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N-*tert*-Butyl-*N*-benzoylhydrazine was prepared in a new and convenient procedure with good yield. Triphosgene underwent reaction with three equivalents of *N*-*t*-butyl-*N*-benzoylhydrazine using six equivalents of triethylamine as a base to yield the cyclic tetramer of *N*-*t*-butyl-*N*-isocyanatobenzoylamide. Treatment of triphosgene with three equivalents of *N*-*t*-butyl-*N*-benzoylhydrazine either in the presence of three equivalents of triethylamine or in the absence of triethylamine afforded the cyclic pentamer of isocyanate, from which *tert*-butyl is eliminated.

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Introduction.

It was our original intent to synthesize *N*-*t*-butyl-*N*'-aminocarbonyl-*N*-benzoylhydrazines as a new class of insect growth regulators [1] by the addition of primary or secondary amines to *N*-*t*-butyl-*N*-isocyanatobenzoylamide (**5**). According to the literatures, [2a-e] triphosgene (**4**) has been used extensively to prepare isocyanates by reacting with primary alkyl- and arylamines or their salts. However, it has not been reported that triphosgene reacts with *N*,*N*-disubstitutedhydrazines to yield the corresponding isocyanates. Our attempts to convert *N*-*t*-butyl-*N*-benzoylhydrazine (**3**) to the corresponding isocyanate **5** using triphosgene were unsuccessful. The only product formed was cyclic tetramer **6** of **5** or cyclic pentamer **7**. These structures of heterocumulenes macrocyclic oligomers are unique. The present paper deals with the new reactions of *N*-*t*-butyl-*N*-benzoylhydrazine with triphosgene.

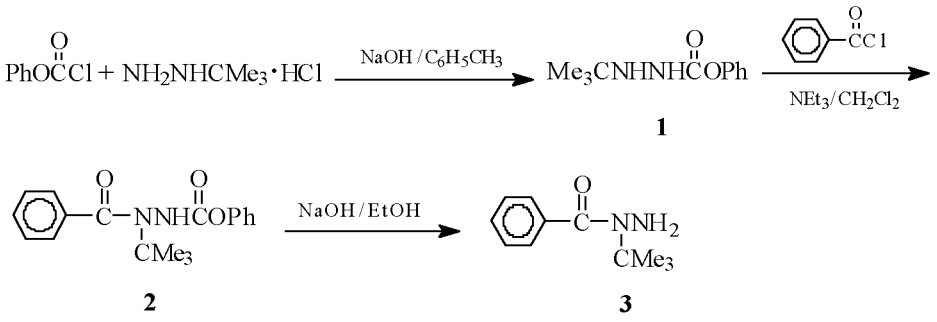
Results and Discussion.

Phenyl chloroformate was treated with *tert*-butylhydrazine hydrochloride to obtain *N*-*tert*-butyl-*N*'-phenyloxycarbonylhydrazine (**1**), and subsequent acylation with benzoyl chloride yielded the *N*-*tert*-butyl-*N*'-phenyloxycarbonyl-*N*-benzoylhydrazine (**2**). Further deprotection using sodium hydroxide provided *N*-*tert*-butyl-*N*-benzoylhydrazine (**3**) as shown in Scheme 1. This new method for the synthesis of *N*-*tert*-butyl-*N*-benzoylhydrazine enjoys a number of advantages in that the reaction is carried out under mild conditions, starting materials are easily prepared, and the experimental procedure is very simple. As a consequence of its practical simplicity and high efficiency, this novel method can be applied to the preparation of other *N*-*t*-butyl-*N*-substitutedbenzoylhydrazines.

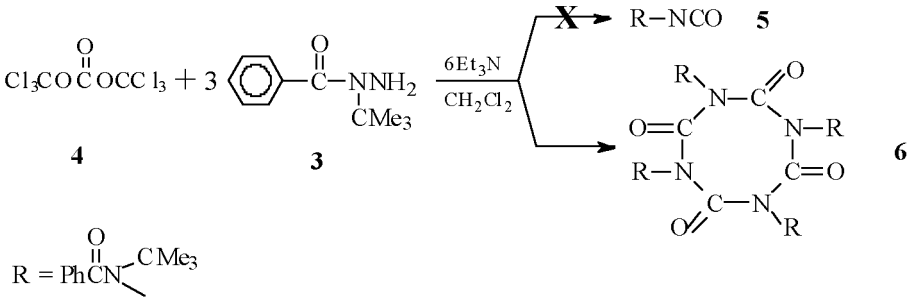
In previous work, [2e] we demonstrated that triphosgene was reacted with three equivalents of primary amines to yield isocyanates. In our attempts to synthesize **5** from *N*-*t*-butyl-*N*-benzoylhydrazine (**3**), we found that the method mentioned above did not result in the desired product **5**. Unexpectedly, triphosgene (**4**) underwent reaction with three equivalents of *N*-*t*-butyl-*N*-benzoylhydrazine (**3**) using six equivalents of triethylamine as acid acceptor to yield the compound **6** in 65.4% yield, which is cyclic tetramer of the isocyanate **5** as shown in Scheme 2. The compound **6** doesn't show absorption band (at approximately 2200 cm^{-1}) of the cumulative double bond of N=C=O in the infrared spectrum. Absence of N=C=O absorption in the infrared and carbonyl absorption comparable to that of dimer or trimer of isocyanate suggested that the compound **6** is a cyclic polymer. The compound **6** does not yield the molecular ion mass spectra under electron impact (EI), but fast atom bombardment (FAB) mass spectra shows the molecular ion to be in high abundance. The compound **6** doesn't react with any primary or secondary amines in toluene at refluxed temperature.

Formation of cyclic dimers and trimers from monoisocyanates has been reported [3,4]. For example, phenyl

Scheme 1



Scheme 2



isocyanate can be converted to a cyclic trimer in the presence of triethylamine. However, to the best of our knowledge, cyclic tetramer of monoisocyanate is not known.

Therefore, we believe that employment of an excess amount of triethylamine may result in the formation of the compound **6**. Based on the above consideration, we decreased the amount of triethylamine or did not use triethylamine, and performed a systematic survey for the reaction of triphosgene (**4**) with *N*-*t*-butyl-*N*-benzoylhydrazine (**3**). Interestingly, we found that treatment of triphosgene with three equivalents of *N*-*t*-butyl-*N*-benzoylhydrazine either in the presence of three equivalents of triethylamine or in the absence of triethylamine afforded a new product **7** in 95.2% and 90.5% yields respectively (shown in Scheme 3). After workup, ^{1}H NMR, IR, FAB-MS and elemental analysis surprisingly identified the colorless crystalline product **7** as a ten-membered ring. This structure of the compound **7** is unique of cyclic urea. It is worth noting that *tert*-butyl is eliminated from compound **7**. The compound **7** doesn't react with any primary or secondary amines in refluxing toluene.

In summary, *N*-*tert*-butyl-*N*-benzoylhydrazine was prepared in a new and convenient procedure with good yield, and these new reactions of *N*-*t*-butyl-*N*-benzoylhydrazine with triphosgene were studied. And the first cyclic tetramer and pentamer of monoisocyanate were obtained.

EXPERIMENTAL

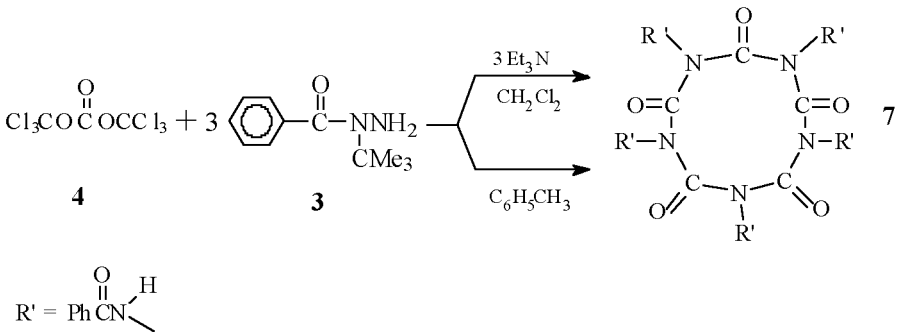
Melting points were taken on a Thomas-Hoover melting-point apparatus and are uncorrected. Proton NMR spectra were obtained at 200 MHz with a Bruker AC-P 200 spectrometer using tetramethylsilane as an internal standard. Chemical shift values (δ) are given in ppm. Infrared spectra were recorded on a Shimadzu-435 spectrometer. Mass spectra were recorded with HP5988A spectrometer using the EI method and VG ZAB-HS using the FAB method. Elemental analysis were carried out with a Yanaco CHN Corder MT-3 elemental analyzer.

Triphosgene (**4**) was synthesized by chlorination of dimethylcarbonate [2a-b], mp 79 °C, IR(KBr) ν/cm^{-1} 1820, 1178, 925, 810, 675, 517.

N-*t*-Butyl-*N*'-phenyloxycarbonylhydrazine (**1**).

To a mechanically stirred suspension of *t*-butylhydrazine hydrochloride (0.092 mol) in toluene (100 mL) was added dropwise a solution of 10% aqueous sodium hydroxide (0.092 mol) at room temperature. After 15 minutes, the reaction mixture was cooled to -15 °C, and solutions of phenyl chloroformate (0.088 mol) in toluene (30 mL) and 10% aqueous sodium hydroxide (0.088 mol) were added dropwise and simultaneously from separate addition funnels, while maintaining the temperature below –10 °C. Following the addition, the reaction mixture was warmed to room temperature and stirred for 2 h. The water phase was extracted three times with 100 mL of chloroform. The extraction solvent was combined with the organic phase, and dried with anhydrous magnesium sulfate and filtered. The solvent was removed by distillation to give a white solid. The solid was then recrystallized from isopropyl alcohol and petroleum ether to

Scheme 3



obtain a colorless crystalline solid in 70.8% yield, m.p. 106-108 °C. ^{1}H NMR($CDCl_3$, 200 MHz) δ: 1.12(s, 9H, Bu^t), 5.14(br., 2H, NHNH), 7.08-7.56(m, 5H, Ph).

N-t-Butyl-*N*'-phenyloxycarbonyl-*N*-benzoylhydrazine (**2**).

A solution of benzoyl chloride (0.054 mol) in methylene dichloride (15 mL) was added dropwise to a solution of *N-t*-butyl-*N*'-phenyloxycarbonylhydrazine (**1**) (0.054 mol) and triethylamine (0.065 mol) in methylene dichloride (40 mL) under magnetic stirring at 0°C, then the resulting mixture was stirred at room temperature for 2 h. Then the solid was filtered off and the filtrate was washed successively with 2% aqueous hydrochloric acid and 10% aqueous sodium bicarbonate, and dried with anhydrous magnesium sulfate and filtered. The solvent was removed by distillation to give a white solid. The solid was then recrystallized from ethanol to obtain a colorless crystalline solid in 81.4% yield, m.p. 141-143 °C. ^{1}H NMR($CDCl_3$, 200 MHz) δ: 1.40(s, 9H, Bu^t), 6.74-7.32(m, 10H, Ph).

N-tert-Butyl-*N*-benzoylhydrazine (**3**).

N-t-Butyl-*N*'-phenyloxycarbonyl-*N*-benzoylhydrazine (**2**) (8.00 mmol) was dissolved in lukewarm ethanol (40 mL). While the reaction mixture was stirred, a 15% aqueous solution of sodium hydroxide (50 mL) was added. Following the addition, the mixture was stirred at 60 °C for 1 hr, then cooled, and extracted three times with 100 mL of chloroform. The extraction solvent was dried with anhydrous magnesium sulfate and filtered. The solvent was removed by distillation to give a white solid. The solid was then recrystallized from isopropanol and petroleum ether to obtain a colorless crystalline solid in 76.4% yield, m.p. 127-129 °C. ^{1}H NMR($CDCl_3$, 200 MHz) δ: 1.48(s, 9H, Bu^t), 3.90(s, 2H, NH_2), 7.28-7.56(m, 5H, Ph). IR(KBr): 3276.0 (NH_2); 1620.5 (C=O); 1573.1, 1529.5, 1508.8 (Ph); 1375.6, 1350.0 (Bu^t); 719.6, 696.7 (Ph).

1,3,5,7-Tetra-(*N-tert*-butylbenzamido)-[1,3,5,7]tetrazocane-2,4,6,8-tetrone (**6**).

To the stirred and cooled (-15 °C) solution of triphosgene (**4**) (0.26 g, 0.87 mmol) in methylene chloride (10 mL) was added dropwise a solution of *N-t*-butyl-*N*-benzoylhydrazine (**3**) (0.5 g, 2.6 mmol) and distilled triethylamine (0.53 g, 5.22 mmol) in methylene chloride (10 mL). After the addition, stirring was continued for 3 h at –15 °C and 2 h at room temperature. The solvent was removed under vacuum and the residue was dissolved in 20 mL ethyl acetate. The solid was filtered off and the filtrate was evaporated. The residue was purified by column chromatography on a silica gel using a mixture of petroleum ether (60-90 °C) and ethyl acetate as the eluent. Finally, an analytical sample **6** was obtained in 65.4% yield, mp 160-162 °C. IR(KBr) ν/cm^{-1} 1774 (vs) (NC=O), 1611 (t-BuN-C=O). ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 9H, t-Bu), 7.42-7.63 (m, 5H, Ph). MS (EI, 15ev) m/z 218.20 (PhCON(t-Bu)NCO, 4%), 162.15 (PhCONHNCO, 54%), 118.20 (PhCONH, 16%), 105.15 (PhCO, 100%).

Anal. Calcd for $(C_{12}H_{14}N_2O_2)_4$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.34; H, 6.51; N, 12.54. MS (FAB) m/z 873.7 $(M+H)^+$.

The Compound **7**.

In the Presence of 3 Equivalents of Triethylamine.

To the stirred and cooled (-15 °C) solution of triphosgene (**4**) (0.26 g, 0.87 mmol) in methylene chloride (10 mL) was added dropwise a solution of *N-t*-butyl-*N*-benzoylhydrazine (**3**) (0.5 g, 2.6 mmol) and distilled triethylamine (0.26 g, 2.61 mmol) in methylene chloride (10 mL). The reaction mixture was stirred at –15 °C for 3 h and at room temperature for 12 h. The solvent was removed under vacuum, and the residue was dissolved in 20 mL ethyl acetate and filtered, then the filtrate was evaporated to give a white solid. The crude solid was recrystallized from methylene chloride/petroleum ether (60-90 °C) to obtain a colorless crystalline solid **7** in 95.2% yield, mp 140-142 °C. IR(KBr) ν/cm^{-1} 3192 (s) (NH), 1760 (vs) (NC=O), 1612 (NHC=O). ^{1}H NMR (DMSO): δ 7.52-7.55 (m, 3H, Ph), 7.76-7.80 (m, 2H, Ph). MS (FAB) m/z 833 $(M+Na)^+$. MS (EI, 15ev) m/z 162.15 (PhCONHNCO, 90%), 118.20 (PhCONH, 100%), 105.15 (PhCO, 56%).

Anal. Calcd for $(C_8H_6N_2O_2)_5$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.30; H, 3.74; N, 17.23.

In the Absence of Triethylamine.

To the stirred and cooled (-15 °C) solution of triphosgene (**4**) (0.26 g, 0.87 mmol) in toluene (10 mL) was added dropwise a solution of *N-t*-butyl-*N*-benzoylhydrazine (**3**) (0.5 g, 2.6 mmol) in toluene (10 mL). After the addition, the resulting mixture was stirred at –15 °C for 2 h, and at room temperature for 3 h, then at reflux temperature for 12 h. After a similar workup, a colorless crystalline solid **7** was obtained in 90.5% yield.

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