International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Impact Factor (2012): 3.358

# An Unconventional Method for the Synthesis of Ether Analogue of Cyclic-Alkyl-Amino-Carbenes

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**Abstract:** ***We report on the synthesis and characterization of ether analogue of cyclic-alkyl-amino-carbenes using singlet biradicoloids dicarbene zinc compounds. Singlet biradicoloids dicarbene zinc compounds (3–4) on reaction with water under normal conditions produce ether analogues (5–6) of respective carbene. Synthesized compound were characterized with various spectroscopic techniques and analysis.***

**Keywords:** Ether analogue, Cyclic-alkyl-amino-carbenes, Biradicoloids

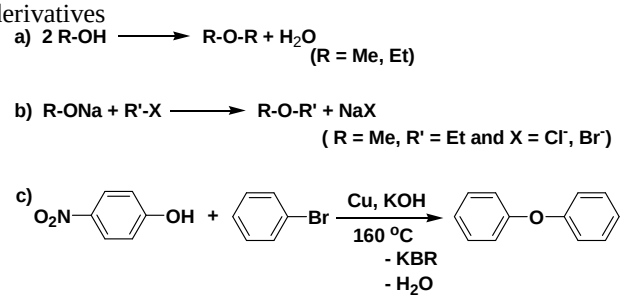
## 1. Introduction

Radicals and biradicals are very reactive chemical species that play an important role in combustion, atmospheric, plasma and polymerization chemistry, biochemistry, and in a number of other chemical processes [1]. Metal ions with radical centers in their coordination sphere are key participants in biological and catalytic processes [2]. Roesky and Coworker's [3] report on the synthesis of a biradicaloid dicarbene zinc compound of composition $(cAAC)_2Zn$ (**3**) using a cyclic-alkyl-amino carbene (cAAC) ligand [4]. The biradicaloid nature of compound **3** was further proved by the synthesis of a non-radical counterpart $(cAACH)_2Zn$. In addition, the utility of compound **3** has been explored in the $CO_2$ activation at -30 $^oC$ without using any catalysts.

Herein, we report on the synthesis and characterization of an analogues biradicaloid compound $(CycAAC)_2Zn$ (**4**) using cyclic-alkyl-amino carbene (CycAAC) [4]. The compounds **3** and **4** are used to synthesize ether derivatives $(cAACH)_2O$ (**5**) and $(CycAACH)_2O$ (**6**) of cAAC and CycAAC, respectively. Compounds **5** and **6** are synthesized by the reaction of water with the toluene solution of compounds **3** and **4**, respectively. So far from best of our knowledge no reports are available where a singlet biradicaloid compound on reaction with water gives corresponding ether product.

In literature, several other methods are available for ether preparation. The dehydration of alcohols affords ethers [5]. This direct nucleophillic substitution reaction requires elevated temperatures (about 125 °C) [6]. The reaction is catalyzed by acids, usually sulfuric acid. Diethyl ether is produced from ethanol by this method (Scheme 1-a). Another method for the synthesis of unsymmetrical ether is Williamson ether synthesis, *i.e*. the nucleophilic displacement of alkyl halides by alkoxides [7-10]. It involves treatment of a parent alcohol with a strong base to form the alkoxide, followed by addition of an appropriate aliphatic compound bearing a suitable leaving group (R-X). Suitable leaving groups (X) include iodide, bromide, or sulfonates (Scheme -1 b). The Ullmann condensation [11-15] or Ullmann ether synthesis is a variation of the Ullmann reaction, in which a phenol is coupled to an aryl halide to create a diaryl ether in the presence of a copper compound. The reaction often requires high-boiling polar solvents such as N-methylpyrrolidone, nitrobenzene or dimethylformamide and high temperatures (often in excess of 210 °C) (Scheme -1 c). In this context, compounds **3** and **4** easily produce the ether derivatives of respective carbene at room temperature under very mild reaction conditions. We assume that the biradicaloid nature of compounds **3** and **4** play an important role in water activation resulting in the formation of ether analogues **5** and **6**, respectively.

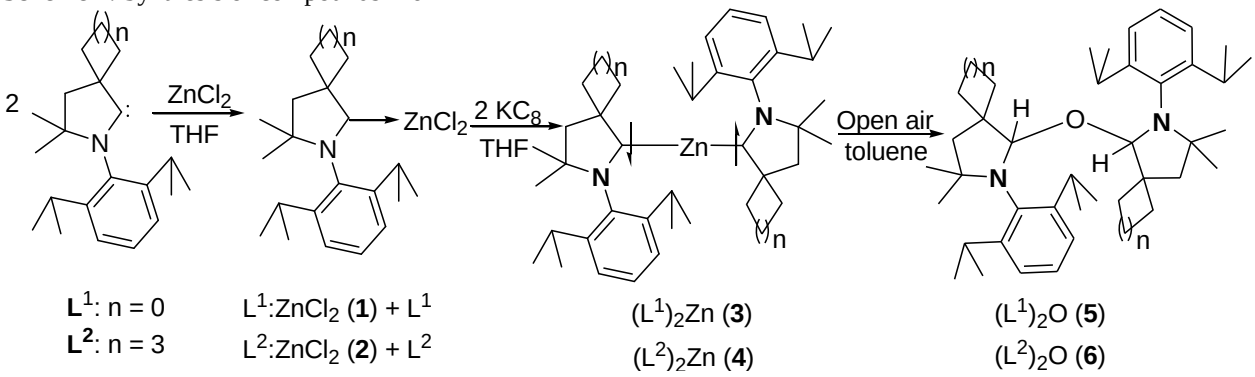
**Scheme 1**: Conventional methods for the synthesis of ether derivatives




## 2. Result and Discussion

We synthesized compound **4** by following a recently reported procedure [3]. The synthesis of **4** was carried out in two steps: in the first step two equivalents of CycAAC were treated with one equivalent of $ZnCl_2$ in THF to give a 1:1 adduct of CycAAC:$ZnCl_2$ (**2**). One equivalent of carbene remained unreactive. In the second step the reaction mixture was treated with two equivalents of $KC_8$ at -78 °C. A deep blue color appeared in the solution at -40 °C. After one hour of stirring the reaction mixture was filtered and the filtrate was stored for one day at -4 °C to give deep blue color crystal of compound **4**. In an alternative route for the synthesis of **4**, we reacted CycAAC and $ZnCl_2$ in a 1:1 ratio to prepare the CycAAC: $ZnCl_2$ adduct (**2**) and this adduct was then treated with CycAAC and $KC_8$ in the ratio of 1: 2.1 to give **4**. In another experiment, when the quantitative amount of water was added to the toluene solution of **3** and **4** at room temperature an immediate color change from blue to

**Scheme 2**: Synthesis of compounds **1-6**




$L^1$: n = 0 $L^1$:$ZnCl_2$ (**1**) + $L^1$ $(L^1)_2Zn$ (**3**) $(L^1)_2O$ (**5**)
$L^2$: n = 3 $L^2$:$ZnCl_2$ (**2**) + $L^2$ $(L^2)_2Zn$ (**4**) $(L^2)_2O$ (**6**)

light yellow was observed. The concentrated toluene solution of reaction mixture gives colorless crystals of **5** and **6** suitable for single-crystal x-ray analysis. Compounds **5** and **6** have been fully characterized by elemental analysis, various spectroscopic methods and single-crystal X-ray structural analysis. The $^1$HNMR spectrum of compounds 5 and 6 show signals for each chemically different proton of respective carbene ligands. The positions of signals are slightly different when compared with that of the respective parent compounds **3** and **4**. Additionally compound **5** and **6** show a singlet in their $^1$H NMR spectra at 4.83 ppm and 4.77 ppm, respectively for CH−O protons. Furthermore, to confirm that CH−O protons come from water we used $D_2O$ in place of water and the reaction product was confirmed by NMR spectroscopy which shows the absence of CH−O signals in their $^1$H NMR spectrum.

### 2.1 Crystal Structure Analysis

In order to establish unambiguously the structural feature of compounds **5** and **6**, single-crystal X-ray structural analysis was carried out. The molecular structures of compounds **5** and **6** are shown in figures 1 and 2, respectively while the structure refinement parameters for compounds **5** and **6** are summarized in table 1. Both the compounds **5** and **6** crystallized in triclinic crystal system with the space group *P*ī. Molecular structure of compound **5** and **6** reveals that two carbene molecules (cAAC for **5** and CycAAC for **6**) are bonded to the oxygen atom making V-shape structures like in water with the C1−O−C1'angle of 115.18° and 115.04°, respectively for compounds **5** and **6**. The C−O bond distances in **5** and **6** are 1.4531(13) Å and 1.4532(14) Å, respectively. In heterocyclic ring each carbon atoms have tetrahedral geometry.

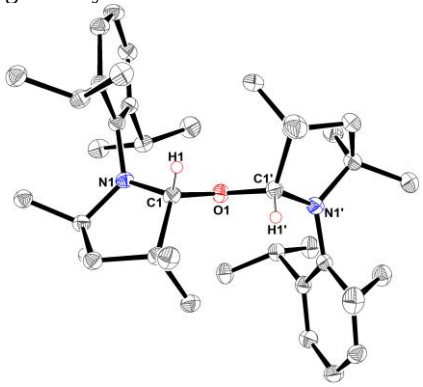



**Figure 1**: The molecular structure of compound **5** is shown. H atoms (except CH−O) and solvent molecules are omitted for clarity. Anisotropic displacement parameters are depicted at the 50% probability level. Selected bond lengths [Å] and angles [°]: C1−O 1.4531(13), C1−N1 1.4354(14), C1−O−C1' 115.18(8)

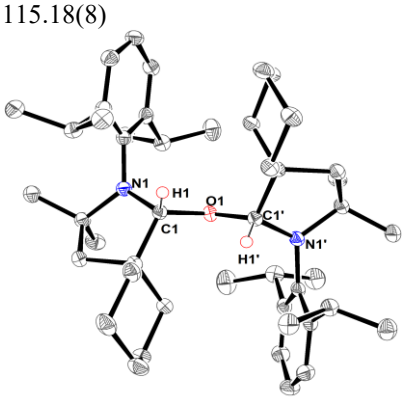



**Figure 2**: The molecular structure of compound **6** is shown. H atoms (except CH−O) and solvent molecules are omitted for clarity. Anisotropic displacement parameters are depicted at the 50% probability level. Selected bond lengths [Å] and angles [°]: C1−O 1.4532(14), C1−N1 1.4536(14), C1−O−C1' 115.04(8)

## 3. Conclusions

The synthesis of radical and biradical compounds is a rapidly growing field in chemistry because of their extensive use in various applications. In present study we have shown the synthesis of biradicaloid compounds by using cyclic-alkyl-amino-carbene ligands. These compounds on further treatment with water yield ether analogues of carbene. This is the first report where a biradicoloid compound used in water activation.

## 4. Experimental

All reactions and handling of reagents were performed under an atmosphere of dry nitrogen or argon using standard Schlenk techniques. The cyclic-alkyl-amino-carbene cAAC and CycAAC were synthesized following a reported procedure [4]. Solvents were purified and dried by following reported procedures. Solution NMR spectra were recorded on Bruker Avance 200, Bruker Avance 300, and Bruker Avance 500 MHz NMR spectrometers. Melting points were measured in sealed glass tubes on a Büchi B-540 melting point apparatus.

### 4.1 Synthesis

Compounds **1** and **3** are synthesized by following recently published procedures [3]. Compounds **2** and **4** were synthesized by using similar procedures.

#### 4.1.1 Synthesis of CycAAC: $ZnCl_2$ (2)

Tetrahydrofuran (30 mL) was cooled to -50 °C and added to a 1:1 mixture of CycAAC (3.07 mmol, 1.00 g) and $ZnCl_2$ (3.07 mmol, 419 mg). The reaction mixture was slowly warmed to room temperature and stirred for 3 hours. A white-colored precipitate appeared which was then filtered over a frit and dried under vacuum to obtain pure **2**. Yield: 1.20 g, 80 %. mp: 179-183 °C. Anal. Calcd. for $C_{23}H_{35}Cl_2NZn$: C, 59.82; H, 7.64; N, 3.03. Found: C, 59.72; H, 7.21; N, 2.95. $^1$H NMR ($CD_3CN$, 298 K, 500 MHz, δ ppm): 7.53-7.50 (*m*, 1Har, p-H), 7.45-7.43 (*d*, 2Har, m-H), 2.75-2.71 (*m*, 2H, $CHMe_2$), 2.23 (*s*, 2H, $CH_2$), 2.17-2.15 (*m*, 20H, $CyCH_2$), 1.65 (*s*, 6H, $CH_3$), 1.43-1.40 (*m*, 12H, $CHCH_3$). $^{13}$C NMR ($CD_3CN$, 298 K, 126 MHz, δ ppm): 152.7, 140.2, 134.1, 128.1, 126.4, 53.8, 51.1, 32.2, 28.8, 27.4, 26.8, 25.2, 24.1.

#### 4.1.2 Synthesis of $(CycAAC)_2Zn$ (4)

Tetrahydrofuran (50 mL) was cooled to -78 °C and added to a 1:1:2.1 mixture of **2** (1.08 mmol, 500 mg), CycAAC (1.08 mmol, 352 mg) and $KC_8$ (1.29 mmol, 176 mg) while stirring. The reaction mixture was slowly warmed to room temperature and stirred for an additional hour to give a solution of deep blue-color. The solution was then filtered, the volume of the filtrate was reduced to half and stored at - 4 °C to give blue-colored crystals suitable for single-crystal X-ray analysis of **4**. Yield: 0.67 g, 68 %. mp: 167-172 °C. Anal. Calcd. for $C_{46}H_{70}N_2Zn$: C, 77.12; H, 9.85; N, 3.91. Found: C, 77.35; H, 10.16; N, 4.12. UV/Vis $\lambda$ab = 632 nm. $^1$H NMR (THF-$d^8$, 298 K, 500 MHz, δ ppm): 7.42-7.38 (*m*, 2Har, p-H), 7.36-7.35 (*d*, 4Har, m-H), 3.27-3.24 (*m*, 4H, $CHMe_2$), 1.93 (*s*, 4H, $CH_2$), 1.85-1.82 (*m*, 40 H, $CyCH_2$), 1.43 (*s*, 12H, $CH_3$), 1.12-1.10 (*d*, 12H, $CHCH_3$), 0.89-0.87(*d*, 12H, $CHCH_3$). $^{13}$C NMR (THF-$d^8$, 298 K, 126 MHz, δ ppm): 156.1, 141.4, 133.2, 129.1, 126.2, 124.3, 69.4, 57.9, 48.5, 36.0, 31.6, 30.4, 29.1, 27.9, 25.9.

#### 4.1.3 Synthesis of $(cAACH)_2O$ (5)

To a toluene solution of compound **3** (0.78 mmol, 500 mg), the equivalent amount of water (0.78 mmol, 0.014 ml) was added with stirring. An immediate color change was observed from deep-blue to colorless and a metallic fall was observed which was confirmed as zinc metal by elemental analysis. The reaction mixture stirred for an additional hour at room temperature. The solution was then filtered; the volume of the filtrate was reduced to half and stored at - 4 °C to give colorless crystals suitable for single-crystal X-ray analysis of **5**. Yield: 0.54 g, 78 %. mp: 182-185 °C. Anal. Calcd. for $C_{40}H_{64}N_2O$: C, 81.57; H, 10.95; N, 4.76. Found: C, 81.15; H, 10.68; N, 4.59. $^1$H NMR ($C_6D_6$, 298 K, 500 MHz, δ ppm): 7.21-7.08 (*m*, 6Har), 4.83 (*s*, 2H, CH-O), 4.20-4.18 (*m*, 2H, $CHMe_2$), 3.16-3.14 (*m*, 2H, $CHMe_2$), 1.82 (*s*, 4H, $CH_2$), 1.62 (*d*, 12H, $CHCH_3$), 1.55 (*s*, 12H, $CH_3$), 1.42(*d*, 12H, $CHCH_3$), 1.31 (*s*, 12H, $CH_3$). $^{13}$C NMR ($C_6D_6$, 298 K, 126 MHz, δ ppm): 152.6, 148.82, 141.4, 101.4, 61.5, 42.3, 33.7, 32.2, 28.3, 27.8, 25.6, 24.8.

#### 4.1.4 Synthesis of $(CYcAACH)_2O$ (6)

A similar procedure like compound **5**, was adopted for the synthesis of to compound **6**. In a toluene solution of compound **4** (0.69 mmol, 500 mg), the equivalent amount of water (0.69 mmol, 0.012 ml) was added with stirring. An immediate color change was observed from deep-blue to colorless. Similar to reaction mixture **5**, zinc fall was observed during the reaction. The reaction mixture stirred for an additional hour at room temperature. The solution was then filtered; the volume of the filtrate was reduced to half and stored at - 4 °C to give colorless crystals suitable for single-crystal X-ray analysis of **6**. Yield: 0.53 g, 73 %. mp: 179-183 °C. Anal. Calcd. for $C_{46}H_{72}N_2O$: C, 82.58; H, 10.85; N, 4.19. Found: C, 82.34; H, 10.74; N, 4.09. $^1$H NMR (THF-$d^8$, 298 K, 500 MHz, δ ppm): 7.17-7.08 (*m*, 6Har), 4.77 (*s*, 2H, CH-O) 3.97-3.95 (*m*, 2H, $CHMe_2$), 3.17-3.14 (*m*, 2H, $CHMe_2$), 2.46 (*s*, 4H, $CH_2$), 1.42 (*m*, 20H, $CyCH_2$), 1.20 (*d*, 12H, $CHCH_3$), 1.10 (*d*, 12H, $CHCH_3$). $^{13}$C NMR (THF-$d^8$, 298 K, 126 MHz, δ ppm): 153.2, 149.4, 142.3, 138.4, 129.6, 128.8, 127.4, 126.0, 125.2, 124.3, 104.0, 62.0, 53.8, 47.5, 43.1, 32.9, 30.9, 28.8, 28.2, 25.1.

### 4.2 Crystal Structure Determinations

Molecular structures of compounds **5** and **6** were established by single-crystal X-ray crystallographic studies and corresponding ORTEP-representations are shown in Figures 1 and 2, respectively. Crystallographic data for **5** and **6** are summarized in Table 1. Crystals for compounds **5** and **6** were measured on a Bruker three-circle diffractometer equipped with a SMART 6000 CCD area detector and a CuKα rotating anode. Integrations were performed with SAINT [16]. Intensity data for all compounds were corrected for absorption and scaled with SADABS [17]. Structures were solved by direct methods and initially refined by full-matrix least-squares methods on $F_2$ with the program SHELXL-97, [18] utilizing anisotropic displacement parameters for non-hydrogen atoms.

**Table 1:** Crystal and Structure Refinement Parameters for Compounds **5** and **6**

| Parameter | Compound **5** | Compound **6** |
|---|---|---|
| Empirical formula | $C_{40}H_{64}N_2O$ | $C_{53}H_{80}N_2O$ |
| Formula Weight | 588.94 | 761.19 |
| Crystal system | triclinic | triclinic |
| Space group | $P\bar{1}$ | $P\bar{1}$ |
| $a$ / Å<br>$b$ / Å<br>$c$ / Å<br>$\alpha$ (°)<br>$\beta$ (°)<br>$\gamma$ (°) | 10.774(2)<br>11.886(2)<br>14.699(3)<br>79.59(3)<br>86.69 (3)<br>78.09(3) | 13.515(3)<br>15.286(3)<br>23.944(5)<br>90.37(3)<br>105.39(3)<br>105.90(3) |
| V / Å$^3$ | 18011.1(6) | 4570(2) |
| Z | 2 | 4 |
| D calcd [g cm$^{-3}$] | 1.080 | 1.106 |
| $\mu$ / [mm$^{-1}$] | 1.138 | 0.479 |
| F (000) | 692 | 1680 |
| Completeness | 0.981 | 0.977 |
| Refinement method | Full-matrix least-squares of $F^2$ | Full-matrix least-squares of $F^2$ |
| Goodness - of -fit on $F^2$ | 1.806 | 1.016 |
| Final R indices[$F > 4\sigma(F)$] | $R1$ = 0.0405, $wR2$ = 0.1861 | $R1$ = 0.0377, $wR2$ = 0.0935 |
| R indices (all data) | $R1$ = 0.0421, $wR2$ = 0.1903 | $R1$ = 0.0450, $wR2$ = 0.0987 |

## 5. Acknowledgments

APS thanks to Department Science and Technology (DST) New Delhi for financial support under INSPIRE Faculty Award.

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