Electronic Supplementary Information

Synthetic and Computational Investigation of Neighboring Group Participation by Nucleophilic Disulfide Bond

Takuhei Yamamoto[ab]*, Koki Fukuta[a], Yuki Kariya[a], Taiki Matsuura[a], Hiroaki Hagiwara[c], Bunji Uno[d], Yukihiro Esaka[ab]

a. Gifu Pharmaceutical University, 1-25-4, Daigaku-nishi, Gifu 501-1196, Japan
b. United Graduate School of Drug Discovery and Medical Information Science, Gifu University, 1-1 Yanaido, Gifu 501-1194, Japan
c. Department of Chemistry, Faculty of Education, Gifu University, Yanaido 1-1, Gifu 501-1193, Japan
d. Faculty of Pharmacy, Gifu University of Medical Science, 4-3-3 Nijigaoka, Kani, Gifu 509-0923, Japan

E-mail: yamamotot@gifu-pu.ac.jp

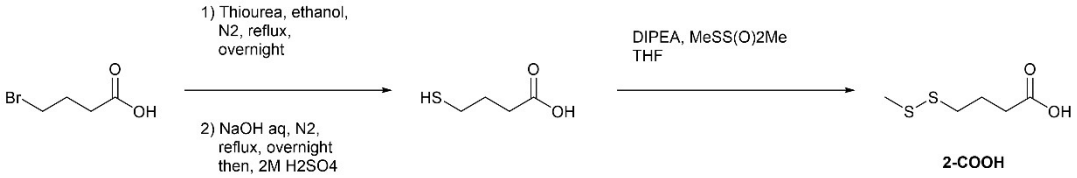
Table of Contents

Experimental Section

All reagents were purchased from Tokyo Chemical Inc. and were used without further purification unless otherwise stated. All solvents and hydrochloric acid were purchased from Nacalai Tesque. Column chromatography was performed using Nacalai Tesque Silica gel 60 (70~230 mesh). All reactions were carried under nitrogen unless otherwise stated. NMR spectra were recorded on a JEOL ECA-400. Chemical shifts were reported as the delta scale in ppm relative to tetramethylsilane (δ = 0.00 ppm) for ^{1}H NMR and $CDCl_3$ (δ = 77.0 ppm) for ^{13}C NMR. IR absorption spectra were recorded on a PerkinElmer FT-IR Frontier MIR spectrometer. All melting points are uncorrected and were recorded on a SANSYO SMP-300 melting point apparatus. X-ray diffraction data were collected by a Rigaku AFC7R Mercury CCD diffractometer using graphite monochromated Mo Kα radiation (λ = 0.71075 Å) operated at 5 kW power (50 kV, 100 mA) at Institute for Molecular Science (IMS), Okazaki, Japan.

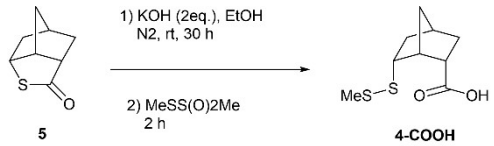
Model compound preparation

4-(methyldisulfanyl)butanoic acid (2-COOH)



4-(methyldisulfanyl)butanoic acid was prepared using a modified procedure reported by Watson *et al*.[1] A solution of 4-bromobutyric acid (2.00 g, 12.0 mmol) and thiourea (1.00 g, 13.1 mmol) in ethanol (30 mL) was refluxed under N_2 overnight. After the ethanol was removed under reduced pressure, 5M NaOH (20 mL) was added to the flask. The solution was bubbled with N_2 for 30 min and refluxed overnight. The reaction mixture was then cooled to 0 ℃, acidified using 2 M aq H_2SO_4, and extracted using CH_2Cl_2 (20 mL × 3). The organic layers were combined and dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude 4-mercaptobutanoic acid was then dissolved in THF (30 mL). After the solution was bubbled with N_2 for 30 min, DIPEA (4.40 mL,25.2 mmol) was added to the solution at 0 ℃, followed by the addition of *S*-methyl methanethiosulfonate (1.14 mL, 12.0 mmol). The mixture was then allowed to warm up to room temperature and stirred overnight. The solvent was removed under reduced pressure. The crude product was purified by silica gel chromatography using a 1:1 mixture of ethyl acetate and *n*-hexane ramped up to 4:1 as eluent to give **2-COOH** as a colorless oil (2.00 g, quantitative yield). ^{1}H NMR (400 MHz, $CDCl_3$ with a few drops of CD_3OD) δ 2.76 (t, *J* = 7.2 Hz, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 2.06 (quint, *J* = 7.2 Hz, 2H)

Synthesis of 6-*endo*-(methyldisulfanyl)bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (4-COOH)



5 **4-COOH**

The procedure for synthesis of 6-*endo*-(methylthio)bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid previously reported[2] was modified and used. KOH (408 mg, 7.27 mmol) was dissolved in 30 mL of ethanol and the solution was bubbled with N_2 for 30 min. Thiolactone **5** (560 mg, 3.64 mmol) was added to the solution at room temperature. After the reaction was stirred for 3 h at room temperature, a white precipitate had formed. *S*-Methyl methanethiosulfonate (0.340 mL, 3.64 mmol) was then added. The precipitate dissolved immediately. After being stirred for 2 h, the solvent was removed under pressure. The residue was acidified with 1 N citric acid and extracted with ethyl acetate (50 mL × 3). The combined organic layer was washed with H_2O (100 mL), dried with $MgSO_4$, filtered, and evaporated to dryness. The crude product was purified by silica gel chromatography using a 1:3 mixture of ethyl acetate and hexane as eluent to give **4-COOH** as a white solid (682 mg, 86%). The product was further purified by recrystallization from a 1:1 mixture of diethyl ether and hexane: mp 124-125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.41 (dddd, J = 12.0, 6.4, 3.6, 1.2 Hz, 1H), 3.05 (br s, 1H), 2.86 (dddd, J = 11.2, 6.8, 4.4, 0.8 Hz, 1H), 2.42 (s, 3H), 2.35 (br s, 1H), 2.15 (ddt, J = 2.8, 4.4, 12.8 Hz, 1H), 1.85 – 1.73 (m, 2H), 1.59 (ddt, J = 1.6, 2.4, 10.4 Hz, 1H). 1.52 (dd, J = 1.2, 10.4 Hz, 1H), 1.09 (ddd, J = 2.4, 6.4, 13.2, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 181.1, 52.8, 44.9, 44.4, 41.2, 37.0, 36.9, 31.2, 22.6; IR (neat) 2963, 1687, 1425, 1309, 1274, 1237, 924, 770, 740, 697 cm^{-1}; Elemental Analysis. Calcd for $C_9H_{14}O_2S_2$: C, 49.51; H, 6.46. Found: C, 49.26: H, 6.38.

General Procedure for synthesis of thiocarbamates

To a solution of carboxylic acid, disulfide (1.0 equiv), and triethylamine (2.2 equiv) in toluene (1.0 M) was added diphenylphosphoryl azide (1.1 equiv) under N_2. The reaction mixture was stirred at room temperature for 30 min and then warmed to 65 °C for 4 h. After the solvent was removed under reduced pressure, a 5:4 mixture of 5 M HCl and dioxane (0.5 M) was added to the mixture and the solution was stirred at room temperature overnight. After the solvent was removed under reduced pressure, ethyl acetate was added to the mixture. The organic layer was washed with saturated $NaHCO_3$ and brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure.

Intermolecular interaction

Synthesis of a thiocarbamate from dimethyl disulfide **1** and bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid was attempted using the general procedure. The corresponding thiocarbamate could not be

obtained based on ^{1}H NMR analysis.

Flexible intramolecular interaction

Synthesis of a thiocarbamate from 4-(methyldisulfanyl)butanoic acid **2-COOH** was attempted using the general procedure. The corresponding thiocarbamate could not be obtained based on ^{1}H NMR analysis.

Phenyl-enforced intramolecular interaction

Synthesis of a thiocarbamate from 2-(methyldisulfanyl)benzoic acid **3-COOH** was attempted using the general procedure. The crude product was purified by preparative thin-layer chromatography using a 1:19 mixture of methanol and chloroform as eluent to give the thiocarbamate **3-S(CO)N** (56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (bs, NH), 7.41 (d, *J* = 6.4, 1H), 7.28 (t, *J* = 6.0 Hz, 1H), 7.17 (d, *J* = 6.4 Hz, 1H), 7.13 (d, *J* = 6.8 Hz, 1H)

Norbornyl-enforced intramolecular interaction

Synthesis of a thiocarbamate from 6-*endo*-(methyldisulfanyl)bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid **4-COOH** was attempted using the general procedure. The crude product was purified by flush chromatography using a mixture of 4:1 EtOAc and *n*-hexane as eluent to give the thiocarbamate **4-S(CO)N** (65%): mp = 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ7.59 (bs, NH), 3.85 (m, 1H), 3.33 (m, 1H), 2.35-2.45 (m, 2H), 2.31 (s, 1H), 2.15 (m, 1H), 1.51- 1.60 (m, 2H), 1.21 (dt, J = 12.8, 3.2 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 165.9, 53.4, 42.1, 39.7 (two overlapped peaks), 39.3, 37.2, 34.9; IR (neat) 3162, 2957, 1630, 1398, 1328, 1292, 1250, 1142, 1129, 1065, 782, 724, 690 cm^{-1}; Elemental Analysis. Calcd for $C_8H_{11}NOS$: C, 56.78; H, 6.55; N, 8.28. Found: C, 56.38: H, 6.49: N, 8.18.

NMR spectra

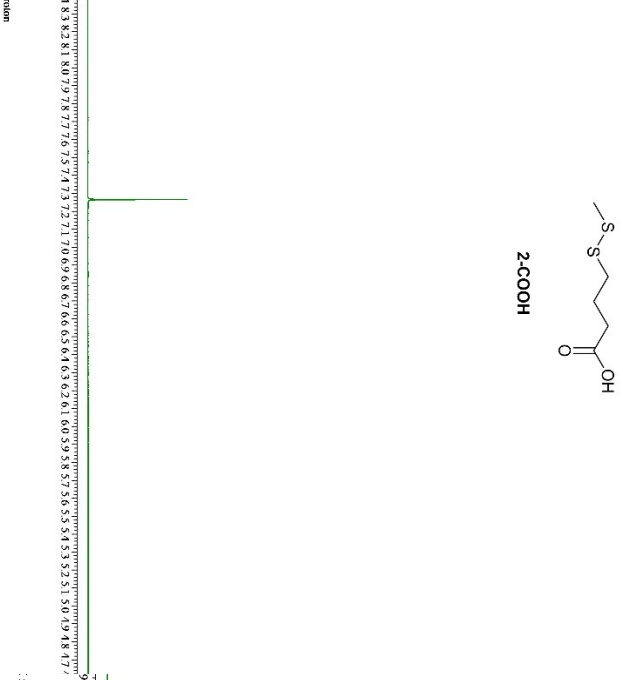


Fig. S1 ^{1}H NMR spectrum of **2-COOH**.

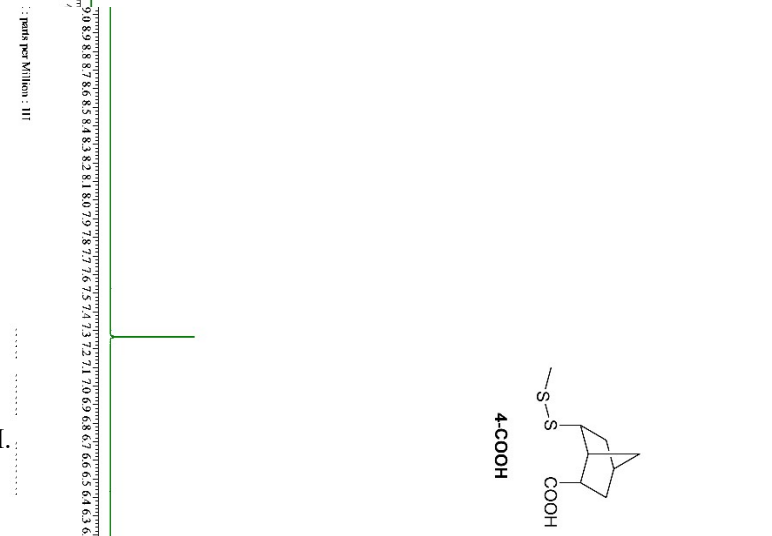


Fig. S2 ^{1}H NMR spectrum of **4-COOH**

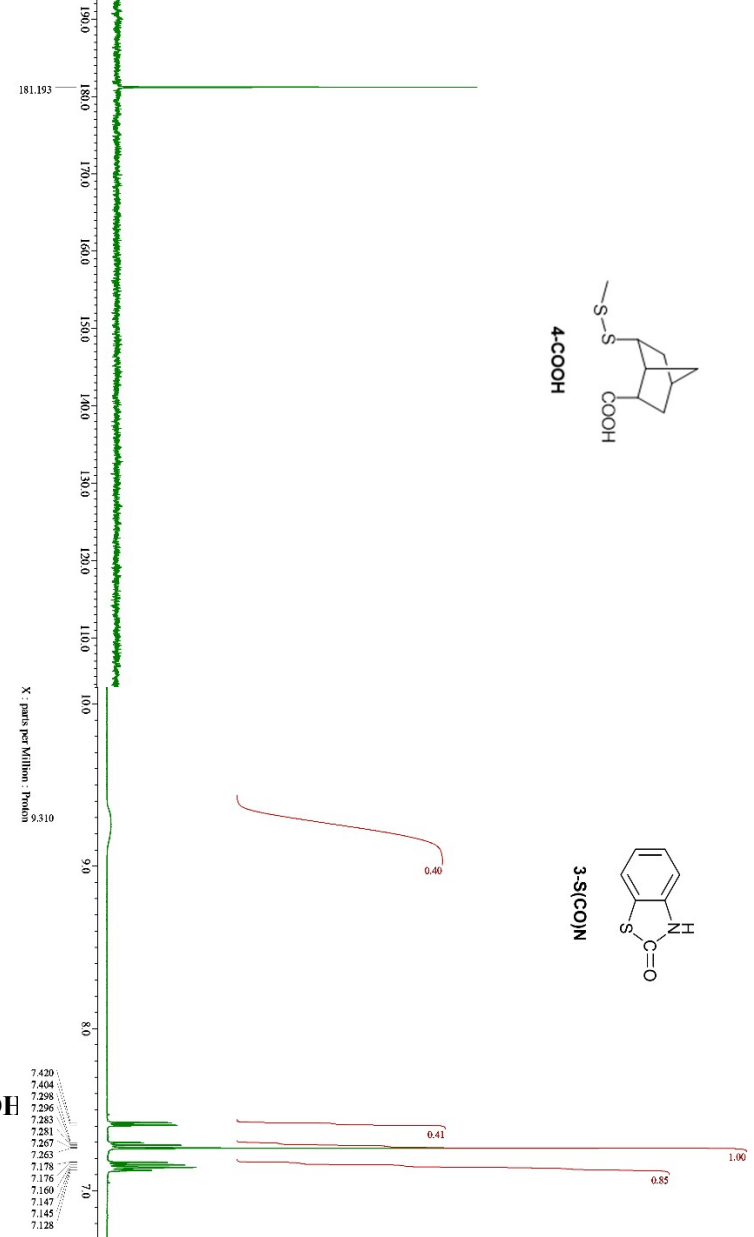


Fig. S3 ^{13}C NMR spectrum of **4-COOH**

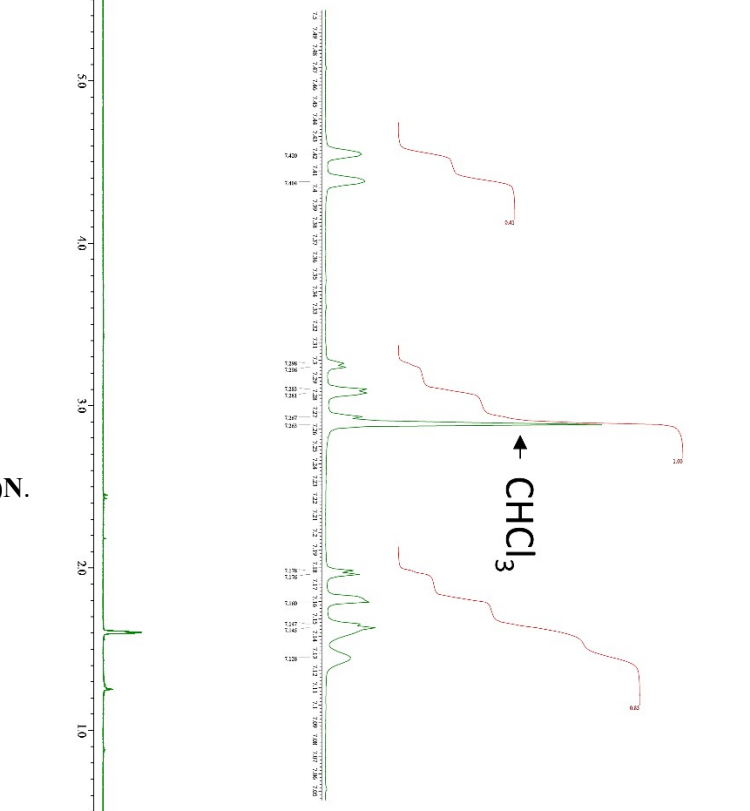


Fig. S4 ^{1}H NMR spectrum of **3-S(CO)N**.

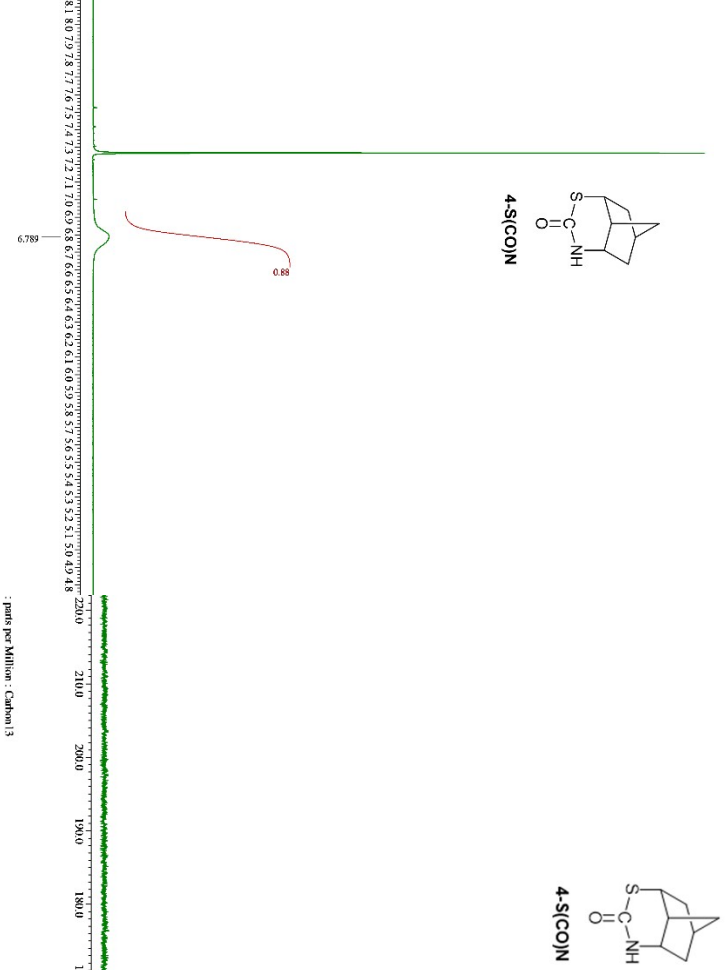


Fig. S5 ^{1}H NMR spectrum of **4-S(CO)N**

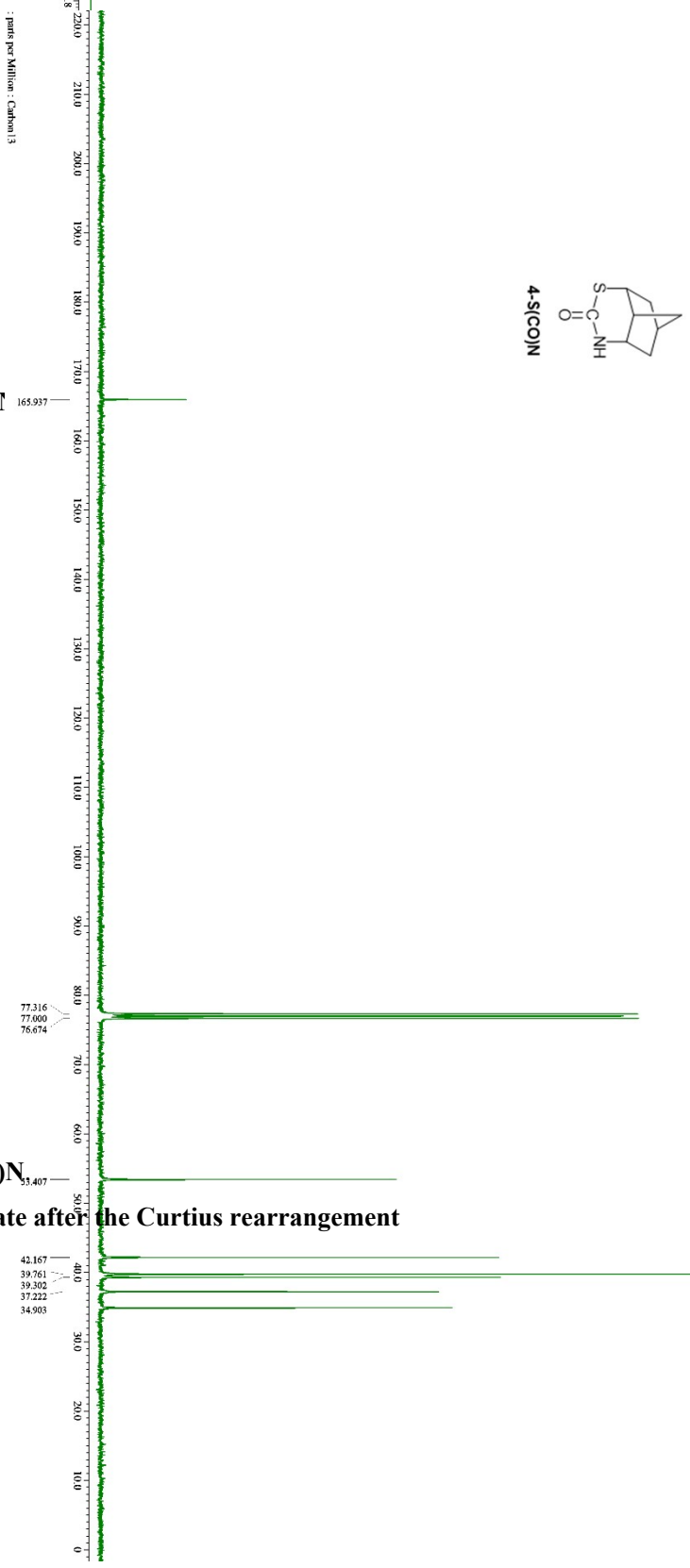
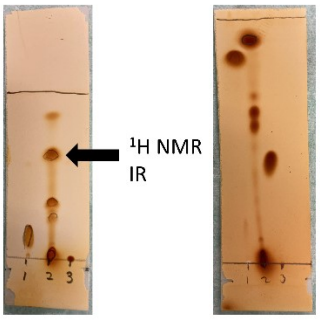


Fig. S6 ^{13}C NMR spectrum of **4-S(CO)N**

Analysis of the isocyanate intermediate after the Curtius rearrangement

TLC analysis

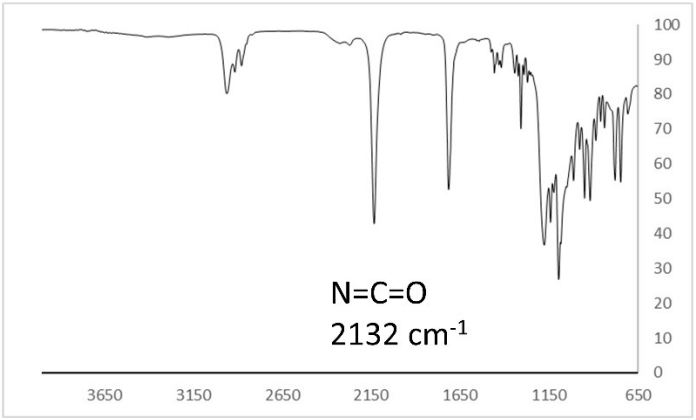


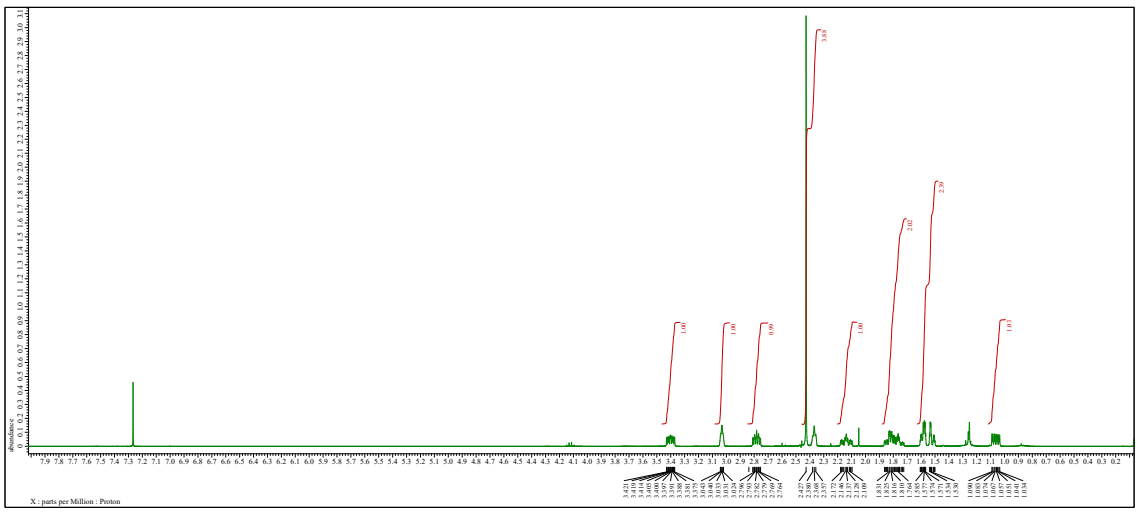
Left TLC
Mobile phase = 1:8 Hexane and Ethylacetate

Right TLC
Mobile phase = 5% Methanol in $CHCl_3$

1. 4-COOH
2. Reaction mixture
3. 4-S(CO)N

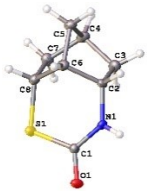
TLCs showed **4-COOH** was consumed and **4-S(CO)N** was not produced yet after the Curtius rearrangement. The major spot was chromatographed and measured on IR and ^{1}H NMR. IR showed an isocyanate peak. ^{1}H NMR spectrum showed different peaks from **4-COOH** and **4-S(CO)N**.





Single Crystal X-ray Diffraction Study

A single crystal was mounted on a glass fiber and the temperature of the crystal was maintained at 100 K by means of a Rigaku cooling device with liquid nitrogen flow to within an accuracy of ± 2 K. Data reductions and empirical absorption correction using spherical harmonics, implemented in a SCALE3 ABSPACK scaling algorithm (multi-scan method)[3] were performed using the CrysAlis^{Pro} software package (version 1.171.41.93a).[4] All the structures were solved with intrinsic phasing algorithm with SHELXT[5] and refined on F^2 data using the full-matrix least-squares algorithm using SHELXL,[6] both of which were implemented in the program OLEX2 (version 1.5)[7] with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were placed in calculated positions with idealized geometries and refined by using a riding model and isotropic displacement parameters.



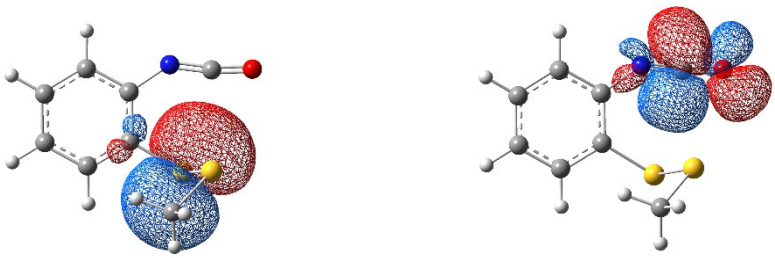
4-S(CO)N

Empirical formula	$C_8H_{11}NOS$
Formula weight	169.24
Temperature	100(2) K
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 9.0019(4) Å b = 7.9707(3) Å c = 11.5272(5) Å α = 90° β = 106.536(4) ° γ = 90°
Volume	792.89(6) Å^3
Z	4
Calculated density	1.418 g/cm^3
Absorption coefficient	0.345 μ/mm^{-1}
F(000)	360
Crystal size	0.41×0.22×0.16 mm^3
2θ range for data collection	4.72 to 60.628°
Radiation	Mo K_α (λ = 0.71073)
Index ranges	-11 ≤ h ≤ 9, -10 ≤ h ≤ 10, -14 ≤ h ≤ 14
Reflections collected	7728
Independent reflections	1975 [R_{int} = 0.0112, R_{sigma} = 0.0095]
Data / restraints / parameters	1975/0/110
Goodness-of-fit on F^2	1.032
Final R indixes [I>2σ(I)]	R_1 = 0.0409, wR_2 = 0.0964

Final R indixes (all data)	$R_1 = 0.0420$, $wR_2 = 0.0971$
Largest diff. peak and hole	0.92 and -0.29 e $Å^{-3}$

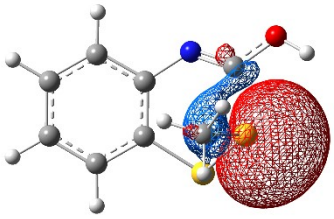
Computational Methods

Conformational search was carried out by Merck molecular force field (MMFF) in conjunction with Monte Carlo search method in Spartan' 18 program.[8] Lowest conformers within <40 kJ/mol for each compound were generated. Then, the equilibrium geometries of these conformers were determined using the semiempirical PM6 method. The resulting geometries were fully optimized at the M06-2X/6-311+G(d,p) level, and solvent effects were included by the use of PCM model in the Gaussian 09 program.[9] Natural bond order (NBO) analyses of all conformers were performed using NBO program as implemented in the Gaussian program package.[10]



Lone pair of S_{ph} (HOMO -4) Antibonding orbital of CO (LUMO +5)

Fig. S7 Lone pair of S_{ph} and antibonding orbital of C=O in **3-toluene**.



Lone pair of SMe (HOMO -15)

Antibonding orbital of N=C (LUMO +24) Antibonding orbital of N=C (LUMO +2)

Fig. S8 Lone pair of S_{Me} and antibonding orbital of N=C in **3-NCOH$^+$-water**.
Cartesian coordinates calculated at M06-2X/6-311+G(d,p) level of theory

3-toluene

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1235.261062

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	2.547545	2.072372	-1.105738
2	6	0	2.312472	1.135019	-0.617618
3	6	0	1.658506	-1.250962	0.643825
4	6	0	1.024234	0.953680	-0.117064
5	6	0	3.265222	0.134082	-0.484929
6	6	0	2.943433	-1.061462	0.148701
7	6	0	0.689080	-0.255807	0.519256
8	1	0	4.262022	0.291336	-0.878678
9	1	0	3.684616	-1.843584	0.255741
10	1	0	1.390726	-2.177518	1.137897
11	16	0	-0.922456	-0.534117	1.217286
12	16	0	-2.065492	-0.814240	-0.511178
13	6	0	-1.473250	-2.449729	-1.025748
14	1	0	-1.681899	-3.189591	-0.254908
15	1	0	-0.406053	-2.411001	-1.243474
16	1	0	-2.017850	-2.701348	-1.936480
17	7	0	0.117915	1.996959	-0.276565
18	6	0	-1.042040	2.236761	-0.060298
19	8	0	-2.132909	2.613104	0.078389

3-water

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1235.265196

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	1	0	2.574710	2.051700	-1.106861
2	6	0	2.328232	1.117282	-0.618620
3	6	0	1.648992	-1.266071	0.640818
4	6	0	1.039285	0.945621	-0.118581
5	6	0	3.271188	0.105936	-0.485424
6	6	0	2.936424	-1.087167	0.146279
7	6	0	0.690602	-0.260503	0.516642
8	1	0	4.269583	0.253625	-0.878516
9	1	0	3.669265	-1.877210	0.251581
10	1	0	1.373139	-2.192099	1.131118
11	16	0	-0.924939	-0.519539	1.212858
12	16	0	-2.071367	-0.799322	-0.513496
13	6	0	-1.526646	-2.458578	-1.006369
14	1	0	-1.761039	-3.180866	-0.226855
15	1	0	-0.458044	-2.453181	-1.218800
16	1	0	-2.075596	-2.702652	-1.916244
17	7	0	0.136824	1.995213	-0.278575
18	6	0	-1.016380	2.252640	-0.061106
19	8	0	-2.104885	2.642624	0.080372

3-NCOH$^+$-water

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1235.622149

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	-1.773728	2.667984	0.295896
2	6	0	-1.902759	1.601086	0.162364
3	6	0	-2.176032	-1.153043	-0.178662
4	6	0	-0.789099	0.843967	-0.207209
5	6	0	-3.134647	0.993336	0.349316
6	6	0	-3.275904	-0.381103	0.168411
7	6	0	-0.937601	-0.541308	-0.372414
8	1	0	-3.989125	1.593803	0.635047

9	1	0	-4.238224	-0.856005	0.311090
10	1	0	-2.270699	-2.225305	-0.299596
11	16	0	0.411342	-1.562971	-0.891051
12	16	0	1.911267	-0.694337	0.260995
13	6	0	1.297865	-0.657006	1.965759
14	1	0	0.284067	-0.263851	1.994076
15	1	0	1.992360	-0.023490	2.516508
16	1	0	1.344789	-1.684226	2.321444
17	7	0	0.414843	1.527176	-0.406305
18	6	0	1.565656	1.075590	-0.272073
19	8	0	2.652983	1.779720	-0.519383
20	1	0	3.476184	1.290908	-0.387323

4-toluene

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1276.889664

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	-2.254251	-2.715278	1.116433
2	6	0	-1.309617	-2.418111	0.654654
3	6	0	-1.452444	-2.006753	-0.825547
4	6	0	-0.036994	-1.491392	-1.139270
5	6	0	0.408087	-0.862652	0.212424
6	6	0	-0.825610	-1.030721	1.122423
7	1	0	-0.567876	-3.202932	0.814762
8	1	0	-1.804799	-2.779417	-1.507267
9	1	0	0.631584	-2.307765	-1.418058
10	1	0	-0.031463	-0.760099	-1.949366
11	1	0	1.210812	-1.456154	0.653816
12	1	0	-0.601213	-0.913930	2.182042
13	6	0	-2.023514	-0.182098	0.662019
14	1	0	-2.835201	-0.348424	1.374376
15	6	0	-2.393576	-0.792174	-0.722495

16	1	0	-2.228791	-0.075396	-1.529456
17	1	0	-3.443548	-1.089446	-0.739250
18	16	0	1.088120	0.839500	0.110743
19	16	0	2.959048	0.405422	-0.680299
20	6	0	3.899775	0.022681	0.828051
21	1	0	4.913743	-0.223550	0.510320
22	1	0	3.468588	-0.833826	1.345245
23	1	0	3.921868	0.888288	1.487242
24	7	0	-1.760842	1.236861	0.656765
25	6	0	-2.051934	2.246686	0.091937
26	8	0	-2.261661	3.291043	-0.391309

4-water

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1276.895329

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	-2.118361	-2.747019	1.223398
2	6	0	-1.180083	-2.435997	0.758597
3	6	0	-1.311716	-2.144912	-0.750407
4	6	0	0.079950	-1.575693	-1.078582
5	6	0	0.462182	-0.830970	0.232154
6	6	0	-0.781728	-0.993230	1.129136
7	1	0	-0.400743	-3.163428	0.992269
8	1	0	-1.605654	-2.985507	-1.376908
9	1	0	0.797058	-2.372054	-1.285306
10	1	0	0.059229	-0.905289	-1.939919
11	1	0	1.280599	-1.349886	0.733138
12	1	0	-0.586422	-0.788811	2.181152
13	6	0	-2.008579	-0.246788	0.582282
14	1	0	-2.828519	-0.382747	1.290318
15	6	0	-2.320739	-0.982848	-0.755899
16	1	0	-2.185623	-0.319708	-1.612142

17	1	0	-3.351393	-1.340143	-0.756987
18	16	0	1.067394	0.890233	0.021738
19	16	0	2.986903	0.499013	-0.674884
20	6	0	3.891368	0.214892	0.877244
21	1	0	4.922602	-0.005195	0.598823
22	1	0	3.475566	-0.637497	1.412721
23	1	0	3.861081	1.106895	1.499665
24	7	0	-1.800072	1.175282	0.444317
25	6	0	-2.265696	2.203965	0.075819
26	8	0	-2.622179	3.273121	-0.255271

4-SSH$^+$-water

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1277.275710

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	2.601174	-1.313707	-1.958225
2	6	0	1.936635	-1.628664	-1.152074
3	6	0	2.484795	-1.315962	0.252988
4	6	0	1.290815	-1.701867	1.144293
5	6	0	0.083465	-1.331204	0.232523
6	6	0	0.709698	-0.700495	-1.023019
7	1	0	1.667609	-2.676398	-1.293457
8	1	0	3.407382	-1.819701	0.532600
9	1	0	1.266797	-2.770253	1.357456
10	1	0	1.297526	-1.166423	2.096053
11	1	0	-0.489129	-2.212720	-0.049981
12	1	0	0.032760	-0.655435	-1.874844
13	6	0	1.421447	0.629451	-0.725561
14	1	0	1.809043	1.017256	-1.668383
15	6	0	2.589407	0.218259	0.219569
16	1	0	2.474332	0.666949	1.207455
17	1	0	3.541703	0.547068	-0.196870

18	16	0	-1.105726	-0.271040	1.157001
19	16	0	-2.606610	0.254095	-0.190799
20	6	0	-3.089703	-1.356668	-0.871612
21	1	0	-3.946133	-1.123919	-1.505725
22	1	0	-3.402747	-2.037551	-0.082579
23	1	0	-2.298382	-1.780054	-1.485392
24	7	0	0.534177	1.627568	-0.158874
25	6	0	0.452815	2.817611	-0.066055
26	8	0	0.268075	3.960992	0.084507
27	1	0	-1.724634	-1.267655	1.832403

4-NCOH$^+$-water

Imaginary frequencies = 0

Sum of electronic and thermal Free Energies = -1277.258138

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	3.224163	-1.147879	-1.572414
2	6	0	2.497467	-1.379435	-0.791994
3	6	0	2.817626	-0.703755	0.552901
4	6	0	1.554926	-1.014252	1.382357
5	6	0	0.453870	-1.063345	0.284505
6	6	0	1.163415	-0.634312	-0.999935
7	1	0	2.368132	-2.461205	-0.724456
8	1	0	3.738229	-1.016742	1.040724
9	1	0	1.614281	-1.985344	1.872623
10	1	0	1.372777	-0.261498	2.152521
11	1	0	0.012835	-2.055577	0.184065
12	1	0	0.605618	-0.858767	-1.907536
13	6	0	1.625820	0.831490	-0.884337
14	1	0	2.005870	1.154701	-1.852813
15	6	0	2.791135	0.777785	0.157163
16	1	0	2.604214	1.441159	1.002592
17	1	0	3.729586	1.074983	-0.310931

18	16	0	-1.005113	-0.044112	0.700082
19	16	0	-2.387917	-0.488684	-0.803347
20	6	0	-3.670955	-1.265671	0.224699
21	1	0	-4.462096	-1.501739	-0.488239
22	1	0	-4.046246	-0.564622	0.965455
23	1	0	-3.302084	-2.181776	0.677732
24	7	0	0.633324	1.824306	-0.501942
25	6	0	-0.426061	1.630461	0.099846
26	8	0	-1.321364	2.582953	0.357153
27	1	0	-1.882613	2.381470	1.118053

References

1 L. M. Miller, W.-J. Keune, D. Castagna, L. C. Young, E. L. Duffy, F. Potjewyd, F. Salgado-Polo, P. E. García, D. Semaan, J. M. Pritchard, A. Perrakis, S. J F. Macdonald, C. Jamieson, A. J. B. Watson, *J. Med. Chem.*, 2017, **60**, 722-748

2 R. S. Glass, J. R. Duchek, U. D. G. Prabhu, W. N. Setzer, G. S. Wilson, *J. Org. Chem.*, 1980, **45**, 3640-3646

3 SCALE3 ABSPACK, version 1.0.4; gui: 1.03; An oxford diffraction program; Oxford Diffraction Ltd.: Abingdon, UK, 2005.

4 Rigaku Oxford Diffraction, CrysAlisPro Software system, version 1.171.41.93a; Rigaku Corporation, Oxford, UK, 2020.

5 G. M. Sheldrick, *Acta Crystallogr. Sect. A Found. Adv.*, 2015, **71**, 3–8.

6 G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.*, 2015, **71**, 3–8.

7 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339–341.

8 Spartan 18; Wavefunction Inc., Irvine, CA.

9 Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

10 E. D. Glendening, A. E. Reed, J. E. Carpenter, F. Weinhold, NBO, version 3.1, 1992