

Intramolecular N–H insertion of α -diazocarbonyls catalyzed by $\text{Cu}(\text{acac})_2$: An efficient route to derivatives of 3-oxoazetidines, 3-oxopyrrolidines and 3-oxopiperidines

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$\text{Cu}(\text{acac})_2$ was found to be an efficient catalyst for the intramolecular N–H insertion by carbenoids. The competitive intramolecular C–H insertion by carbenoids is not a problem in the diazo decomposition reaction with $\text{Cu}(\text{acac})_2$ as catalyst. The reaction provided derivatives of 3-oxoazetidine, 3-oxopyrrolidine and 3-oxopiperidine in moderate to good yields.

Introduction

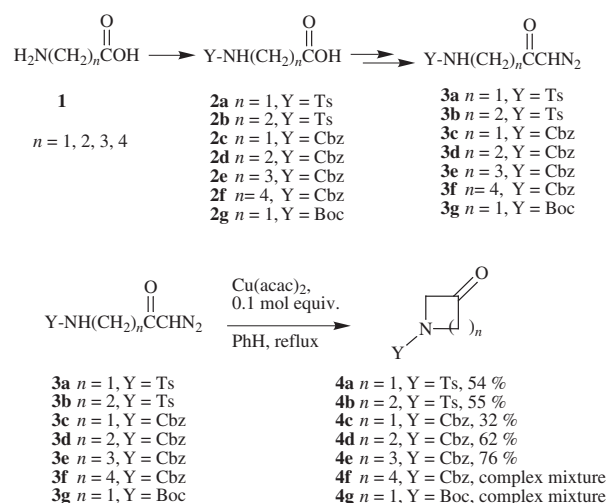
Along with the intramolecular C–H insertion reactions by carbenoids, intramolecular N–H insertion reactions of α -diazocarbonyl substrates catalyzed by metal complex have received considerable attention in recent years.¹ This type of insertion reaction has been shown to be a mild and efficient route to 4-, 5-, and 6-membered aza rings. A frequently cited example of this powerful approach is the Merck industrial synthesis of the bicyclic β -lactam thienamycin, in which the intramolecular N–H insertion by Rh^{II} -carbenoid is the key step.² The corresponding asymmetric N–H insertion was early exploited with a chiral-auxiliary approach,³ and recent efforts in this area are concentrated on the application of chiral Rh^{II} catalysts.⁴

Although N–H insertions by metalcarbenoids were originally promoted by copper-mediated diazo decomposition,^{3,5} most of the intramolecular N–H insertions recently reported are based on Rh^{II} -catalyzed diazo decomposition, particularly with $\text{Rh}_2(\text{OAc})_4$ as the catalyst.^{4,6} Rh^{II} complexes have been extensively used in diazo decomposition, and they have been shown to be the most efficient catalysts in intramolecular C–H insertions as well as in cyclopropanations. Despite great success demonstrated by Rh^{II} catalysts, their application in intramolecular N–H insertion has been limited by the competing C–H insertion,^{4,6b,7} which is a very easily accomplished Rh^{II} -mediated reaction. For example, Rapoport reported that intramolecular C–H insertion, which led to the formation of 5-membered carbocycles, was a significant by-product in the synthesis of 3-oxopiperidine by $\text{Rh}_2(\text{OAc})_4$ -catalyzed intramolecular carbenoid N–H insertion.^{6b} McKervery also recently reported the competing C–H insertion in asymmetric intramolecular N–H insertions by a chiral Rh^{II} complex.⁴ This possible side reaction may be the reason that the intramolecular N–H insertion by carbenoids has still not been widely applied in the synthesis of molecules with complicated structures, except for the β -lactams syntheses by Rh^{II} -carbene intramolecular N–H insertion in which the reaction occurs in a conformationally restricted ring system. To avoid the complexity caused by this side reaction, it would be desirable to look for other metal complexes which can efficiently promote intramolecular N–H insertion but not C–H insertion. We report in this paper our investigation on the intramolecular N–H insertion catalyzed by copper(II) acetylacetonate [$\text{Cu}(\text{acac})_2$]. The results suggest that this catalyst can efficiently promote intramolecular N–H insertions.

Results and discussion

First, we investigated the simple diazocarbonyl substrates

devoid of unnecessary functionality. Three typical amino-protecting groups, *p*-tolylsulfonyl (Ts), *tert*-butoxycarbonyl (Boc), and benzyloxycarbonyl (Cbz), were selected in order to investigate the effect of protecting group on the N–H insertion. The diazo substrates **3a–g** were prepared from corresponding amino acids **2a–g** according to the known procedure.^{8,9} Diazo decomposition by a catalytic amount of $\text{Cu}(\text{acac})_2$ was performed by adding the α -diazocarbonyl substrate in benzene to a refluxing benzene solution containing 10% (mol) $\text{Cu}(\text{acac})_2$. Upon completion of the reaction as indicated by TLC, the mixture of products was subjected to column chromatography with silica gel and the structure of the product was established by spectroscopic analysis. As shown in Scheme 1, for diazo sub-



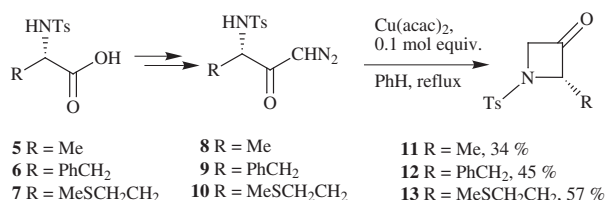
Scheme 1

strates with *N*-tosyl or *N*-Cbz protecting group **3a–e**, the intramolecular N–H insertion was the major reaction pathway, leading to the formation of 3-oxoazetidine, 3-oxopyrrolidine and 3-oxopiperidine systems in moderate to good yields. It is noteworthy that in diazo substrate **3e** there is the possibility of a competing intramolecular C–H insertion to give a 5-membered carbocycle. Nevertheless, the N–H insertion product was isolated as the only major product, thus suggesting that $\text{Cu}(\text{acac})_2$ -mediated carbenoids can selectively promote N–H insertion. While the formation of 4-, 5- and 6-membered aza rings is a simple procedure, it was observed that the formation of a seven-membered ring in this reaction was difficult, as shown by the $\text{Cu}(\text{acac})_2$ -catalyzed diazo decomposition of **3f**. On the other hand, the diazo substrates with an *N*-Boc protecting

group yielded inseparable complex mixtures, suggesting that amino protecting groups have a marked influence over the reaction.

$\text{Cu}(\text{acac})_2$ has been widely used to promote cyclopropanation by carbenoids.¹ The application of this catalyst in carbenoid X–H (X = C, N, O, S) insertion is rare. Hon *et al.* reported intramolecular C–H insertion using $\text{Cu}(\text{acac})_2$ as the catalyst.¹⁰ Intermolecular O–H insertion of a α -diazo ketone catalyzed by $\text{Cu}(\text{acac})_2$ has been recently investigated by Ohfuné's group.¹¹ However, to the best of our knowledge, $\text{Cu}(\text{acac})_2$ has not been reported to promote intramolecular carbenoid N–H insertion,¹² and so our results seem to be the first example of this.

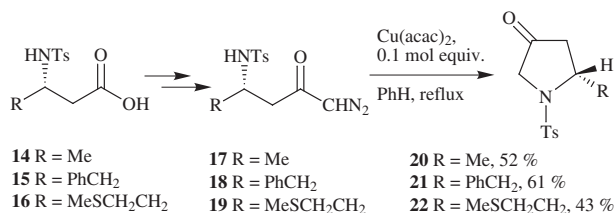
To examine whether $\text{Cu}(\text{acac})_2$ -catalyzed N–H insertion could be extended to diazo substrates with other functionality or alkyl substituents, the diazocarbonyl compounds **8**–**10** and **17**–**19** were prepared from the corresponding optically pure α - and β -amino acids **5**–**7** and **14**–**16**, respectively.⁸ For the diazo substrates derived from α -amino acids, the $\text{Cu}(\text{acac})_2$ -catalyzed reaction gave corresponding N–H-insertion products **11**, **12** and **13** in 34, 45 and 57% yield, respectively (Scheme 2).



Scheme 2

L-methionine, the possible C–H insertion into the C–H bond adjacent to the methylthio group was not observed.

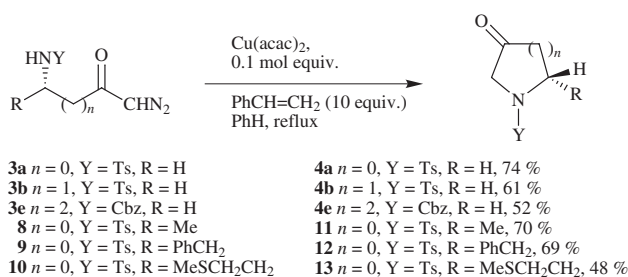
Similarly, the optically active 2-substituted 3-oxopiperidines **20**–**22** were obtained in the $\text{Cu}(\text{acac})_2$ -catalyzed reaction of the diazo substrates **17**–**19** derived from β -amino acids **14**–**16** (Scheme 3). Again, intramolecular C–H-insertion products



Scheme 3

were not observed in these cases. The result with diazo substrate **18** indicates that a phenyl group, which can possibly react with Rh^{II} -carbene, remains intact in the $\text{Cu}(\text{acac})_2$ -catalyzed reaction.

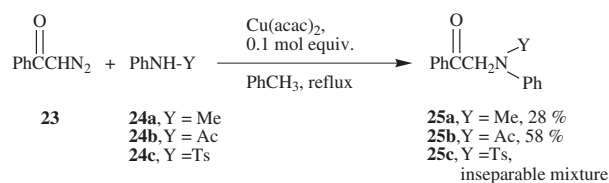
The intramolecular N–H-insertion reactions under $\text{Cu}(\text{acac})_2$ catalysis conditions were further investigated by the competition reaction with intermolecular cyclopropanation, since this catalyst has been most frequently used in cyclopropanation by carbenoids. Thus, as shown in Scheme 4, the $\text{Cu}(\text{acac})_2$ -catalyzed diazo decomposition was performed in the presence of an excess of styrene. To our surprise, the formation of cyclopropanation products was not observed in all cases; the intramolecular N–H-insertion products were again isolated as the major products. Interestingly, compared with the results shown in Schemes 2 and 3 in which the corresponding $\text{Cu}(\text{acac})_2$ reactions were run in the absence of styrene, the presence of styrene seems to have an influence over the yields of the N–H-insertion products. For the diazo substrates **3a**, **3b**, **8** and **9**, the presence of styrene markedly increases the yield of the N–H-insertion



Scheme 4

products. The detailed mechanism of this styrene effect is not clear.

Lastly, we examined the corresponding intermolecular carbenoids N–H insertion catalyzed by $\text{Cu}(\text{acac})_2$. As shown in Scheme 5, diazoacetophenone **23** was decomposed by



Scheme 5

$\text{Cu}(\text{acac})_2$ in the presence of *N*-methylaniline **24a**, acetanilide **24b** and *N*-tosylaniline **24c**, respectively. The corresponding N–H-insertion products were indeed isolated as major products from the reaction with *N*-methylaniline and acetanilide, albeit in comparatively low yields. The reaction with *N*-tosylaniline, however, gave an inseparable mixture.

In conclusion, we have demonstrated that $\text{Cu}(\text{acac})_2$ -mediated carbenoids intramolecular N–H insertion is an efficient and chemoselective approach for the construction of azetidines, pyrrolidines and piperidines. Although the yields were only moderately high, the competing C–H intramolecular insertion was not a problem in the $\text{Cu}(\text{acac})_2$ -catalyzed reaction. Thus, the readily available and inexpensive $\text{Cu}(\text{acac})_2$ can be a choice as the catalyst in carbenoid intramolecular N–H insertions.

Experimental

Mps were recorded with a Yanaco micro melting point apparatus and are uncorrected. All reactions with air- and moisture-sensitive components were performed under a nitrogen atmosphere in a flame-dried reaction flask, and the components were added *via* syringe. All solvents were distilled prior to use. The distillation range of petroleum spirit is 30–60 °C. MeOH and CH₂Cl₂ were freshly distilled from CaH₂ before use. THF was distilled from sodium. For chromatography, 100–200 mesh silica gel (Qingdao Haiyang Chemical Factory, Qingdao, China) was employed. For preparative TLC, 10–40 μm silica gel GF₂₅₄ (Qingdao Haiyang Chemical Factory, Qingdao, China) was used. Recrystallization was from petroleum spirit–ethyl acetate. ¹H and ¹³C NMR spectra were recorded at 200 MHz and 50 MHz with a Varian Mercury 200 spectrometer, and chemical shifts are reported in ppm using tetramethylsilane as internal standard. *J*-Values are given in Hz. IR spectra were recorded with a Nicolet 5MX-S infrared spectrometer. Mass spectra were obtained on a VG ZAB-HS mass spectrometer. Elemental analyses were performed in the Institute of Chemistry, Chinese Academy of Sciences. Optical activities were measured on a Perkin-Elmer 291 polarimeter, and [α]_D-values are given in units of 10^{−1} deg cm² g^{−1}.

Diazomethane solution in dry diethyl ether was prepared from *N*-methyl-*N*-nitrosourea.¹³ Copper(II) acetylacetonate

[Cu(acac)₂] was prepared from copper(II) sulfate and acetylacetone according to a literature procedure.¹⁴

The experimental procedure and the analytical data for *N*-tosyl-protected α -diazocarbonyl compounds have been reported in our previous paper.⁸ The *N*-Cbz- and *N*-Boc-protected α -diazocarbonyl compounds were prepared from the corresponding *N*-protected amino acids according to literature procedure.⁹

General procedure for the preparation of diazo ketones 3c–g

The *N*-protected amino acid **2c–g** (1.0 mmol) was dissolved in anhydrous diethyl ether (4 cm³) and anhydrous THF (4 cm³). The solution was cooled to $-20\text{ }^{\circ}\text{C}$ under N₂ atmosphere. Triethylamine (0.14 cm³, 1.0 mmol) and isobutyl chloroformate or benzyl chloroformate (1.0 mmol) were added and the mixture was stirred for 30 min, and then the temperature of the reaction was allowed to rise to $-10\text{ }^{\circ}\text{C}$. A solution of diazomethane (≈ 2 mmol) in diethyl ether was added dropwise. The mixture was stirred for 4 h, during which the temperature slowly rose to $20\text{ }^{\circ}\text{C}$. Excess of diazomethane was removed by bubbling the reaction mixture with N₂. The solvent was removed by evaporation and the residue was dissolved in diethyl ether. The ethereal solution was washed successively with water, 10% aq. NaHCO₃, and saturated aq. NaCl, and then dried over anhydrous MgSO₄. Removal of the drying agent and the solvent gave a crude product, which was purified by silica gel column chromatography with petroleum spirit–ethyl acetate as the eluent.

Diazo-(*N*-benzyloxycarbonylglycyl)methane 3c. Mp $68\text{--}69\text{ }^{\circ}\text{C}$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3426, 3296 (NH), 3089, 2107 (CHN₂), 1697, 1649, 1561, 1381; δ_{H} 3.97 (2 H, d, *J* 4.8, NHCH₂), 5.12 (2 H, s, PhCH₂), 5.37 (1 H, br s, CHN₂), 5.54 (1 H, br s, NH), 7.35 (5 H, m, C₆H₅); δ_{C} 48.05, 53.57, 67.05, 128.01, 128.15, 128.46, 136.11, 156.25, 190.09; *m/z* (EI) 233 (M⁺, 2%), 205 [(M – N₂)⁺, 10], 120 (16), 107 (100), 91 (71) [Found: (M – N₂)⁺, 205.0737. C₁₀H₁₁NO₃ requires *m/z*, 205.0738].

Diazo-(*N*-benzyloxycarbonyl- β -alanyl)methane 3d. Oil; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3353 (NH), 3082, 2110 (CHN₂), 1687, 1626, 1532, 1390, 1259; δ_{H} 2.65 (2 H, m, CH₂CO), 3.48 (2 H, q, *J* 5.8, NHCH₂), 5.08 (2 H, s, CH₂), 5.25 (1 H, br s, CHN₂), 5.37 (1 H, br s, NH), 7.34 (5 H, s, C₆H₅); δ_{C} 36.43, 40.11, 55.01, 66.60, 127.97, 128.45, 136.45, 156.28, 179.21, 193.19; *m/z* (EI) 233 [(M – N₂)⁺, 2%], 142 (7), 127 (14), 107 (100), 91 (51) [Found: (M – N₂)⁺, 219.0891. C₁₂H₁₃NO₃ requires *m/z*, 219.0882].

1-Diazo-5-(benzyloxycarbonylamino)pentan-2-one 3e. Mp $31\text{--}32\text{ }^{\circ}\text{C}$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3333 (NH), 3089, 2943, 2107 (CHN₂), 1709 (C=O), 1633, 1533, 1375, 1255, 1141; δ_{H} 1.83 (2 H, m, CH₂), 2.35 (2 H, br t, *J* 5.2, CH₂CO), 3.21 (2 H, q, *J* 6.6, CH₂NH), 5.08 (2 H, s, CH₂O), 5.12 (1 H, br s, CHN₂), 5.26 (1 H, br s, NH), 7.34 (5 H, s, C₆H₅); δ_{C} 25.02, 37.57, 40.37, 54.54, 66.51, 127.75, 127.98, 128.39, 136.50, 156.48, 194.31; *m/z* (EI) 233 [(M – N₂)⁺, 3%], 142 [(M – C₆H₅CH₂ – N₂)⁺, 17], 127 (15), 107 (100) [Found: (M – N₂)⁺, 233.1067. C₁₃H₁₅NO₃ requires *m/z*, 233.1051].

1-Diazo-6-(benzyloxycarbonylamino)hexan-2-one 3f. Mp $35\text{--}36\text{ }^{\circ}\text{C}$; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3355 (NH), 2948, 2104 (CHN₂), 1691 (C=O), 1626, 1525, 1385, 1258; δ_{H} 1.58 (4 H, m, 2 \times CH₂), 2.34 (2 H, br d, *J* 6.4, CH₂), 3.20 (2 H, m, CH₂N), 4.92 (1 H, br s, NH), 5.08 (2 H, s, CH₂O), 5.23 (1 H, s, CHN₂), 7.34 (5 H, s, C₆H₅); δ_{C} 21.76, 29.33, 33.29, 40.46, 54.34, 66.57, 128.02, 128.44, 128.44, 136.55, 156.42, 194.65; *m/z* (EI) 247 [(M – N₂)⁺, 3%], 174 (4), 141 (8), 91 (100) [Found: (M – N₂)⁺, 247.1213. C₁₄H₁₇NO₃ requires *m/z*, 247.1208].

Diazo-(*N*-tert-butoxycarbonylglycyl)methane 3g. Oil [Found: C, 47.93; H, 6.45; N, 21.01. C₈H₁₃N₃O₃ requires C, 48.23; H,

6.58; N, 21.09%]; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3296 (NH), 2979, 2114 (CHN₂), 1704 (C=O), 1625, 1537, 1369, 1279, 1251; δ_{H} 1.45 (9 H, s, CH₃), 3.90 (2 H, d, *J* 4.4, CH₂), 5.34 (1 H, br s, CHN₂), 5.45 (1 H, br s, NH); δ_{C} 28.24, 47.79, 53.32, 80.05, 155.50, 196.89; *m/z* (EI) 144 (3%), 130 (9), 126 (32), 115 (44), 69 (32), 57 (33), 41 (100); *m/z* (FAB) 200 [(M + 1)⁺, 13%], 144 (42), 116 (58), 73 (30), 57 (100).

General procedure for the Cu(acac)₂-catalyzed diazo compound decomposition in benzene

The diazo compound (0.3 mmol) in anhydrous benzene (6 cm³) was added dropwise during 1.5 h to a refluxing solution of Cu(acac)₂ (8 mg, 0.03 mmol) in benzene (15 cm³) under nitrogen atmosphere. The reflux was continued for another 1.5 h after addition. After cooling of the reaction mixture to room temperature, the solvent was removed by evaporation and the crude residue was subjected to silica gel column chromatography with petroleum spirit–ethyl acetate as eluent. The structures of *N*-tosylazetidin-3-one **4a** and its 4-substituted derivatives **11**, **12** and **13** were confirmed with the samples obtained from our previous investigation.⁸

***N*-Tosylpyrrolidin-3-one 4b.** 55%; mp $121\text{--}122\text{ }^{\circ}\text{C}$ (lit.¹⁵ $122\text{--}123\text{ }^{\circ}\text{C}$); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3442, 1752 (C=O), 1430, 1339, 1156; δ_{H} 2.54 (3 H, s, CH₃), 2.50 (2 H, d, *J* 7.6, CH₂), 3.48 (2 H, s, CH₂), 2.49 (2 H, t, *J* 7.6, CH₂), 7.37 (2 H, d, *J* 8.2, 4-MeC₆H₄), 7.72 (2 H, d, *J* 8.2, 4-MeC₆H₄); δ_{C} 21.51, 37.11, 44.95, 53.63, 127.88, 129.86, 129.95, 144.43, 208.17.

***N*-(Benzyloxycarbonyl)azetidin-3-one 4c.** 32%; oil; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3360, 2925, 1827 (C=O), 1709 (C=O), 1497, 1409, 1354, 1205; δ_{H} 4.78 (4 H, s, CH₂), 5.16 (2 H, s, CH₂O), 7.37 (5 H, s, C₆H₅); δ_{C} 67.71, 71.28, 128.22, 128.39, 128.59, 136.58, 156.10, 200.45; *m/z* (EI) 205 (M⁺, 27%), 179 (15), 151 (8), 107 (100), 91 (93) [Found: M⁺, 205.0738. C₁₁H₁₁NO₃ requires *M*, 205.0748].

***N*-(Benzyloxycarbonyl)pyrrolidin-3-one 4d.** 62%; oil; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2923, 1760 (C=O), 1706 (C=O), 1422, 1360, 1173, 1106; δ_{H} 2.53 (2 H, t, *J* 7.8, CH₂CO), 3.75 (2 H, s, CH₂NHCbz), 3.78 (2 H, t, *J* 7.8, CH₂NHCbz), 5.10 (2 H, s, PhCH₂), 7.29 (5 H, s, C₆H₅); δ_{C} 29.65, 42.62, 52.46, 67.27, 128.03, 128.19, 128.52, 136.31, 156.40, 209.53; *m/z* (EI) 219 (M⁺, 72%), 191 [(M – CO)⁺, 8], 146 (12), 128 [(M – C₆H₅CH₂)⁺, 7], 91 (100) [Found: M⁺, 219.0897. C₁₂H₁₃NO₃ requires *M*, 219.0895].

***N*-(Benzyloxycarbonyl)piperidin-3-one 4e.** 76%; oil; $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3377, 2955, 1705 (C=O), 1425, 1265, 1114, 1010; δ_{H} 2.00 (2 H, m, CH₂), 2.46 (2 H, t, *J* 6.7, CH₂), 3.65 (2 H, d, *J* 6.0, CH₂N), 4.07 (2 H, s, CH₂N), 5.14 (2 H, s, CH₂N), 7.34 (5 H, s, C₆H₅); δ_{C} 22.16, 38.00, 42.08, 53.90, 67.42, 127.92, 128.10, 128.25, 136.21, 155.07, 205.10; *m/z* (EI) 233 (M⁺, 32%), 203 (51), 127 (10), 91 (100) [Found: M⁺, 233.1055. C₁₃H₁₅NO₃ requires *M*, 233.1051].

(5*S*)-5-Methyl-*N*-tosylpyrrolidin-3-one 20. 52%; mp $98\text{--}99\text{ }^{\circ}\text{C}$ [Found: C, 57.17; H, 5.79; N, 5.35. C₁₂H₁₅NO₃S requires C, 56.90; H, 5.97; N, 5.53%]; $[\alpha]_{\text{D}}^{20} -63.9$ (*c* 0.61, CH₂Cl₂); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3429, 1761, 1715, 1642, 1438, 1345, 1157; δ_{H} 1.37 (3 H, d, *J* 6.4, CH₃), 2.17 (1 H, m, CH₂), 2.40 (1 H, d, *J* 8.4, CH₂), 2.44 (3 H, s, CH₃C₆H₄), 3.70 (2 H, s, CH₂), 4.24 (1 H, m, MeCHNTs), 7.34 (2 H, d, *J* 8.2, MeC₆H₄), 7.73 (2 H, d, *J* 8.2, MeC₆H₄); δ_{C} 21.55, 21.87, 44.98, 53.13, 53.63, 115.99, 127.38, 130.02, 144.19, 209.13; *m/z* (EI) 253 (M⁺, 12%), 238 [(M – Me)⁺, 22], 184 (40), 155 (100), 91 (95).

(5*S*)-5-Benzyl-*N*-tosylpyrrolidin-3-one 21. 61%; mp $122\text{--}123\text{ }^{\circ}\text{C}$ [Found: C, 65.42; H, 5.68; N, 4.06. C₁₈H₁₉NO₃S requires C, 65.63; H, 5.81; N, 4.25%]; $[\alpha]_{\text{D}}^{20} -50.6$ (*c* 0.6, CH₂Cl₂); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3439, 1754 (C=O), 1635, 1438, 1156; δ_{H} 2.25 (2 H, m, PhCH₂), 2.43 (3 H, s, CH₃), 2.85 (1 H, dd, *J* 13.6, 4.8,

CH₂), 3.12 (1 H, dd, *J* 13.6, 4.1, CH₂), 3.46 (1 H, d, *J* 18.8, CH₂), 3.69 (1 H, d, *J* 18.8, CH₂), 4.49 (1 H, m, CHN), 7.12–7.30 (5 H, m, C₆H₅), 7.32 (2 H, d, *J* 8.2, 4-MeC₆H₄), 7.73 (2 H, d, *J* 8.2, 4-MeC₆H₄); δ_{C} 21.51, 41.61, 41.91, 53.14, 58.43, 127.09, 127.21, 128.74, 129.71, 130.07, 135.07, 135.97, 144.20, 209.04; *m/z* (FAB) 330 [(M + 1)⁺, 23%], 274 (7), 238 (13), 184 (8), 155 (42), 91 (100).

(5*R*)-5-[2-(Methylthio)ethyl]-*N*-tosylpyrrolidin-3-one **22**. 43%; mp 71–72 °C (Found: C, 54.03; H, 6.09; N, 4.14. C₁₄H₁₉NO₃S₂ requires C, 53.65; H, 6.11; N, 4.47%); $[\alpha]_{\text{D}}^{20}$ –29.4 (*c* 0.61, CH₂Cl₂); ν_{max} (KBr)/cm^{–1} 3438, 2920, 1754 (C=O), 1632, 1436, 1349, 1156; δ_{H} 1.60–2.38 (4 H, m, CH₂), 2.14 (3 H, s, CH₃), 2.44 (3 H, s, CH₃), 2.60 (2 H, m, CH₂), 3.67 (1 H, d, 19.2, CH₂), 3.82 (1 H, d, *J* 19.2, CH₂), 4.36 (1 H, m, NHCH), 7.35 (2 H, d, *J* 8.2, 4-MeC₆H₄), 7.74 (2 H, d, *J* 8.2, 4-MeC₆H₄); δ_{C} 15.45, 21.52, 30.14, 34.84, 42.29, 52.88, 56.64, 127.30, 130.15, 135.20, 144.37, 290.50; *m/z* (EI) 313 (M⁺, 3%), 238 [(M – MeSCH₂CH₂)⁺, 8], 159 (18), 158 (100), 110 (42), 91 (98).

The Cu(acac)₂-catalyzed decomposition of diazoacetophenone in the presence of aniline derivatives

The *N*-substituted aniline **24a–c** (5 mmol) was dissolved in dry toluene (20 cm³). To the solution was added Cu(acac)₂ (26 mg, 0.1 mmol) and the mixture was heated under reflux. Diazoacetophenone **23** (146 mg, 1 mmol) in toluene (8 cm³) was added dropwise. The reflux was continued until the disappearance of the starting material as indicated by TLC. The reaction mixture was cooled and toluene was removed under reduced pressure to leave a crude product, which was purified by column chromatography with petroleum spirit–ethyl acetate (8:1) as eluent.

2-[Methyl(phenyl)amino]acetophenone **25a** was isolated in 28% yield when *N*-methylaniline **24a** was used. For **25a**: most of this molecule exists in its enol form in solution. Mp 118–120 °C (Found: C, 79.80; H, 6.30; N, 5.92. C₁₅H₁₅NO requires C, 79.97; H, 6.71; N, 6.22%); ν_{max} (KBr)/cm^{–1} 3437, 2924, 1664, 1600, 1497, 1442, 1272, 1114; δ_{H} 2.57 (3 H, s, CH₃), 6.07 (1 H, s, C=CH), 6.70–6.79 (3 H, m, C₆H₅), 7.15–7.53 (5 H, m, C₆H₅), 7.90–7.97 (2 H, m, C₆H₅); δ_{C} 34.05, 61.22, 113.35, 117.68, 128.35, 128.54, 128.99, 129.17, 133.29, 148.15, 198.88; *m/z* (EI) 225 (M⁺, 9%), 120 (100), 106 [(M – C₆H₅COCH₂)⁺, 95], 77 (81).

2-[Acetyl(phenyl)amino]acetophenone **25b** was isolated in 58% yield when acetanilide **24b** was used. For **25b**: mp 67–69 °C (Found: C, 75.87; H, 5.94; N, 5.11. C₁₆H₁₅NO₂ requires C, 75.87; H, 5.97; N, 5.53%); ν_{max} (KBr)/cm^{–1} 3434, 1703, 1672, 1592, 1446, 1376, 1224; δ_{H} 1.96 (3 H, s, CH₃), 5.47 (2 H, s, CH₂), 6.70–6.72 (2 H, m, C₆H₅), 7.00–7.02 (1 H, m, C₆H₅), 7.20–7.30 (2 H, m, C₆H₅), 7.46–7.58 (3 H, m, C₆H₅), 7.93–8.07 (2 H, m, C₆H₅); δ_{C} 15.73, 67.27, 120.88, 123.06, 127.75, 128.66, 128.88, 133.44, 134.92, 148.16, 160.09, 193.89; *m/z* (EI) 253 (M⁺, 13%), 180 (100), 118 (46), 105 (66), 77 (84).

The reaction with *N*-tosylaniline **24c** gave an inseparable mixture.

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