THE STUDIES OF CARBENOID REACTIONS OF α-O-ALLYL- or α-N-ALLYL-α'-DIAZOPROPANONE DERIVATIVES CATALYZED BY VARIOUS METAL IONS

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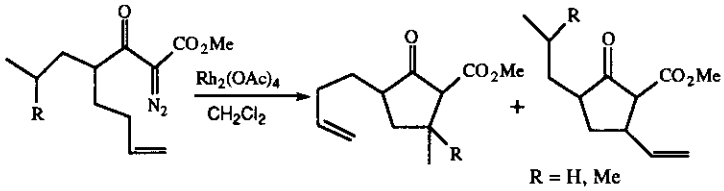
Abstract- Both cupric acetylacetonate and palladium(II) acetate are good catalysts to induce the carbon-carbon double bond addition reaction for α-O-allyl- or α-N-allyl-α'-diazopropanone derivatives. The heteroatom did not play an important role in enhancing the carbon-hydrogen bond insertion for compound (3).

The intramolecular cyclization via carbenoid C-H bond insertion reaction has been widely used for C-C bond formation.[1-6] The reactivity of the C-H bond insertion is dependent on its electron density as the diazoketone is the precursor of the carbenoid center.[7-10](Scheme 1) It is noteworthy to point out that the formation of 5-membered ring via C-H bond insertion was the only process occurred and the formation of bicyclo[4.1.0]heptane ring system via the C=C double bond addition was excluded.[8](Scheme 1) Moreover, the C-H bond adjacent to the ether oxygen was found to be the preferred site of insertion, compared with an aliphatic C-H bond.[11-14](Scheme 2) Recently, we reported that the cupric acetylacetonate ($Cu(acac)_2$) is the best catalyst to induce C-H bond insertion for α-alkoxy-α'-diazoketone derivatives.[15] By using this catalyst, the side reactions such as aromatic C-H bond insertion and rearrangement could be prevented. These observations could not simply be explained by inductive effect since the C-H bond adjacent to the oxygen atom is electron deficient based on its chemical shift of the ^{1}H-Nmr. We might ascribe this preference to the stereoelectronic effect. The carbenoid insertion reaction will occur preferentially when the oxygen has a lone pair orbital antiperiplanar to the C-H bond as ahown in structure (**A**).[16] In combination with the results described in Schemes 1 and 2, it is interesting to know whether the heteroatom of structure (**B**) will enhance chemoselectivity of the carbenoid center to the C-H bond in the presence of a C=C double bond. The oxygen atom of β- or γ-allyloxy-α'-diazoketone could displace the diazo group to form the oxonium ylide, followed by [2,3] sigmatropic shift, to give the tetrahydrofuranone.(Scheme 3) This type of reaction should not occur in structure (**B**) because the formation of the four-membered ring intermediate is not a favored process. In this paper, we describe the effects of the heteroatom and the metal catalyst on the chemoselectivity in the reaction of the carbenoid centers derived from mandelic acid and glycine.

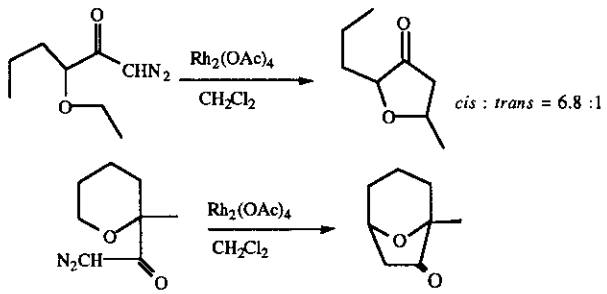
The mono-O-allylated compound (**2**) was made in 98% yield by treatment of mandelic acid (**1**) (0.3 M in THF) with sodium hydride and allyl bromide in refluxing THF. 2-Allyl-2-allyloxyphenylacetic acid was formed as the side product in a very significant amount if the concentration of the mandelic acid was lowered to 0.1 M. The diazoketone (**3**) was formed in 61% yield by treating carboxylic acid (**2**) with oxalyl chloride to give acyl chloride, followed by reacting with diazomethane.(Scheme 4) The signal

corresponding to the CHN_2 appeared at δ 5.83 (br s, 1H) in ^{1}H-Nmr and δ 52.42 (d) in ^{13}C-Nmr and ν_{max} 2104 cm^{-1} (CH=N=N stretching) in ir spectrum.

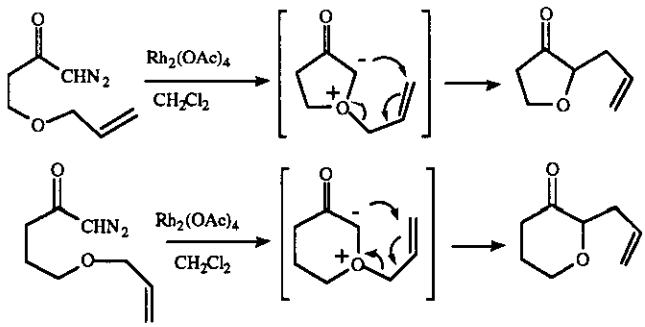
Scheme 1

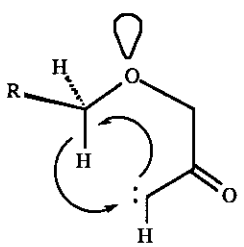


Scheme 2



Scheme 3



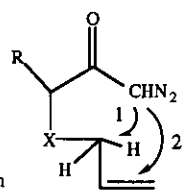


A

X= N, O

1. C-H Insertion

2. C=C Addition

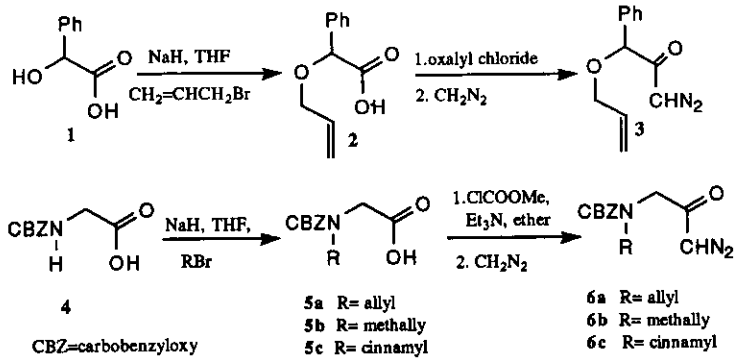


B

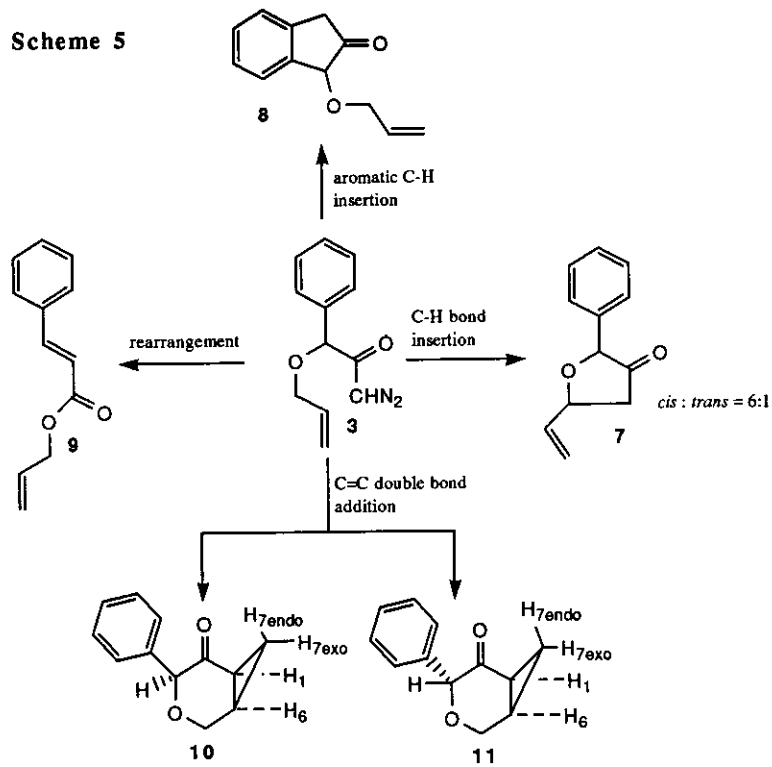
In order to prepare nitrogen analogues, carbobenzyloxyglycine (CBZ-glycine) (4) was treated with sodium hydride and alkyl halide (alkyl=allyl, methallyl, cinnamyl) in refluxing THF to give N-alkylated CBZ-glycines (**5a-5c**) in moderate yield (62-81%). The

carboxyl group was then treated with methyl chloroformate and triethylamine in anhydrous ether to form the corresponding mixed anhydrides, which were reacted with diazomethane to give diazoketones (**6a-6c**) in moderate yield (69-73%).(Scheme 4)

Scheme 4



Scheme 5



When diazoketone (**3**) was treated with 3 weight % $Rh_2(OAc)_4$ in dichloromethane, five products (**7-11**) were isolated and characterized by their spectral data.(Scheme 5) Both the aliphatic C-H bond insertion product (**7**) and the aromatic C-H bond insertion product (**8**) were formed in a ratio of 3:1.(Table 1, entry 1) The signal corresponding to methylene group of the *cis*-2-

tetrahydofuranone ring in compound (**7**) appeared as two doublet-doublet at δ 2.45 and 2.74, respectively. The *cis-trans* isomer ratio (6:1) of compound (**7**) was determined by their gc integration and the *cis* isomer is the major product.[17] The signals corresponding to two protons in the 2-indanone ring of compound (**8**) appeared at δ 3.54 (s, 2H, C_3-H) and 4.89 (s, 2H, C_1-H). To our surprise, very little of *trans*-allyl cinnamate (**9**), identified by their olefinic coupling constant (J=16 Hz), was formed.(Table 1, entry 1) The possible mechanisms of the cinnamate formation were described in previous reports.[15,18] Compounds (**10**) and (**11**) were formed via carbenoid addition to the double bond. The structures of compounds (**10**) and (**11**) were speculated by the following explanations. First, the polarity of the *trans* isomer is usually less than that of *cis* isomer for the cyclic compound.[15,19] The major isomer is a less polar one on tlc.(entries 2-5) Therefore, the *trans* isomer should be the major one (i.e. compound (**11**)) and this conclusion is also consistent with the steric requirement during the cyclization process. Second, the chemical shift of the H_{7endo} from the *cis* isomer (**10**) will be deshielded by the *endo* phenyl group due to the anisotropic effect and moved slightly to downfield (δ 1.89-2.01). In other words, only *cis* isomer could cause the larger chemical shift difference between H_{7endo} and H_{7exo}. The chemical shift difference between H_{7endo} and H_{7exo} for minor isomer (Δδ=0.7 ppm, δ_1=1.22-1.30, δ_2=1.89-2.01) is larger than that of major isomer (Δδ=0.4 ppm) Therefore, the minor isomer (**10**) should be the polar one with its phenyl group *cis* to the three-membered ring.(Scheme 5) The chemoselectivity of the carbenoid center to the C-H bond insertion and C=C bond addition reaction is only about 3:1, which is not as good as those shown in Scheme 1.(entry 1, Table 1) The poor chemoselectivity of the above reaction encourages us to look for the other catalysts to improve the results. Six other catalysts were tried and their results were listed in Table 1. The product distributions were quite dependent on the catalysts used. None of C-H bond insertion products were formed when the copper and palladium catalysts were used. Both $Cu(acac)_2$ and $Pd(OAc)_2$ afforded only the C=C double bond addition products in very high yields. Moreover, $Cu(acac)_2$ is the best catalyst concerning the matter of stereoselectivity (93:7).(Table 1)

Table 1 The Reactions of Compound (**3**) with Various Catalysts

entry	Catalyst	**7**	**8**	**9**	**10**	**11**	Overall Yield[b]
		product distributions (%)[a]					
1	$Rh_2(OAc)_4$	52	17	5	15	11	66%
2	Cu	0	0	13	14	73	83%
3	CuCl	0	0	25	25	50	92%
4	$CuSO_4$	0	0	23	16	61	90%
5	$Cu(acac)_2$	0	0	0	7	93	84%
6	$Pd(OAc)_2$	0	0	0	50	50	70%

a. The product distributions were determined based on the amount of each isolated products.
b. The isolated yield of all the insertion products was reported.

Scheme 6

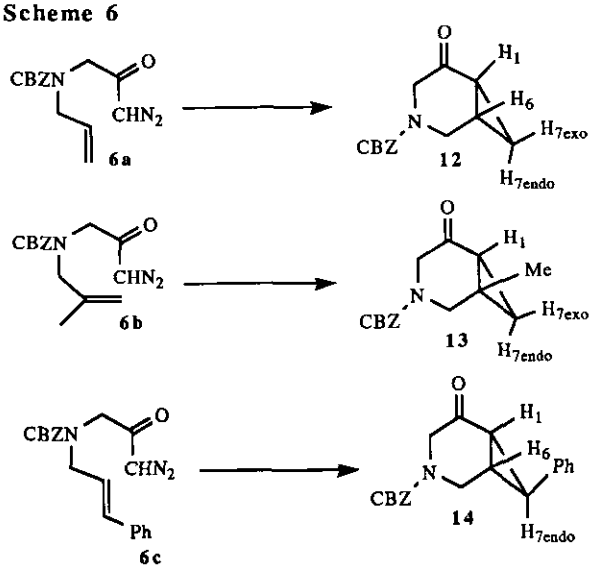


Table 2 The Reaction of Compounds (**6a-6c**) with Various Catalysts

Catalysts	Yields (%)[a]		
	6a → **12**	**6b** → **13**	**6c** → **14**
Cu/benzene	23	57	42
Cu/cyclohexane	31	56	42
$Rh_2(OAc)_4$	17	24	30
$Pd(OAc)_2/CH_2Cl_2$	40	51	51
$CuSO_4$/cyclohexane	—[b]	—[b]	22
CuCl/benzene	—	—	44
$Cu(acac)_2$/benzene	41	46	52

a. The purified yields were reported.
b. They had not been tried by using these conditions.

The nitrogen analogues (**6a-6c**) were also treated with various catalysts.(Scheme 6) Similar to the results described above, none of the C-H bond insertion products were isolated for all the catalysts, including $Rh_2(OAc)_4$, we tried. While the reactions appeared to be clean (as judged by tlc) the yields tended to be rather low, particularly when the less electron rich double bond was used as the trapping group.(Table 2) The C-H bond between olefin and carbamyl group is electron deficient due to the inductive effect and, therefore, it is not favorable to react with electron deficient carbenoid center. Again, both $Pd(OAc)_2$ and $Cu(acac)_2$ are good catalysts for the C=C double bond addition.(Table 2) These results are consistent with those shown in the literature that copper or copper salts are the catalysts of choice for intramolecular addition reactions of the carbenoid to an olefinic moiety but not for

intramolecular C-H insertion reactions.[20] The structures of compound (**12-14**) are determined unambiguously by their spectral data. The signals corresponding to the 3-membered ring carbons appeared at rather upfield of ^{13}C-Nmr and they were listed as follows: δ 9.82 (C_7), 17.42 (C_6), 25.30 (C_1) for compound (**12**); 17.89 (C_7), 24.58 (C_6), 33.68 (C_1) for compound (**13**) and 25.67 (C_7), 27.21 (C_6), 36.00 (C_1) for compound (**14**). Compound (**14**) was formed stereoselectively and its phenyl group was oriented *exo* face to the bicyclo[4.1.0]heptane system. The signal corresponding to its C_1-H appeared at δ 2.77, which was much downfield than that of compound (**12**) due to the anisotropic effect of the phenyl group.

In conclusion, the metal carbenoids of α-diazoketones, which were derived from O-allylmandelic acid and CBZ-N-allylglycine, preferentially added to the C=C double bond rather than inserted to the C-H bond. The proposed stereoelectronic effect from oxygen atom did not play an important role in compound (**3**) for the C-H insertion channel. However, we discovered that $Cu(acac)_2$ is the best catalyst for the three-membered ring formation with regard to chemical yields and stereoselectivity.

EXPERIMENTAL

All reactions were carried out under nitrogen. The ^{1}H and ^{13}C-Nmr spectra were recorded on a Bruker AC 200 Spectrometer, and chemical shifts are given in ppm downfield from tetramethylsilane (TMS). ^{1}H-Nmr data are tabulated in the order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant(s) in hertz, number of protons. Ir spectra were taken with a Perkin Elmer 882 spectrophotometer and only noteworthy absorptions were listed. Mass spectra were measured on a VG 70-250S mass spectrometer by electronic impact at 70 eV (unless otherwise indicated). The elemental analyses were performed on a Perkin-Elmer 2400 Elemental Analyzer.

O-Allylmandelic acid (**2**) To a suspension solution of NaH (2.467 g, 82.2 mmol, 80% NaH in mineral oil) in 50 ml of anhydrous THF was added a solution of mandelic acid (5.00 g, 32.9 mmol) in 50 ml of THF slowly at 0°C. Once the hydrogen bubbling ceased, allyl bromide (5.56 ml, 65.8 mmol) was added into the above heterogeneous solution and the reaction mixture was heated to reflux for 12 h. The reaction mixture was cooled down to 0°C and quenched by 1N HCl to become acidic (pH=2). The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The crude product was chromatographed on silica gel column ($MeOH/CH_2Cl_2$ = 1 : 19) to afford 6.12 g (98% yield) of product (**2**) as a colorless oil. ^{1}H-Nmr ($CDCl_3$) δ 4.04 (m, 2H, O-CH_2-C=C), 4.94 (s, 1H, Ph-CH), 5.18-5.32 (m, 2H, C=CH_2), 5.84-5.97 (m, 1H, CH=C), 7.33-7.34 (m, 5H, Ph-H), 9.76 (br s, 1H, COOH); ^{13}C-Nmr ($CDCl_3$) δ 70.28 (O-C-C=C), 79.13 (Ph-C-O), 118.37 (C=CH_2), 127.24, 128.58, 128.81, 133.29 (aromatic), 135.53 (C=CH_2), 175.66 (COOH); ir (neat) ν_{max} (cm^{-1}) 2450-3600 (brs,

OH), 1747 (C=O); ms (m/z): 147 (M^+-45); hrms (m/z): 147.0805 (M^+-COOH, $C_{10}H_{11}O$, calcd 147.0809); Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found : C, 68.53; H, 6.20.

1-Phenyl-1-allyloxy-1'-diazopropanone (3) To a solution of carboxylic acid (2) (200 mg, 1.05 mmol) in 5 ml of CH_2Cl_2 was added oxalyl chloride (0.11 ml, 1.27 mmol). The reaction mixture was stirred at room temperature for 2 h. The solvent and excess oxalyl chloride were removed. The residue was dissolved in 5 ml of CH_2Cl_2 and was added into the etheral solution of CH_2N_2. The reaction mixture was stirred at room temperature for 1 h and then concentrated. The crude products were chromatographed (hexane/ethyl acetate = 10:1) to give 137 mg (61%) of **3** as a form of yellow oil. ^{1}H-Nmr ($CDCl_3$) δ 4.03-4.07 (m, 2H, O-CH_2-C=C), 4.82 (s, 1H, Ph-CH-O), 5.20-5.36 (m, 2H, C=CH_2), 5.83 (s, 1H, CHN_2), 5.84-5.91 (m, 1H, -CH=C), 7.25-7.42 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 52.42 (CHN_2), 70.23 (C-O-CH_2-C=C), 84.73 (Ph-CH-O-C), 117.57 (C=CH2), 126.48, 128.304, 128.47 (aromatic),133.69 (-CH=C), 136.69 (aromatic), 193.93 (C=O); ir (neat) ν_{max} (cm^{-1}) 2104 (CH=N=N), 1640 (C=O), 1350; ms (m/z): 188 (M^+-28); hrms (m/z): 188.0828 (M^+-N_2, $C_{12}H_{12}O_2$, calcd 188.0837); Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found : C, 66.39; H, 5.45; N, 13.09.

N-Carbobenzyloxy-N-allylglycine (5a) To a suspended solution of NaH (5.74 g, 119.50 mmol, 80% NaH in mineral oil) in 50 ml of anhydrous THF was added a solution of CBZ-glycine (5.00 g, 23.90 mmol) in 50 ml of THF slowly at 0°C. Once the hydrogen evolution ceased, allyl bromide (3.1 ml, 35.85 mmol) was added into the above heterogeneous solution and the reaction mixture was heated to reflux for 12 h. The reaction mixture was cooled down to 0°C and quenched by 1N HCl to become acidic (pH=2). The mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, and concentrated. The crude product was chromatographed on silica gel column (MeOH/CH_2Cl_2= 1 : 19) to afford 4.76 g (80%) of product (**5a**) as a colorless oil. ^{1}H-Nmr ($CDCl_3$) δ 4.00 (br s, 4H, N-CH_2), 5.16 (br s, 4H, Ph-CH_2-O, C=CH_2), 5.71-5.85 (m, 1H, N-C-CH=C), 7.26-7.34 (m, 5H, Ph), 9.77 (br s, 1H, COOH); ^{13}C-Nmr ($CDCl_3$) (There are two sets of ^{13}C-Nmr peaks due to the C=N double bond character of the carbamyl group) δ 47.06, 47.62 (N-CH_2-C), 50.34, 50.65 (N-CH_2-COOH), 67.67 (Ph-CH_2-O), 117.60, 118.14 (-C=CH_2), 127.58, 127.68, 128.29 (aromatic), 132.65 (CH=C), 136.01 (aromatic), 155.90, 156.45 (N-C=O), 174.02 (COOH); ir (neat) ν_{max} (cm^{-1}) 2450-3600 (OH), 1712, 1710 (C=O); ms (m/z): 249 (M^+), 91 (base peak); hrms (m/z): 249.1001 (M^+, $C_{13}H_{15}NO_4$, calcd 249.0998); Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found : C, 62.51; H, 6.03; N, 5.84.

N-Carbobenzyloxy-N-methallylglycine (5b) Compound (**5b**) was made in 62% yield as a colorless oil by following the procedures described in the preparation of compound (**5a**) . ^{1}H-Nmr ($CDCl_3$) δ 1.67 (d, J= 10Hz, 3H, CH_3), 3.96 (m, 4H, N-CH_2-C), 4.87 (m, 2H, -C=CH_2), 5.16 (m, 2H, Ph-CH_2-O), 7.32 (m, 5H, Ph-H); ir (neat) ν_{max} (cm^{-1}) 2800-3650 (OH), 1685 (C=O), 1651 (C=O); ms (m/z): 263 (M^+); Anal. Calcd for $C_{15}H_{17}NO_4$: C, 63.87 ; H, 6.51 ; N, 5.32. Found : C, 64.02; H, 6.30; N, 5.56.

N-Carbobenzyloxy-N-cinnamylglycine (5c) Compound (**5c**) was made in 81% yield as a colorless oil by following the procedures described in the preparation of compound (**5a**). ^{1}H-Nmr ($CDCl_3$) δ 3.96-4.17 (m, 4H, N-CH_2-C), 5.15 (s, 2H, Ph-CH_2-O), 6.05-6.16 (m, 1H, -C=CHPh), 6.36-6.52 (m, 1H, -CH=CPh), 7.16-7.30 (m, 10H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 47.15, 47.90 (N-CH_2-C), 50.09, 50.25 (N-CH_2-COOH), 67.72, 67.86 (Ph-CH_2-O), 124.02 (-C=CHPh), 126.42, 127.81, 128.04, 128.06, 128.53 (aromatic), 133.01, 133.56 (-CH=C), 136.21 (aromatic), 155.64, 156.57 (N-C=O), 173.89, 174.19 (COOH); ir (neat) ν_{max} (cm^{-1}) 2500-3600 (OH), 1738 (C=O), 1456; ms (m/z): 325 (M^+), 91 (base peak); hrms (m/z): 325.1309 (M^+, $C_{19}H_{19}NO_4$, calcd 325.1314); Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30. Found : C, 69.85; H, 5.82; N, 4.35.

1-(N-Carbobenzyloxy-N-allyl)amino-1'-diazopropanone (6a) To a mixtures of CBZ-glycine (500 mg, 2.0 mmol) in 6 ml of ether were added Et_3N (0.34 ml, 2.4 mmol) and then methyl chloroformate (0.18 ml, 2.4 mmol). The white precipitate formed rapidly. The precipitates were filtered and washed with anhydrous ether. The filtrates were concentrated. The crude products were dissolved in anhydrous ether and then added into the etheral solution of CH_2N_2. The reaction was stirred for 2 h and concentrated. The crude products were purified by chromatography on a silica gel column (hexane/ethyl acetate = 5 : 1) to give 394 mg (72%) of the yellow oil . ^{1}H-Nmr ($CDCl_3$) δ 3.98 (br s, 4H, N-CH_2-C), 5.16 (br s, 5H, -C=CH_2, Ph-CH_2-O, CHN_2), 5.70-5.78 (m, 1H, -CH=C), 7.19-7.33 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 50.64, 50.96 (N-CH_2-C), 53.34 (CHN_2), 67.67 (Ph-CH_2-O), 117.76 (CH=C), 118.40, 127.87, 128.10, 128.45 (aromatic), 132.59 (C=CH2), 136.19 (aromatic), 155.71, 156.25 (N-C=O), 191.01 (COOH); ir (neat) ν_{max} (cm^{-1}) 2108 (CH=N=N), 1691, 1653 (C=O), 1246; ms (m/z): 204 (M^+-69); hrms (m/z): 204.1019 (M^+-$COCHN_2$, $C_{12}H_{14}NO_2$, calcd 204.1024); Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found : C, 61.38; H, 5.29; N, 15.52.

1-(N-Carbobenzyloxy-N-methallyl)amino-1'-diazopropanone (6b) Compound (**6b**) was made in 69% yield as a yellow oil by following the procedures described in the preparation of compound (**5a**). ^{1}H-Nmr ($CDCl_3$) δ 1.69 (d, J=6.9 Hz, 3H, CH_3), 3.94 (br s, 4H, N-CH_2-C), 4.77 (s, 1H, C=CH_2), 4.89 (s, 1H, C=CH_2), 5.17 (s, 2H, Ph-CH_2-O), 5.23 and 5.36 (br s, 1H, CHN_2), 7.30-7.34 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 19.48 (CH_3), 52.88 (N-CH_2-C), 53.28 (CHN_2), 53.60 (N-CH_2-CO), 67.31 (Ph-CH_2-O), 112.48, 112.86 (-C=CH_2), 127.49, 127.76, 128.13, 135.97 (aromatic), 139.88 (N-C-C=C), 155.67, 156.16 (N-C=O), 190.52 (C=O); ir (neat) ν_{max} (cm^{-1}) 2104 (CH=N=N), 1688, 1652 (C=O) 1119; ms (m/z): 259 (M^+-28); hrms (m/z): 259.1220 (M^+-N_2, $C_{15}H_{17}NO_3$, calcd 259.1208); Anal. Calcd for $C_{15}H_{17}N_3O_3$: C, 62.71; H, 5.96; N, 14.62. Found : C, 62.47; H, 5.93; N, 14.86.

1-(N-Carbobenzyloxy-N-cinnamyl)amino-1'-diazopropanone (6c) Compound (**6c**) was made in 73% yield as a yellow oil by following the procedures described in the preparation of compound (**5a**). ^{1}H-Nmr ($CDCl_3$) δ 4.00 (d, J= 6.1 Hz, 2H, N-CH_2-C=C), 4.14 (br s, 2H, N-CH_2-C=O), 5.17-5.35 (m, 3H, Ph-CH_2-O, CHN_2), 6.05-6.14 (m, 1H, -C=CH-Ph), 6.41-6.52 (m, 1H, CH=C-Ph),

7.19-7.33 (m, 10 H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 50.14 (<u>C</u>HN$_2$), 53.18 (N-<u>C</u>H$_2$-C), 67.61 (Ph-<u>C</u>H$_2$-O), 123.77 (-C=<u>C</u>HPh), 126.32, 127.80, 128.03, 128.40 (aromatic), 133.05 (-<u>C</u>H=CPh), 133.66, 136.120 (aromatic), 155.64, 156.31 (N-<u>C</u>=O), 190.80 (<u>C</u>=O); ir (neat) ν_{max} (cm^{-1}) 2108 (CH=N=N), 1709, 1650 (C=O), 1356; ms (m/z): 321 (M$^+$-28); <u>Anal.</u> Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found : C, 68.74; H, 5.44; N, 12.05.

<u>General procedure of the metal ion catalyzed carbenoid reaction of compound (3) and (6a-6c).</u>

(1) When $Rh_2(OAc)_4$ or $Pd(OAc)_2$ was used as catalyst: To a solution of diazo compound (**3**) (100 mg, 0.47 mmol) in 10 ml of anhydrous CH_2Cl_2 was added $Rh_2(OAc)_4$ or $Pd(OAc)_2$ (3 mg, 3 wt %) in one portion at room temperature. After stirring 3 h, the solution was concentrated and the crude products were chromatographed on silica gel column to isolate each product.

(2) When Cu, CuCl, $CuSO_4$ or $Cu(acac)_2$ was used as catalyst: To a solution of diazoketone (1 mmol) in 100 ml of benzene or cyclohexane (0.01 M solution was prepared) was added copper species (15 mmol for Cu; 3 mmol for CuCl or $CuSO_4$; 1 mmol for $Cu(acac)_2$). The reaction mixture was refluxed for 6 h. The catalyst was filtered off through celite. The filtrate was concentrated and chromatographed on silica gel column to isolate each product. The yield of each product was dependent on the catalyst used and they were listed in the Tables of the main text.

<u>*cis*-2-Phenyl-5-vinyl-3-tetrahydrofuranone (7)</u> Colorless oil; ^{1}H-Nmr ($CDCl_3$) δ 2.45 (dd, J=17.8 and 10.7 Hz, 1H, CH_2-C=O), 2.74 (dd, J=17.8 and 5.7 Hz, 1H, CH_2-C=O), 4.74-4.77 (m, 1H, O-CH-C=C), 4.80 (s, 1H, Ph-CH-), 5.31-5.55 (m, 2H, -C=CH_2), 6.02-6.19 (m, 1H, -CH=C), 7.30-7.42 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 42.57 (O=C-<u>C</u>H$_2$-C-O-), 82.83 (C=C-<u>C</u>H-O), 118.01 (O-<u>C</u>H-C=O), 126.28 (-C=<u>C</u>H$_2$), 127.98, 128.29, 128.49, 135.77 (aromatic), 136.52 (-<u>C</u>H=C), 212.26 (<u>C</u>=O); ir (neat) ν_{max} (cm^{-1}) 1720 (C=O); ms (m/z): 188 (M$^+$); hrms (m/z): 188.0828 (M$^+$, $C_{12}H_{12}O_2$, calcd 188.0837); <u>Anal.</u> Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found : C, 76.45; H, 6.48. The polarity of *cis* and *trans* isomer are quite close on silica gel tlc. Therefore, their ratio is determined by gc-ms technique.[17] The signal corresponding to the C_5-H of the *trans* isomer appeared at δ 4.77-4.80 (m). The other proton absorptions are almost overlapped with those of *cis* isomer.

<u>1-Allyloxy-2-indanone (8)</u> Colorless oil; ^{1}H-Nmr ($CDCl_3$) δ 3.54 (s, 2H, CH_2-C=O), 4.27 (dd, J= 12.5 and 6.2 Hz, 1H, O-CH_2-C=C), 4.44 (dd, J= 12.5 and 5.4 Hz, 1H, O-CH_2-C=C), 4.89 (s, 1H, Ph-CH-C=O), 5.22-5.40 (m, 2H, -C=CH_2), 5.90-6.10 (m, 1H, -CH=C), 7.26-7.51 (m, 4H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 41.37 (Ph-<u>C</u>H$_2$-C=O), 70.92 (O-<u>C</u>H$_2$-C=C), 79.69 (Ph-<u>C</u>H-C=O), 117.87 (-C=<u>C</u>H$_2$), 125.12 , 125.74, 127.81, 129.25, 134.32, 136.72 (aromatic), 138.41 (-<u>C</u>H=C), 213.76 (<u>C</u>=O); ir (neat) ν_{max} (cm^{-1}) 1717 (C=O), 1258; ms (m/z): 187 (M$^+$-1); <u>Anal.</u> Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found : C, 76.48; H, 6.46.

trans-Allyl cinnamate (9) Colorless oil; ^{1}H-Nmr ($CDCl_3$) δ 4.69-4.73 (m, 2H, -O-CH_2-C), 5.24-5.42 (m, 2H, C=CH_2), 5.90-6.09 (m, 1H, C-CH=C), 6.47 (d, J=16 Hz, 1H, Ph-C=CH), 7.36-7.55 (m, 5H, Ph-H), 7.72 (d, J= 16 Hz, 1H, Ph-CH=C); ^{13}C-Nmr ($CDCl_3$) δ 65.01 (O-CH_2-C), 117.73 (Ph-C=CH-C=O), 118.13 (O-C-C=CH_2), 127.95, 128.75, 130.19 (aromatic), 132.16 (O-C-CH=C), 134.23 (aromatic), 144.92 (Ph-CH=C), 166.42 (C=O); ir (neat) ν_{max} (cm^{-1}) 1715 (C=O), 1637, 1457; ms (m/z): 188 (M^+), 131 (base peak); hrms (m/z): 188.0828 (M^+, $C_{12}H_{12}O_2$, calcd 188.0837); Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found : C, 76.43; H, 6.45.

cis-3-Phenyl-4-oxabicyclo[4.1.0]heptan-2-one (10) Colorless oil (more polar isomer); ^{1}H-Nmr ($CDCl_3$) δ 1.22-1.30 (m, 1H, C_7-H), 1.89-2.01 (m, 3H, C_1-H, C_6-H and C_7-H), 3.99 (d, J=11.5 Hz, 1H, C_5-H), 4.40 (d, J=11.5 Hz, 1H, C_5-H), 4.68 (s, 1H, C_3-H), 7.29-7.37 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 9.33 (C_7), 18.19 (C_6), 25.70 (C_1), 62.86 (C_5), 84.91 (C_3), 127.10, 128.05, 128.23, 136.12 (aromatic), 204.76 (C_2); ir (neat) ν_{max} (cm^{-1}) 1702 (C=O), 1450, 1275; ms (m/z): 188 (M^+), 105 (base peak); hrms (m/z):188.0835 (M^+, $C_{12}H_{12}O_2$, calcd 188.0837). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found : C, 76.41; H, 6.47.

trans-3-Phenyl-4-oxabicyclo[4.1.0]heptan-2-one (11) Colorless oil (less polar isomer); ^{1}H-Nmr ($CDCl_3$) δ 1.21-1.34 (m, 1H, C_7-H), 1.67-1.79 (m, 2H, C_6-H, C_7-H), 1.91-2.11 (m, 2H, C_1-H), 3.83 (m, 2H, C_5-H), 5.03 (s, 1H, C_3-H), 7.27-7.52 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 10.48 (C_7), 16.05 (C_6), 27.75 (C_1), 57.35 (C_5), 80.29 (C_3), 127.81, 128.10, 128.38, 135.45 (aromatic), 205.64 (C_2); ir (neat) ν_{max} (cm^{-1}) 1691 (C=O), 1264; ms (m/z): 188 (M^+), 82 (base peak); hrms (m/z): 188.0832 (M^+, $C_{12}H_{12}O_2$, calcd 188.0837). Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found : C, 76.48; H, 6.49.

N-CBZ-4-azabicyclo[4.1.0]heptan-2-one (12) Colorless oil; ^{1}H-Nmr ($CDCl_3$) δ 1.21-1.36 (m, 2H, C_7-H), 1.88-1.95 (m, 2H, C_1-H, C_6-H), 3.30-3.55 (m, 2H, C_5-H), 4.41-4.54 (m, 2H, C_3-H), 5.41 (s, 2H, Ph-CH_2-O), 7.31 (s, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 9.82 (C_7), 17.42 (C_6), 25.30 (C_1), 39.96 (C_5), 52.10 (C_3), 67.56 (Ph-CH_2), 127.82, 128.11, 128.41, 135.94 (aromatic), 155.18 (-N-C=O), 220.83 (C_2); ir (neat) ν_{max} (cm^{-1}) 1698 (C=O), 1427, 1316, 1234; ms (m/z): 245 (M^+); hrms (m/z): 245.1053 (M^+, $C_{14}H_{15}NO_3$, calcd 245.1051). Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.16; N, 5.71. Found : C, 68.62; H, 6.10; N, 5.86.

N-CBZ-4-aza-6-methylbicyclo[4.1.0]heptan-2-one (13) Colorless oil; ^{1}H-Nmr ($CDCl_3$) δ 1.07-1.12 (m, 1H, C_7-H), 1.26 (s, 3H, CH_3), 1.47 (t, J=9.8 Hz, 1H, C_7-H), 1.71-1.79 (m, 1H, C_1-H), 2.96-3.18 (m, 1H, C_5-H), 3.40-3.60 (m, 1H, C_5-H), 4.20-4.51 (m, 2H, C_3-H), 5.15 (s, 2H, Ph-CH_2-O), 7.15 (s, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 17.89 (C_7), 20.20 (CH_3), 24.58 (C_6), 33.68 (C_1), 45.27 (C_5), 51.55 (C_3), 67.61 (Ph-CH_2), 127.87, 128.15, 128.45, 135.99 (aromatic), 155.02 (N-C=O), 202.92 (C=O); ir (neat) ν_{max} (cm^{-1}) 1711, 1670 (C=O), 1450, 1284; ms (m/z): 260 (M^++1), 259 (M^+); hrms (m/z): 259.1217 (M^+, $C_{15}H_{17}NO_3$, calcd 259.1208). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found : C, 69.71; H, 6.37; N, 5.62.

N-CBZ-4-aza-*cis*-7-phenylbicyclo[4.1.0]heptan-2-one (14) Colorless oil; ^{1}H-Nmr ($CDCl_3$) δ 2.21-2.23 (m, 2H, C_6-H, C_7-H), 2.77 (t, J= 4.5 Hz, 1H, C_1-H), 3.34-3.61 (m, 2H, C_5-H), 4.50-4.60 (m, 2H, C_3-H), 5.19 (s, 2H, $PhCH_2$-O), 7.03-7.35 (m, 5H, Ph-H); ^{13}C-Nmr ($CDCl_3$) δ 25.67 (C_7), 27.03 (C_6), 36.03 (C_1), 40.06 (C_5), 52.13 (C_3), 67.68 ($PhCH_2$), 126.18, 126.88, 127.92, 128.19, 128.49, 135.94, 137.58 (aromatic), 155.21 (N-C=O), 200.22 (C=O); ir (neat) ν_{max} (cm^{-1}) 2280, 1680 (C=O), 1420, 1345; ms (m/z): 322 (M^++1), 321 (M^+); hrms (m/z): 321.1355 (M^+, $C_{20}H_{19}NO_3$, calcd 321.1364). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.74; H, 5.96; N, 4.36. Found : C, 74.62; H, 6.16; N, 4.68.

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