Palladium(II)-Catalyzed Intramolecular Diamination of Unfunctionalized Alkenes

Jan Streuff, Claas H. Hövelmann, Martin Nieger and Kilian Muñiz

Kekulé-Institut für Organische Chemie und Biochemie,
Universität Bonn
Gerhard-Domagk-Str. 1,
D-53121 Bonn,
Germany
kilian.muniz@uni-bonn.de

SUPPORTING INFORMATION

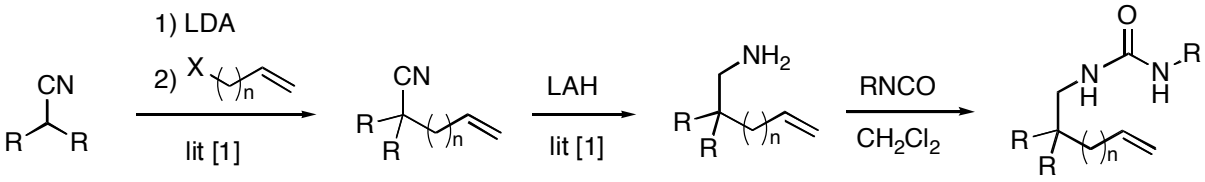
Experimental Section

General.

All organic reagents were purchased from Acros. Palladium acetate and i...odosobenzene diacetate were purchased from Aldrich. Dichloromethane, ethyl acetate and hexanes were dried over calcium chloride, distilled and used without further manipulation. Column chromatography was performed with silica gel (Merck, type 60, 0.063-0.2 mm and Machery Nagel, type 60, 0.015-0.025 mm). Nmr spectra were recorded on a Bruker DPX 300 MHz and Bruker DRX 500 MHz spectrometer. All chemical shifts in nmr experiments are reported as ppm downfield from TMS. The following calibrations were used: $CDCl_3$ δ = 7.26 and 77.00 ppm, C_6D_6 δ = 7.16 and 128.00 ppm. MS and HRMS experiments were performed on a Kratos MS 50 within the service centers at the Kekulé-Department, Bonn.

Synthesis of starting materials

All *N*-tosylated urea-derivates were prepared from the corresponding nitriles. These were synthesized and reduced using a literature procedure [Y. Tamaru, M. Hojo, H. Higashimura, Z.-I. Yoshida, *J. Am. Chem. Soc.* **1988**, *110*, 3994]. The free amine was then directly used without prior purification and reacted with p-toluolsulfonylisocyanate (or phenylsulfonylisocyanate) to give the urea starting materials as white solids:



Diamination of Alkenes: General Procedures

General procedure A, preparation of 5-membered diamines:

To a solution of $Pd(OAc)_2$ (0.025 mmol, 11.3 mg) and $PhI(OAc)_2$ (2.00 mmol, 322 mg) in 5 ml CH_2Cl_2 were added the unsaturated urea (0.50 mmol), Me_4NCl (0.50 mmol, 55 mg) and NaOAc (0.50 mmol, 40 mg). The mixture was stirred overnight and product formation was followed by tlc where the products appeared as an UV-active spot with a higher retention than the starting compound (R_f = 0.5-0.7). The reaction was reductively quenched by addition of an aqueous saturated $Na_2S_2O_3$-solution. The aqueous layer was extracted several times with CH_2Cl_2 and the organic layers were extracted with brine. The combined organic layers were

dried over $MgSO_4$. The solvent was removed under reduced pressure and the product purified by flash-chromatography (hexanes/CH_2Cl_2/diethylether, 3/3/1, v/v).

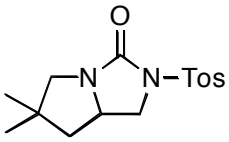
General procedure B, catalytic preparation of 6-membered diamines:

Preparation and workup were the same as in procedure A employing 25 mol% of $Pd(OAc)_2$ and no base. Stirring was continued for about 3 days to complete the conversion of all starting material and product formation was followed by tlc where the products appeared as an UV-active spot with a higher retention than the starting compound (R_f = 0.5-0.6). The reaction was worked up as described and the product was purified by flash-chromatography (hexanes/CH_2Cl_2/diethylether, 3/3/1, v/v).

Procedure C:

Preparation and workup were the same as in procedure A employing 10 mol% of $Pd(OAc)_2$ and no base. Stirring was continued for 12 hours to complete the conversion of all starting material and product formation was followed by tlc where the product appeared as an UV-active spot with a higher retention than the starting compound (R_f = 0.6). The reaction was worked up as described and the product was purified by flash-chromatography (hexanes/CH_2Cl_2/diethylether, 3/3/1, v/v).

Hexahydro-6,6-dimethyl-2-(p-tolylsulfonyl)pyrrolo-[1,2-*e*]imidazol-3-one



Synthesized according to procedure A.

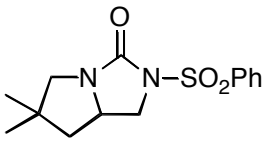
^{1}H nmr (300 MHz, $CDCl_3$): δ = 0.96 (s, 3H), 1.05 (s, 3H), 1.27 (dd, *J* = 9.2, 12.4 Hz, 1H), 1.78 (dd, *J* = 6.1, 12.4 Hz, 1H), 2.40 (s, 3H), 3.76 (d, *J* = 11.3 Hz, 1H), 3.28 (d, *J* = 11.3 Hz, 1H), 3.63 (dd, *J* = 4.2, 9.2 Hz, 1H), 3.92 (m, 1H), 4.03 (dd, *J* = 8.7, 9.3 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H).

^{13}C nmr (75 MHz, $CDCl_3$): δ = 21.52, 27.53, 28.08, 40.62, 46.02, 48.19, 54.69, 58.41, 127.89, 129.51, 134.97, 144.65, 156.16.

MS: 293.2 $[M\text{-}CH_3]^+$, 252.1 (18), 244.2 (100), 229.2 (8), 188.1 (25), 155.1 (16), 153.2 (32), 133.1 (3), 105.1 (4), 97.1 (36), 91.1 (38), 82.1 (3), 65.1 (8), 55.1 (58).

HRMS: calc. for $C_{14}H_{17}N_2O_3S$ (M-CH_3): 293.0960, found: 293.0962.

Hexahydro-6,6-dimethyl-2-phenylsulfonylpyrrolo-[1,2-*e*]imidazol-3-one



Synthesized according to procedure A.

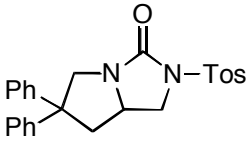
^{1}H nmr (300 MHz, $CDCl_3$): δ = 0.96 (s, 3H), 1.06 (s, 3H), 1.28 (dd, *J* = 9.0, 12.4 Hz, 1H), 1.79 (dd, *J* = 6.3, 12.4 Hz, 1H), 2.77 (d, *J* = 11.3 Hz, 1H), 3.29 (d, *J* = 11.3 Hz, 1H), 3.64 (dd, *J* = 4.3. 9.3 Hz, 1H), 3.94 (m, 1H), 4.04 (dd, *J* = 8.7, 9.3 Hz, 1H), 7.52 (m, 2H), 7.62 (tt, *J* = 1.3, 7.4 Hz, *J* = 1.3 Hz, 1H), 8.03 (m, 2H).

^{13}C nmr (75 MHz, $CDCl_3$): δ = 27.56, 28.11, 40.69, 46.09, 48.33, 54.76, 48.45, 127.92, 128.96, 133.68, 137.93, 156.09.

MS: 279.2 $[M\text{-}CH_3]^+$, 238.1 (40), 230.2 (84), 215.2 (8), 202.2 (4), 174.1 (28), 153.2 (40), 141.1 (12), 97.1 (30), 82.1 (8), 77.1 (42), 55.1 (100).

HRMS: calc. for $C_{13}H_{15}N_2O_3S$ (M-CH_3): 279.0803, found: 279.0803.

Hexahydro-2-(p-tolylsulfonyl)-6,6-diphenylpyrrolo-[1,2-*e*]imidazol-3-one



Synthesized according to procedure A.

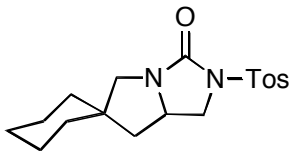
^{1}H nmr (300 MHz, $CDCl_3$, TMS): δ = 2.15 (dd, *J* = 9.6, 12.0 Hz, 1H), 2.34 (s, 3H), 2.47 (dd, *J* = 5.2, 12.0 Hz, 1H), 3.53 (dd, *J* = 5.3, 9.3 Hz, 1H), 3.77 (d, *J* = 11.7 Hz, 1H), 3.81 (m, 1H), 3.94 (d, *J* = 12.0 Hz, 1H), 3.97 (dd, *J* = 8.7, 9.4 Hz, 1H), 6.98-7.17 (m, 10H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 8.2 Hz, 2H).

^{13}C nmr (75 MHz, $CDCl_3$): δ = 21.54, 43.60, 47.99, 54.00, 56.06, 56.78, 126.41, 126.65, 127.94, 128.47, 129.58, 134.94, 144.68, 145.16, 145.37, 156.14.

MS: 432.2 $[M]^+$ (100), 368.2 (2), 277.2 (35), 252.1 (40), 205.1 (4), 193.1 (10), 179.1 (8), 115.1 (5), 97.1 (35), 91.1 (18), 65.1 (2), 55.1 (32).

HRMS: calc. for $C_{25}H_{24}N_2O_3S$: 432.1508, found: 432.1508.

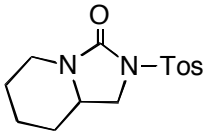
Spiro[cyclohexan-1',6-hexahydro-2-(p-tolylsulfonyl)pyrrolo-[1,2-*e*]imidazol-3-one]



Synthesized according to procedure A.

^{1}H nmr (300 MHz, $CDCl_3$): □ = 1.15-1.50 (m, 11H), 1.89 (dd, *J* = 6.4, 12.6 Hz, 1H), 2.42 (s, 3H), 2.77 (d, *J* = 11.7 Hz, 1H), 3.39 (d, *J* = 11.7 Hz, 2H), 3.64 (dd, *J* = 3.8, 9.6 Hz, 1H), 3.85 (m, 1H), 3.99 (dd, *J* = 8.4, 9.6 Hz, 1H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.90 (d, *J* = 8.3 Hz, 2H).
^{13}C nmr (75 MHz, $CDCl_3$): □ = 21.59, 23.15, 23.67, 25.49, 36.28, 37.72, 43.92, 44.74, 48.08, 54.16, 56.41, 127.97, 129.55, 135.02, 144.68, 156.28.
MS: 347.2 $[M]^+$, 332.2 (2), 298.3 (1), 284.3 (100), 253.1 (25), 227.2 (1), 193.2 (24), 175.1 (3), 155.1 (20), 138.2 (9), 109,1 (2), 105.1 (4), 97.1 (24), 91.1 (30), 65.1 (4), 55.1 (30).
HRMS: calc. for $C_{18}H_{24}N_2O_3S$ (M-H): 347.1429, found: 347.1426.

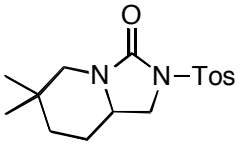
Hexahydro-2-(p-tolylsulfonyl)imidazo[1,5-*a*]pyridine-3(5*H*)-one



Synthesized according to procedure B.

^{1}H nmr (300 MHz, $CDCl_3$): □ = 1.15-1.43 (m, 3H), 1.62 (m, 1H), 1.83 (m, 2H), 2.42 (s, 3H), 2.64 (td, *J* = 3.6, 13.2 Hz, 1H), 3.35-3.49 (m, 2H), 3.80 (dd, *J* = 4.2, 13.6, 1H), 3.95 (dd, *J* = 7.8, 8.7 Hz, 1H), 7.32 (d, *J* = 8.3 Hz, 2H), 7.90 (d, *J* = 8.3 Hz, 2H).
^{13}C nmr (75 MHz, $CDCl_3$): □ = 21.58, 22.77, 24.00, 30.66, 41.97, 48.45, 51.87, 128.01, 129.55, 135.15, 144.55, 152.65.
MS: 293.1 $[M]^+$, 244.2 (4), 230.2 (100), 215.2 (8), 187.1 (6), 174.1 (4), 155.1 (12), 139.1 (50), 119.1 (8), 97.1 (5), 91.1 (43), 82.1 (4), 65.1 (8), 55.1 (10).
HRMS: calc. for $C_{14}H_{17}N_2O_3S$ (M-H): 293.0959, found: 293.0962.

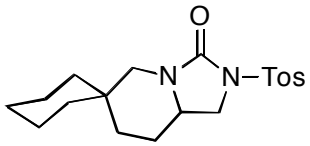
Hexahydro-6,6-dimethyl-2-(p-tolylsulfonyl)imidazo[1,5-*a*]pyridine-3(5*H*)-one



Synthesized according to procedure B.

^{1}H nmr (300 MHz, $CDCl_3$): δ = 0.82 (s, 3H), 0.91 (s, 3H), 1.28 (td, *J* = 3.7, 14.0 Hz, 1H), 1.47 (m, 2H), 1.66 (m, 1H), 2.40 (d, *J* = 11.5 Hz, 1H), 2.41 (s, 3H), 3.39-3.47 (m, 3H), 3.95 (dd, *J* = 8.1, 9.0 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.90 (d, *J* = 8.5 Hz, 2H).
^{13}C nmr (75 MHz, $CDCl_3$): δ = 21.58, 23.10, 27.10, 28.59, 30.27, 36.34, 48.23, 51.54, 51.75, 128.00, 129.54, 135.15, 144.53, 152.94.
MS: 321.1 $[M]^+$, 307.1 (5), 258.2 (100), 243.2 (25), 239.1 (2), 189.1 (38), 167.1 (28), 155.0 (32), 119.1 (2), 112.1 (8), 91.0 (30), 69.1 (3), 55.1 (6).
HRMS: calc. for $C_{16}H_{21}N_2O_3S$ (M-H): 321.1272, found: 321.1269.

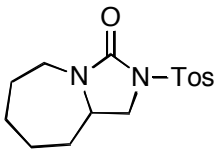
Spiro[cyclohexan-1',6-hexahydro-2-(p-tolylsulfonyl)imidazo[1,5-*a*]pyridine-3(5*H*)-one]



Synthesized according to procedure B.

^{1}H nmr (300 MHz, $CDCl_3$): δ = 1.09-1.70 (m, 14H), 2.26 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 3.37 (m, 1H), 3.42 (dd, *J* = 5.3, 9.4 Hz, 1H), 3.79 (dd, *J* = 2.2, 13.2 Hz, 1H), 3.88 (dd, *J* = 8.7, 9.2 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H).
^{13}C nmr (75 MHz, $CDCl_3$): δ = 21.34, 21.46, 21.57, 26.25, 26.34, 30.63, 32.73, 34.89, 37.96, 48.15, 49.13, 51.95, 127.99, 129.51, 135.09, 144.51, 152.91.
MS: 362.2 $[M]^+$, 298.3 (100), 253.1 (20), 207.2 (50), 189.1 (20), 155.1 (40), 139.1 (4), 111.1 (16), 99.1 (28), 91.1 (64), 81.1 (10), 67.1 (12), 55.1 (12).
HRMS: calc. for $C_{19}H_{26}N_2O_3S$: 362.1664, found: 362.1662.

Octahydro-2-(p-tolylsulfonyl) imidazo[1,5-*a*]azepin-3-one



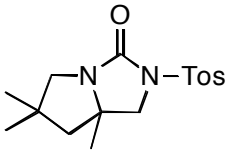
Synthesized according to procedure C.

^{1}H nmr (300 MHz, $CDCl_3$): □=1.16-1.60 (m, 6H), 1.63-1.72 (m, 1H), 1.91-2.02 (m, 1H), 2.43 (s, 3H), 3.21 (m, 2H), 3.65 (dd, *J* = 7.5, 11.2Hz, 1H), 3.74(dd, *J* = 5.1, 11.4 Hz, 1H), 3.99 (m, 1H), 7.31(d, *J* = 8.2, 2H), 7.77(d, *J* = 8.2, 2H).

^{13}C nmr (75 MHz, $CDCl_3$): □=21.58, 25.39, 26.00, 29.32, 34.82, 40.09, 48.13, 60.90, 126.89, 129.88,136.74, 144.75, 151.88

MS: 347.2 $[M]^+$, 332.2 (2), 298.3 (1), 284.3 (100), 253.1 (25), 227.2 (1), 193.2 (24), 175.1 (3), 155.1 (20), 138.2 (9), 109,1 (2), 105.1 (4), 97.1 (24), 91.1 (30), 65.1 (4), 55.1 (30).

Hexahydro-2-(p-tolylsulfonyl)-6,6,8-trimethylpyrrolo-[1,2-*e*]imidazol-3-one



Synthesized according to procedure A.

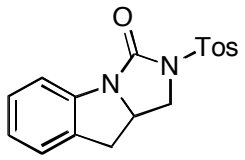
^{1}H nmr (300 MHz, $CDCl_3$): □= 0.66 (s, 3H), 1.07 (s, 3H), 1.29 (s, 3H), 1.59 (d, *J* = 4.9 Hz, 2H), 2.41 (s, 3H), 2.73 (d, *J* = 12.1 Hz, 1H), 3.41 (d, *J* = 11.9 Hz, 1H), 3.69 (d, *J* = 1.0 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H).

^{13}C nmr (75 MHz, $CDCl_3$): □= 21.55, 27.48, 27.69, 28.42, 41.08, 52.90, 56.80, 57.48, 62.16, 128.02, 129.47, 134.75, 144.66, 156.19.

MS: 321.2 $[M]^+$, 307.2 (61), 266.1 (82), 258.2 (96), 202.2 (14), 167.2 (42), 155.1 (39), 111.1 (59), 01.1 (77), 69.1 (100).

HRMS: calc. for $C_{16}H_{21}N_2O_3S$ [M-H]: 321.1272. Found: 321.1276.

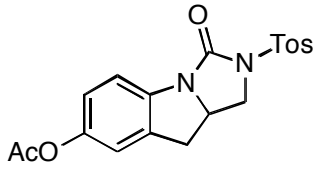
Tricyclic urea 2a



Synthesized according to procedure A.

^{1}H nmr (500 MHz, $CDCl_3$): δ = 2.42 (s, 3H), 2.92 (dd, *J* = 9.6, 15.8 Hz, 1H), 3.27 (dd, *J* = 8.7, 15.8 Hz, 1H), 3.65 (ps-t, *J* = 9.0 Hz, 1H), 4.45 (dd, *J* = 8.4, 9.3 Hz, 1H), 4.66 (pseudo-quin, *J* = 8.7 Hz, 1H), 7.04 (td, *J* = 1.0, 7.5 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 1H) 7.18 (d, *J* = 1.0, 7.7 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 2H).
^{13}C nmr (125 MHz, $CDCl_3$): δ = 21.63, 35.78, 51.19, 55.67, 115.17, 124.56, 125.16, 128.14, 128.27, 129.73, 132.04, 134.81, 140.12, 145.01, 151.22.
MS: 328.1 $[M]^+$ (100), 272.1 (35), 264.2 (10), 173.1 (16), 155.0 (32), 130.1 (56), 117.1 (16), 91.1 (48), 84.0 (12), 65.1 (10), 56.1 (15).
HRMS: calc. for $C_{17}H_{16}N_2O_3S$: 328.0882, found: 328.0877.

Tricyclic urea 2b



Obtained as side-product from a reaction according to procedure A in the absence of base.

^{1}H nmr (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H), 2.42 (s, 3H), 2.93 (dd, *J* = 9.5, 16.0 Hz, 1H), 3.26 (dd, *J* = 8.8, 16.0 Hz, 1H), 3.64 (pseudo-t, *J* = 9.0 Hz, 1H), 4.44 (dd, *J* = 8.5, 9.2 Hz, 1H), 4.68 (pseudo-quin, *J* = 8.8 Hz, 1H), 6.90 (m, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 2H).
^{13}C nmr (75 MHz, $CDCl_3$): δ = 20.97, 21.62, 35.86, 51.12, 55.92, 115.56, 118.97, 121.14, 128.24, 129.78, 133.34, 134.59, 138.02, 145.15, 147.49, 151.38, 169.75

MS: 386.1 $[M]^+$, 344.1 (100), 328.1 (6), 189.1 (25), 155.0 (16), 146.1 (32), 133.0 (12), 130.1 (8), 91.1 (40), 65.1 (5).

HRMS: calc. for $C_{19}H_{18}N_2O_3S$: 386.0936, found: 386.0940.

Details concerning the X-ray structure of 2a

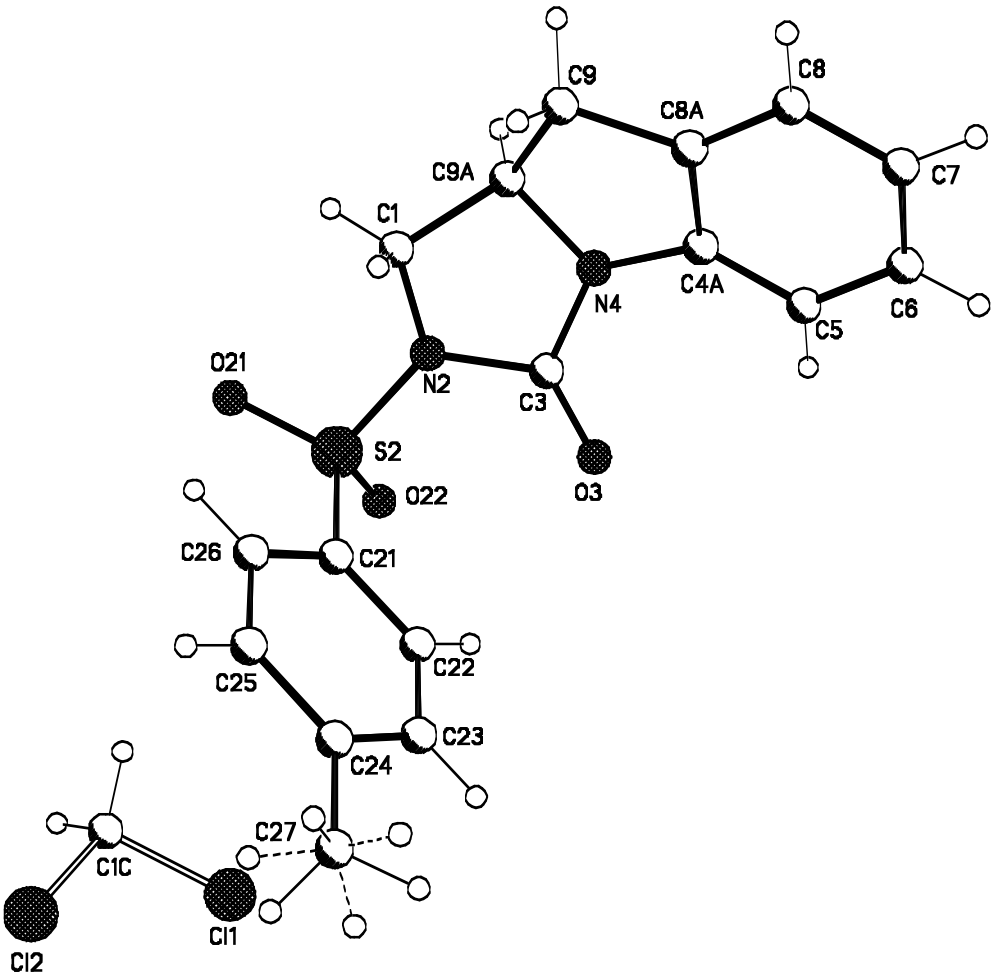


Table 1. Crystal data and structure refinement for **2a.**

Empirical formula	C17.50 H17 Cl N2 O3 S C17 H16 N2 O3 S - 0.5 CH2Cl2
Formula weight	370.84
Temperature	123(2) K
Wavelength	0.71073 A
Crystal system, space group	Triclinic, P-1 (No.2)
Unit cell dimensions	a = 5.9460(3) A alpha = 96.432(3) deg. b = 11.5541(7) A beta =95.564(4) deg. c = 12.6351(9) A gamma = 103.692(2) deg.

Volume	831.18(9) A^3
Z, Calculated density	2, 1.482 Mg/m^3
Absorption coefficient	0.375 mm^-1
F(000)	386
Crystal size	0.50 x 0.40 x 0.05 mm
Diffractometer	Nonius KappaCCD
Theta range for data collection	3.52 to 25.02 deg.
Limiting indices	-6<=h<=7, -13<=k<=13, -14<=l<=14
Reflections collected / unique	6439 / 2898 [R(int) = 0.0384]
Completeness to theta = 25.02	99.2 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2898 / 21 / 231
Goodness-of-fit on F^2	1.103
Final R indices [I>2sigma(I)]	R1 = 0.0644, wR2 = 0.1822
R indices (all data)	R1 = 0.0855, wR2 = 0.1948
Largest diff. peak and hole	0.651 and -1.036 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for **2a.**
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)	
C(1)	3232(7)	3880(3)	758(3)	30(1)	
N(2)	1365(5)	4333(3)	1238(2)	29(1)	
S(2)	1571(2)	5773(1)	1604(1)	29(1)	
O(21)	3121(5)	6389(2)	937(2)	35(1)	
O(22)	-756(5)	5918(2)	1588(2)	34(1)	
C(21)	2935(7)	6125(3)	2945(3)	30(1)	
C(22)	1569(7)	5942(4)	3767(3)	38(1)	
C(23)	2649(7)	6219(4)	4826(3)	41(1)	
C(24)	5047(7)	6681(4)	5057(3)	38(1)	
C(25)	6349(8)	6862(4)	4215(3)	47(1)	
C(26)	5315(7)	6581(4)	3152(3)	38(1)	
C(27)	6188(8)	6982(5)	6205(3)	55(1)	
C(3)	-173(6)	3395(3)	1648(3)	29(1)	
O(3)	-1502(4)	3518(2)	2296(2)	35(1)	
N(4)	181(5)	2354(3)	1155(2)	30(1)	
C(4A)	20(7)	1254(3)	1573(3)	31(1)	
C(5)	-1601(7)	711(3)	2192(3)	38(1)	
C(6)	-1379(8)	-388(4)	2498(4)	46(1)	
C(7)	356(8)	-902(4)	2178(4)	47(1)	
C(8)	1974(8)	-339(4)	1560(3)	41(1)	
C(8A)	1794(7)	754(3)	1251(3)	32(1)	
C(9)	3347(7)	1587(3)	624(3)	37(1)	
C(9A)	2010(7)	2554(3)	437(3)	33(1)	
C(1C)	4290(20)	9730(20)	4344(10)	141(7)	s.o.f.= 0.50
Cl(1)	1892(9)	9173(7)	4948(4)	160(2)	s.o.f.= 0.50
Cl(2)	6661(9)	10367(7)	5285(5)	153(2)	s.o.f.= 0.50

Table 3. Bond lengths [A] and angles [deg] for **2a.**

C(1)-N(2)	1.486(4)
C(1)-C(9A)	1.522(5)
N(2)-C(3)	1.424(5)
N(2)-S(2)	1.648(3)
S(2)-O(21)	1.428(3)
S(2)-O(22)	1.431(3)
S(2)-C(21)	1.766(4)
C(21)-C(26)	1.376(6)
C(21)-C(22)	1.384(5)
C(22)-C(23)	1.394(5)
C(23)-C(24)	1.389(6)
C(24)-C(25)	1.381(6)
C(24)-C(27)	1.507(5)
C(25)-C(26)	1.391(6)
C(3)-O(3)	1.212(4)
C(3)-N(4)	1.363(5)
N(4)-C(4A)	1.417(4)
N(4)-C(9A)	1.475(5)
C(4A)-C(5)	1.380(5)
C(4A)-C(8A)	1.390(5)
C(5)-C(6)	1.400(5)
C(6)-C(7)	1.378(6)
C(7)-C(8)	1.387(6)
C(8)-C(8A)	1.387(5)
C(8A)-C(9)	1.516(5)
C(9)-C(9A)	1.543(5)
C(1C)-Cl(1)	1.709(10)
C(1C)-Cl(2)	1.711(10)

N(2)-C(1)-C(9A)	100.9(3)
C(3)-N(2)-C(1)	110.6(3)
C(3)-N(2)-S(2)	123.3(2)
C(1)-N(2)-S(2)	123.2(2)
O(21)-S(2)-O(22)	120.48(15)
O(21)-S(2)-N(2)	105.05(15)
O(22)-S(2)-N(2)	107.18(16)
O(21)-S(2)-C(21)	108.45(17)
O(22)-S(2)-C(21)	108.21(17)
N(2)-S(2)-C(21)	106.67(15)
C(26)-C(21)-C(22)	121.5(4)
C(26)-C(21)-S(2)	119.7(3)
C(22)-C(21)-S(2)	118.9(3)
C(21)-C(22)-C(23)	118.8(4)
C(24)-C(23)-C(22)	120.9(4)
C(25)-C(24)-C(23)	118.6(4)
C(25)-C(24)-C(27)	121.1(4)
C(23)-C(24)-C(27)	120.3(4)
C(24)-C(25)-C(26)	121.6(4)
C(21)-C(26)-C(25)	118.6(4)
O(3)-C(3)-N(4)	128.3(3)
O(3)-C(3)-N(2)	126.5(3)
N(4)-C(3)-N(2)	105.2(3)
C(3)-N(4)-C(4A)	127.8(3)
C(3)-N(4)-C(9A)	113.2(3)
C(4A)-N(4)-C(9A)	111.1(3)
C(5)-C(4A)-C(8A)	123.0(3)
C(5)-C(4A)-N(4)	128.0(4)
C(8A)-C(4A)-N(4)	109.0(3)
C(4A)-C(5)-C(6)	116.6(4)
C(7)-C(6)-C(5)	121.2(4)

C(6)-C(7)-C(8)	121.2(4)
C(7)-C(8)-C(8A)	118.6(4)
C(8)-C(8A)-C(4A)	119.3(4)
C(8)-C(8A)-C(9)	130.1(4)
C(4A)-C(8A)-C(9)	110.5(3)
C(8A)-C(9)-C(9A)	103.6(3)
N(4)-C(9A)-C(1)	103.1(3)
N(4)-C(9A)-C(9)	104.3(3)
C(1)-C(9A)-C(9)	120.0(3)
Cl(1)-C(1C)-Cl(2)	110.6(8)

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for **2a**.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	27(2)	35(2)	31(2)	8(2)	8(2)	7(2)
N(2)	24(2)	32(2)	31(2)	9(1)	7(1)	4(1)
S(2)	29(1)	31(1)	28(1)	10(1)	5(1)	7(1)
O(21)	40(2)	35(1)	31(1)	14(1)	12(1)	4(1)
O(22)	33(2)	42(2)	32(1)	10(1)	4(1)	14(1)
C(21)	29(2)	33(2)	30(2)	8(2)	6(2)	7(2)
C(22)	27(2)	50(2)	34(2)	12(2)	6(2)	2(2)
C(23)	34(2)	59(3)	29(2)	14(2)	8(2)	6(2)
C(24)	34(2)	51(2)	29(2)	5(2)	3(2)	11(2)
C(25)	25(2)	67(3)	45(2)	2(2)	3(2)	9(2)
C(26)	26(2)	49(2)	37(2)	4(2)	9(2)	5(2)
C(27)	41(3)	84(3)	36(2)	4(2)	-1(2)	15(2)
C(3)	23(2)	34(2)	31(2)	10(2)	1(2)	4(2)
O(3)	26(2)	42(2)	42(2)	15(1)	14(1)	7(1)
N(4)	25(2)	30(2)	36(2)	12(1)	6(1)	3(1)
C(4A)	28(2)	30(2)	32(2)	7(2)	-2(2)	2(2)
C(5)	32(2)	38(2)	43(2)	14(2)	6(2)	3(2)
C(6)	46(3)	40(2)	51(3)	19(2)	11(2)	1(2)
C(7)	56(3)	30(2)	54(3)	15(2)	4(2)	5(2)
C(8)	39(2)	33(2)	46(2)	3(2)	-2(2)	8(2)
C(8A)	30(2)	33(2)	30(2)	4(2)	-1(2)	3(2)
C(9)	36(2)	38(2)	40(2)	7(2)	9(2)	11(2)
C(9A)	29(2)	37(2)	32(2)	8(2)	7(2)	5(2)
Cl(1)	106(4)	264(7)	84(3)	48(3)	18(3)	-16(4)
Cl(2)	86(4)	233(7)	108(4)	-22(4)	-21(3)	11(4)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for **2a.**

	x	y	z	U(eq)	
H(1A)	4632	3995	1289	36	
H(1B)	3682	4274	127	36	
H(22)	-74	5632	3613	45	
H(23)	1731	6090	5396	49	
H(25)	7989	7186	4365	56	
H(26)	6234	6702	2580	45	
H(27A)	5170	6531	6664	82	s.o.f.= 0.50
H(27B)	6449	7846	6439	82	s.o.f.= 0.50
H(27C)	7687	6764	6260	82	s.o.f.= 0.50
H(27D)	7701	7563	6244	82	s.o.f.= 0.50
H(27E)	6421	6248	6469	82	s.o.f.= 0.50
H(27F)	5184	7330	6649	82	s.o.f.= 0.50
H(5)	-2806	1066	2401	45	
H(6)	-2445	-787	2933	55	
H(7)	446	-1657	2386	57	
H(8)	3179	-694	1352	49	
H(9A)	3553	1152	-67	44	
H(9B)	4900	1950	1043	44	
H(9A1)	1269	2416	-326	39	
H(1C1)	3970	10345	3902	169	s.o.f.= 0.50
H(1C2)	4631	9075	3863	169	s.o.f.= 0.50

Table 6. Torsion angles [deg] for **2a**.

C(9A)-C(1)-N(2)-C(3)	26.7(3)
C(9A)-C(1)-N(2)-S(2)	-172.3(2)
C(3)-N(2)-S(2)-O(21)	-174.7(3)
C(1)-N(2)-S(2)-O(21)	26.6(3)
C(3)-N(2)-S(2)-O(22)	-45.5(3)
C(1)-N(2)-S(2)-O(22)	155.9(2)
C(3)-N(2)-S(2)-C(21)	70.3(3)
C(1)-N(2)-S(2)-C(21)	-88.4(3)
O(21)-S(2)-C(21)-C(26)	-18.6(4)
O(22)-S(2)-C(21)-C(26)	-150.9(3)
N(2)-S(2)-C(21)-C(26)	94.1(3)
O(21)-S(2)-C(21)-C(22)	160.9(3)
O(22)-S(2)-C(21)-C(22)	28.6(3)
N(2)-S(2)-C(21)-C(22)	-86.4(3)
C(26)-C(21)-C(22)-C(23)	-0.5(6)
S(2)-C(21)-C(22)-C(23)	180.0(3)
C(21)-C(22)-C(23)-C(24)	0.5(6)
C(22)-C(23)-C(24)-C(25)	0.0(6)
C(22)-C(23)-C(24)-C(27)	179.7(4)
C(23)-C(24)-C(25)-C(26)	-0.7(6)
C(27)-C(24)-C(25)-C(26)	179.6(4)
C(22)-C(21)-C(26)-C(25)	-0.1(6)
S(2)-C(21)-C(26)-C(25)	179.4(3)
C(24)-C(25)-C(26)-C(21)	0.7(6)
C(1)-N(2)-C(3)-O(3)	161.2(3)
S(2)-N(2)-C(3)-O(3)	0.2(5)
C(1)-N(2)-C(3)-N(4)	-18.8(4)
S(2)-N(2)-C(3)-N(4)	-179.8(2)
O(3)-C(3)-N(4)-C(4A)	-32.1(6)
N(2)-C(3)-N(4)-C(4A)	147.9(3)
O(3)-C(3)-N(4)-C(9A)	-177.9(3)
N(2)-C(3)-N(4)-C(9A)	2.2(4)
C(3)-N(4)-C(4A)-C(5)	39.7(6)
C(9A)-N(4)-C(4A)-C(5)	-173.9(4)
C(3)-N(4)-C(4A)-C(8A)	-140.9(4)
C(9A)-N(4)-C(4A)-C(8A)	5.4(4)
C(8A)-C(4A)-C(5)-C(6)	0.3(6)
N(4)-C(4A)-C(5)-C(6)	179.6(4)
C(4A)-C(5)-C(6)-C(7)	-0.9(6)
C(5)-C(6)-C(7)-C(8)	1.2(7)
C(6)-C(7)-C(8)-C(8A)	-1.0(6)
C(7)-C(8)-C(8A)-C(4A)	0.4(6)
C(7)-C(8)-C(8A)-C(9)	177.2(4)
C(5)-C(4A)-C(8A)-C(8)	-0.1(6)
N(4)-C(4A)-C(8A)-C(8)	-179.5(3)
C(5)-C(4A)-C(8A)-C(9)	-177.5(3)
N(4)-C(4A)-C(8A)-C(9)	3.2(4)
C(8)-C(8A)-C(9)-C(9A)	173.2(4)
C(4A)-C(8A)-C(9)-C(9A)	-9.8(4)
C(3)-N(4)-C(9A)-C(1)	14.2(4)
C(4A)-N(4)-C(9A)-C(1)	-137.3(3)
C(3)-N(4)-C(9A)-C(9)	140.2(3)
C(4A)-N(4)-C(9A)-C(9)	-11.3(4)
N(2)-C(1)-C(9A)-N(4)	-23.2(3)
N(2)-C(1)-C(9A)-C(9)	-138.5(3)
C(8A)-C(9)-C(9A)-N(4)	12.2(4)
C(8A)-C(9)-C(9A)-C(1)	126.8(3)

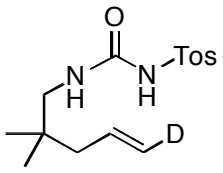
Table 7. Hydrogen bonds for **2a** [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(25)-H(25)...Cl(1)#1	0.95	2.82	3.679(7)	150.5
C(26)-H(26)...O(22)#1	0.95	2.56	3.369(5)	143.5
C(1)-H(1B)...O(21)#2	0.99	2.64	3.233(4)	118.8
C(1)-H(1B)...O(22)#3	0.99	2.60	3.237(4)	122.3

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z #2 -x+1,-y+1,-z #3 -x,-y+1,-z

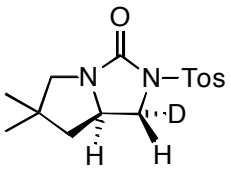
Diamination of deuterated material 3:

Trans-deuterated urea **3** was prepared using the selectively labelled allylic bromide which was obtained through hydrozirconation with the Schwartz reagent followed by subsequent quenching with D_2O as described previously [D. Orain, J.-C. Guillemin, *J. Org. Chem.* **1999**, *64*, 3563]. Urea **3** was then elaborated via a sequence as described above for the unlabelled compound.



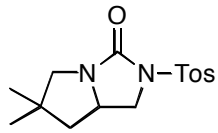
^{1}H nmr (300 MHz, $CDCl_3$): □ = 0.82 (s, 6H), 1.88 (dd, *J* = 1.3, 7.5 Hz, 2H), 2.42 (s, 3H), 3.95 (d, *J* = 6.0 Hz, 2H), 5.00 (dt, *J* = 1.3, 17.0 Hz, 1H), 5.75 (dt, *J* = 7.5, 17.0 Hz, 1H), 6.63 (t, *J* = 6.0 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 9.27 (br s, 1H).
^{13}C nmr (75 MHz, $CDCl_3$): □ = 21.54, 24.67, 34.58. 44.06, 49.67, 117.50 (t, *J* = 24.0 Hz), 126.87, 129.83, 134.14, 136.89, 144.61, 152.34.

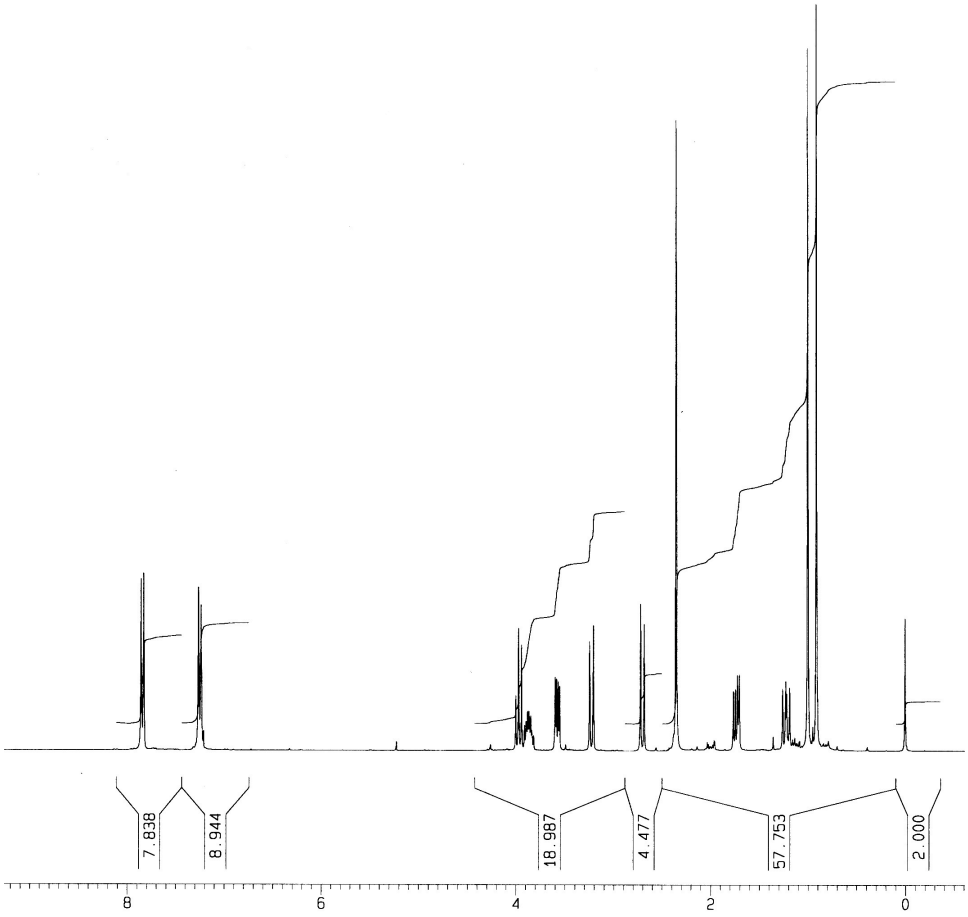
Hexahydro-1-deutero-6,6-dimethyl-2-(p-tolylsulfonyl)pyrrolo-[1,2-e]imidazol-3-one

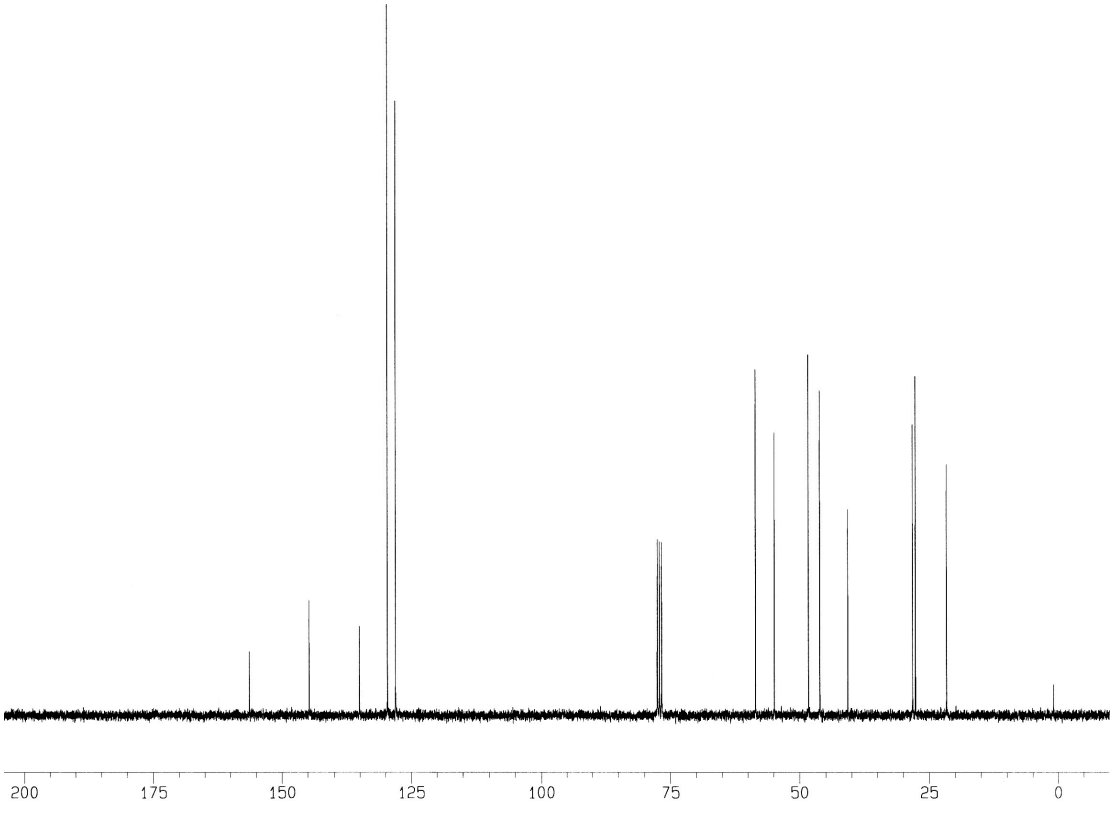


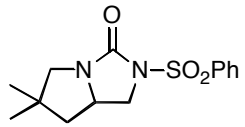
Synthesized according to procedure A.

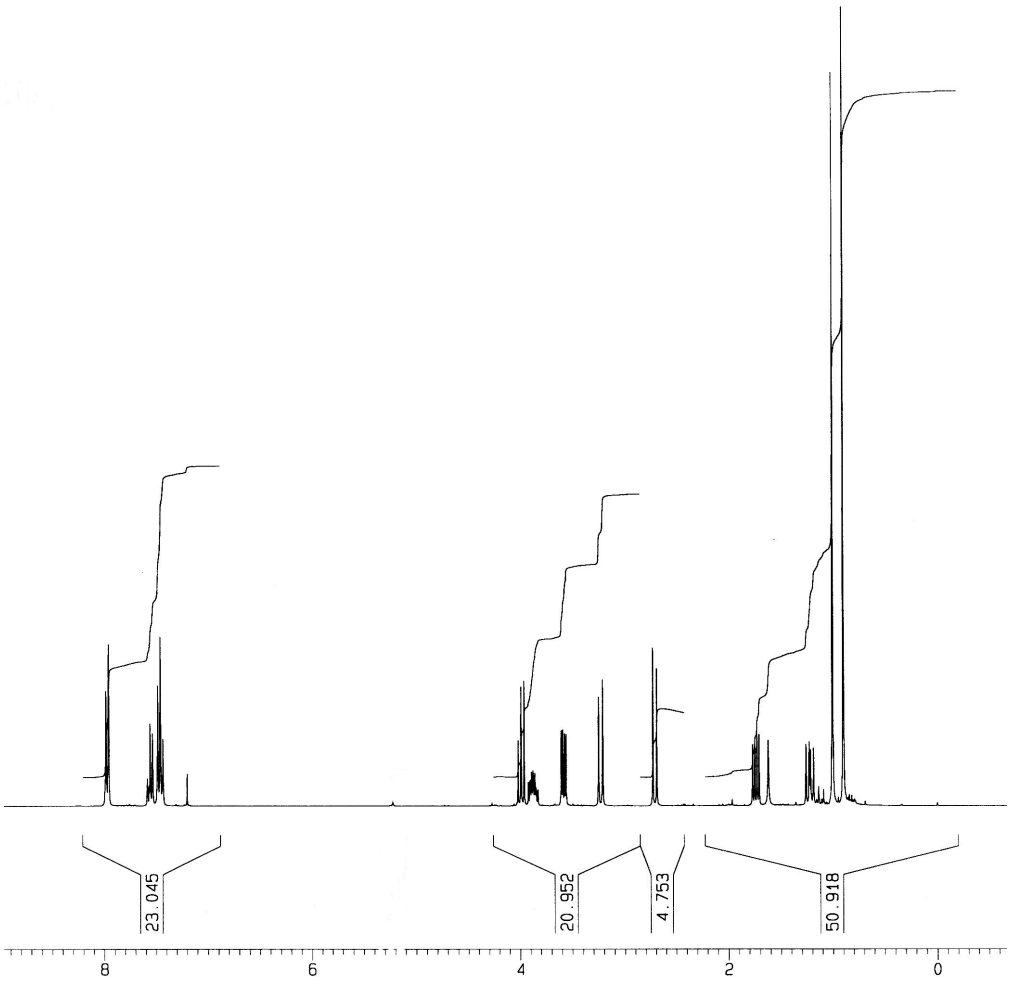
^{1}H nmr (300 MHz, $CDCl_3$): □ = 0.96 (s, 3H), 1.05 (s, 3H), 1.27 (dd, *J* = 12.4 Hz, *J* = 9.2 Hz, 1H), 1.78 (dd, *J* = 12.4 Hz, *J* = 6.1 Hz, 1H), 2.40 (s, 3H), 3.76 (d, *J* = 11.3 Hz, 1H), 3.28 (d, *J* = 11.3 Hz, 1H), 3.92 (ddd, *J* = 5.9, 8.6, 8.8 Hz, 1H), 4.03 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H).

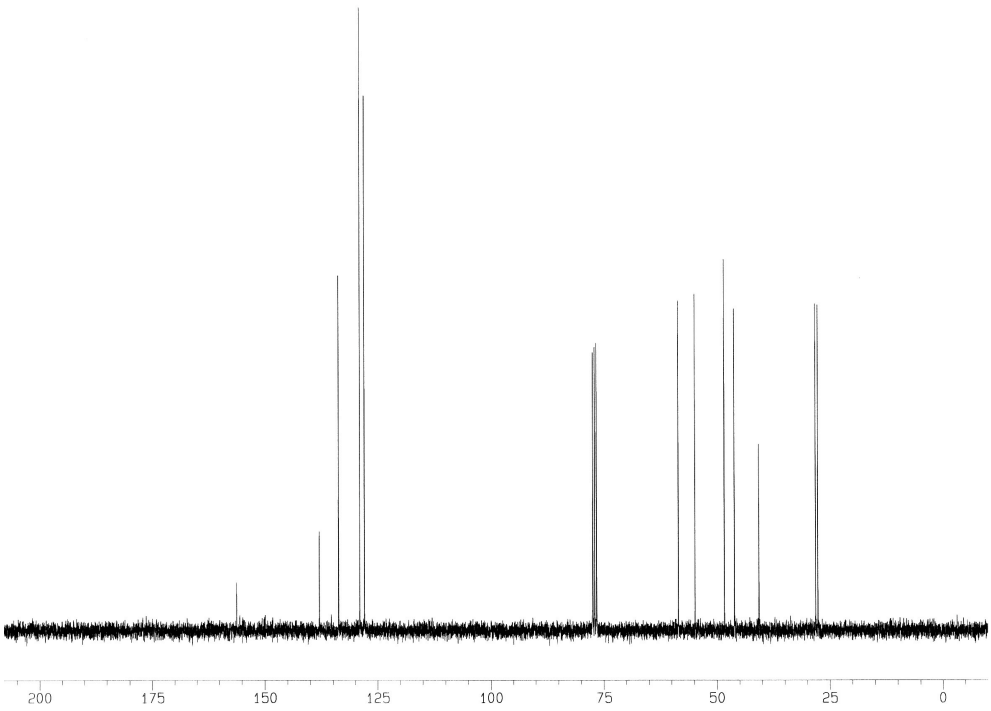

O
N
N–Tos

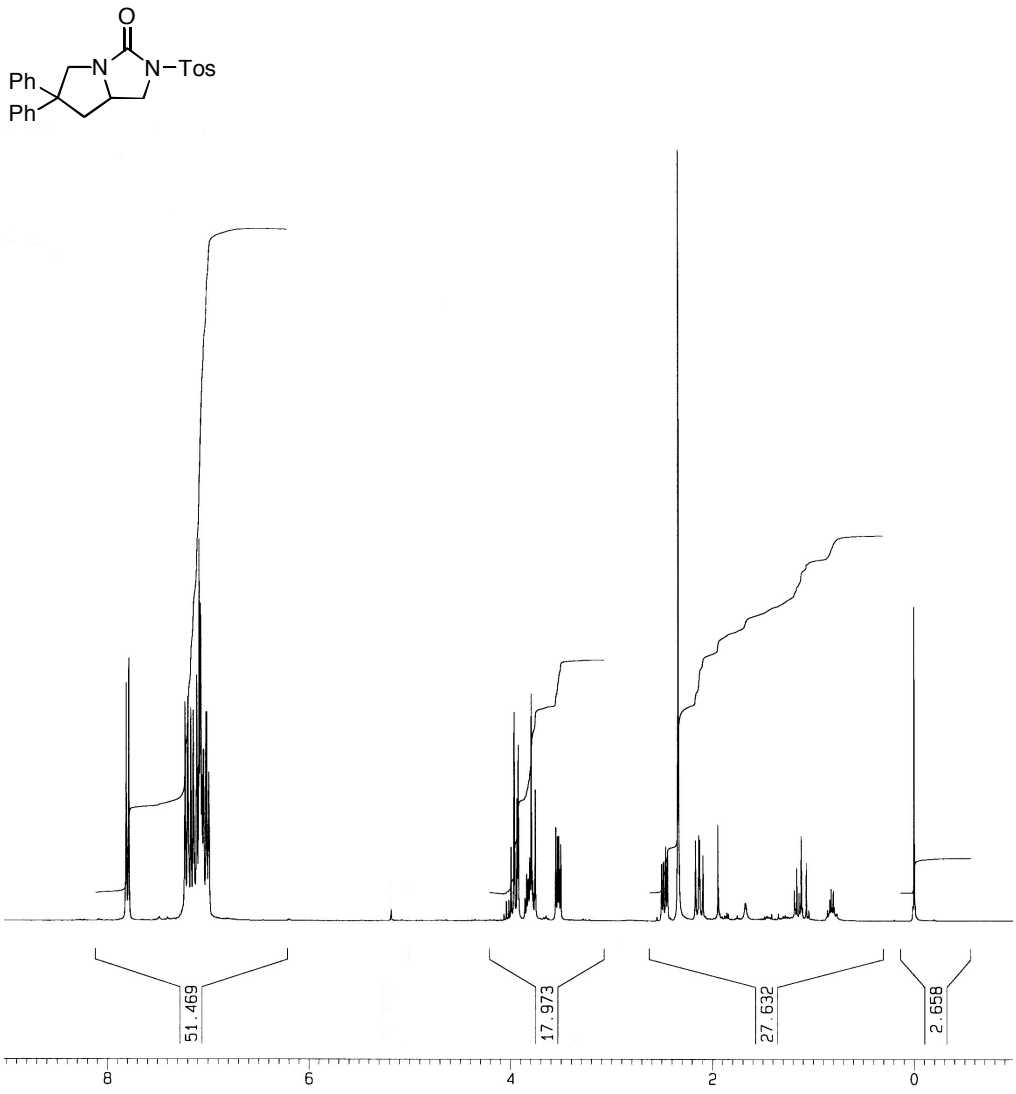

7.838
8.944
18.987
4.477
57.753
2.000
8
6
4
2
0

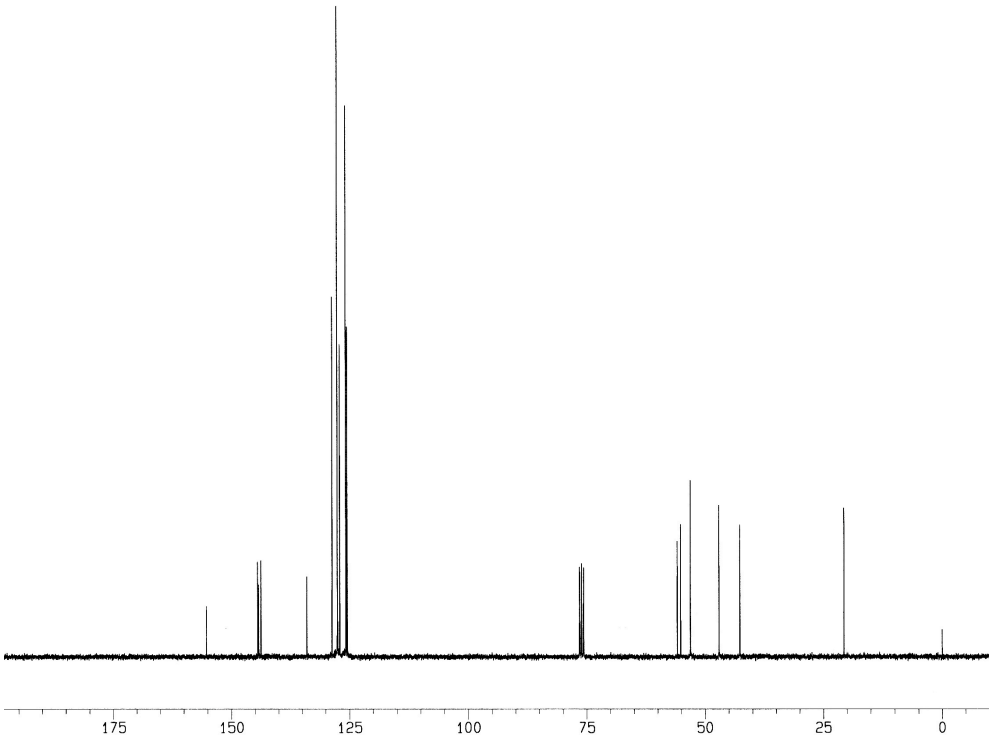

200
175
150
125
100
75
50
25
0

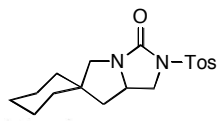

O
N
N–SO2Ph

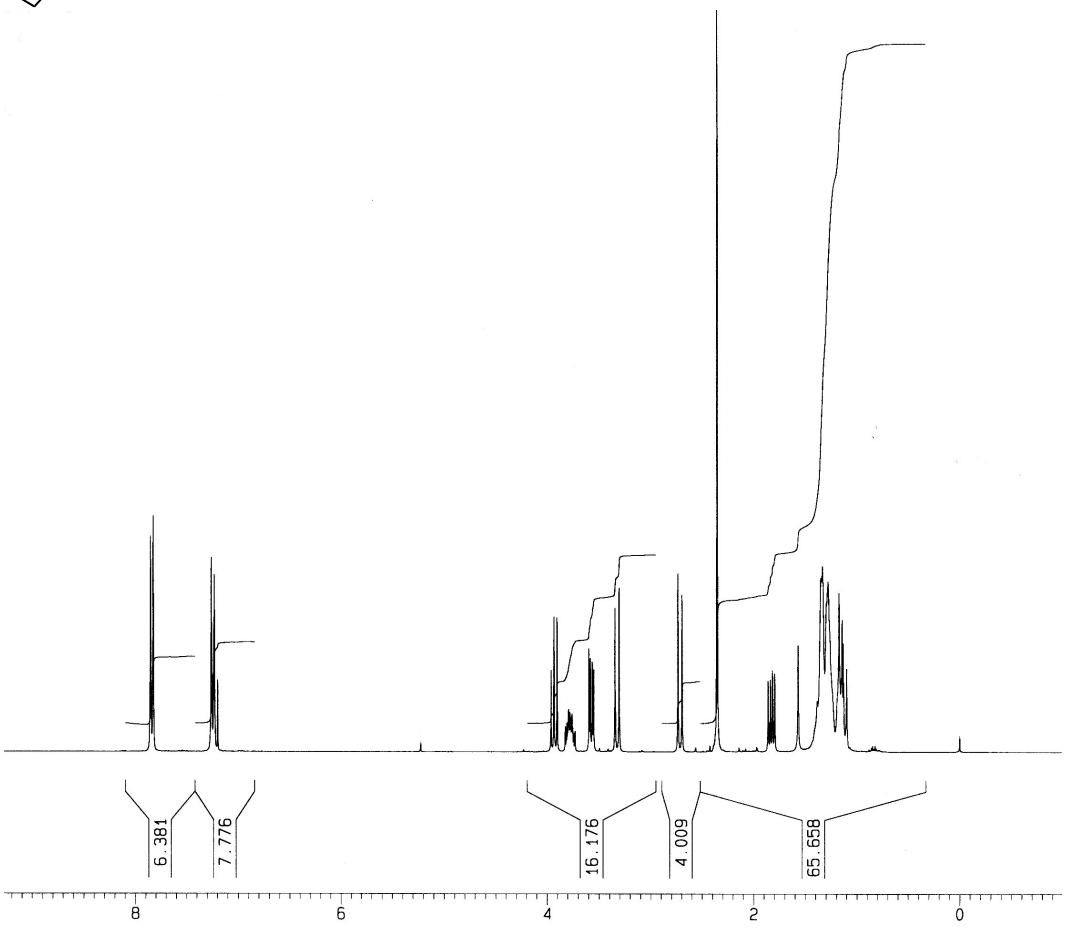

23.045
20.952
4.753
50.918
8
6
4
2
0

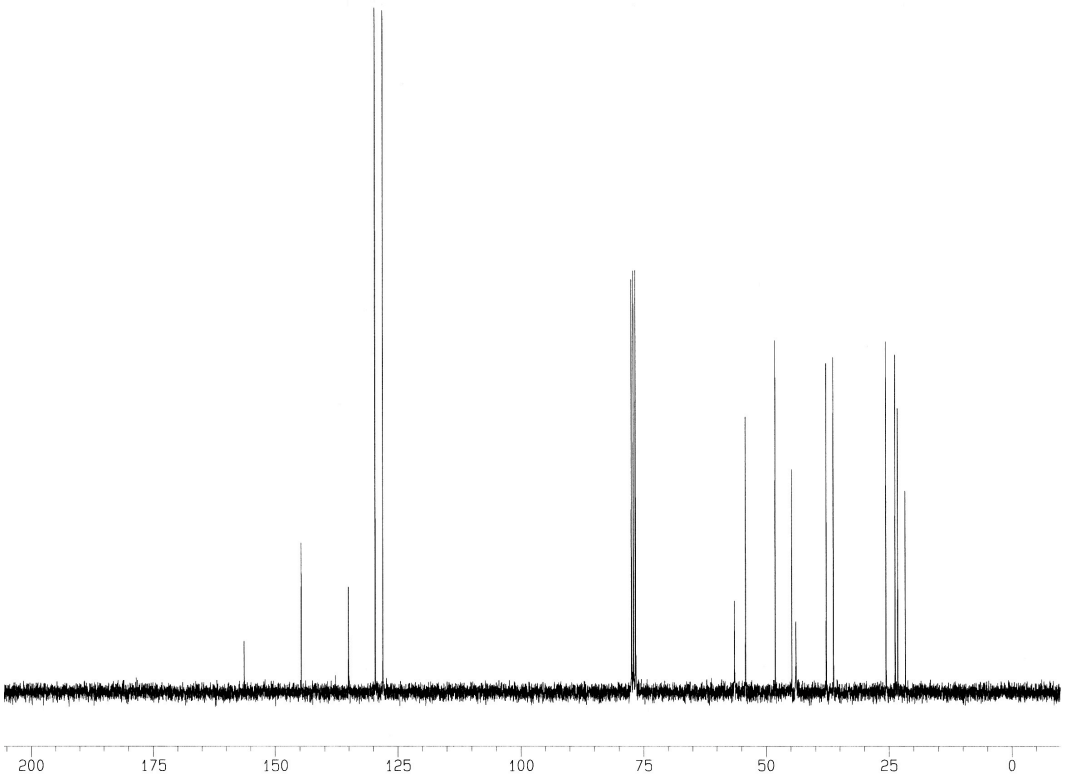

200
175
150
125
100
75
50
25
0

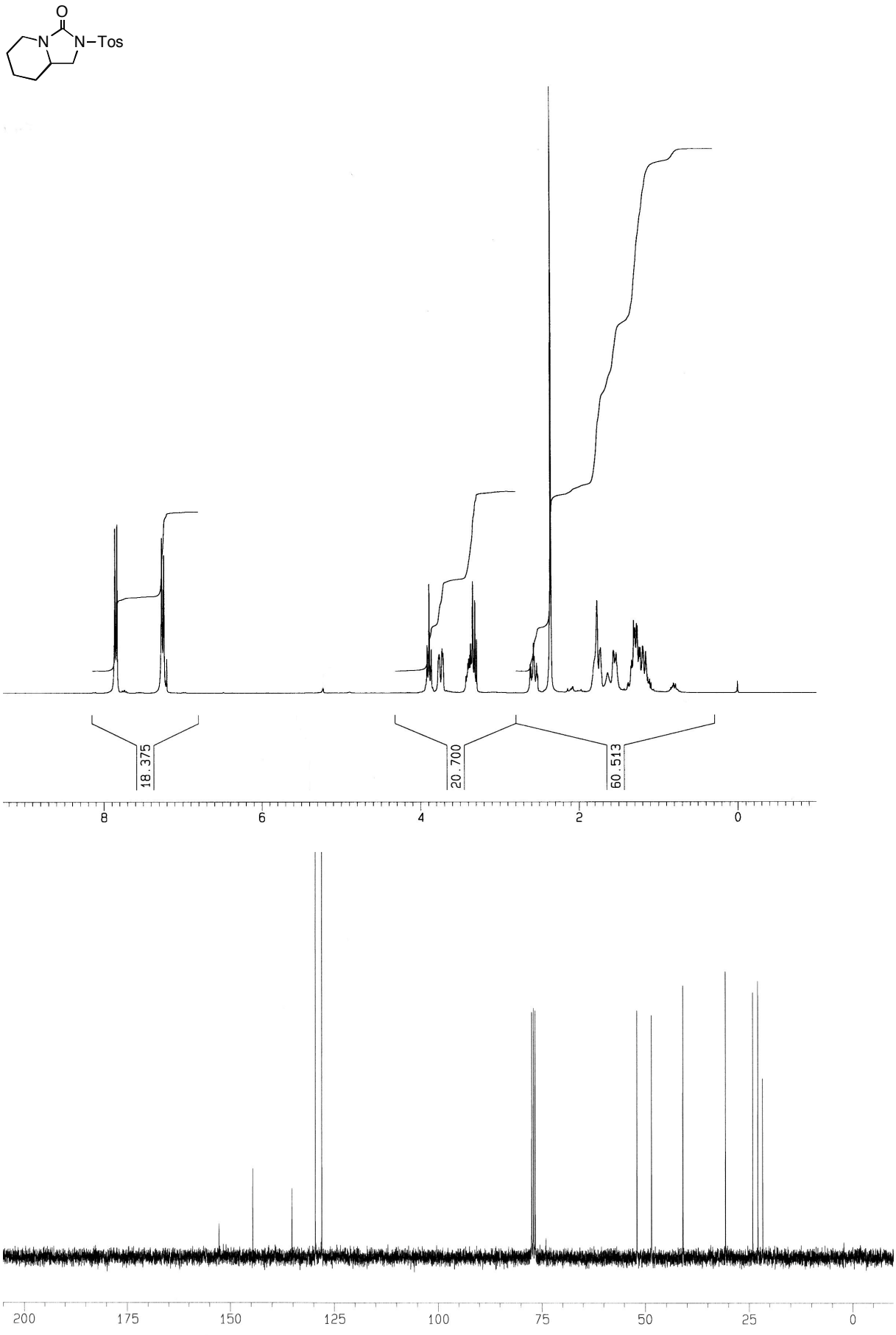

O
N
N−Tos
Ph
Ph
51.469
17.973
27.632
2.658
8
6
4
2
0

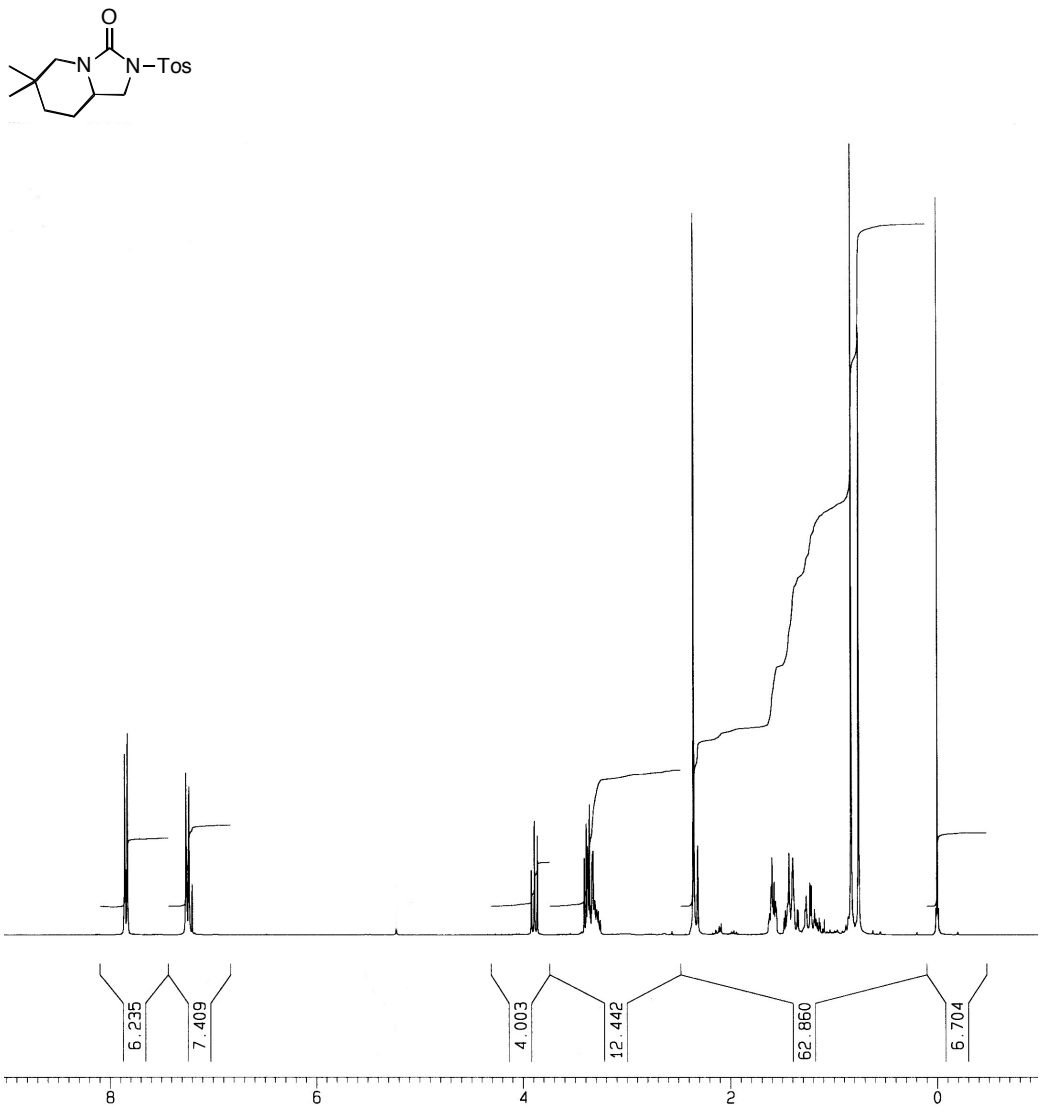

175
150
125
100
75
50
25
0

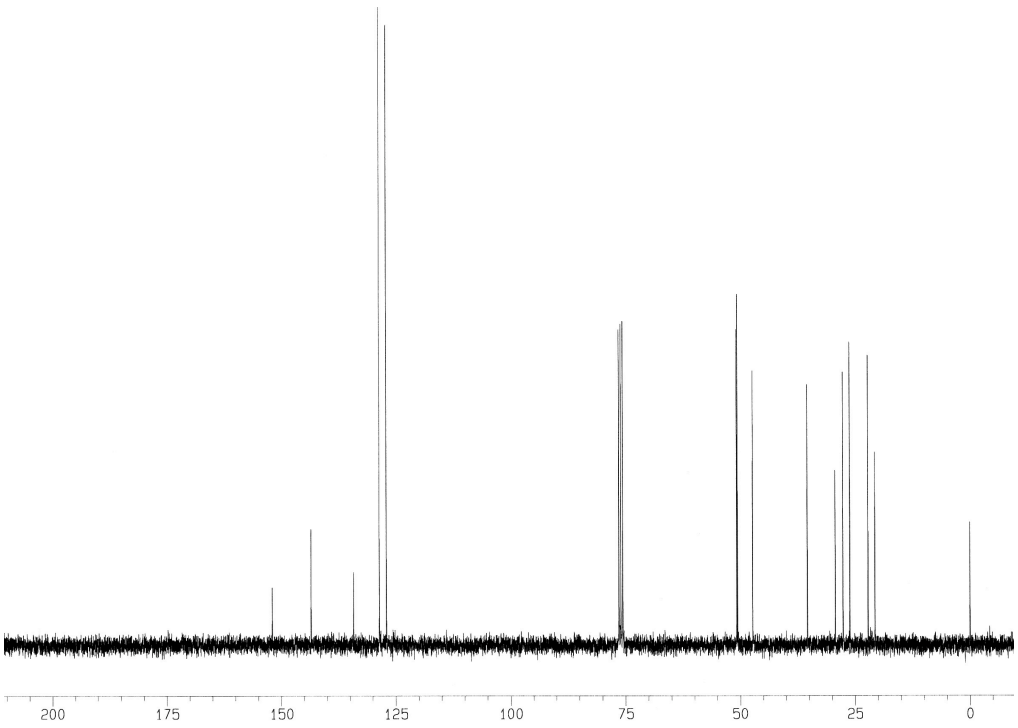

O
N
N–Tos

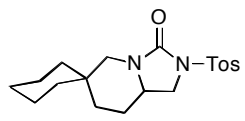

6.381
7.776
16.176
4.009
65.658
8
6
4
2
0

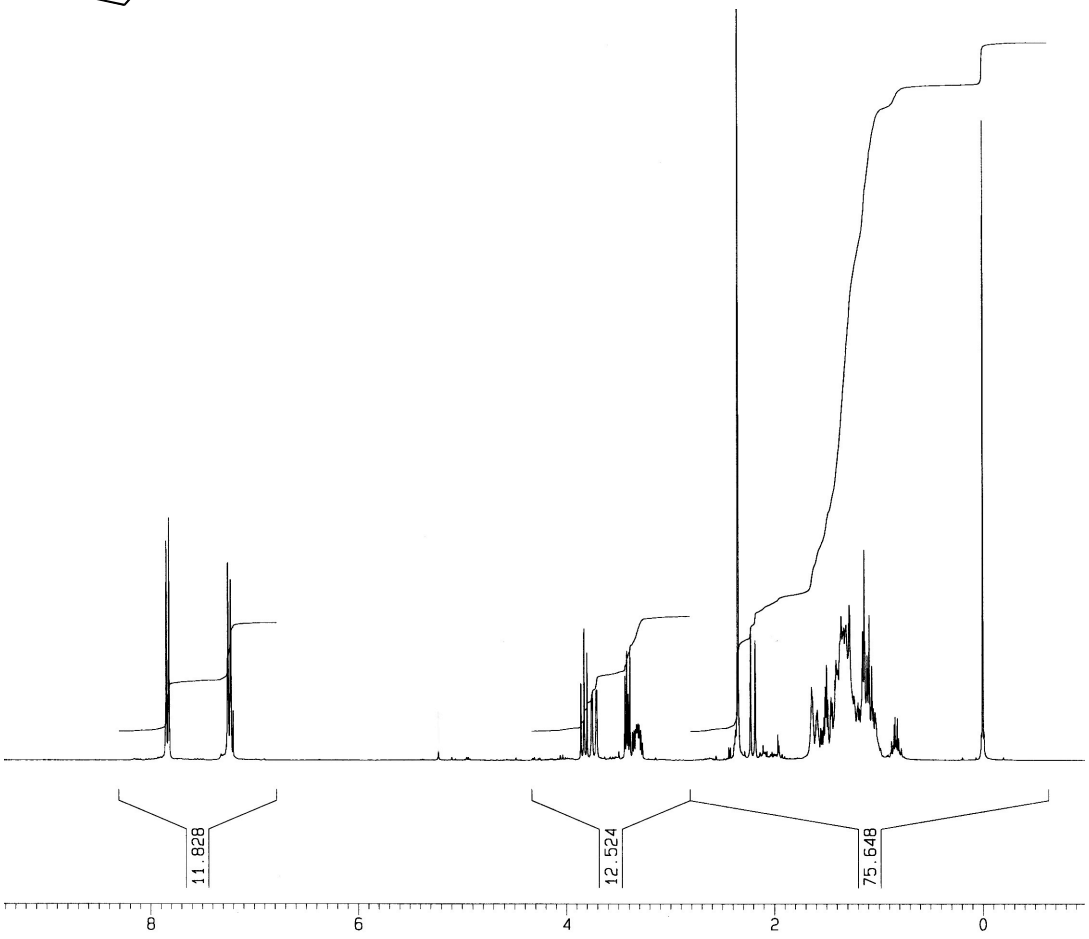

200
175
150
125
100
75
50
25
0

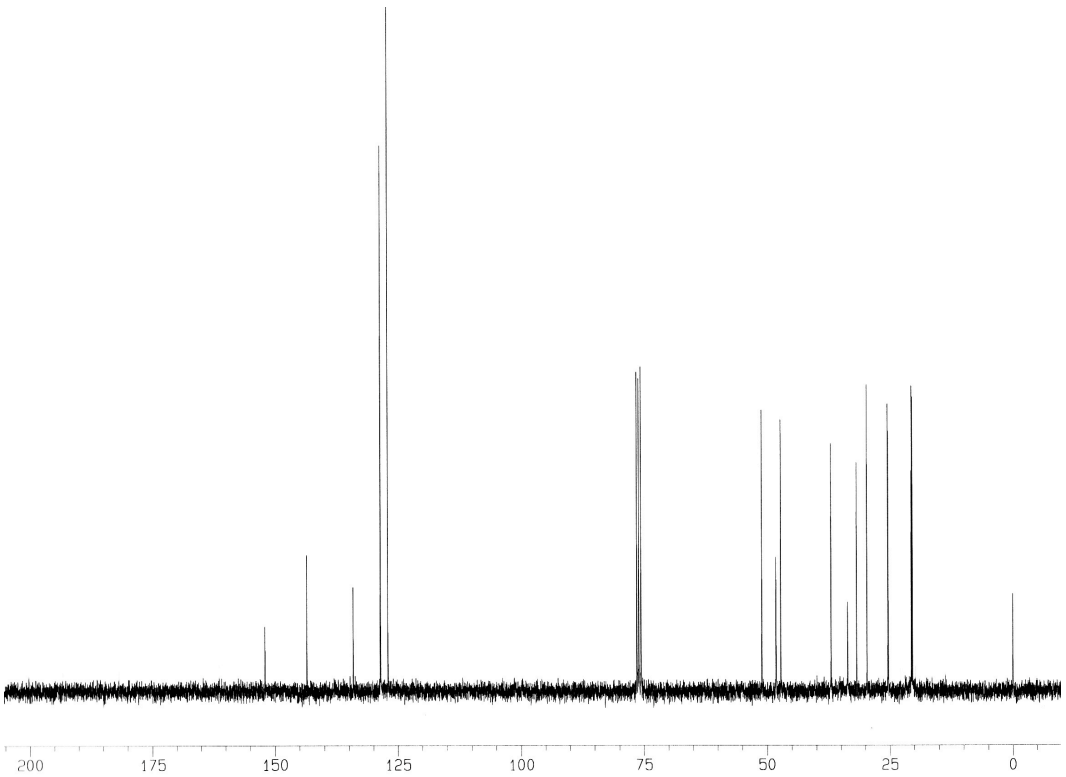

O
N
N–Tos
18.375
20.700
60.513
8
6
4
2
0
200
175
150
125
100
75
50
25
0

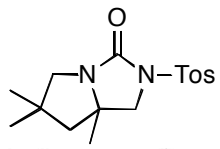

O
N
N–Tos
6.235
7.409
4.003
12.442
62.860
6.704
8
6
4
2
0

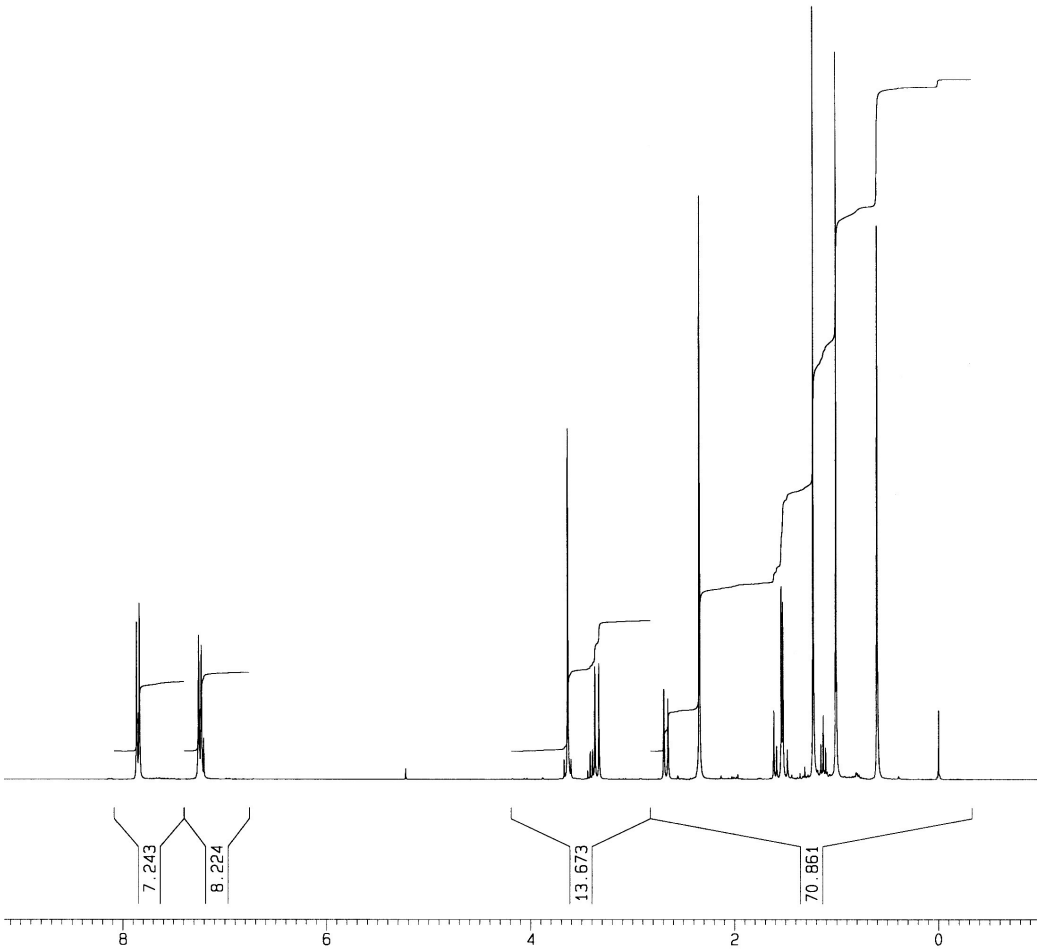

200
175
150
125
100
75
50
25
0

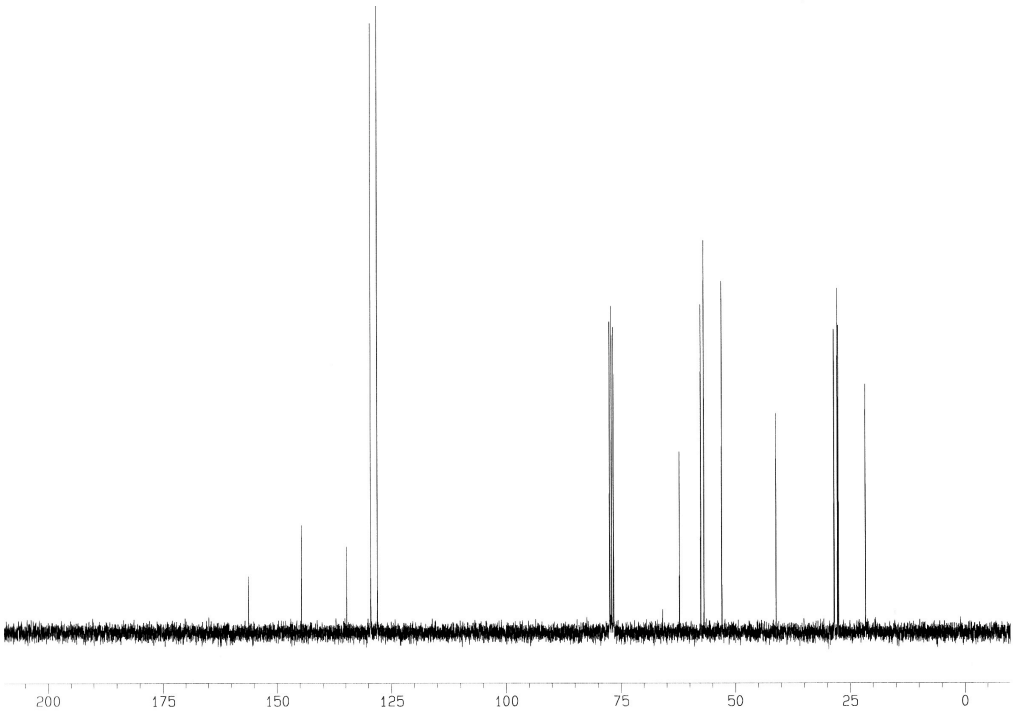

O
N
N–Tos

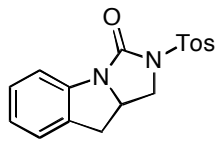

11.828
12.524
75.648
8
6
4
2
0

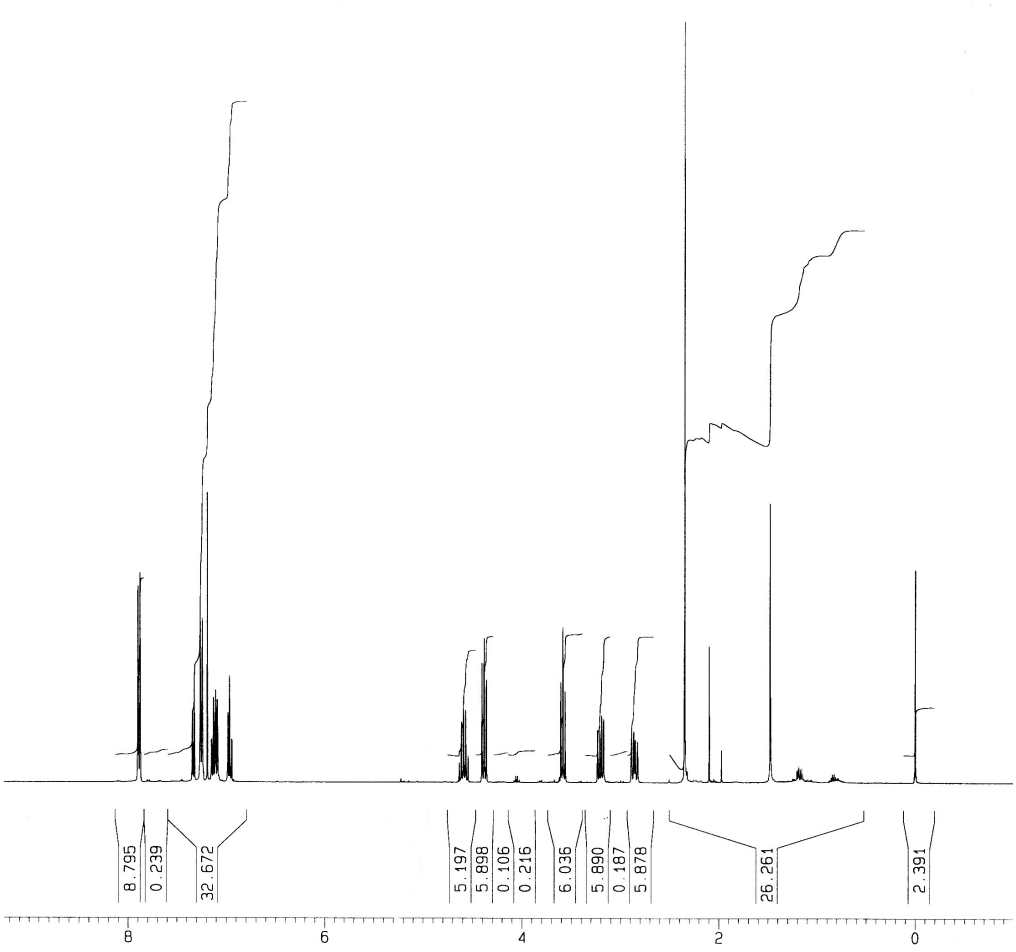

200
175
150
125
100
75
50
25
0

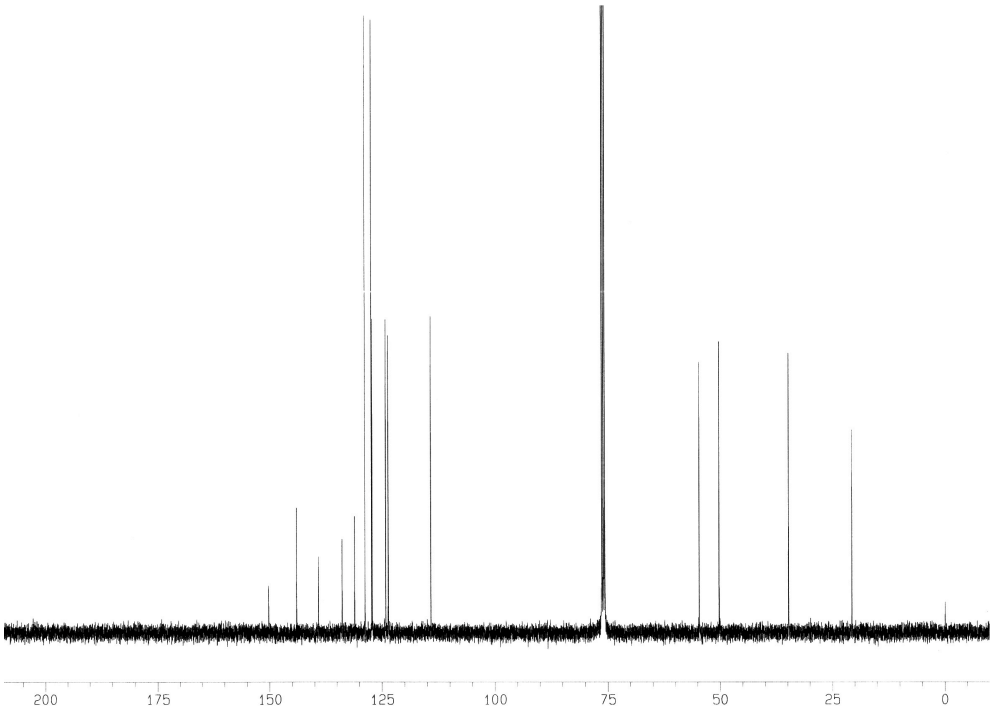

O
N
N–Tos

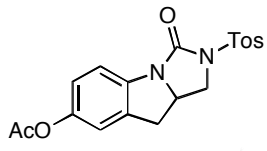

7.243
8.224
13.673
70.861
8
6
4
2
0

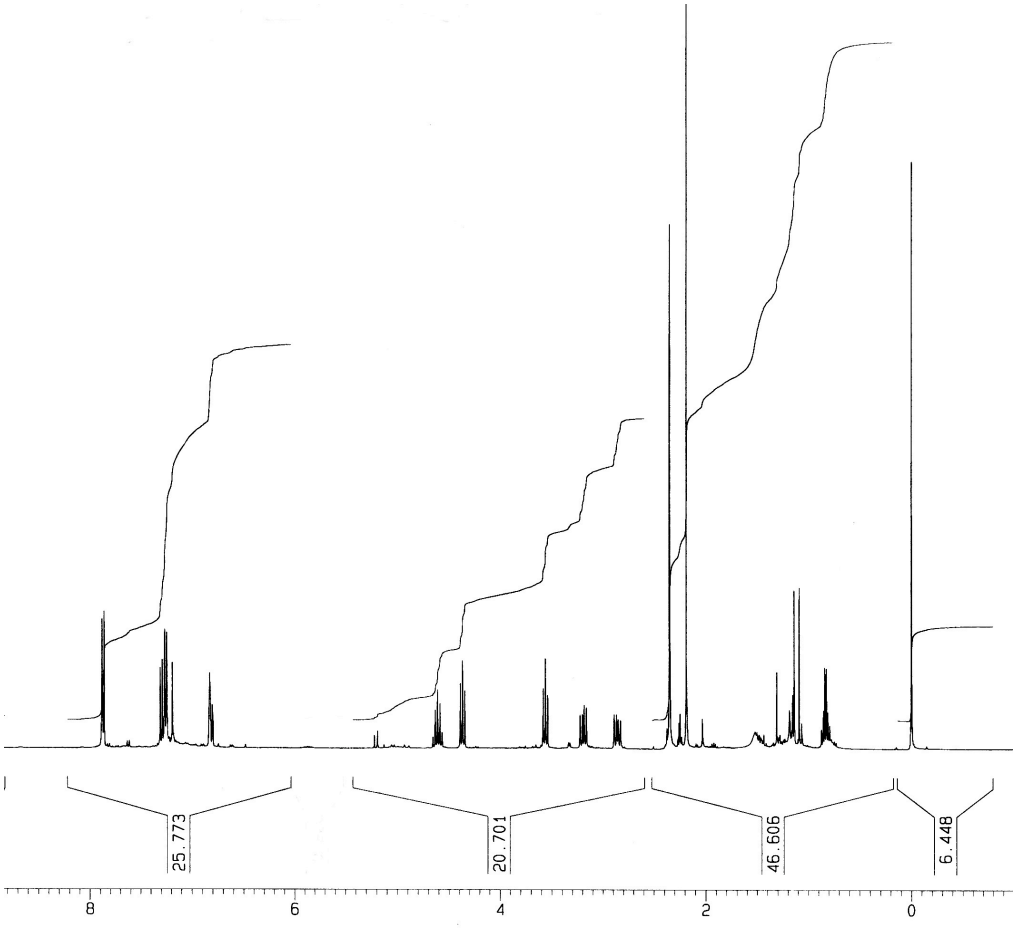

200
175
150
125
100
75
50
25
0

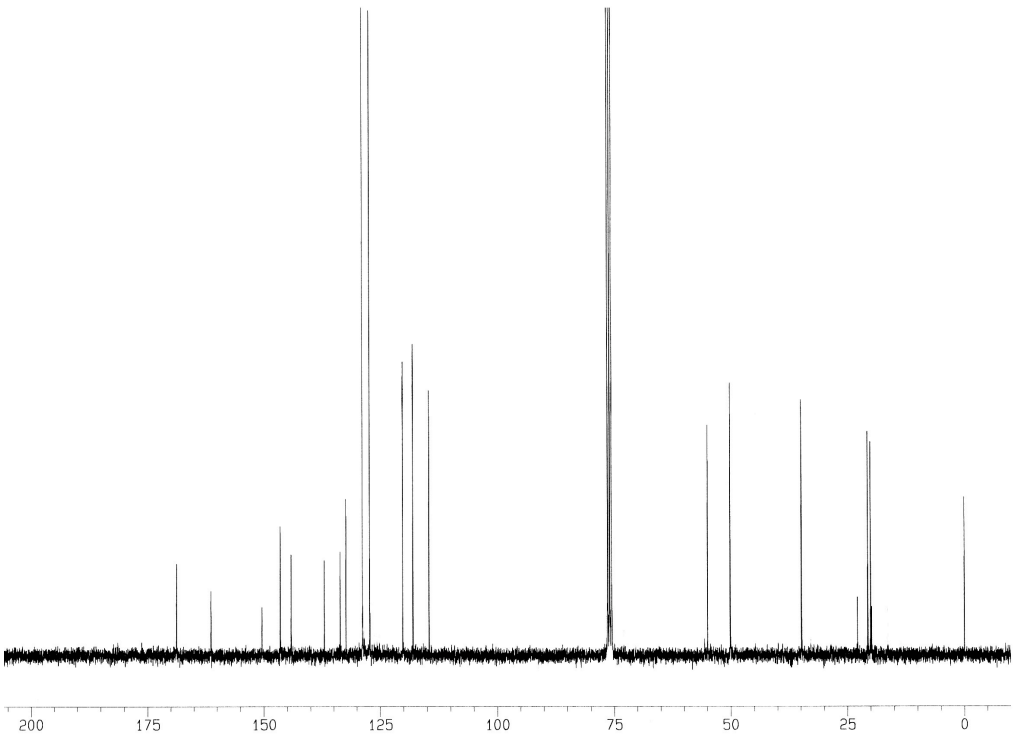

O
N
Tos
N


8.795
0.239
32.672
5.197
5.898
0.106
0.216
6.036
5.890
0.187
5.878
26.261
2.391
8
6
4
2
0


200
175
150
125
100
75
50
25
0


O
N
Tos
N
AcO


25.773
20.701
46.606
6.448
8
6
4
2
0


200
175
150
125
100
75
50
25
0