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A USEFUL DENDRITIC BUILDING BLOCK: DI-*tert*-BUTYL 4-[(2-*tert*-BUTOXYCARBONYL)ETHYL]-4-ISOCYANATO-1,7-HEPTANEDICARBOXYLATE[1]

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Abstract: The facile preparation of the title compound, which is a crystalline alkyl isocyanate capable of dendrimerizing (poly)functional materials, is reported. The structure is proven by X-ray analysis and its chemistry is confirmed by its versatile reactivity with diverse molecules. © 1997 Elsevier Science Ltd.

The rapidly expanding field of dendritic chemistry[2] has reached a state of development whereby the application of iterative technology is being examined from many different perspectives. We herein report the preparation and preliminary chemistry of the first example in a series of novel, 1 → 3 *C*-branched isocyanate monomers, namely di-*tert*-butyl 4-isocyanato-4-[2-(*tert*-butoxycarbonyl)ethyl]-1,7-heptanedicarboxylate (2), which is envisioned to be particularly useful for the "dendrimerization" of appropriately functionalized substances, such as dendrimers, classical polymers and oligomers, as well as various surfaces.

The use of alkyl isocyanates for branched building blocks is a logical extension of our amine-based monomers[3] with respect to the simplicity of tier construction and product purification. However, tertiary aliphatic isocyanates have been rarely mentioned in the literature, due in part to sterically promoted diminished chemical reactivity of the reactive moiety.[4,5] General methods for their preparation involved: (a) hydrolysis of trialkylacetonitriles to the corresponding acetamides, and subsequent treatment with sodium hypobromite; or (b) the treatment with highly branched amines with phosgene in the presence of an inorganic or organic base, as an hydrogen chloride acceptor.

Recently, a series of 1 → 3 branched, simple amine building blocks[3] has been widely used in the

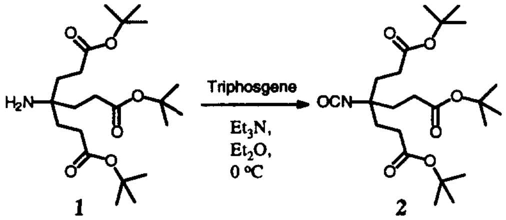

Figure 1. Preparation of the alkyl isocyanate **2**.

construction of cascade macromolecules.[2a] Due to their limited use in amide preparation, the simplest amine[7] ("Behera's Amine"; **1**) was transformed (>95%) by the treatment with triphosgene (Et_3N, Et_2O, 0 °C) into the corresponding stable, crystalline isocyanate[6] (**2**; Figure 1). This solid, isocyanate derivative (mp 62-63 °C) is remarkably air stable and need not be stored or manipulated under inert conditions. Presumably the stability of this isocyanate is rooted, at least partially, in the juxtaposition of the tertiary alkyl center adjacent to the reactive moiety. Although phosgene has been generally used for the conversion of an amine[7] to the corresponding isocyanate, we have employed as a matter of convenience on a laboratory scale the readily available solid triphosgene (hexachlorodimethylcarbonate), as the source of phosgene.[8]

In order to establish the constitution and position of the isocyanate substituents, the X-ray structure of this crystalline monomer was determined. The ORTEP drawing of monomer **2** is depicted in Figure 2 along with the pertinent bond distances and angles. Isocyanate **2** crystallizes in the $P2_1/c$ space group and the observed distance between N^1 and C^1 (1.475 Å) as well as the noted angles formed by C^{23}-N^1-C^1 (140.2°) and N^1-C^{23}-O^7 (174.0°) correspond well with literature values.[9] Additional pertinent supporting spectroscopic data for **2** include ^{13}C NMR absorptions 171.7, 122.2, 80.0, and 61.8 ppm corresponding to the C=O, NCO, CMe$_3$, and NC_{4°, respectively, as well as the IR peak at 2262 cm^{-1} (N=C=O).

To test the general utility of this isocyanate, **2** was reacted with simple alcohols, amines, and carboxylic acids. Thus, treatment of **2** with methyl, ethyl, n-propyl, and n-butyl alcohols afforded (86-95%) the corresponding series of carbamates as demonstrated by the presence (^{13}C NMR) of absorptions in the 154.2-154.9 ppm [O(C=O)NH] range. Reaction of **2** with acetic and propionic acids afforded (55-60%), after loss of CO_2, the desired amide derivatives,[10] identical to that generated from simple amide conversion with DCC/1-HOBT.[11] Whereas, treatment of **2** with piperidine and aniline resulted in the formation of the corresponding urea as indicated by the appearance (^{13}C NMR) of a signal attributed to the new -NHC=ONH- unit coupled with the distinct loss of the absorption produced by the N=C=O moiety.

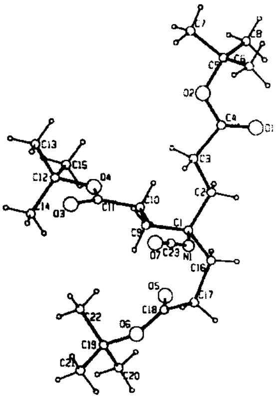

Figure 2. ORTEP structure for **2**: O7-C23, 1.180(2); N1-C1, 1.475(2); N1-C23, 1.166(2); C1-C2, 1.536(2); C1-C9, 1.533(2); C1-C16, 1.535(2) Å.

Amine-terminated poly(propyleneimine) dendrimers[12] possessing 8, 16, 32, and 64 termini, commercially available from DSM, when treated with

2, resulted in dendritic polyesters having ideally 24, 48, 96, and 192 terminal ester groups, respectively. In each case, reaction of a stoichiometric amount of **2** with the appropriate dendrimer in boiling *tert*-butyl alcohol afforded (~95% conversion based on recovered mass and NMR detection limits) of the desired polyesters (e.g., **3**; Figure 3). Observed ^{13}C and ^{1}H NMR spectra for each member of the dendritic series was similar, as expected. Supportive, as well as representative, absorptions (^{13}C NMR) recorded for these typical polyfunctional macromolecules exhibited and demonstrated the expected first order analysis.[13] The polyesters were readily deprotected affording the corresponding polycarboxylic acids as evidenced in the related ^{13}C NMR spectra with the loss of peaks at 172.6, 79.6, and 27.9 ppm assigned to the *tert*-butyl ester moieties.

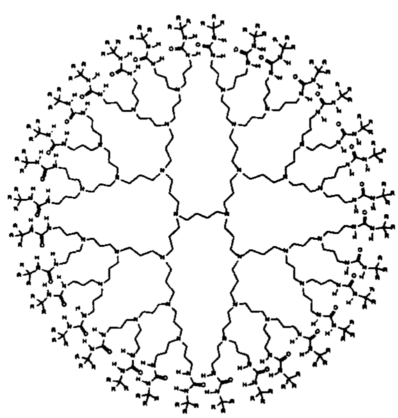

Figure 3. The polyester-coated DSM dendrimer (**3**).

It is envisioned that these demonstrated general transformations utilizing this 1 → 3 branched monomer can be applied to the functionalization of other nucleophilic moieties in high overall yields. Additionally, the thermal and hydrolytic stabilities of monomeric isocyanate **2** suggest that it has great potential in polymer construction and materials surface modification.

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13. Typical polyester assignments - ^{13}C NMR: 172.6 (ester), 157.8 (C=O), 79.6 ($\mathrm{O}\mathit{C}\mathrm{Me_3}$), 52.5, 51.5 ($\mathrm{N}\mathit{C}\mathrm{H_2CH_2}\mathit{C}\mathrm{H_2N_{internal}}$), 37.5 ($\mathrm{N}\mathit{C}\mathrm{H_2CH_2CH_2N_{external}}$), 30.1 ($\mathit{C}\mathrm{H_2}\mathit{C}\mathrm{H_2CO_2}$), 29.5 ($\mathrm{NCH_2CH_2}\mathit{C}\mathrm{H_2N_{external}}$), 24.0 ($\mathrm{NCH_2}\mathit{C}\mathrm{H_2CH_2N_{external}}$).

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