 Hz, two *o*-arom-C), and 128.25 (dm, *m*-arom-C of Ph) (carbons of the two *p*-ClC₆H₄ groups appear to be equivalent.); MS (*m/e*): 483 (M⁺-2, 25), 448 (2), 344 (100, 483-ClC₆H₄CO), 331 (5), 232 (10), 208 (15), 165 (18), 139 (75, ClC₆H₄CO), 111 (20) and 77 (5). Found: C, 71.66; H, 4.15; N, 2.92%. Calcd for C₂₉H₂₁NO₂Cl₂: C, 71.60; H, 4.32; N, 2.88%.
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