# Sustainable Synthesis Routes towards Urazole Compounds

Laetitia Vlaminck, Babs Van de Voorde, Filip E. Du Prez*

Polymer Chemistry Research Group, Centre of Macromolecular Chemistry (CMaC), Department of Organic and Macromolecular Chemistry, Ghent University, Krijgslaan 281 S4bis, 9000 Ghent, Belgium

*Corresponding author: Filip.Duprez@Ugent.be

**Experimental Procedures**

Materials and methods

Allylamine (Sigma-Aldrich, ≥ 99%), 3-amino-1-propanol (Sigma-Aldrich, 99%), aniline (Sigma-Aldrich, 99%), benzylamine (Sigma-Aldrich, 99%), butylamine (Acros organics, ≥99), cyclohexanemethylamine (TCI, ≥98%), 1,8-diazabicyclo[5.4.0]undec-7-ene (Acros organics, 98%), DMSO-d6 (Eurisotop, 99.8%), diphenylcarbonate (Acros organics, 99%), ethyl carbazate (Sigma-Aldrich, 97%), ethylenediamine (Acros organics, ≥ 99%), ethanol (Sigma-Aldrich, 99.8%), isobutyric acid (VWR, 99%), octylamine (Sigma-Aldrich, 99%), oleylamine (Sigma-Aldrich, ≥98%), potassium carbonate (Roth, ≥ 99%), tetrahydrofurfuryl amine (TCI, ≥ 98%) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (Sigma-Aldrich, 98%) were used as received.

*$^1$H-NMR spectra* were recorded in DMSO-$d_6$ on a Bruker Avance 300 (300 MHz). Chemical shifts are presented in parts per million (δ) relative to DMSO-$d_6$ (2.50 ppm) as internal standard. The resonance multiplicities are described as s (singlet), d (doublet), t (triplet), q (quadruplet) or m (multiplet). *LC-MS analyses* were performed on an Agilent Technologies 1100 series LC/MSD system with a diode array detector (DAD) and single quad MS.IR spectra were collected using a Perkin–Elmer Spectrum1000 FTIR infrared spectrometer with a diamond ATR probe.

General procedure for the synthesis of urazoles via an activated carbamate

Diphenyl carbonate (1 eq.) was heated to 80 °C under inert atmosphere. A primary amine (1 eq.) was added and the reaction mixture stirred for 10 minutes. Ethyl carbazate (1 eq.) was added to the reaction mixture and stirred for 2.5 h at 140 °C. The reaction mixture was further heated for 1 h at 250 °C under a gentle nitrogen flow.

Synthesis of ethyl phenyl hydrazine-1,2-dicarboxylate (EPHD)

20 g Diphenyl carbonate (1 eq., 0.093 mol) was melted in a 250 mL flask and 20 g ethyl carbazate (2 eq., 0.192 mol) was added. The mixture stirred under inert atmosphere for 1 h at 80 °C. The product was precipitated in water and dried overnight under vacuum at 40 °C. The pure white powder was obtained. (76 %)

Chemical formula: $C_{10}H_{12}N_2O_4$. Molecular weight: 224.22 g/mol. $^1$H-NMR (300 MHz, DMSO-$d_6$): δ(ppm) = 1.17 (t, 3H, O-$CH_2$-$CH_3$), 4.08 (q, 2H, O-$CH_2$-$CH_3$), 7.01-7.47 (m, 5H, Ar-*H*), 9.25 (s, 1H, N*H*-CO-O-Et), 9.67 (s, 1H, Ar-O-CO-N*H*).

General procedure for the synthesis of urazoles via an activated intermediate

- Thermal cyclization

Ethyl phenyl hydrazine-1,2-dicarboxylate (1 eq.) was melted at 80 °C under inert atmosphere. A primary amine (1 eq) was added and the mixture was stirred for 10 minutes. Subsequently, the temperature of the reaction mixture was increased to 250 °C for 1 h and a gentle nitrogen flow was applied.

- Basic cyclization

Ethyl phenyl hydrazine-1,2-dicarboxylate (1 eq.) was melted at 80 °C under inert atmosphere. A primary amine (1 eq) was added and the mixture was stirred for 10 minutes. Subsequently, ethanol and $K_2CO_3$ (5 eq) were added and the mixture was refluxed overnight. The reaction mixture was cooled to room temperature and acidified to pH 1 with HCl in propanol (5-6 N). The precipitate was filtered off, the reaction mixture was concentrated *in vacuo* and residual phenol was removed under vacuum at 80°C for 3 hours.

Synthesis of the activated carbamate of aniline

2.14 g Diphenyl carbonate (1 eq., 10 mmol) was heated to 80°C under inert atmosphere ($N_2$). 1.1 mL aniline (1.2 eq., 12 mmol) and 0.18 mL isobutyric acid (0.2 eq., 2 mmol) were added and the mixture was stirred for 4 h. The mixture was dissolved in DCM (10 mL) and extracted with 4M KOH (2 x 2 mL) and brine (1 x 1 mL). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. A mixture of the product and aniline was obtained.

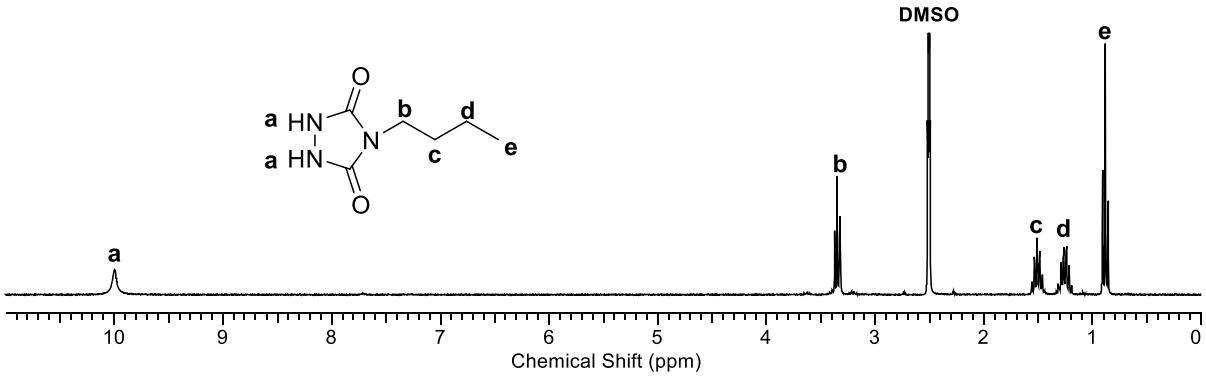
Urazoles via route A and B

**Butylamine**

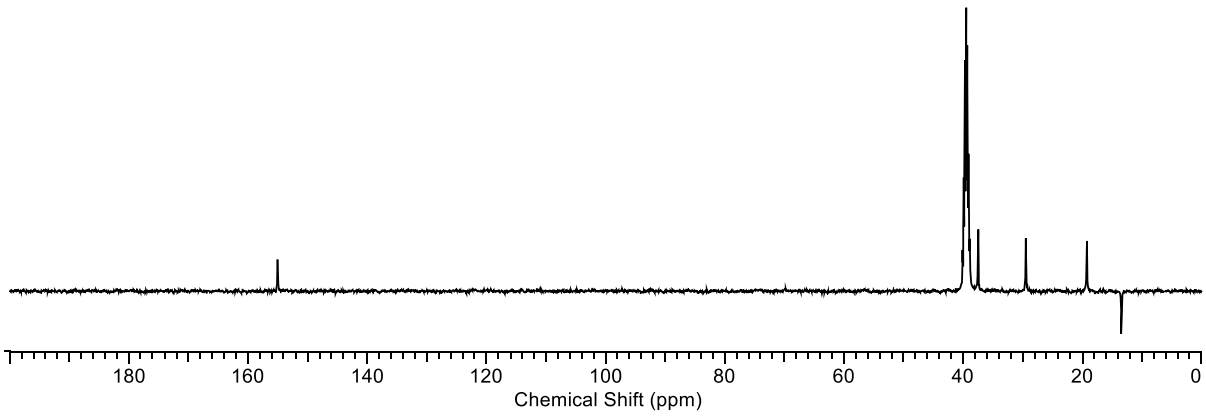
*Carbamate*
$^{1}$H-NMR (400MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.89 (t, 3H, $CH_2$-C*H*$_3$), 1.32 (sext, 2H, $CH_2$-C*H*$_2$-$CH_3$), 1.45 (quint, 2H, C*H*$_2$-$CH_2$-$CH_3$), 3.06 (q , 2H, $CH_2$-C*H*$_2$-NH), 6.74-7.41 (m, 10H, Ar-*H*), 7.72 (t, 1H, $CH_2$-$CH_2$-N*H*), 9.30 (s, 1H, PhO*H*).

*Semicarbazide*
$^{1}$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.85 (t, 3H, $CH_2$-C*H*$_3$), 1.17 (t, 3H, O-$CH_2$-C*H*$_3$), 1.26 (sext, 2H, $CH_2$-C*H*$_2$-$CH_3$), 1.35 (quint, 2H, C*H*$_2$-$CH_2$-$CH_3$), 2.98 (q, 2H, $CH_2$-C*H*$_2$-NH), 4.02 (q, 2H, $CH_3$-C*H*$_2$-O) 6.27 (s, 1H, $CH_2$-N*H*-CO), 6.7-7.2 (m, 10H, Ar-*H*), 7.61 (s, 1H, O-CO-N*H*), 8.71 (s, 1H, NH-N*H*-CO-NH), 9.32 (s, 2H, PhO*H*).

*Urazole*[1]
Yield: A = 86 %, B = 89 %
Chemical formula: $C_6H_{11}N_3O_2$
Molecular weight: 157.17 g/mol
LC-MS (m/z): 156.1 $[M-H]^-$
HRMS (m/z for $[M-H]^-$): 156.0778 (calculated), 156.0782 (experimental)
FT-IR: $\nu_{max}$ ($cm^{-1}$): 3320 and 3166 (NH), 2956 ($sp^3$ CH), 1764 and 1656 (CO).
$^{1}$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.88 (t, 3H, $CH_2$-C*H*$_3$), 1.25 (sext, 2H, $CH_2$-C*H*$_2$-$CH_3$), 1.50 (quint, 2H, C*H*$_2$-$CH_2$-$CH_3$), 3.35 (q, 2H, $CH_2$-C*H*$_2$-NH), 10.00 (s, 2H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 13.34 ($CH_3$), 19.25 ($CH_2$), 29.55 ($CH_2$), 37.55 ($CH_2$), 155.17 (CO).



**Octylamine**

*Carbamate*

$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.85 (t, 3H, $CH_2$-C$H_3$), 1.27 (d, 10H, (C$H_2$)$_5$-$CH_3$), 1.43 (t, 2H, C$H_2$-$CH_2$-NH), 3.04 (q, 2H, C$H_2$-NH), 5.69 (t, 1H, $CH_2$-N*H*-CO), 6.7-7.41 (m, 10 H, Ar-*H*), 9.18 (s, 1H, PhO*H*).

*Semicarbazide*

$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.85 (t, 3H, $CH_2$-C$H_3$), 1.17 (t, 3H, O-$CH_2$-C$H_3$), 1.25 (s, 10H, (C*H*2)$_5$-$CH_3$), 1.35 (t, 2H, C$H_2$-$CH_2$-NH), 2.97 (q, 2H,C$H_2$-NH), 4.02 (q, 2H, O-C$H_2$-$CH_3$), 6.26 (t, 1H, N*H*-$CH_2$-$CH_2$), 6.7-7.2 (m, 5H, Ar-*H*), 7.60 (s, 1H, O-CO-N*H*), 8.69 (s, 1H, NH-N*H*-CO-NH), 9.27 (s, 1H, PhO*H*).

*Urazole*[1]

Yield: A = 96 %, B = 95 %

Chemical formula: $C_{10}H_{19}N_3O_2$

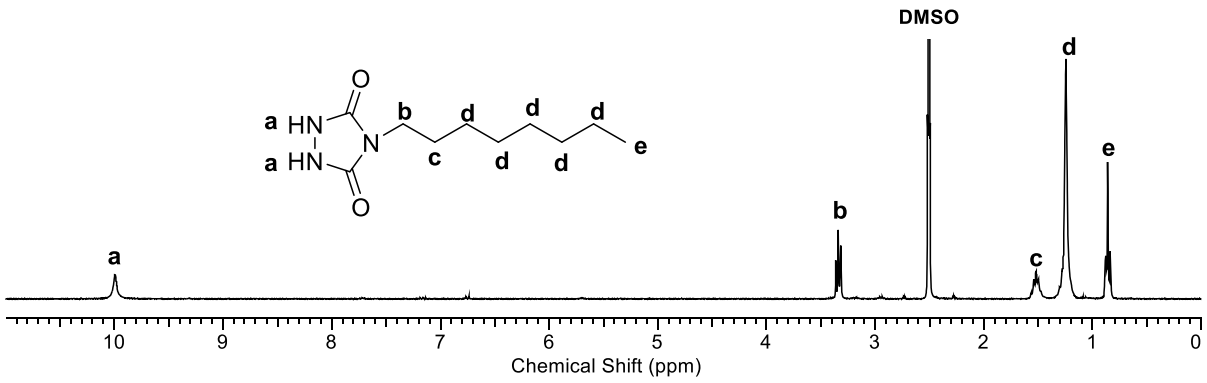
Molecular weight: 213.28 g/mol

LC-MS (m/z): 214.2 $[MH]^+$

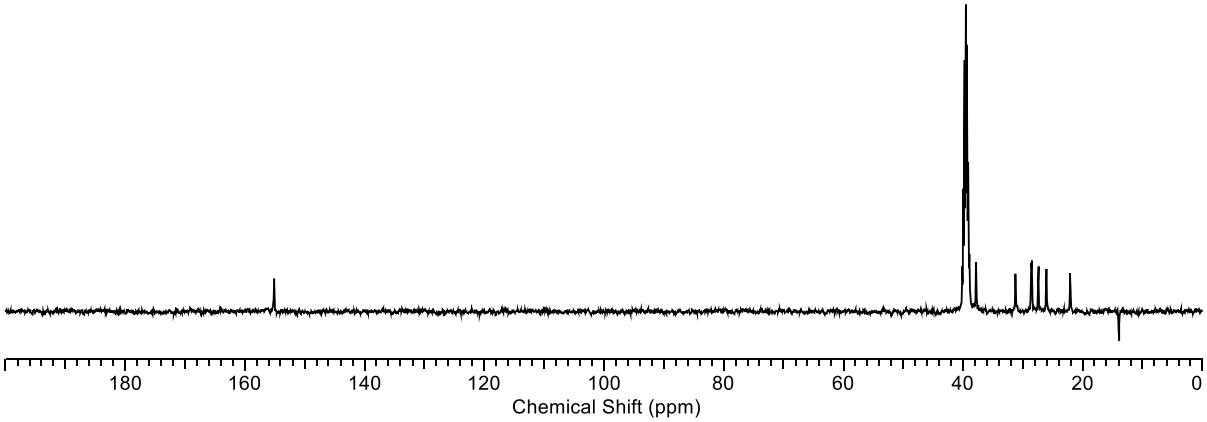
HRMS (m/z for $[M-H]^-$): 212.1405 (calculated), 212.1415 (experimental)

FT-IR: $\nu_{max}$ ($cm^{-1}$): 3328 and 3166 (NH), 2920 and 2852 ($sp^3$ CH), 1760 and 1662 (CO).

$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.85 (t, 3H, $CH_2$-C$H_3$), 1.24 (m, 10H, (C$H_2$)$_5$-$CH_3$), 1.51 (quint, 2H, N-$CH_2$-C$H_2$), 3.35 (t, 2H, N-C$H_2$), 10.00 (s, 2H,N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 13.90 ($CH_3$), 22.04 ($CH_2$), 26.00 ($CH_2$),27.38 ($CH_2$), 28.40 ($CH_2$), 28.55 ($CH_2$), 31.13 ($CH_2$), 37.80 ($CH_2$), 155.00 (CO).

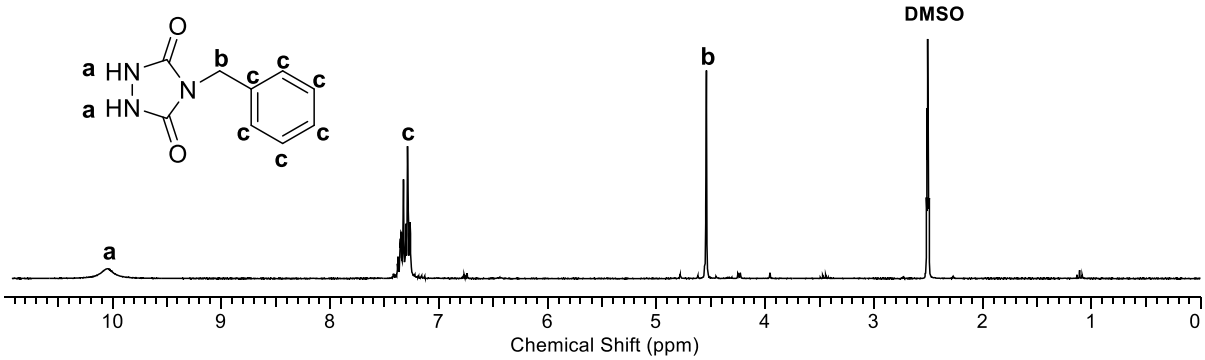


**Benzylamine**

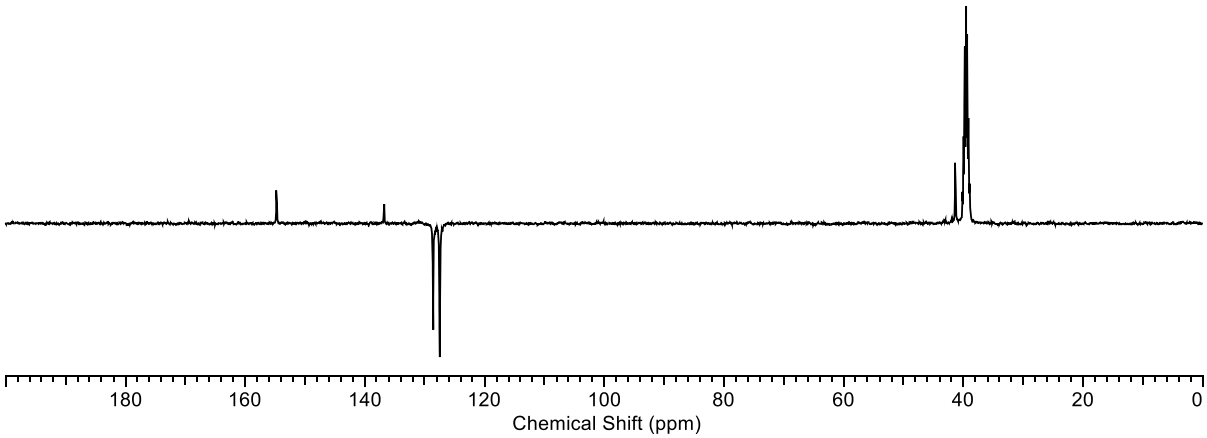
*Carbamate*
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 4.28 (d, 2H, Ar-C*H*$_2$), 6.7-7.7 (m, 15H, Ar-*H*), 8.31 (t, 1H, Ar-CH$_2$-N*H*), 9.32 (s, 1H, PhO*H*).

*Semicarbazide*
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.18 (t, 3H, O-CH$_2$-C*H*$_3$), 4.04 (q, 2H, O-C*H*$_2$-CH$_3$), 4.22 (d, 2H, Ar-C*H*$_2$-NH), 6.7-7.73 (m, 15 H, Ar-*H*), 6.91 (s, 1H, CH$_2$-N*H*-CO), 7.82 (s, 1H, O-CO-N*H*), 8.82 (s, 1H, NH-N*H*-CO-NH), 9.31 (s, 2H, PhO*H*).

*Urazole*[2]
Yield: A = 87 %, B = 85 %
Chemical formula: $C_9H_9N_3O_2$
Molecular weight: 191.19 g/mol
LC-MS (m/z): 190 $[M-H]^-$
HRMS (m/z for $[M-H]^-$): 190.0622 (calculated), 190.0625 (experimental)
FT-IR: $\nu_{max}$ ($cm^{-1}$): 3155 (NH), 3020 (aromatic CH), 2790 ($sp^3$ CH), 1762 and 1665 (CO), 1475 and 1447 (aromatic C=C).
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 4.54 (s, 2H, Ar-C*H*$_2$-N), 7.2-7.4 (m, 5H, Ar-*H*), 10.18 (s, 2H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 41.20 (CH$_2$), 127.46 (CH), 128.44 (CH),136.69 (C), 154.73 (CO).



**Tetrahydrofurfurylamine**

*Carbamate*

$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.56 (m, H, $CH_2$-C$H_2$-$CH_2$), 1.82 (m, 2H, $CH_2$-$CH_2$-C$H_2$), 1.92 (m, 1H, $CH_2$-C$H_2$-$CH_2$), 3.10 (t, 2H, CH-C$H_2$-NH), 3.63(q, 1H, O-C$H_2$-$CH_2$), 3.75 (quint, 1H, O-C$H_2$-$CH_2$), 3.89 (quint, 1H, O-C*H*-$CH_2$), 6.7-7.4 (m, 10H, Ar-*H*), 7.82 (t, 1H, $CH_2$-N*H*), 9.31 (s, 1H, PhO*H*).

*Semicarbazide*

$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.16 (t, 3H, O-$CH_2$-C$H_3$), 1.50 (m, 1H, $CH_2$-C$H_2$-$CH_2$), 1.80 (m, 3H, $CH_2$-C$H_2$-C$H_2$), 3.05 (m, 2H, CH-C$H_2$-NH), 3.60(q, 1H, O-C$H_2$-$CH_2$), 3.74 (q, 1H, O-C$H_2$-$CH_2$), 3.80 (t, 1H, O-C*H*-$CH_2$), 4.02 (q, 2H, O-C$H_2$-$CH_3$), 6.24 (t, 1H, $CH_2$-N*H*-CO), 6.7-7.2 (d, 10H, Ar-*H*), 7.71 (s, 1H, O-CO-N*H*), 8.75 (s, 1H, NH-N*H*-CO-NH), 9.31 (s, 2H, PhO*H*).

*Urazole*

Yield: A = 87 %, B = 90 %

Chemical formula: $C_7H_{11}N_3O_3$

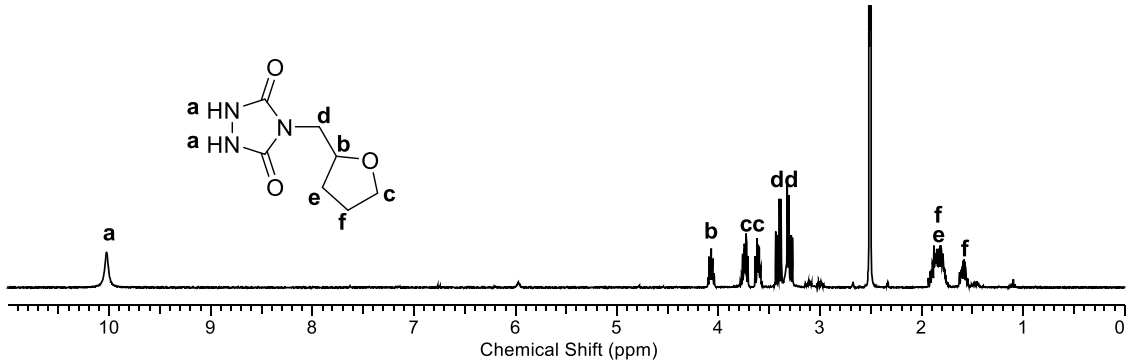
Molecular weight: 185.18 g/mol

LC-MS (m/z): 186.1 $[MH]^+$, 184 $[M-H]^-$

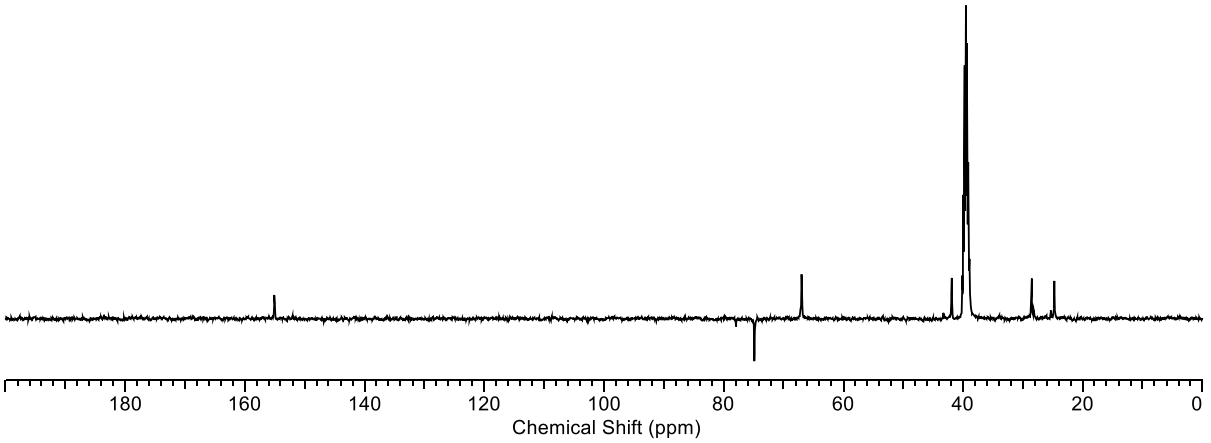
HRMS (m/z for $[M-H]^-$): 184.0728 (calculated), 184.0727 (experimental)

FT-IR: $\nu_{max}$ ($cm^{-1}$): 3168 (NH), 2928 ($sp^3$ CH), 1762 and 1670 (CO).

$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.60 (m, 1H, $CH_2$-C$H_2$-$CH_2$), 1.83 (m, 3H, $CH_2$-C$H_2$-C$H_2$), 3.28 (m, 1H, CH-C$H_2$-NH), 3.39 (m, 1H, CH-C$H_2$-NH), 3.62 (q, 1H, O-C$H_2$-$CH_2$), 3.73(q, 1H, O-C$H_2$-$CH_2$), 4.07 (t, 1H, O-C*H*-$CH_2$), 10.03 (s, 2H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 24.73 ($CH_2$), 28.52 ($CH_2$), 41.87 ($CH_2$), 66.93 ($CH_2$), 74.85 (CH), 155.03 (CO).

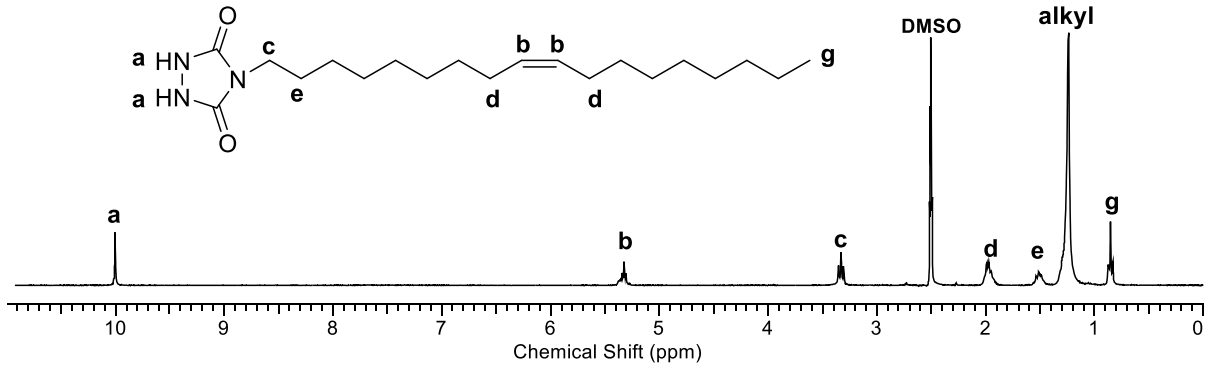


**Oleylamine**

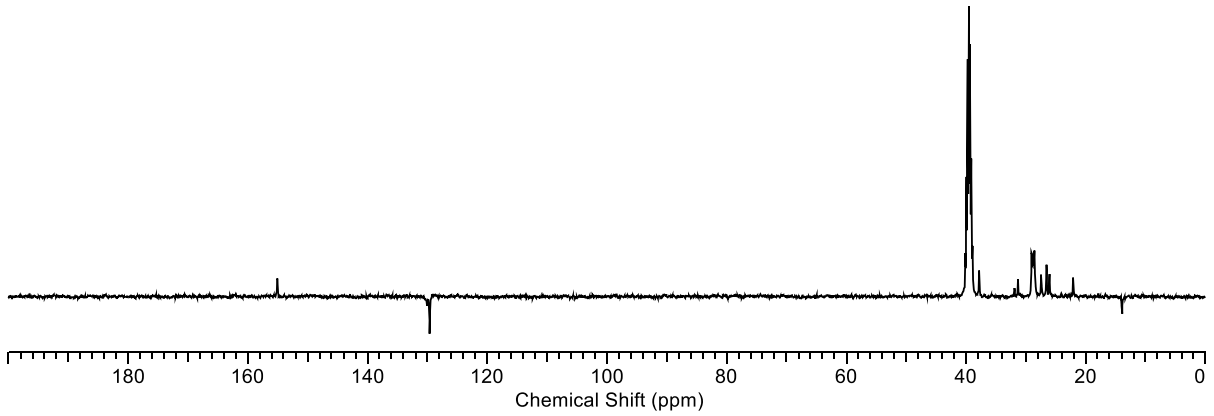
*Carbamate*
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.89 (t, 3H, $CH_2$-C$H_3$), 1.30 (d, 22H, 11x$CH_2$), 1.58 (t, 2H, C$H_2$-$CH_2$-NH), 2.03 (q, 4H, C$H_2$-CH-CH-C$H_2$), 3.26 (q, 2H, $CH_2$-C$H_2$-NH), 5.08 (s, 1H, $CH_2$-N*H*-*C*O), 5.35 (t, 2H, C*H*-*CH*), 6.76-7.43 (m, 10H, Ar-H).

*Semicarbazide*
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.86 (t, 3H, $CH_2$-C$H_3$), 1.17 (t, 3H, O-$CH_2$-C$H_3$), 1.24 (m, 24H, 12x(C$H_2$)), 2.01 (q, 4H, C$H_2$-CH-CH-C$H_2$), 2.97 (q, 2H, $CH_2$-C$H_2$-NH), 4.02 (d, 2H, O-C$H_2$-$CH_3$), 5.33 (t, 2H, C*H*-*CH*), 6.26 (t, 1H, $CH_2$-N*H*-*C*O), 6.69-7.21 (m, 10H, Ar-H), 7.60 (s, 1H, O-CO-N*H*), 8.67 (s, 1H, NH-N*H*-*C*O-NH).

*Urazole*[3]
Yield: A = 96 %, B = 95 %
Chemical formula: $C_{20}H_{37}N_3O_2$
Molecular weight: 351.54 g/mol
LC-MS (m/z): 352,3 $[MH]^+$, 350,2 $[M-H]^-$
HRMS (m/z for $[M-H]^-$): 350.2813 (calculated), 350.2809 (experimental)
FT-IR: $\nu_{max}$ ($cm^{-1}$): 3166 (NH), 3093 and 3037 ($sp^2$ CH), 2920 and 2852 ($sp^3$ CH), 1756 and 1665 (CO).
$^1$H-NMR (300MHz, $CDCl_3$): $\delta$ (ppm) = 0.86 (t, 3H, $CH_2$-C$H_3$), 1.24 (d, 22H, 11x$CH_2$), 1.66 (t, 2H, C$H_2$-$CH_2$-NH), 2.01 (q, 4H, C$H_2$-CH=CH-C$H_2$), 3.53 (q, 2H, $CH_2$-C$H_2$-NH), 5.35 (t, 2H, C*H*=*CH*), 9.96 (s, 2H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) = 13.92 ($CH_3$), 22.11 ($CH_2$), 26.00 ($CH_2$),16.55 ($CH_2$), 27.42 ($CH_2$), 28.66 ($CH_2$), 28.74 ($CH_2$), 28.80 ($CH_2$), 29.00 ($CH_2$),29.07 ($CH_2$), 31.25 ($CH_2$), 37.80 ($CH_2$), 129.61 (CH), 155.03 (CO).

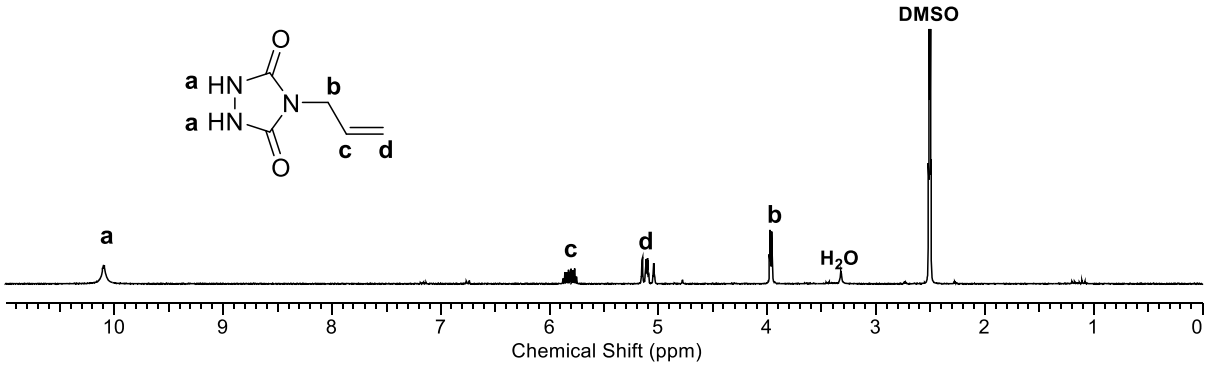


**Allylamine**

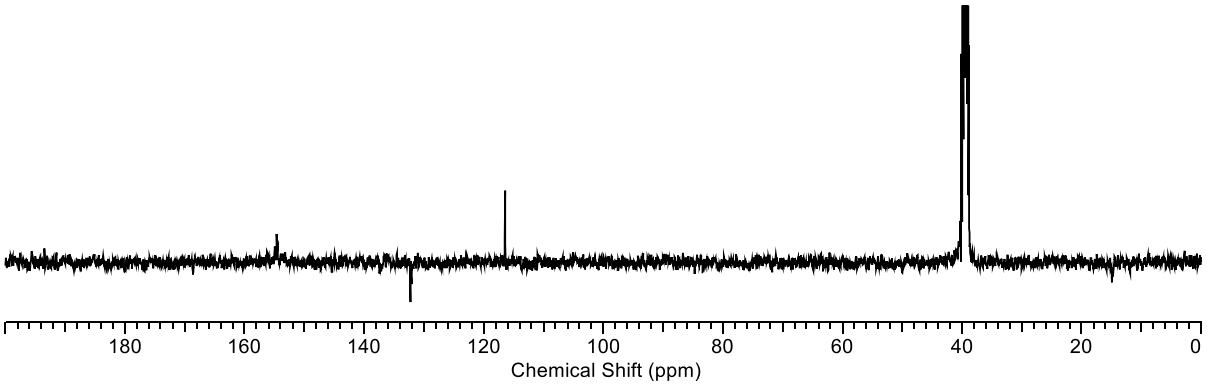
*Carbamate*
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 3.69 (t, 2H, CH-C*H*$_2$-NH), 5.15 (m, 2H, CH=C*H*$_2$), 5.85 (m, 1H, C*H*=*C*H$_2$), 6.7-7.42 (m, 10H, Ar-H), 7.93 (t, 1H, CH$_2$-N*H*-*C*O), 9.31 (s, 1H, PhO*H*).

*Semicarbazide*
$^1$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.16 (t, 3H, O-CH2-C*H*3), 3.63 (t, 2H, CH-C*H*$_2$-NH), 4.02 (q , 2H, O-C*H*$_2$-CH$_3$), 5.05 (m, 2H, CH=C*H*$_2$), 5.79 (m, 1H, C*H*=*C*H$_2$), 6.48 (t, 1H, CH$_2$-N*H*-*C*O), 6.7-7.22 (m, 10H, Ar-H), 7.73 (s, 1H, O-CO-N*H*), 8.76 (s, 1H, NH-N*H*-*C*O-NH), 9.30 (s, 2H, PhO*H*).

*Urazole*[2]
Yield: A = 89 %, B = 84 %
Chemical formula: $C_5H_7N_3O_2$
Molecular weight: 141.13 g/mol
LC-MS (m/z): 283,1 $[MH]^+$, 281 $[2M-H]^-$, 422,1 $[3M-H]^-$
HRMS (m/z for $[M-H]^-$): 140.0466 (calculated), 140.0472 (experimental)
FT-IR: $\nu_{max}$ ($cm^{-1}$): 3323 and 3155 (NH), 3021 ($sp^2$ CH), 2813 ($sp^3$ CH), 1751 and 1662 (CO).
$^1$H-NMR (400MHz, DMSO-$d_6$): $\delta$ (ppm) = 3.95 (t, 2H, CH-C*H*$_2$-NH), 5.11 (m, 2H, CH=C*H*$_2$), 5.80 (m, 1H, C*H*=*C*H$_2$), 10.11 (s, 2H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 116.45 ($CH_2$), 132.27 (CH), 154.59(CO).

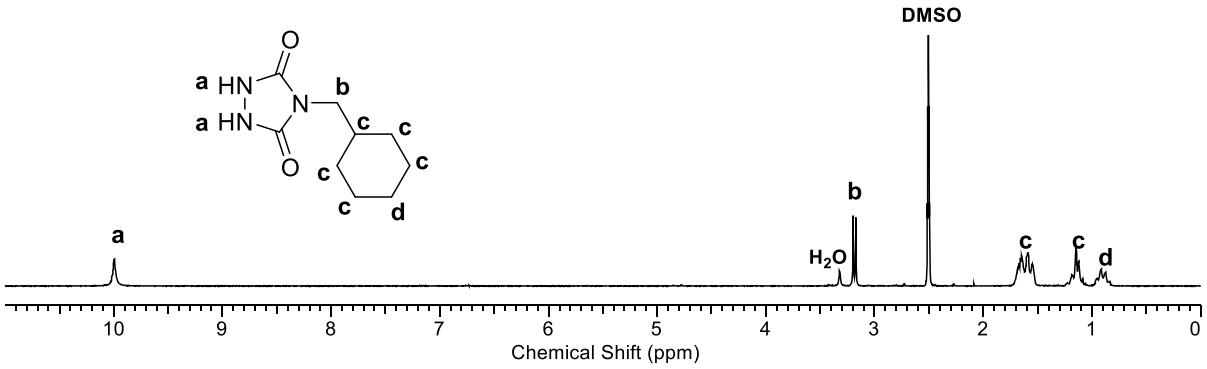


**Cyclohexanemethylamine**

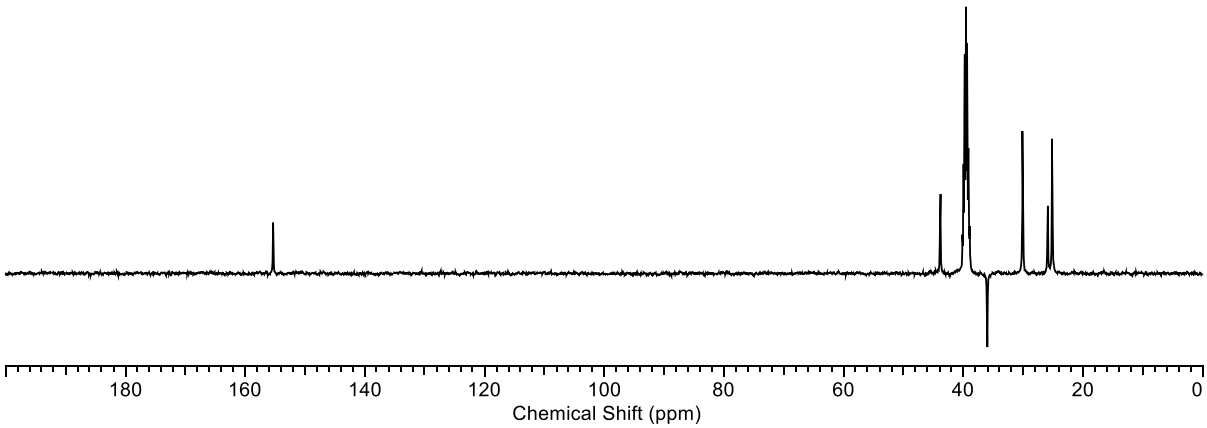
*Carbamate*
$^{1}$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.9 (t, 2H, $CH_2$-$CH_2$-C*H*$_2$-$CH_2$-$CH_2$), 1-1.75 (m, 9H, C*H*$_2$-C*H*$_2$-C*H*-*CH*$_2$-C*H*$_2$), 3.17 (t, 2H, C*H*$_2$-NH), 6.7-7.4 (m, 10H, Ar-H), 7.84 (t, 1H, $CH_2$-N*H*-*C*O), 9.60 (s, 1H, PhO*H*).

*Semicarbazide*
$^{1}$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.9 (t, 2H, $CH_2$-$CH_2$-C*H*$_2$-$CH_2$-$CH_2$), 1.04-1.77 (m, 12H, C*H*$_2$-C*H*$_2$-C*H*-*CH*$_2$-C*H*$_2$ and O-$CH_2$-C*H*$_3$), 2.85 (t, 2H, C*H*$_2$-NH), 4.02 (q, 2H, O-C*H*$_2$-$CH_3$), 6.27 (t, 1H, $CH_2$-N*H*-*C*O), 6.7-7.22 (m, 10H, Ar-H), 7.57 (s, 1H, O-CO-N*H*), 8.70 (s, 1H, NH-N*H*-*C*O-NH), 9.30 (s, 2H, PhO*H*).

*Urazole*
Yield: A = 93 %, B = 95 %
Chemical formula: $C_9H_{15}N_3O_2$
Molecular weight: 197.24 g/mol
LC-MS (m/z): 198,1 $[MH]^+$, 196,1 $[M-H]^-$
HRMS (m/z for $[M-H]^-$): 196.1092 (calculated), 196.1096 (experimental)
FT-IR: $\nu_{max}$ ($cm^{-1}$): 3164 (NH), 2922 and 2847 ($sp^3$ CH), 1761 and 1680 (CO).
$^{1}$H-NMR (400MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.90 (t, 2H, $CH_2$-$CH_2$-C*H*$_2$-$CH_2$-$CH_2$), 1.04-1.73 (m, 9H, C*H*$_2$-C*H*$_2$-C*H*-*CH*$_2$-C*H*$_2$), 3.19 (t, 2H, C*H*$_2$-N), 10.00 (s, 2H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 25.07 ($CH_2$), 25.88 ($CH_2$), 30.03 ($CH_2$),35.91 (CH), 43.75 ($CH_2$), 155.24 (CO).

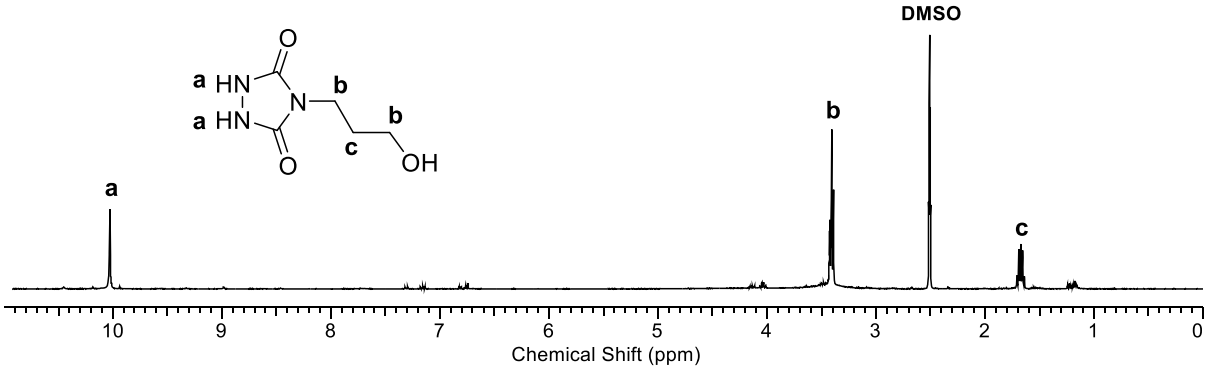


Urazoles via route B

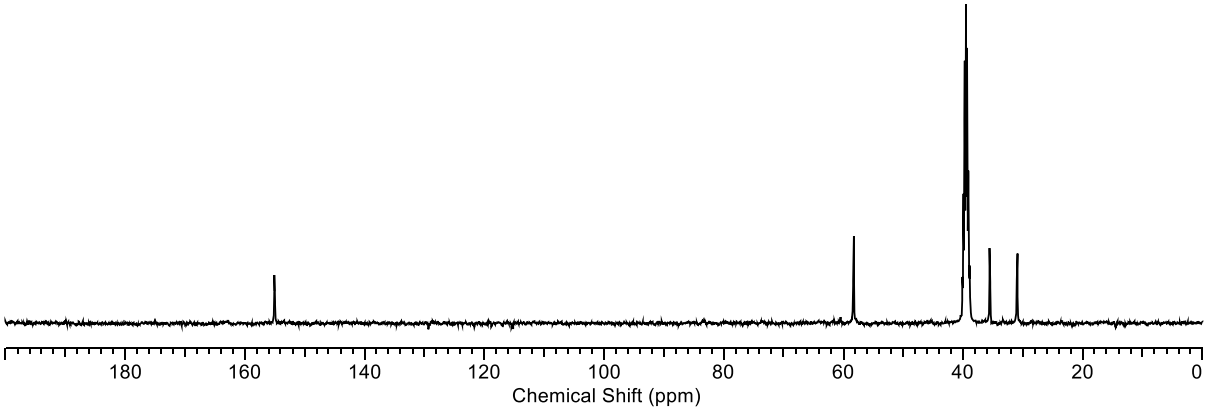
**3-Amino-1-propanol**

*Semicarbazide*
$^{1}$H-NMR (300MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.17 (t, 3H, O-$CH_2$-C$H_3$), 1.52 (quint, 2H, $CH_2$-C$H_2$-$CH_2$), 3.05 (q, 2H, C$H_2$-NH), 3.38 (q, 2H, HO-C$H_2$), 4.03 (q, 2H, O-C$H_2$-$CH_3$), 4.41 (t, 1H, *H*O-$CH_2$), 6.31 (s, 1H, $CH_2$-N*H*), 6.7-7.2 (m, 5 H, Ar-H),7.68 (s, 1H, O-CO-N*H*), 8.75 (s, 1H, NH-N*H*-*C*O-NH), 9.30 (s, 1H, PhO*H*).

*Urazole*
Yield: 78 %
Chemical formula: $C_5H_9N_3O_3$
Molecular weight: 159.15 g/mol
LC-MS (m/z): 160 $[MH]^+$, 158.05 $[M-H]^-$
HRMS (m/z for $[M-H]^-$): 158.0571 (calculated), 158.0576 (experimental)
FT-IR: $\nu_{max}$ ($cm^{-1}$): 3326 (OH), 3192 (NH), 2954 and 2754 ($sp^3$ CH), 1742 and 1672 (CO).
$^{1}$H-NMR (400MHz, DMSO-$d_6$): $\delta$ (ppm) = 0.77 (quint, 2H, $CH_2$-C$H_2$-$CH_2$), 1.6 (m, 4H, C$H_2$-$CH_2$-C$H_2$), 9.12 (s, 2H, N*H*-N*H*).



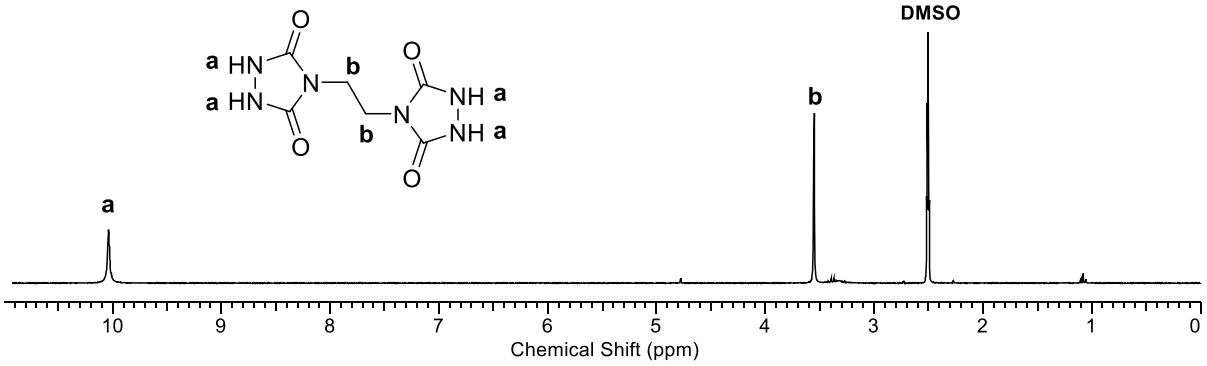

$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 31.00 ($CH_2$), 35.60 ($CH_2$), 58.30 ($CH_2$), 155.10 (CO).



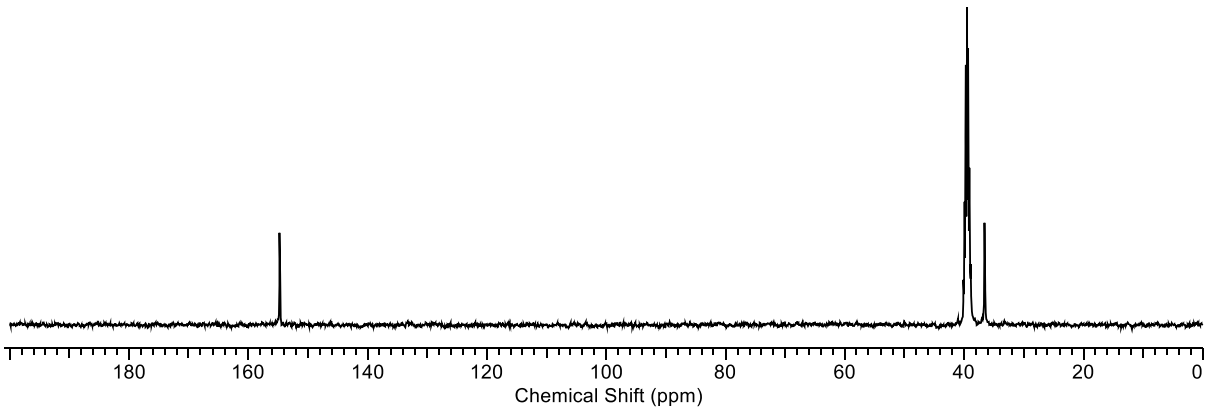
**Ethylenediamine**

*Semicarbazide*
$^{1}$H-NMR (400MHz, DMSO-$d_6$): $\delta$ (ppm) = 1.17 (t, 6H, O-$CH_2$-C$H_3$), 3.05 (t, 4H, C$H_2$-C$H_2$), 4.02 (q, 4H, O-C$H_2$-$CH_3$), 6.43 (s, 2H, N*H*-*C*$H_2$-$CH_2$-N*H*), 6.7-7.2(m, 10H, Ar-H), 7.78 (s, 2H, O-CO-N*H*), 8.72 (s, 2H, NH-N*H*-*C*O-NH), 9.28 (s, 2H, PhO*H*).

*Urazole*
Yield: 92 %
Chemical formula: $C_6H_8N_6O_4$
Molecular weight: 228.17 g/mol
LC-MS (m/z): insoluble
FT-IR: 3152 (NH), 2934 ($sp^3$ CH), 1696 and 1666 (CO)
$^{1}$H-NMR (400MHz, DMSO-$d_6$): $\delta$ (ppm) = 3.55 (s, 4H, C$H_2$-C$H_2$), 10.03 (s, 4H, N*H*-N*H*).




$^{13}$C-NMR (400 MHz, DMSO-$d_6$): $\delta$ (ppm) = 36.5 ($CH_2$), 154.6 (CO).



## Supplementary Figures

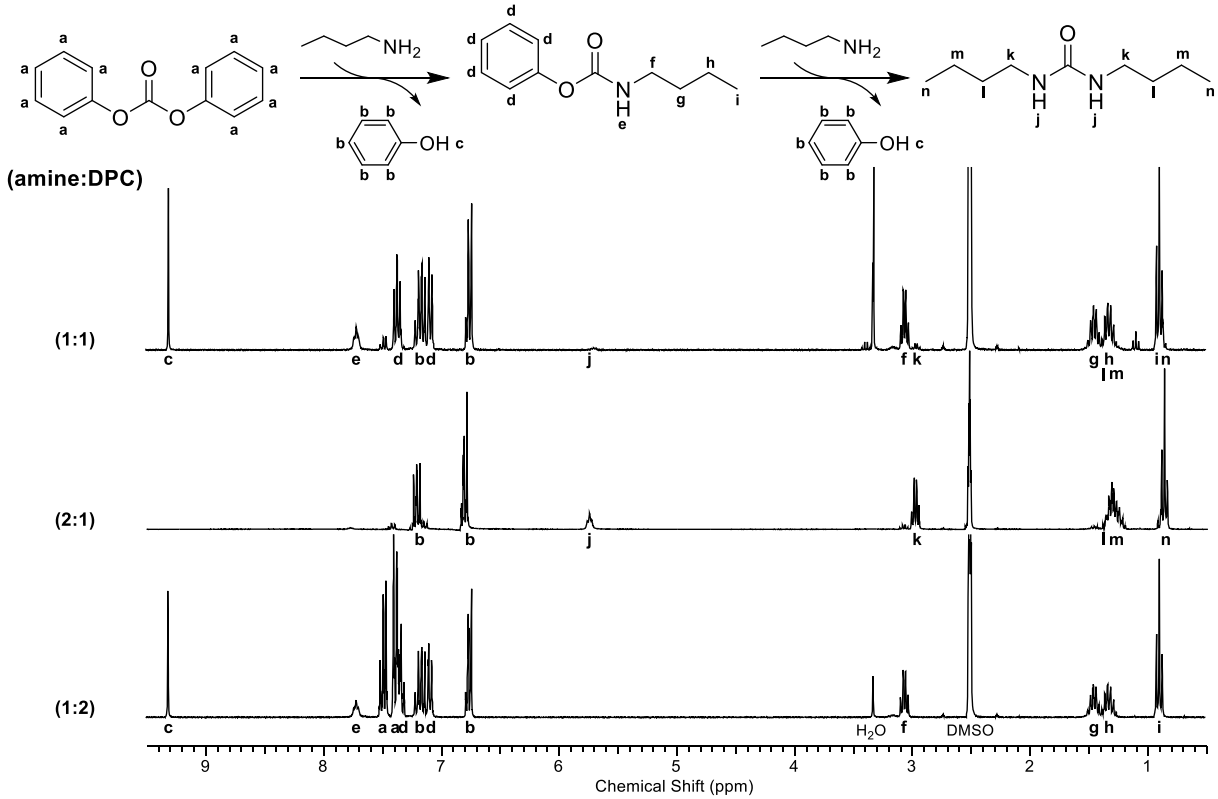



*Figure S1 - A side reaction was observed during the first reaction step, as a second amine addition leads to the urea rather than the carbamate. NMR analysis showed that this side product can be avoided when an excess of DPC is used.*

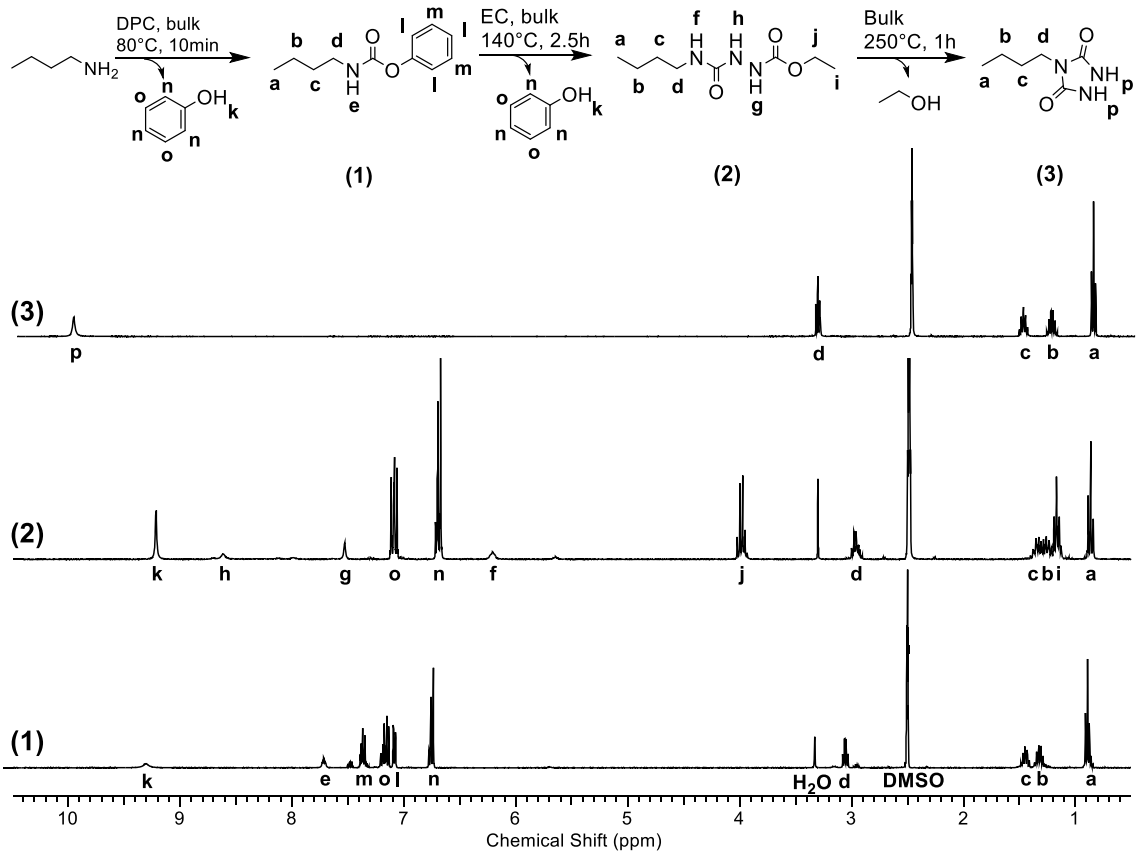



*Figure S2 - Complete [1]H-NMR analysis of the synthesis of butyl urazole via reaction route A.*

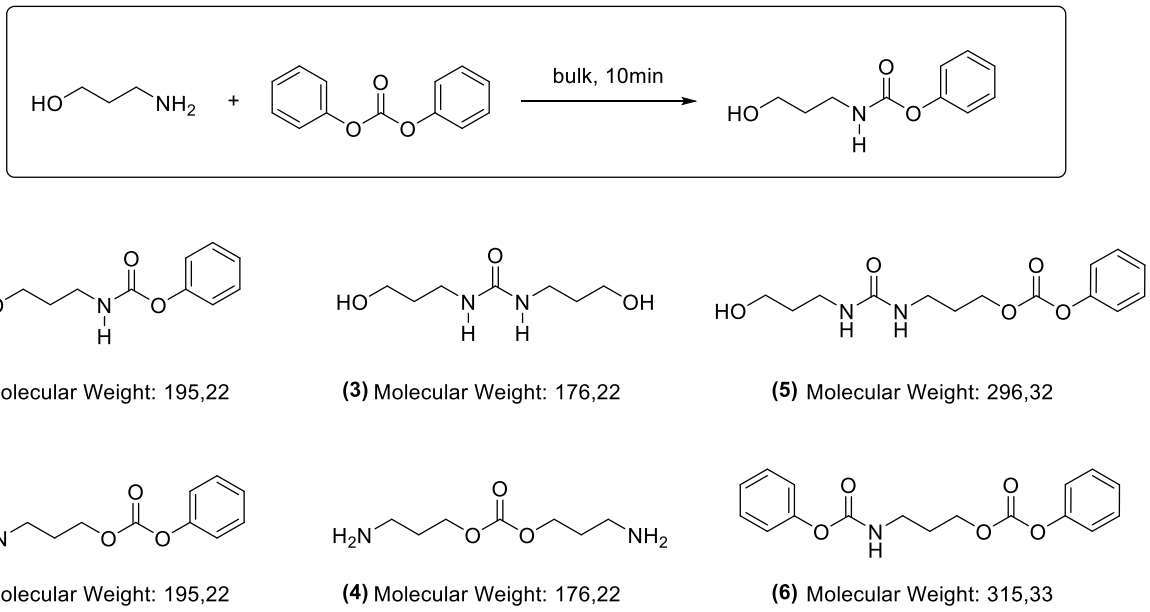



*Figure S3 – Product and side products of the carbamate formation of DPC and 3-amino-propanol.*

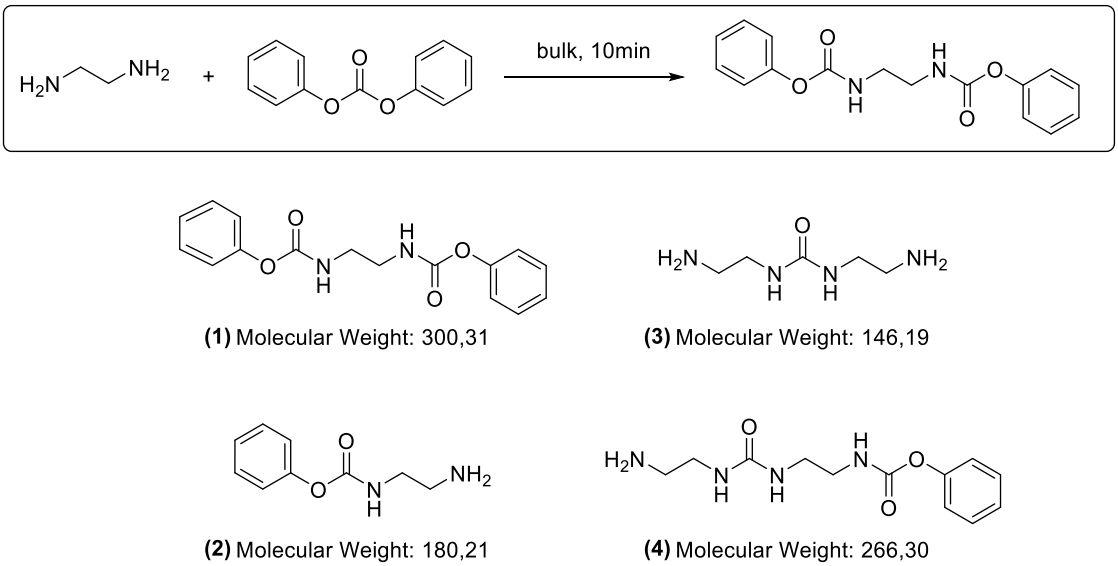



*Figure S4 – Product and side products of the carbamate formation of DPC and ethylenediamine.*

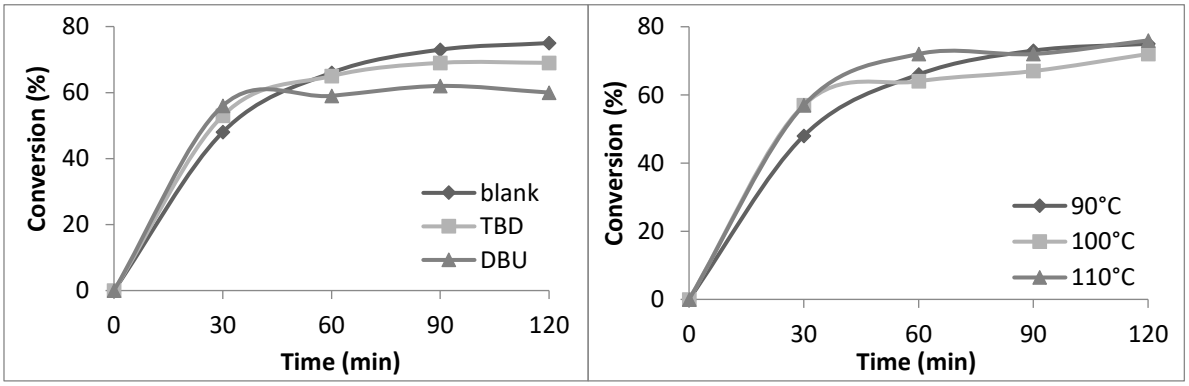



*Figure S5 - Conversion of EC and DPC towards EPHD as a function of the reaction time with varying (a) catalyst and (b) reaction temperature.*

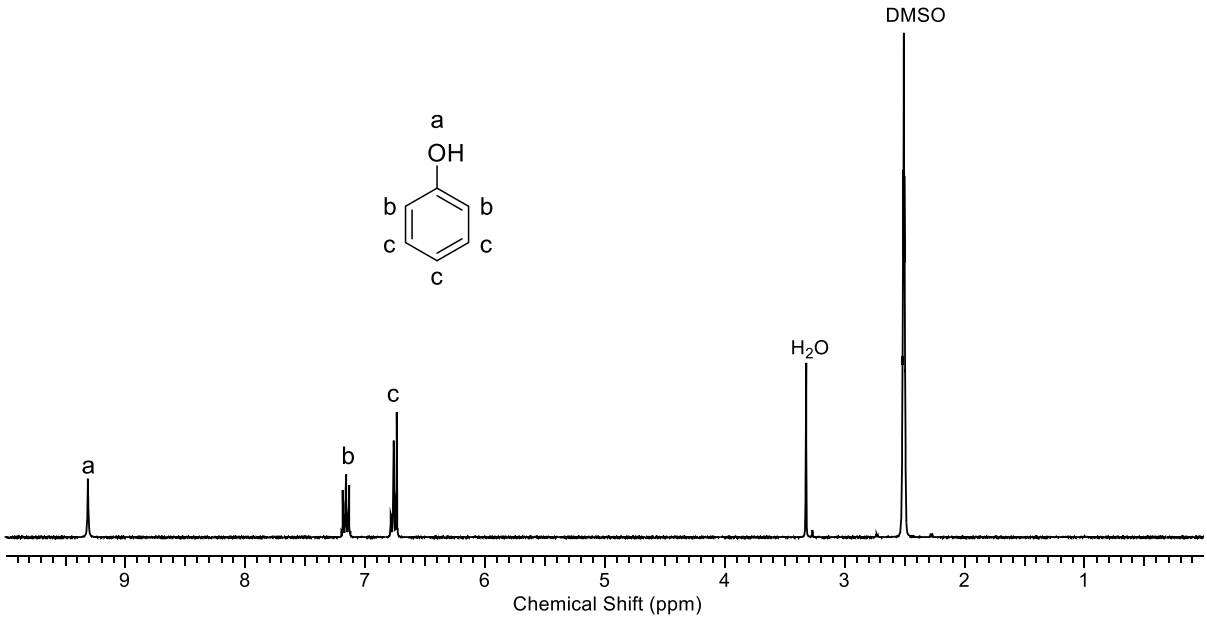



*Figure S 1 - NMR of the phenol recuperated from the octyl urazole formation via reaction pathway B*

## References


1. T. Tsuji, Pharm. Bull., 1954, **2**, 403.
2. V. Arya and S. Shenoy, Indian J. Chem., Sect. B: Org., 1976, **14**, 883.
3. R. L. Sowerby, Urazole compositions useful as additives for functional fluids, WO8707892, 1988.