Preparation, Characterization and Selective Reactions of Novel [1,3]Diazetidine-2,4-diones (Uretdiones) – A New Route to Generate Asymmetric Substituted Toluylenediisocyanate-Derivatives

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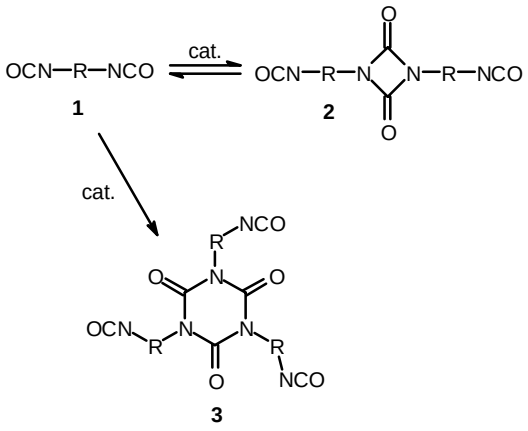
Abstract. The selective cyclodimerization of monomeric diisocyanates like IPDI **4** and TDI **5** yields [1,3]diazetidine-2,4-diones (uretdiones). On this basis, a new method for the selective transformation of the NCO-groups of asymmetric substituted diisocyanates is described. The reaction with different nucleophiles yields carbamates and ureas such as **9**–**11**.

Diisocyanates **1** are important building blocks in polymer chemistry [1]. In the manufacture of elastomers, plastics and coatings they react with polyhydroxylic components to give polyurethanes and with polyamines to give polyureas.

To meet the requirements for advanced materials it is necessary to look for new polymers with enhanced properties concerning optical permeability, viscoelasticity, defined structure *etc*. Special care is necessary in the handling of volatile isocyanates since their vapours are irritant. They are sensitizers at extremely low concentrations and need to be modified to guarantee a safe handling of these compounds. Hence, for industrial application they are often used in the form of blocked isocyanates. Blocked or masked isocyanates are the reaction products of the isocyanate group with low molecular weight alcohols, phenols, and some other compounds such as lactams; these reaction products decompose on heating to reform the isocyanate group. Blocked isocyanate curing agents are used in electrocoat compositions, various solvent applied finishes and in powder coatings. With special catalysts [2–9] it is also possible to dimerize or to trimerize some monomeric diisocyanates to give [1,3]diazetidine-2,4-diones (uretdiones) **2** or isocyanurates **3** (scheme 1).



Scheme 1 Catalytic dimerization and trimerization of monomeric diisocyanates

The production of uretdiones, unlike the trimerisation, is a reversible reaction [10–13]. The dimerisation products are thermally unstable, and at higher temperatures or in the presence of catalysts they are cleaved to reform the monomers. The [1,3]diazetidine-2,4-diones **2** are very useful in the synthesis and technical application of organic polymers, since no toxic by-products are released from the polymer when these cycloaddition products are used as crosslinking agents.

Diisocyanates of technical importance, which contain two -NCO groups of different reactivity, are isophoronediisocyanate **4** (IPDI) and 2,4-tolylenediisocyanate **5** (TDI). After the selective cyclodimerization of these monomers, the free isocyanate groups of the resulting [1,3]diazetidine-2,4-diones should selectively react with nucleophiles. Thus, it could be possible to synthezise tailor made polymers of this type for technical application.

As described by Singh and Boivin [14] it is possible to prepare a series of carbamates and ureas of the dimer TDID **6** of 2,4-tolylene diisocyanate **5**, leaving the [1,3]diazetidine-2,4-dione ring unaffected. However, sometimes amines rupture the 4-membered ring, and diureas of the monomer were obtained. We were interested in the selective synthesis of mixed ureas and carbamates derived from TDID **6** as shown in scheme 2. Another approach was to prepare derivates of benzene (toluene) with carbamoyl and urea functionality.

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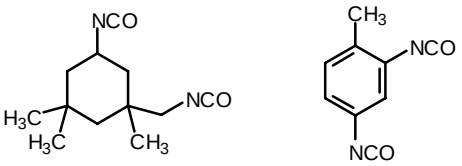
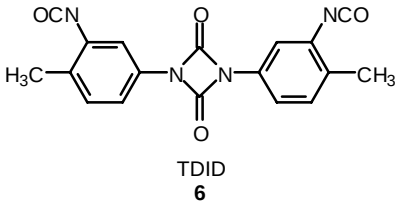
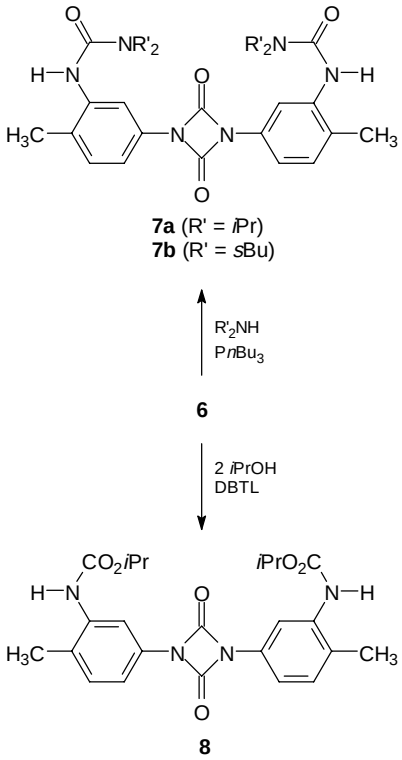
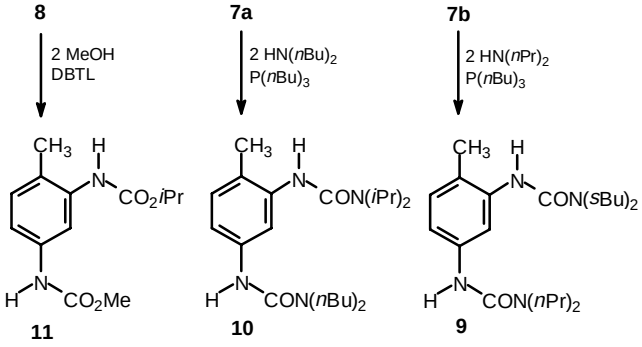




The *p*-isocyanate group of TDI is three times more reactive than the *o*-isocyanate group [15]. We used commercially available TDI as a mixture of 2,4-tolylenediisocyanate (80%) and 2,6-tolylenediisocyanate (20%). After cyclodimerisation in the presence of a catalytic amount of tri-*n*-butylphosphane [4] we obtained the TDI-dimer **6** (TDID) in moderate yields. The 2,6-isomer did not react under these conditions. To prevent cyclotrimerisation it is necessary to carry out the reaction at low temperature and to avoid long reaction times. As shown in scheme 2 the advantage of this methodology is the option to block the isocyanate group at C-4 by the catalytic cyclodimerisation of TDI **5**. This selective protection is the basis for nucleophilic reactions (*i.e.* alcohols, amines) at the C-2 isocyanate group which lead to the formation of the products **7a**, **7b**, and **8**. In one pot, the selective cleavage of the uretdione functionality of **7a**, **7b**, and **8** is followed by the reaction with suitable nucleophiles. The deprotected isocyanate group at C-4 can be used to produce selectively derivatives such as carbamates and ureas, *i.e.* **9**–**11**. In conclusion, these few examples show the flexibility of this approach, which allows a high standard concerning the diversity during the selective synthesis of derivatives of diisocyanates.



Scheme 2 Synthesis of ureas **7** and carbamate **8** derived from TDID **6**



Scheme 3 Selective synthesis of mixed ureas **9**, **10** and carbamate **11** derived from TDID **6**

Experimental

Melting points: Mettler, Model FP 61, uncorrected. – IR spectra: Perkin Elmer 1310 spectrophotometer. – ^{1}H NMR spectra: Bruker WP-80 (80 MHz), Bruker AM-300 (300 MHz). – ^{13}C NMR spectra: Bruker AM-300 (75.4 MHz). Chemical shifts refer to δ_{TMS} = 0.00 ppm according to the chemical shifts of residual solvent signals. – MS: Varian Mat 311-A (70 eV). Elemental analyses: Perkin Elmer elemental analyzer 240. DBTL (dibutyltin dilaurate) was purchased from Lancaster. Tolylene-2,4-diisocyanate (technical grade, 80%) was purchased from Janssen and was used without further purification. Organic solvents were purified by standard procedures. All reactions were carried out under dry nitrogen.

1,3-Bis-(3-isocyanato-4-methylphenyl)-[1,3]diazetidin-2,4-dione (**6**)

A solution of tolylene-2,4-diisocyanate **5** (8.70 g, 50 mmol) and tri-*n*-butylphosphine (300 mg, 1.5 mmol) in dry toluene (70 ml) was stirred vigorously at 0 °C for 1 h. The precipitate was filtered from the solution and washed with a few drops of cold toluene to remove last traces of the catalyst. The crude product was dried *in vacuo*. Recrystallization from petroleum ether (100–140 °C) and removing of solvent traces *in vacuo* yielded 3.70 g (53%) of the pure diazetidin-dione **6** as

fine colorless crystalline powder, *m.p.* 156 °C. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 080, 2 980, 2 920, 2 280 (NCO), 1 750 (CO), 1 610. – ^{1}H NMR (80 MHz, $CDCl_3$/*d*6-DMSO): δ/ppm = 2.30 (s, 6H, Ar–CH_3), 7.11 – 7.36 (m, 6H, Ar-H). – ^{13}C NMR (75.4 MHz, $CDCl_3$/*d*6-DMSO): δ/ppm = 17.96 (q, Ar–CH_3), 113.25, 114.07 (d, 4 C, C–Ar), 124.73 (s, 2C, NCO), 129.86 (s, 2C, C–Ar), 131.53 (d, 2C, C–Ar), 132.54, 133.24, (s, 4C, C–Ar), 150.44 (s, 2C, CO (dione)). – MS (EI), *m*/*z* (%): 348 [M$^+$] (3), 174 (100), 146 (53), 133 (11), 91 (11).

Preparation of the Symmetrical Dimeric Ureas and Carbamates (General Procedure)

350 mg (1 mmol) **6** were solved in 30 ml boiling petroleum ether (100 – 140 °C), and a solution of 4 mmol amine or alcohol, respectively, (reactions with alcohols were catalyzed with DBTL) in 10 ml petroleum ether (100 – 140 °C) was added dropwise. The mixture was kept boiling for further 3 h and allowed to cool to room temperature. The precipitate was filtered off from the solution, washed with a few drops of petroleum ether, dried *in vacuo*, and recrystallized from 1,4-dioxane.

1,3-Bis[3-(3,3-diisopropylureido)-4-methylphenyl]-[1,3]diazetidin-2,4-dione (**7a**)

310 mg colorless crystalline powder (56%), *m.p.* 199 °C. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 200 (NH), 2 960, 2 920, 1 740 (CO dione), 1 620 (CO urea). – ^{13}C NMR (75.4 MHz, $CDCl_3$): δ/ppm = 17.92 (q, 2C, ArCH_3), 21.45 (q, 8C, CH($\underline{C}H_3$)$_2$), 45.52 (d, 4C, $\underline{C}$H($\underline{C}H_3$)$_2$), 111.03, 111.91 (d, 4C, C–Ar), 124.67 (s, 2C, C–Ar), 130.90 (d, 2C, C–Ar), 132.47, 138.56 (s, 4C, C–Ar), 151.28 (s, 2C, CO (dione)), 154.37 (s, 2C, CO (urea)). – MS (EI), *m*/*z* (%): 275 [M^{2+}] (2, 14), 174 (18), 128 (49), 86 (100), 58 (11), 44 (29), 43 (76), 41 (13).

$C_{30}H_{42}N_6O_4$	Calcd.:	C 65.43	H 7.69	N 15.26
(550.70)	Found :	C 65.39	H 7.75	N 15.13.

1,3-Bis-[3-(3,3-di-s-butylureido)-4-methylphenyl]-[1,3]diazetidin-2,4-dione (**7b**)

440 mg colorless crystalline powder (73%), lit. [14] 70%, *m.p.* 188 °C, lit. [14] 176 °C. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 220 (NH), 2 980, 2 920, 2 860, 1 760 (CO dione), 1 610 (CO urea). – ^{13}C NMR (75.4 MHz, $CDCl_3$): δ/ppm = 11.99, 12.14 (q, 4C, $CH_2\underline{C}H_3$), 17.98 (q, 2C, Ar–CH_3) 19.24 (q, 4C, CH$\underline{C}H_3$), 28.78 (t, 4C, N(CH_2R)$_2$), 52.12, 52.44 (d, 4C, $\underline{C}$H(CH_3)), 111.18, 111.98 (d, 4C, C–Ar) 124.66, 124.80 (s, 2C, C–Ar), 130.91 (d, 2C, C–Ar), 132.47, 138.57 (s, 4C, C–Ar), 151.30 (s, 2C, CO (dione)), 154.82 (s, 2C, CO (urea)). – MS (EI) *m*/*z* (%): 303 [M^{2+}] (2, 8), 156 (21), 100 (95), 57 (100), 44 (42), 41 (16).

$C_{34}H_{50}N_6O_4$	Calcd.:	C 67.28	H 8.31	N 13.86
(606.81)	Found:	C 67.21	H 8.40	N 13.75.

1,3-Bis-(3-isopropoxycarbonylamino-methylphenyl)-[1,3]diazetidin-2,4-dione (**8**)

460 mg colorless crystalline powder (95%), *m.p.* 216 °C, lit. [14] 215 °C. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 360 (NH), 3 060, 3 005, 2 950, 1 795 (CO dione), 1 705 (CO carbamate). – MS (EI), *m*/*z* (%): 234 [M$^+$] (2, 69), 192 (71), 175 (29), 174 (28), 148 (73), 147 (37), 145 (14) 77 (12), 43 (100).

$C_{24}H_{28}N_4O_6$	Calcd.:	C 61.53	H 6.02	N 11.96
(468.00)	Found:	C 60.98	H 6.10	N 12.22.

Preparation of Bisureido- and Biscarbamoyltoluenes. Mixed Ureido-carbamoyltoluenes may be Synthesized by a Similar Procedure **(General Procedure)**

0.5 mmol of ureido-[1,3]diazetidine-2,4-dione **7a**, **7b** or carbamoyl-[1,3]diazetidine-2,4-dione **8**, respectively, were solved in 10 ml boiling THF. A solution of 2 mmol amine or alcohol, respectively, in 5 ml THF was added dropwise (reactions with amines were catalyzed with P(*n*-Bu)$_3$, and reactions with alcohols were catalyzed with DBTL). The mixture was kept boiling for further 3 h, and then the solvent was removed in vacuo. The remaining solid was recrystallized and dried *in vacuo*.

3-[3-(3,3-Di-s-butylureido)-4-methylphenyl]-1,1-di-n-propylurea (**9**)

Derived from the reaction of **7b** with di-*n*-propylamine; 180 mg colorless crystalline powder (45%), *m.p.* 155 °C (petroleum ether 100 – 140 °C). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 300 (NH), 2 960, 2 920, 2 860, 1 620 (CO). – ^{13}C NMR (75.4 MHz, $CDCl_3$): δ/ppm = 11.40 (q, 2C, CH_3 (*n*-propyl)), 12.00, 12.14 (q, 2C, $CH_2C\underline{H}_3$ (*s*-butyl)), 17.71 (q, 1C, ArCH_3), 19.26 (q, 2C, CH$C\underline{H}_3$ (*s*-butyl), 21.81 (t, 2C, $C\underline{H}_2CH_3$ (*n*-propyl), 28.80 (t, 2C, $C\underline{H}_2CH_3$ (*s*-butyl), 49.34 (t, 2C, N(CH_2R)$_2$), 52.08, 52.42 (d, 2C, $\underline{C}HCH_3$), 112.64, 113.06, 115.30, 130.48 (d, 3C, C–Ar), 121.26, 121.37, 137.60, 137.96 (s, 3C, C–Ar), 155.10 (s, 2C, CO). – MS (EI), *m*/*z* (%): 404 [M$^+$] (33), 376 (19), 275 (19), 249 (22), 156 (19), 128 (56), 100 (100), 86 (54), 72 (50), 57 (63), 43 (98).

$C_{23}H_{40}N_4O_2$	Calcd.:	C 68.28	H 9.96	N 13.85
(404.60)	Found:	C 68.35	H 9.89	N 13.76.

3-[3-(3,3-Di-i-propylureido)-4-methylphenyl]-1,1-di-n-butylurea (**10**)

Derived from the reaction of **7a** with di-*n*-butylamine; 190 mg colorless crystalline powder (52%), *m.p.* 106 °C (petroleum ether/dioxane 10:1). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 320 (NH), 3 020, 2 990, 2 930, 1 690 (CO carbamate), 1 630 (CO urea). – ^{13}C NMR (75.4 MHz, $CDCl_3$): δ/ppm = 13.92 (q, 2C, $CH_2\underline{C}H_3$), 16.98 (q, 1C, ArCH_3), 20.21 (t, 2C, $\underline{C}H_2CH_3$), 22.08 (q, 1C, CH$\underline{C}H_3$), 30.78 (t, 2C, $\underline{C}H_2CH_2CH_3$), 47.40 (t, 2C, N(CH_2R)$_2$), 68.67 (d, 2C, $\underline{C}$H(CH_3)$_2$), 112.30, 115.92, 130.50 (d, 3C, C–Ar), 121.50, 136.03, 138.08 (s, 3C, C–Ar), 153.53, 155.03 (s, 2C, 2CO). – MS (EI), *m*/*z* (%): 363 [M$^+$], (11), 156 (18), 148 (17), 147 (13), 121 (10), 100 (15), 86 (39), 57 (95), 44 (67), 43 (100), 41 (72).

$C_{20}H_{33}N_3O_3$	Calcd.:	C 66.09	H 9.15	N 11.56
(363.50)	Found:	C 65.96	H 9.22	N 11.44.

(3-Isopropoxycarbonylamino-4-methylphenyl)-carbamicacid-methylester (**11**)

Derived from reaction of **8** with methanol; 200 mg colorless crystalline powder (75%), *m.p.* 175 °C (petroleum ether 100 – 140 °C). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3 320 (NH), 3 290 (NH), 2 980, 1 700 (CO), 1 680 (CO). – ^{13}C NMR (75.4 MHz, $CDCl_3$): δ/ppm = 17.01 (q, 1C, ArCH_3), 22.08 (q, 2C, CH$C\underline{H}_3$), 52.22 (q, C, OCH_3), 68.86 (d, 1C, $\underline{C}$H(CH_3)$_2$), 111.28, 114.25, 130.71 (d, 3C, C–Ar), 121.90, 136.44, 136.78 (s, 3C, C–Ar), 153.41, 154.19 (s, 2C, CO). – MS (EI), *m*/*z* (%): 266 [M$^+$] (100), 224 (25), 207 (18), 180 (47), 165 (21), 148 (35), 147 (17), 43 (53), 41 (15).

$C_{13}H_{18}N_2O_4$	Calcd.:	C	58.63	H	6.81	N 10.52
(266.30)	Found :	C	58.57	H	6.88	N 10.60.

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