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

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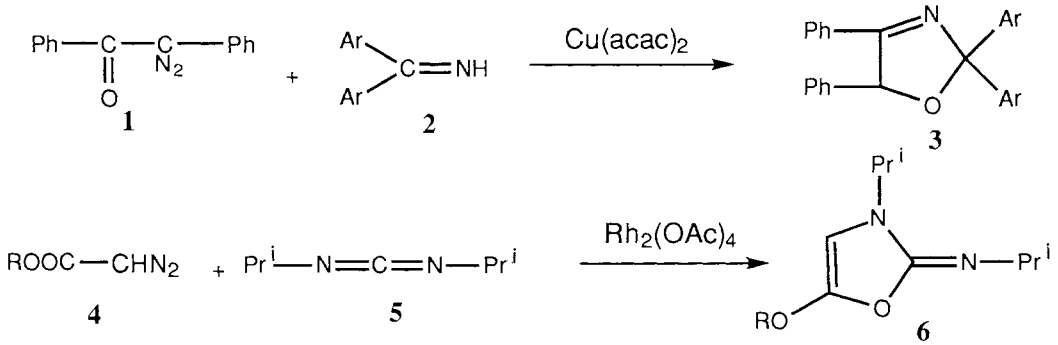
The reaction of α-diazocarbonyl compounds with 1,1-diphenylmethanimine in the presence of $Cu(acac)_2$ afforded the corresponding N-substituted imines in general together with pyrrolidine and 1,4,6-dioxazocine derivatives (in the reaction of α-diazo-4-chloroacetophenone) and 1,1-diphenyl-2-(4-nitrobenzoyl)-ethylene (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 C=N linkage followed by 1,5-cyclization. For example, azibenzil (**1**) reacts with 1,1-diarylmethanimines (**2**) in the presence of $Cu(acac)_2$ to give 3-oxazolines (**3**),[2] and alkyl diazoacetates (**4**) react with diisopropylcarbodiimide (**5**) in the presence of $Rh_2(OAc)_4$ to give 4-oxazolines (**6**).[3]



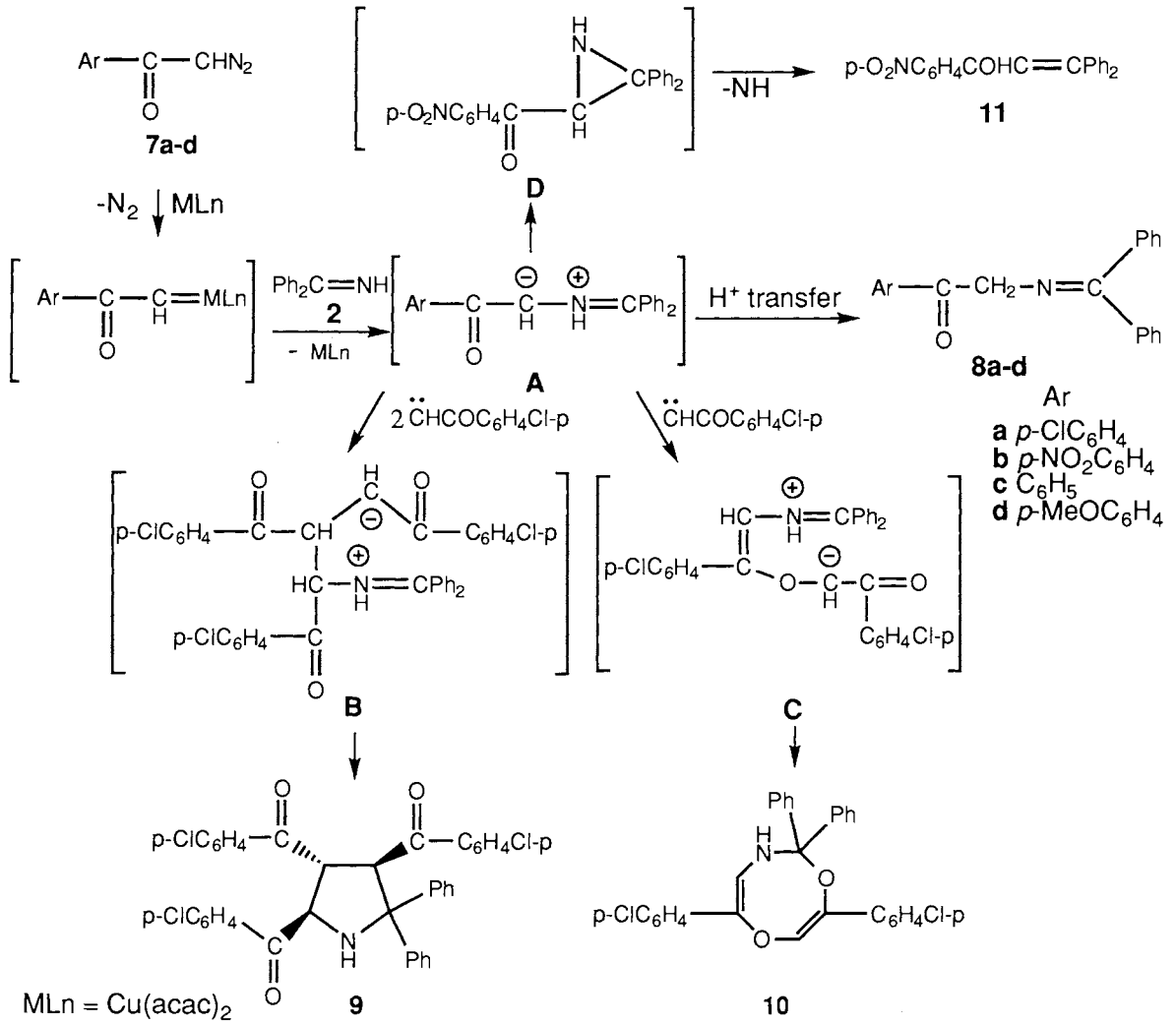
In continuation to our recent studies on the formation and reactions of nitrile ylides[4] and thiocarbonyl ylides[5], we now wish to report the reactions of α-diazocarbonyl compounds (**7**) with 1,1-diphenylmethanimine (**2**) in the presence of $Cu(acac)_2$ leading to products through formal insertion 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 CH_2Cl_2 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 ^{13}C NMR spectra and presence of fragment with *m/e* 139 (*p*-chlorobenzoyl) in the mass spectrum[9] 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-diarylmethanimines[2] 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 CH_2Cl_2 providing sufficient time for further attack of the ketocarbenoid on azomethine ylide **A** to give **B** and **C**.

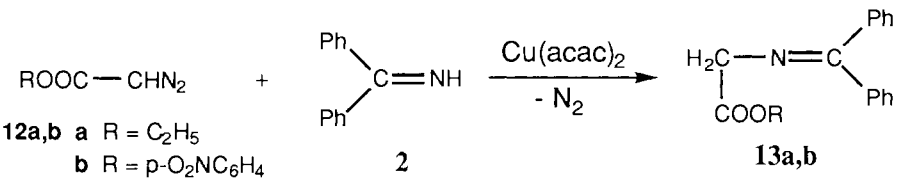
The reaction of α-diazo-4-nitroacetophenone (**7b**) with imine **2** led to *N*-(4-nitrobenzoyl)methyl-1,1-diphenylmethanimine (**8b**, max. yield 32% in CH_2Cl_2 at reflux temperature) through the same mechanism as in case of **8a** and 1,1-diphenyl-2-(4-nitrobenzoyl)ethylene (**11**, yield 11% in 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.

References

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5) H. Nakano and T. Ibata, *Chem. Express*, **7**, 789 (1992).
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7) General procedure: a solution of 1 mmol of **7** in 15 ml of C_6H_6 or CH_2Cl_2 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 N_2 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 ($CDCl_3$, 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, D_2O exchange); ^{13}C NMR ($CDCl_3$, 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-ClC_6H_4CO), 456 (5, three ClC_6H_4COCH), 314 (10, two ClC_6H_4COCH), 165 (15), 139 (100, ClC_6H_4CO) and 111 (ClC_6H_4). Found: C, 69.37; H, 4.33; N, 2.25%. Calcd for $C_{37}H_{26}NO_3Cl_3$: C, 69.66; H, 3.95; N, 2.20%.
10. IR (KBr): 3439 (NH), 3065 (CH) and 1649 (CH=C) cm^{-1}; ^1H NMR ($CDCl_3$, 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); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 140.00 (br, C_2), 133.55 (br, C_7), 129.07 and 128.83 (s, C_3 and C_8), 126.15 (s, C_5), 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*-ClC_6H_4 groups appear to be equivalent.); MS (*m/e*): 483 (M^+-2, 25), 448 (2), 344 (100, 483-ClC_6H_4CO), 331 (5), 232 (10), 208 (15), 165 (18), 139 (75, ClC_6H_4CO), 111 (20) and 77 (5). Found: C, 71.66; H, 4.15; N, 2.92%. Calcd for $C_{29}H_{21}NO_2Cl_2$: C, 71.60; H, 4.32; N, 2.88%.
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