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General and Practical Formation of Thiocyanates from Thiols

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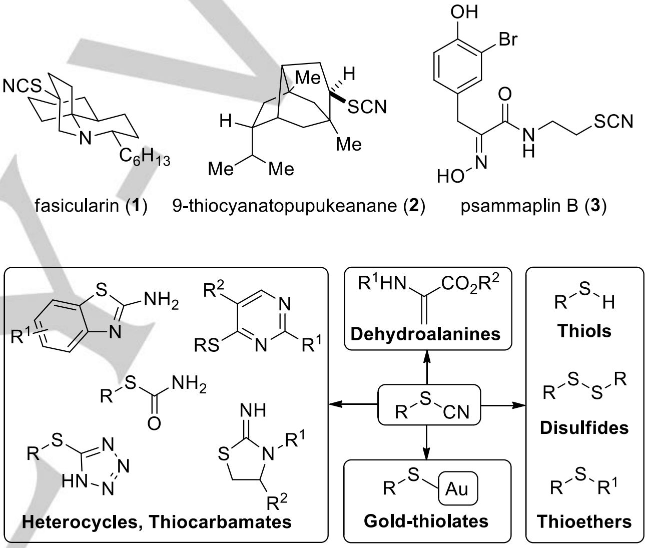
Abstract: A new method for the cyanation of thiols and disulfides using cyanobenziodoxol(on)e hypervalent iodine reagents is described. Both aliphatic and aromatic thiocyanates can be accessed in good yields in a few minutes at room temperature starting from a broad range of thiols with high chemioselectivity. The complete conversion of disulfides to thiocyanates was also possible. Preliminary computational studies indicated a low energy concerted transition state for the cyanation of the thiolate anion or radical. The developed thiocyanate synthesis has broad potential for various applications in synthetic chemistry, chemical biology and materials science.

Introduction

Heteroatom containing functional groups are essential in synthetic and medicinal chemistry, as they have a tremendous influence on the physical and biological properties of molecules and serve as a platform for functionalization. Thiocyanates in particular have attracted broad attention. They can be found in bioactive natural products, such as fasicularin (**1**),[1a-b] 9-thiocyanatopupukeanane (**2**)[1c] and psammaplin B (**3**)[1d] (Scheme 1A). Thiocyanates are also very important precursors in synthetic and medicinal chemistry, chemical biology and materials science (Scheme 1B). They can be converted easily to thiocarbamates and structurally diverse heterocycles.[2] The good leaving group ability of the cyanide group makes them mild electrophilic sulfur-transfer reagents to access disulfides and thioethers.[3a-e] Thiocyanates can also easily be converted into thiols and the cyano group is consequently a useful and atom-economical protecting group for sulfur.[3f-g] Furthermore, thiocyanates derived from cysteine are also important intermediates to access dehydroalanines under mild conditions, to promote cleavage of the amide bonds in peptides and proteins and to study the mechanism of enzymes with vibrational spectroscopy.[4] Finally, thiocyanates are highly useful precursors for the synthesis of gold-thiolate nanoparticles.[5] Traditionally, this functional group has been introduced by nucleophilic or electrophilic thiocyanation of organic molecules, and their accessibility has been limited by the availability and reactivity of the required precursors.[2a] Other disconnections giving access to thiocyanates would be highly desirable.

The synthesis of thiocyanates from thiols would constitute such an alternative disconnection, especially in light of the broad range of commercial or easily accessible thiols. This can be achieved either by nucleophilic cyanation of an activated thiol derivative[6] or direct electrophilic cyanation of the thiol using reagents such as **4**-**9** (Scheme 2A).[4,7] The latter route is more efficient, as it can be done in a single step. Nevertheless, no truly general method for the selective cyanation of both aliphatic and aromatic thiols has been reported and the most often used electrophilic cyanation reagent, cyanogen bromide (**4**), is toxic, difficult to manipulate and highly reactive, which leads to side reactions. Consequently, the discovery of new electrophilic cyanation reagents is an intensive topic of research.[8]



Scheme 1. Thiocyanates in Natural Products (**A**) and as Synthetic Precursors (**B**).

To develop new electrophilic cyanation methods, the use of hypervalent iodine reagents is highly promising, due to the exceptional reactivity of three-center four-electron bonds.[9] Nevertheless, hypervalent iodine compounds are also strong oxidants, which limits their use for the functionalization of thiols due to the easy formation of disulfides via oxidative dimerization. Recently, the use of cyclic hypervalent iodine reagents, especially benziodoxol(on)es, has led to important breakthroughs in atom-transfer reactions.[10] In the field of thiol functionalization in particular, Togni and co-workers reported the first example of trifluoromethylation,[11] whereas our group developed a practical alkynylation of thiols using EthynylBenziodoXolone (EBX) reagents.[12] However, to the best of our knowledge, hypervalent iodine reagents have never been used for the synthesis of thiocyanates starting from thiols. Herein, we report the first use of 1-Cyano-1,2-BenziodoXol-3-(*1H*)-one (CBX, **10**) and 1-Cyano-3,3-Dimethyl-3-(1H)-1,2-BenziodoXol (CDBX, **11**),[9d] for the cyanation of thiols (Scheme 2B). The reaction proceeded at room temperature in a few

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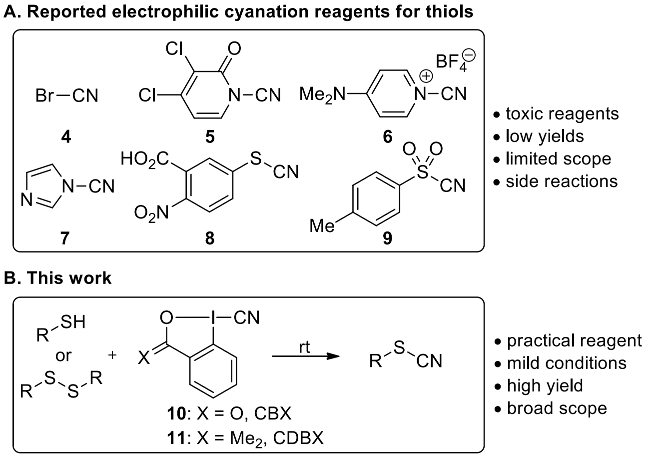
minutes in nearly quantitative yields for a broad range of aromatic and aliphatic thiols and displayed unprecedented functional group tolerance. CBX reagents could also be used for accessing thiocyanates from disulfides in up to 92% yield. In addition, a combined experimental and computational investigation gave a first insight into the reaction mechanism.

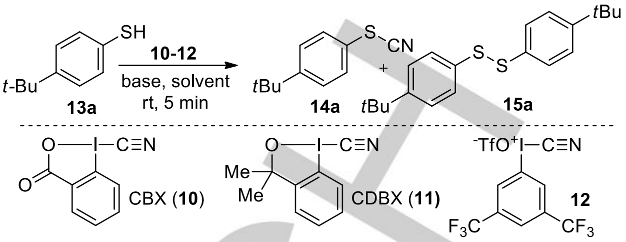


Scheme 2. Previously reported reagents for thiol cyanation (**A**) and our new approach (**B**).

Results and Discussion

We started our study with simple commercially available thiophenol **13a** as a model substrate (Table 1). With 1-cyano-1,2-benziodoxol-3(1*H*)-one (CBX, **10**), we found that the desired thiocyanate **14a** could be obtained in moderate yield using triethylamine as a base (entry 1). The choice of the base was crucial to obtain good yields of the thiocyanate product **14a** and minimize formation of the undesired disulfide **15a** arising from the oxidative dimerization of thiophenol **13a** (entries 1-4). Stronger bases such as tetramethylguanidine (TMG), 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) led to the desired thiocyanate **14a** as the main product (entries 2-4). Among the latter, DBU showed the best result with a yield above 95% (entry 4). In the absence of base, disulfide **15a** was obtained as the major product (entry 5). An important effect of the solvent was also apparent, as significant formation of disulfide **15a** was observed in other solvents (entries **6** and **7**). 1-Cyano-3,3-dimethyl-1,2-benziodoxole (CDBX, **11**), also gave an excellent result (entry 8). The cyclic hypervalent iodine regents **10** and **11** were superior to iodonium salts such as **12**,[9j] which led to the formation of disulfide **15a** as major product (entry 9).

Table 1. Optimization of thiocyanate formation[a]



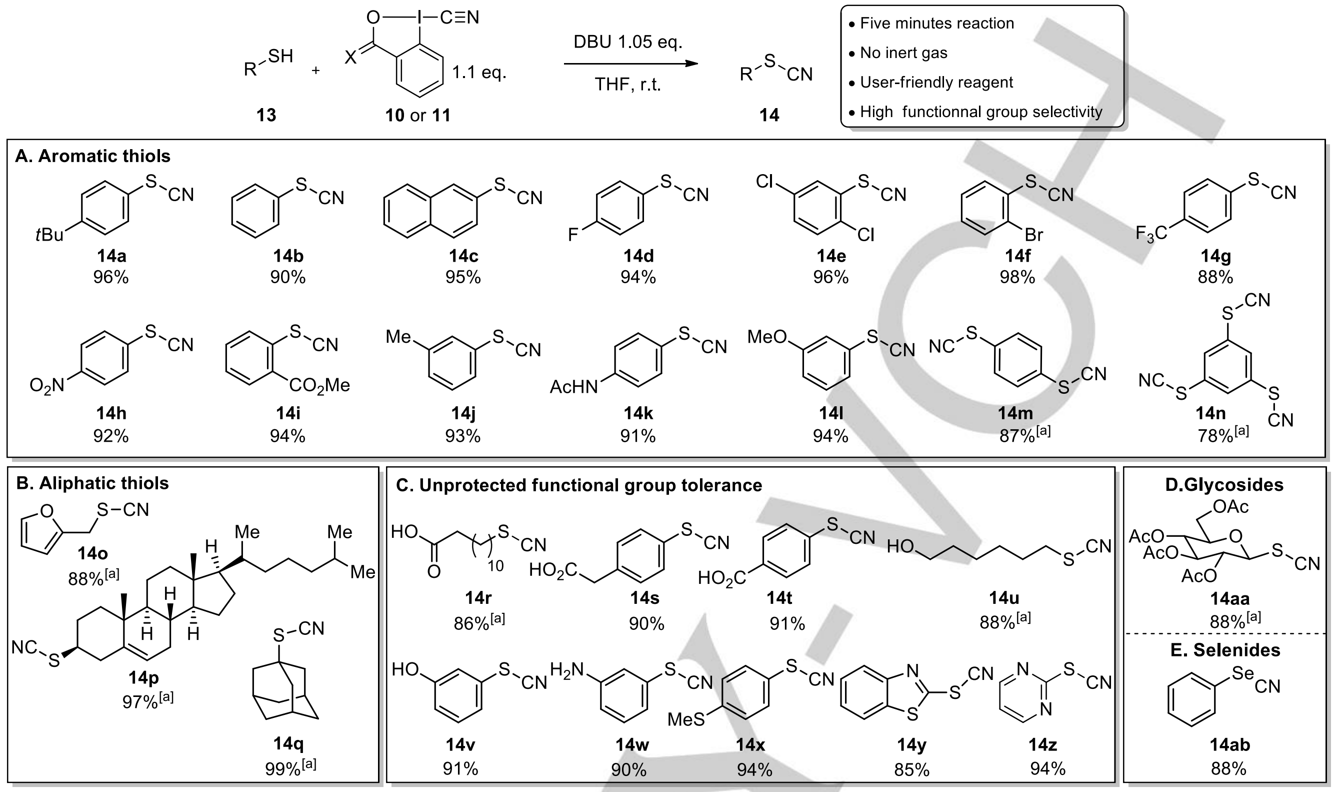
entry	10-12	base	solvent	yield **14a**[b]	yield **15a**[b]
1	**10**	Et_3N	THF	40%	60%
2	**10**	TMG	THF	79%	20%
3	**10**	TBD	THF	74%	26%
4	**10**	DBU	THF	>95%	<5%
5	**10**	-	THF	<10%	90%
6	**10**	DBU	MeOH	64%	35%
7	**10**	DBU	CH_3CN	86%	12%
8	**11**	DBU	THF	>95%	<5%
9	**12**	DBU	THF	17%	81%

[a] 4-*Tert*butylthiophenol (**13a**, 0.50 mmol), cyanide transfer reagent (**10-12**, 0.550 mmol), base (0.525 mmol), solvent (5.0 mL), 23 °C, 5 min, open flask. [b] Isolated yield of spectroscopically pure product.

Under the optimized conditions CBX (**10**) or CDBX (**11**) (1.1 eq) was added in one portion to a solution of the thiol **13a** (1.0 eq) and DBU (1.05 eq) in THF at room temperature and stirred for five minutes in an open-air flask to give the thiocyanate **14a** in 96% isolated yield (Scheme 3A). The cyanation of thiophenol (**13b**) and 2-thionaphthalene (**13c**) gave the corresponding products **14b** and **14c** in 90% and 95% respectively. Both electron-withdrawing (products **14d-i**) or electron-donating (products **14j-l**) groups were well tolerated and gave thiocyanates in 88-98% yield. The cyanation was successful in the presence of numerous functional groups such as halogens (fluorides, chlorides and bromides), nitro groups, esters, amides and ethers. Double and triple cyanation reactions were also possible, as demonstrated by the synthesis of bisthiocyanate **14m** and tristhiocyanate **14n** in 87% and 78% respectively. These compounds are particularly interesting scaffolds for materials science as a platform for dendrimeric heterocycle synthesis.[2a,13]

There are only few methods for the efficient conversion of aliphatic thiols to the corresponding thiocyanates under mild conditions.[7c,14] The use of cyanation reagent **10** allowed us to selectively convert primary, secondary and tertiary aliphatic thiols into thiocyanates in a general and practical fashion (Scheme 3B, products **14o-q**). In particular, the more complex steroid **14p** was obtained in an excellent 97% yield.

Chemoselectivity is a main challenge for cyanation reactions as acidic or nucleophilic functionalities can react with electrophilic cyanation reagents and consequently need to be protected, adding extra steps to the synthetic sequence. In particular, free amines and anilines are known to be efficiently cyanated with electrophilic cyanation reagents.[7e]



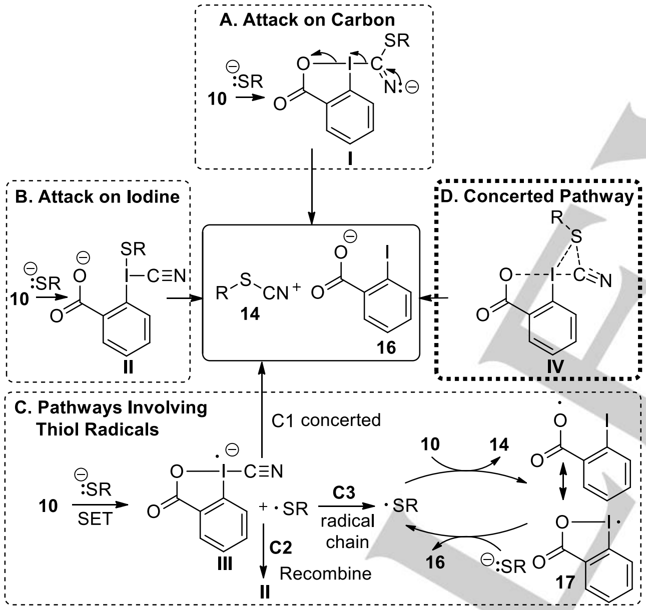
Scheme 3. General and practical thiocyanate synthesis from various thiols. The reaction conditions of Table 1, entry 8 with reagent **11** were used. [a] Reagent **10** was used (conditions of Table 1, entry 4).

To our delight, the cyanation reaction could be selectively done in the presence of unprotected aliphatic (products **14r** and **14s**) and aromatic (product **14t**) carboxylic acids in 86-91% yield (Scheme 3C). With a free aliphatic alcohol and a phenol, the thiocyanates **14u** and **14v** were obtained in 88% and 91% respectively. In the case of aniline **13w**, the cyanation was completely selective for sulfur and **14w** was obtained in 90% yield. This result points to the superior selectivity of hypervalent iodine-based reagents and their strong affinity for sulfur. On the other hand, it was possible to selectively cyanate a thiol in the presence of a thioether to obtain thiocyanate **14x** in 94% yield. The methodology was extended to the use of heterocyclic substrates giving thiocyano-benzothiazole **14y** or thiocyano-pyrimidine **14z** in 85% and 94% yield respectively. Heterocyclic thiocyanates are useful building-blocks for the synthesis of bioactive compounds.[15] Thiocyano-glycosides are known to be very good glycoside donor in glycosylation reactions, especially for 1,2-*cis*-glycosylation.[16] Under our optimized conditions, tetra-acetyl-β-thioglucose **13aa** cleanly gave the desired thiocyanate **14aa** in 88% yield without epimerization to the α form (Scheme 3D). Finally, phenylselenol (**13ab**) was found to be a suitable substrate for this reaction and selenocyanate **14ab** could be obtained in 88% yield (Scheme 3E).

Several pathways can be proposed for the reaction mechanism (Scheme 5).[9] A first possibility would be nucleophilic attack on the carbon of the cyanide group to form thioimidate **I** (pathway **A**). 1,2-Elimination would then give thiocyanate **14** and benzoate **16**. However, this mechanism is less probable when considering that the most electrophilic position is usually on the iodine for this type of reagents.[9] Therefore, attack on the iodine atom appears more probable to give intermediate **II** upon ring-opening of the benziodoxolone heterocycle (pathway **B**). Reductive elimination on iodine would then lead to thiocyanate **14**. This type of mechanism has indeed been often proposed for the functionalization of nucleophiles with hypervalent iodine reagents.[9]

Nevertheless, when considering the strong oxidizing properties of hypervalent iodine reagents, mechanisms involving a single electron transfer and the subsequent formation of radical intermediates also constitute an important alternative (pathway **C**). In the case of related benziodoxolone reagents for trifluoromethylation, the formation of a trifluoromethyl radical has often been proposed.[11] However, when considering the much lower stability of the cyano radical, such an intermediate appears highly improbable.[17] In contrast, a single electron transfer between reagent **10** and a thiolate anion could be possible, although Lewis or Brønsted acid activation of hypervalent iodine reagents is usually needed to promote single electron transfer.[18] Several pathways could then be considered for further reaction of the formed radical anion **III** and the thiol radical: (1) Concerted reaction to give directly the thiocyanate (pathway **C1**), (2) radical recombination to give intermediate **II** followed by reductive elimination (pathway **C2**), or initiating of a radical chain reaction starting with attack of the thiol radical onto reagent **10** (pathway **C3**). In the latter case, the formed benziodoxole radical **17** would be further reduced by a thiolate anion to give benzoate **16** and regenerate a thiol radical. If the reaction would occur via pathway **C3**, it should be possible to intercept the formed thiol radicals with trapping reagents. However, no adduct could be observed in presence of phenylacetylene and 1,1-dicyclopropylethene, which are known to react very quickly with thiol radicals.[19] Consequently, this pathway also appears less probable.

Finally, a last alternative would involve a concerted mechanism via a three-atom transition state **IV** (pathway **D**). Although this alternative has not yet been proposed in the literature for the cyanation of thiols, we have recently discovered by computation that such a transition state was possible in the case of the related alkynylation reaction.[20] We consequently turned to computational chemistry to investigate this intriguing mechanism pathway.



Scheme 4. Speculative mechanism pathways for the cyanation reaction.

Computations (at the PBE0-dDsC/TZ2P//M06-2X/def2-SVP or M06-2X/def2-TZVP//M06-2X/def2-SVP theoretical level, see computational details section) designed to probe the potential energy surface with phenyl thiolate **13b'** allowed us to identify low-energy Van der Waals complexes **V** indeed indicating a significant interaction between the sulfur and the iodine atom (Figure 1). Nevertheless, the sulfur atom is already shifted towards the carbon of the cyanide group (S-I and S-C distances of 2.895 and 3.206 Å respectively). Starting from **V**, no stable intermediate corresponding to either thioimidate **I** or intermediate **II** containing a formal S-I bond was observed. Instead, a low energy (8.8 kcal/mol) transition state **IV** led directly to thiocyanate **14b** and iodobenzoate **23** (complex **VI**).[21,22] This energetically favorable concerted pathway is in accordance with the high reaction rate. As observed for the alkynylation of thiols,[20] the linear geometry at the cyanide carbon was distorted and a significant transfer of negative charge on the nitrogen atom was observed (-0.46 calculated Hirshfeld iterative charge). The higher electronegativity of the nitrogen atom could further stabilize the formed charge and lower the energy of the transition state.

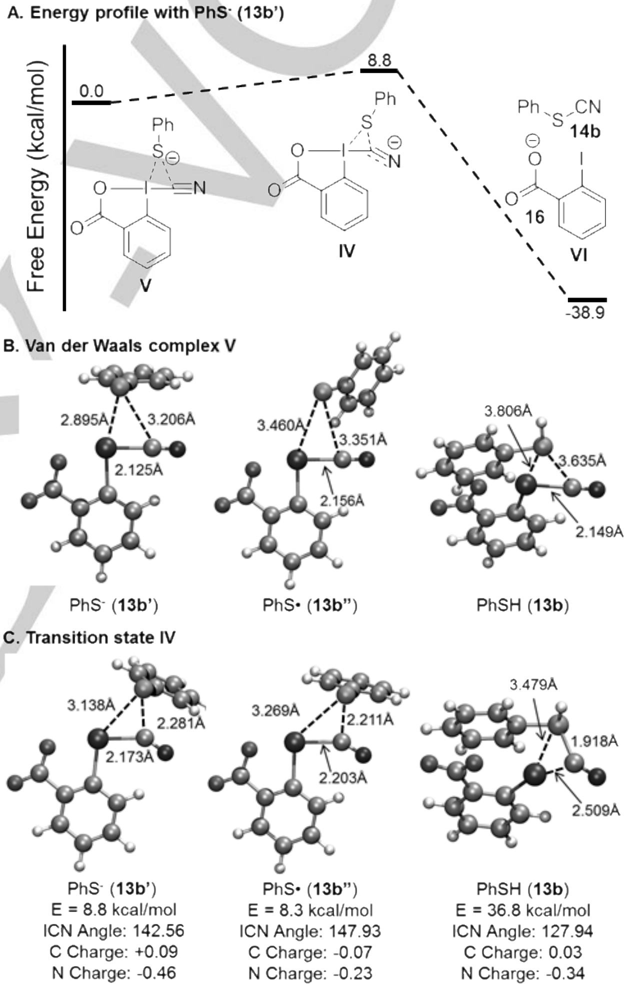
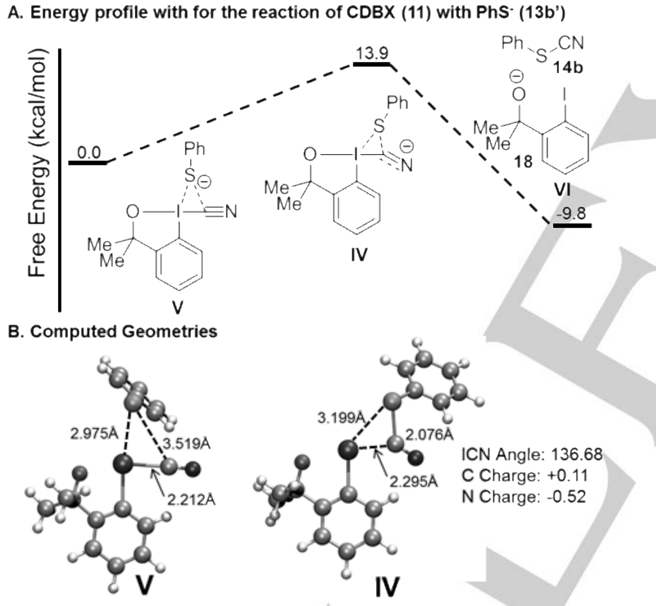


Figure 1. Free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the cyanation of thiophenolate (**13b'**) with CBX (**10**) and computed geometries (M06-2X/def2-SVP level) for Van der Waals complex **V** and transition state **IV** with thiophenolate (**13b'**), thiophenol radical (**13b''**) and thiophenol (**13b**).[21]

In addition to thiophenolate (**13b'**), thiophenol radical (**13b''**) and thiophenol (**13b**) itself could also lead to thiocyanate formation. Consequently, the energies and geometries for Van der Waals complex **V** and transition state **IV** were calculated for these two molecules. Interestingly, the addition of thiophenol radical **13b''** was also a very facile process, with a transition state energy of only 8.3 kcal/mol. The geometries of Van der Waals complexes **V** and transition state **IV** are similar to the ones obtained with thiophenolate **13b'**, except that the distance between the sulfur and the iodine atom was significantly longer in complex **V** (3.460 vs 2.895 Å). It is know that hypervalent iodine reagents are strongly Lewis acidic in *para* position to the aryl ring,[9] and a stronger interaction with the nucleophilic thiolate compared to the neutral radical could be reasonably expected. In contrast, a completely different result was obtained using thiophenol (**13b**) itself as nucleophile: a much higher transition state energy (36.8 kcal/mol) was observed, as well as a nearly complete change of the geometry to trigonal planar (ICN angle of 128°). Consequently, direct reaction of the neutral thiol appears highly improbable, and it is in good agreement with the lack of thiocyanate formation in the absence of base (Table 1, entry 5).

Finally, the energy profile and the computed geometries were also calculated in the case of the reaction of CDBX (**11**) with thiophenolate (**13b'**) (Figure 2).

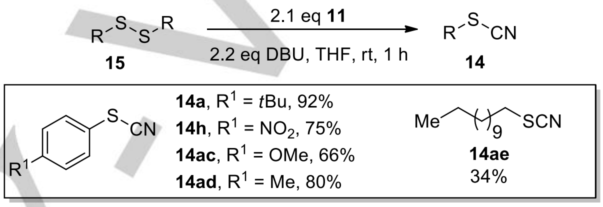

A. Energy profile with for the reaction of CDBX (11) with PhS- (13b')

B. Computed Geometries

Figure 2. Free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the cyanation of thiophenolate (**13b'**) with CDBX (**11**) and computed geometries (M06-2X/def2-SVP level) for Van der Waals complex **V** and transition state **IV**.[23]

A similar profile was obtained, although transition state **IV** was higher in energy (13.9 vs 8.8 kcal/mol with CBX (**10**)). Concerning the geometries, a stronger distortion from linearity was observed (ICN angle of 137° vs 143°) and the C-I distance was larger (2.295 vs 2.173 Å) and the C-S distance shorter (2.076 vs 2.281 Å), corresponding to a later transition state.

During optimization of the reaction conditions with thiolate **13a**, the formation of disulfide **15a** could be avoided by the right choice of reagent, base and solvent. However, even under the optimized conditions, formation of small amounts of disulfide **15a** was still observed by TLC in the first minute of reaction, but gradually disappeared afterwards. We consequently wondered if disulfide **15a** could also be converted into the desired thiocyanate **14a** under the reaction conditions. Indeed, when **15a** was treated with 2.1 equivalents of CDBX (**11**), thiocyanate **14a** was obtained in 92% yield in one hour (Scheme 5). To the best of our knowledge, this constitutes the first report of efficient transformation of a disulfide into a thiocyanate, as most reported methods can reach a maximum of only 50% yield.[6,24] Under the same reaction conditions, thiocyanates **14h** and **14ac-d** bearing either electron-withdrawing or electron-donating groups could be obtained in 66-80% yield. The cyanation of an aliphatic disulfide was also possible, but thiocyanate **14ae** was obtained in lower yield (34%).



Scheme 5. Thiocyanate formation from disulfides.

Conclusions

In conclusion, we have developed a very general and practical methodology to access useful thiocyanates from readily available thiols and disulfides. This methodology utilizes the easily accessible and user-friendly benziodoxoles CBX (**10**) and CDBX (**11**) as electrophilic cyanation reagents. The mild reaction conditions and high chemoselectivity allowed us to successfully prepare aromatic-, benzylic-, and aliphatic thiocyanates, as well as thiocyano-saccharides or thiocyano-steroids. The methodology showed an unprecedented functional group tolerance towards carboxylic acids, alcohols, thioethers and anilines. The high rate and selectivity observed could be tentatively rationalized by a low energy barrier concerted mechanism available to thiolates and thiol radicals as nucleophiles. All attempted trapping experiments for thiol radicals were unsuccessful up to now. Nevertheless, the presence of short-lived radical intermediates cannot be excluded without further investigations. The thiol-cyanation reaction we developed has the potential to become a reference method for thiocyanate formation from thiols and disulfides with various applications in synthetic chemistry, chemical biology and materials science.

Experimental Section

Computational Details.[25]

Geometries were optimized using Truhlar's M06-2X[26] density functional with the def2-SVP basis set in Gaussian09.[27] M06-2X computations employed the "Ultrafine" grid to remove known problems with the size of the integration grid for this functional family.[28] To obtain refined energy estimation that explicitly account for non-bonded interactions, a density dependent dispersion correction (-dDsC)[29] was used appended to the PBE0[30] functional (PBE0-dDsC). PBE0-dDsC single point computations made use of the slater-type orbital 3-ζ basis set, TZ2P, as implemented in ADF.[31] To confirm the accuracy of the PBE0-dDsC computations, a second set of single point energies was obtained at the M06-2X/def2-TZVP level. All reported free energies include the effects of solvation (in THF) using the implicit continuum model for realistic solvents[32] (COSMO-RS), also as implemented in ADF, as well as free energy correction derived from M06-2X/def2-SVP computations. Iterative Hirshfeld charges[33] were computed using Q-Chem.[34]

Experimental Procedures.

Caution: Hypervalent iodine reagents are high energy compounds which should be used with appropriate care. Compounds **10** and **11** are stable at room temperature, but show a strong exothermic decomposition at 151 °C and 133 °C respectively by DSC measurement. We recommend not using these reagents above 40 °C and running reactions behind a protective shield. An advantage of the method is to avoid the use of highly toxic cyanide anions. Nevertheless, as the formation of small amounts of cyanide cannot be excluded, all relevant measures have to be taken when performing the cyanation step.[35] In particular, the aqueous layers were basified and disposed separately. All open flask reactions were set up in well ventilated fume-hoods.

General Procedure for the cyanation of thiols.

A 25 mL round bottom flask was charged with a magnetic stirring bar, thiol derivative (0.500 mmol, 1.00 eq.) and THF (5.0 mL). To this solution was added 1,8-diazabicycloundec-7-ene (DBU, 79.0 µL, 0.525 mmol, 1.05 eq.), followed by 1-cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (CDBX (**11**), 158 mg, 0.550 mmol, 1.10 eq.) or 1-cyano-1,2-benziodoxol-3-(1*H*)-one (CBX (**10**), 150 mg, 0.550 mmol, 1.10 eq.). In case DBU addition yielded a THF-insoluble thiolate, CDBX or CBX was added prior to DBU. An additional equivalent of DBU (total amount: 153 µL, 1.03 mmol. 2.05 eq.) was added for carboxylic acid containing substrates. The resulting reaction mixture was stirred in an open flask for 5 minutes at room temperature (unless otherwise stated). The reaction was quenched with 5% aq. citric acid (10 mL). The aq. mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was further purified by column chromatography.

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Keywords: Cyanation, Chemoselective reaction, Hypervalent Iodine, Thiocyanates, Thiols

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[22] An examination of the intrinsic reaction coordinate (IRC) further supported the concerted nature of the proposed mechanism. See Supporting Information for selected IRC structures.

[23] Electronic energies obtained with M06-2X/def2-TZVP: 17.9 kcal/mol. See Supporting Information for further details.

[24] At this stage, the exact mechanism of the conversion of disulfides to thiocyanates in unknown and will be the topic of future studies.

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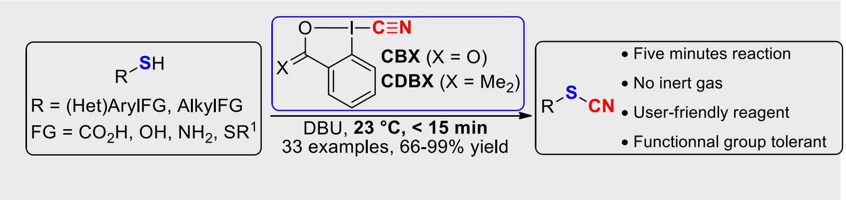
FULL PAPER



Easy and General: A new method for the cyanation of thiols using cyanobenziodoxol(on)e hypervalent iodine reagents is described. Both aliphatic and aromatic thiocyanates can be accessed in good yields in a few minutes at room temperature with high chemioselectivity. The developed thiol-cyanation reaction has broad potential for the formation of thiocyanates with various applications in synthetic chemistry, chemical biology and materials science.

Reto Frei,[b]† Thibaut Courant,† Matthew D. Wodrich and Jerome Waser[a]*

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General and Practical Formation of Thiocyanates from Thiols

Table of Contents

1. List of Abbreviations

EtOAc	Ethyl acetate
Ac_2O	Acetic anhydride
CDBX	1-Cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole
CBX	1-Cyano-1,2-benziodoxol-3-(1*H*)-one
DBU	1,8-Diazabicycloundec-7-ene
TBD	1,5,7-Triazabicyclo[4.4.0]dec-5-ene
TFAA	Trifluoroacetic anhydride
THF	Tetrahydrofuran
TIPS	Triisopropylsilyl
TIPS-EBX	1-[(Triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one
TLC	Thin layer chromatography
TMG	1,1,3,3-Tetramethylguanidine
TMS	Trimethylsilyl
TMS-CN	Trimethylsilyl cyanide
TMS-OTf	Trimethylsilyl trifluoromethanesulfonate
brsm	Based on recovered starting material
Im.	1-*H*-Imidazole
DMSO	Dimethyl sulfoxide

2. Computational Details

Figure S1. Reaction free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the reaction of CBX with a phenylthiol anion. Values in kcal/mol.

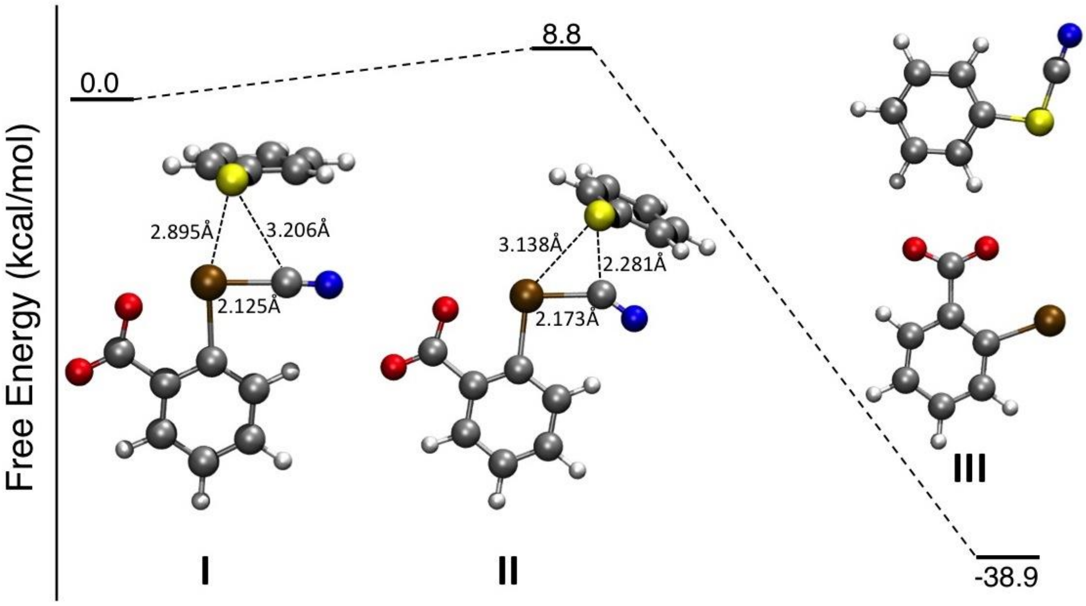

Figure S2. Selected structures along the intrinsic reaction coordinate for the reaction of CBX with a phenylthiol anion. Structures computed at the M06-2X/def2-SVP level. Bond lengths in Angstrom.

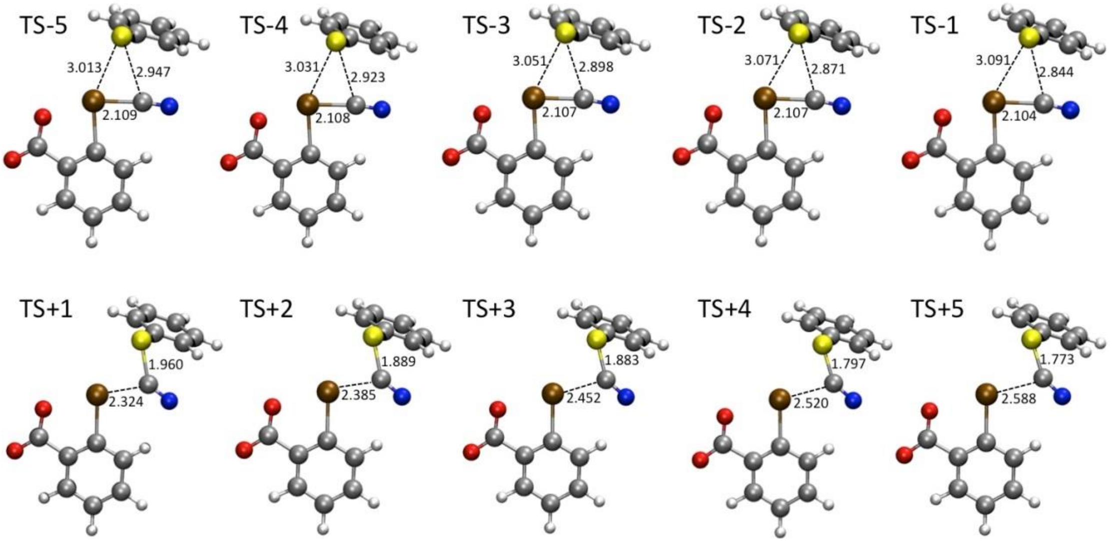

Figure S3. Reaction free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the reaction of CBX with a phenylthiol radical. Values in kcal/mol.

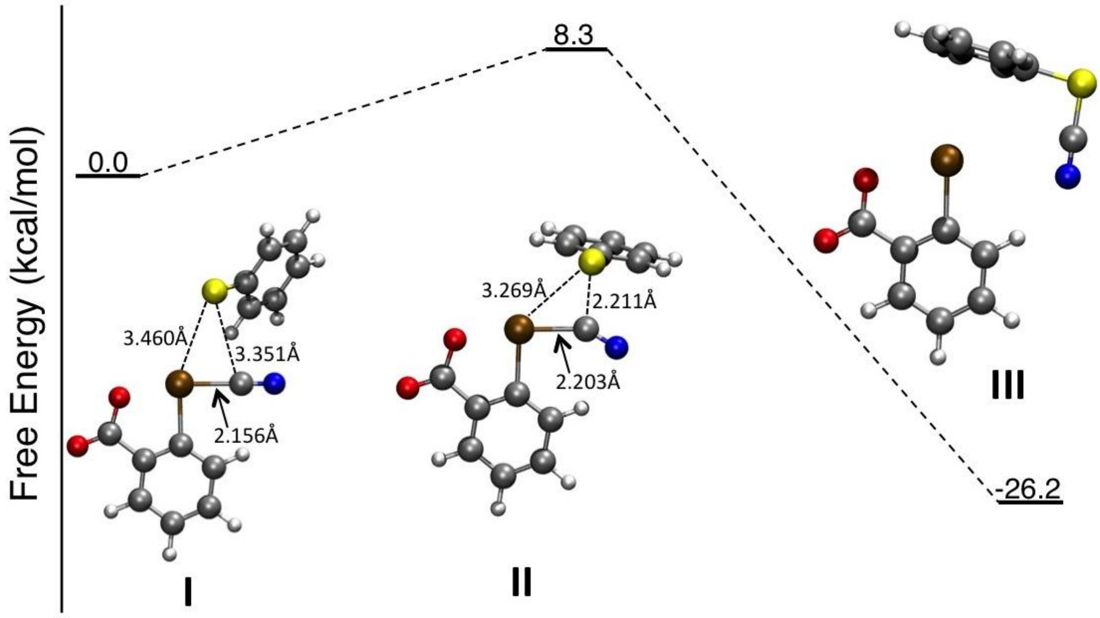

Figure S4. Selected structures along the intrinsic reaction coordinate for the reaction of CBX with a phenylthiol radical. Structures computed at the M06-2X/def2-SVP level. Bond lengths in Angstrom.

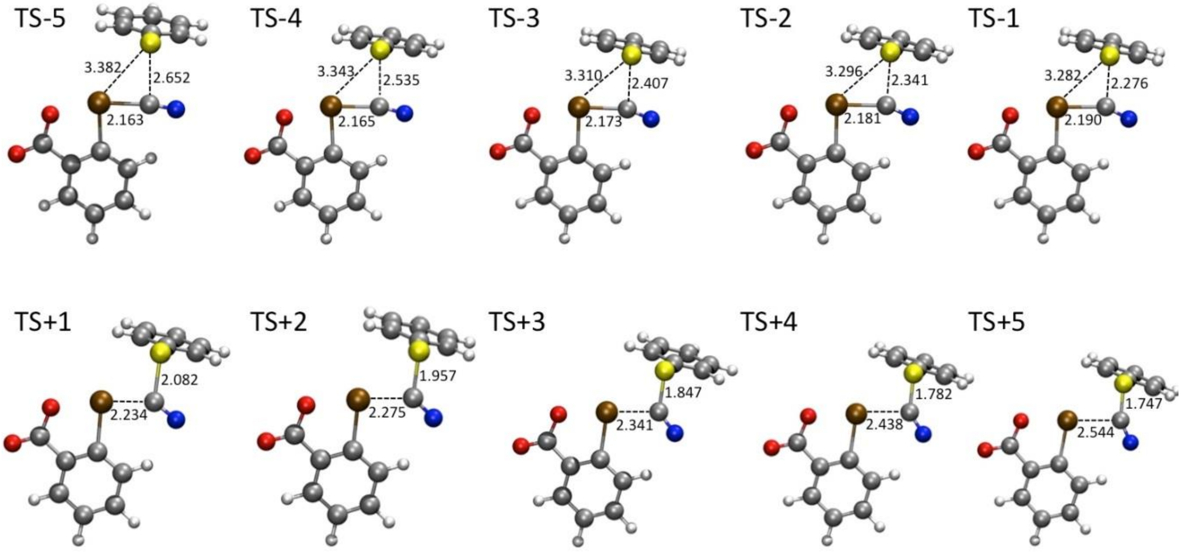

Figure S5. Reaction free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the reaction of CBX with neutral phenylthiol. Values in kcal/mol.

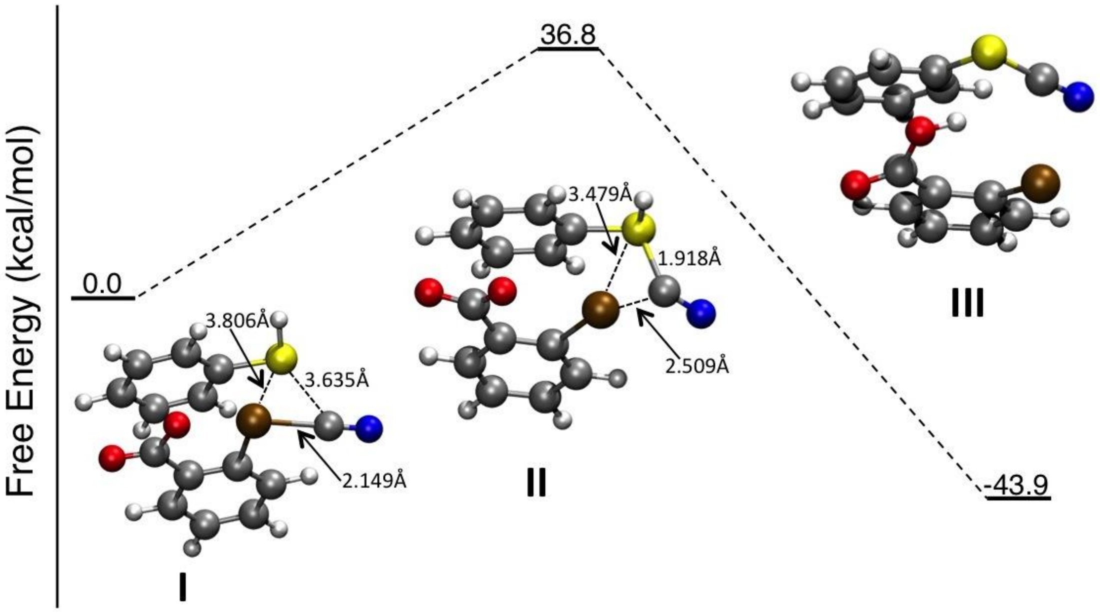

Figure S6. Selected structures along the intrinsic reaction coordinate for the reaction of CBX with neutral phenylthiol. Structures computed at the M06-2X/def2-SVP level. Bond lengths in Angstrom.

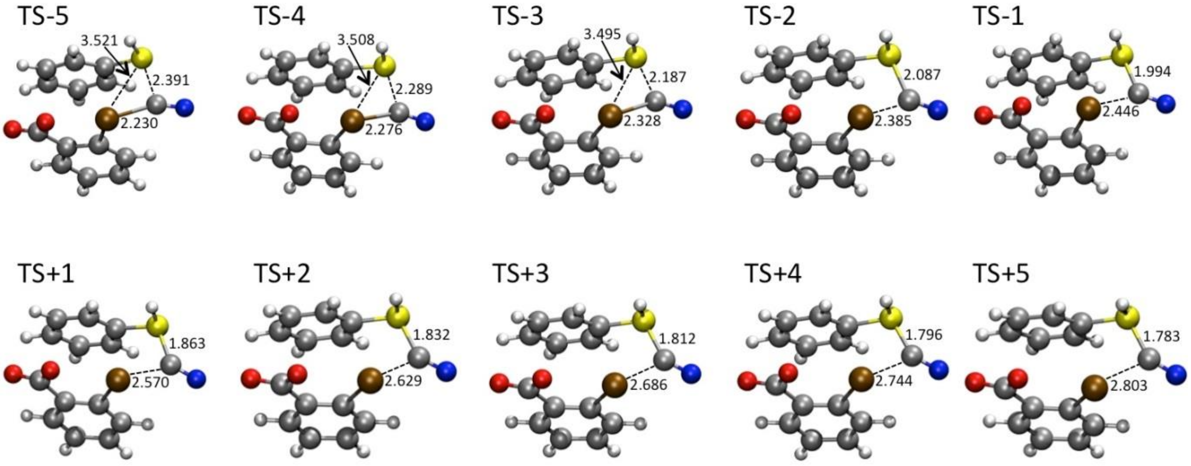

Figure S7. Reaction free energy profile [PBE0-dDsC/TZ2P//M06-2X/def2-SVP level in implicit THF solvent (COSMO-RS)] for the reaction of CDBX with a phenylthiol anion. Values in kcal/mol.

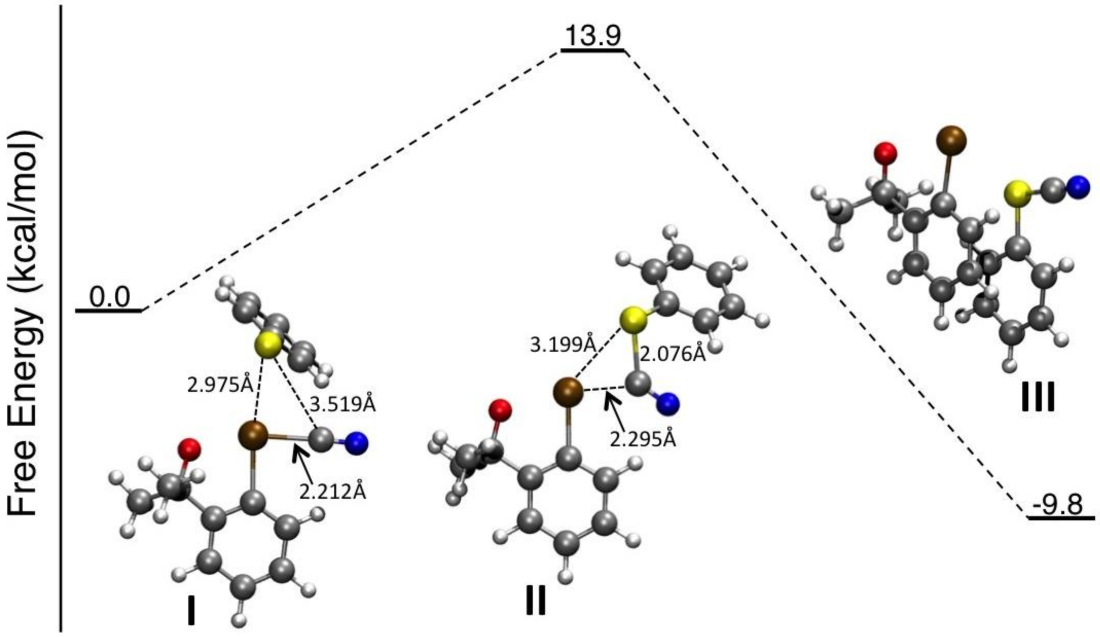

Table S1. Electronic energies, free energy corrections, and solvation corrections of relevant species. PBE0-dDsC/TZ2P and M06-2X/def2-TZVP electronic energies obtained from single point computations on M06-2X/def2-SVP geometries.

Compound	M06-2X/def2-SVP Electronic Energy (hartree)	M06-2X/def2-SVP Free Energy Correction (hartree)	PBE0-dDsC/TZ2P Electronic Energy (hartree)	M06-2X/def2-TZVP Electronic Energy (hartree)	PBE0-dDsC/TZ2P Solvation Energy (kcal/mol)
	CBX/Phenylthiol Anion				
Reactant	-1438.913291	0.143967	-8.361120	-1439.905415	-47.838
TS	-1438.899587	0.145162	-8.347671	-1439.888145	-48.192
Product	-1438.988473	0.143819	-8.420133	-1439.975958	-49.633
	CBX/ Phenylthiol Radical				
Reactant	-1438.794259	0.142637	-8.235568	-1439.781356	-17.754
TS	-1438.779398	0.143964	-8.226017	-1439.765917	-16.238
Product	-1438.842142	0.141754	-8.278477	-1439.824976	-16.511
	CBX/Phenylthiol				
Reactant	-1439.432099	0.156239	-8.432726	-1440.419780	-16.329
TS	-1439.353139	0.157084	-8.363608	-1440.341014	-23.374
Product	-1439.524302	0.159046	-8.508100	-1440.503039	-14.658
	CDBX/ Phenylthiol Anion				
Reactant	-1443.457403	0.214259	-9.768118	-1444.451798	-51.260
TS	-1443.436323	0.214552	-9.748953	-1444.426214	-49.587
Product	-1443.480614	0.213157	-9.781551	-1444.475380	-51.948

Table S2. Free energies for relevant reactions. PBE0-dDsC and M06-2X/def2-TZVP electronic energies computed on M06-2X/def2-SVP optimized geometries. Free energies include unscaled free energy corrections from M06-2X/def2-SVP computations and solvation corrections (in implicit THF) from COSMO-RS (at the PBE0-dDsC/TZ2P level). Values in kcal/mol.

	PBE0-dDsC/TZ2P Free Energy	M06-2X/def2-TZVP Free Energy
CBX/Phenylthiol Anion		
Reactant → TS	8.84	11.23
TS → Product	-47.76	-57.39
CBX/ Phenylthiol Radical		
Reactant → TS	8.34	12.04
TS → Product	-34.58	-38.72
CBX/Phenylthiol		
Reactant → TS	36.86	42.91
TS → Product	-80.72	-91.73
CDBX/ Phenylthiol Anion		
Reactant → TS	13.88	17.91
TS → Product	-23.69	-34.09

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CBX/Phenylthiol Anion - Reactant

I	0.56207	-0.92062	0.42045
S	2.39304	1.28463	0.82992
N	2.89838	-1.62323	-1.77287
C	2.09828	-1.34079	-0.98586
O	-1.33790	-1.03767	1.66523
C	-2.14702	-2.01324	1.44140
O	-3.19756	-2.23874	2.00919
C	-1.67229	-2.94726	0.33224
C	-0.47073	-2.70453	-0.32320
C	-0.01361	-3.53679	-1.34048
H	0.92978	-3.33962	-1.85223
C	-0.79243	-4.63905	-1.69991
H	-0.44617	-5.29967	-2.49730
C	-2.00227	-4.89862	-1.05121
H	-2.60105	-5.76367	-1.34240
C	-2.44097	-4.05295	-0.03649
H	-3.37819	-4.21107	0.50051
C	1.91980	2.07855	-0.66748
C	2.71464	1.98294	-1.82726
C	2.33757	2.60711	-3.01388
C	1.15372	3.34392	-3.08558
C	0.72703	2.82339	-0.75951
C	0.35080	3.44454	-1.94817
H	3.63209	1.39398	-1.77579
H	2.97424	2.51026	-3.89664
H	0.85813	3.82942	-4.01766
H	0.10036	2.90340	0.13118
H	-0.58171	4.01296	-1.98624

28
CBX/Phenylthiol Anion - TS

I	0.12373	-0.93628	0.63290
S	2.53907	1.05635	0.42985
N	2.46782	-1.44818	-1.46519
C	1.91855	-0.88655	-0.59101
O	-1.90104	-1.30164	1.82794
C	-2.54703	-2.35744	1.52608
O	-3.59518	-2.76535	1.99804
C	-1.87229	-3.17930	0.42238
C	-0.67658	-2.76367	-0.14555
C	-0.02967	-3.47323	-1.15404
H	0.90846	-3.11230	-1.57973
C	-0.62659	-4.65519	-1.59725
H	-0.13987	-5.23021	-2.38728
C	-1.82950	-5.10103	-1.04368
H	-2.28253	-6.02728	-1.40247
C	-2.44912	-4.36439	-0.03803
H	-3.38941	-4.66811	0.42581
C	2.06260	2.05362	-0.94086
C	2.62981	1.84322	-2.21102
C	2.26192	2.63919	-3.29296
C	1.33129	3.66808	-3.13587
C	1.11500	3.08173	-0.79784
C	0.76020	3.88319	-1.88087
H	3.34603	1.02866	-2.32993
H	2.70903	2.45320	-4.27217
H	1.04930	4.29294	-3.98541
H	0.66038	3.23928	0.18212
H	0.02367	4.67826	-1.74400

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CBX/Phenylthiol Anion - Product

I	-0.98929	2.67718	2.40521
S	3.56954	-0.48493	-0.49889
N	6.21615	-1.06638	-1.39438
C	5.13366	-0.85580	-1.03793
O	-0.47144	0.17366	0.73984
C	-1.54383	-0.44705	0.79110
O	-1.79511	-1.61641	0.45237
C	-2.77575	0.34507	1.33454
C	-2.76030	1.58754	1.97486
C	-3.94191	2.20253	2.40536
H	-3.89367	3.16882	2.90882
C	-5.17017	1.58436	2.19197
H	-6.08693	2.07427	2.52699
C	-5.21397	0.34345	1.55627
H	-6.17059	-0.15509	1.38574
C	-4.02964	-0.25682	1.14563
H	-4.01016	-1.23298	0.65952
C	2.71047	-2.03411	-0.80726
C	3.32377	-3.16548	-1.34589
C	2.55393	-4.31212	-1.53895
C	1.20055	-4.32203	-1.19893
C	1.35900	-2.02206	-0.46022
C	0.60623	-3.18027	-0.66150
H	4.38191	-3.15715	-1.61170
H	3.02372	-5.20333	-1.96005
H	0.60820	-5.22578	-1.35481
H	0.85706	-1.13771	-0.03335
H	-0.44761	-3.12291	-0.37584

28

CBX/Phenylthiol Radical - Reactant

O	-4.28945	-1.56889	1.73263
I	-0.48482	-0.22530	0.68784
S	1.50487	2.60494	0.66008
N	2.52681	-0.89918	-0.51661
C	1.48223	-0.66348	-0.07883
O	-2.52450	-0.23835	1.37575
C	-3.15351	-1.38512	1.38436
C	-2.28544	-2.52783	0.89139
C	-0.98141	-2.28756	0.49268
C	-0.12269	-3.27339	0.03045
H	0.90072	-3.05535	-0.27632
C	-0.62860	-4.57435	-0.02666
H	0.01804	-5.37642	-0.38489
C	-1.93975	-4.85444	0.36699
H	-2.31251	-5.87791	0.31393
C	-2.76911	-3.83484	0.82572
H	-3.79867	-4.00954	1.14291
C	2.10150	2.89635	-0.92666
C	3.14066	3.83797	-1.12036
C	3.63710	4.08415	-2.39193
C	3.10780	3.40220	-3.49232
C	1.57833	2.21655	-2.05197
C	2.07820	2.47097	-3.32005
H	3.53966	4.35914	-0.24928
H	4.43993	4.80877	-2.53240
H	3.50047	3.59705	-4.49142
H	0.77726	1.49045	-1.90800
H	1.67012	1.94152	-4.18155

28

CBX/Phenylthiol Radical - TS

O	-3.54683	-2.41365	1.90913
I	0.15899	-0.93387	0.71683
S	2.82529	0.90025	0.25356
N	2.61745	-1.55649	-1.33358
C	1.98599	-0.99677	-0.51164
O	-1.71538	-1.14090	1.74892
C	-2.47264	-2.16304	1.43208
C	-1.85154	-3.04090	0.36622
C	-0.61424	-2.71738	-0.16604
C	0.02274	-3.46757	-1.14263
H	0.99749	-3.19271	-1.54557
C	-0.64527	-4.60811	-1.59632
H	-0.17357	-5.22292	-2.36398
C	-1.89467	-4.96478	-1.08321
H	-2.39588	-5.85967	-1.45358
C	-2.49973	-4.18349	-0.10293
H	-3.47417	-4.42439	0.32566
C	2.16369	1.92088	-1.01171
C	2.82987	2.02484	-2.24402
C	2.31233	2.83816	-3.24624
C	1.13908	3.56316	-3.02485
C	0.98003	2.64614	-0.79715
C	0.47682	3.46981	-1.79990
H	3.74482	1.45171	-2.40007
H	2.82764	2.91074	-4.20485
H	0.73891	4.20406	-3.81179
H	0.46888	2.56675	0.16397
H	-0.43809	4.03768	-1.62632

28
CBX/Phenylthiol Radical - Product

O	-3.61016	-2.16210	2.13213
I	0.07276	-0.38938	0.52685
S	3.95784	2.03433	-0.61147
N	1.21913	2.82117	-0.86658
C	2.32402	2.49533	-0.75852
O	-1.48742	-2.07121	1.57999
C	-2.68190	-1.54972	1.65693
C	-2.84959	-0.14760	1.12507
C	-1.79513	0.57540	0.57891
C	-1.94607	1.86785	0.08804
H	-1.09841	2.41061	-0.33333
C	-3.21512	2.44500	0.15575
H	-3.35700	3.45810	-0.22333
C	-4.29262	1.74229	0.69943
H	-5.27814	2.20699	0.74515
C	-4.11015	0.45018	1.18262
H	-4.92459	-0.13370	1.61524
C	3.70881	0.45707	0.21738
C	3.71720	0.40785	1.61204
C	3.52677	-0.81660	2.25062
C	3.33428	-1.97614	1.49835
C	3.53386	-0.69876	-0.54542
C	3.34079	-1.91851	0.10336
H	3.85726	1.32375	2.18742
H	3.51954	-0.86287	3.34008
H	3.17549	-2.93063	2.00174
H	3.53551	-0.63776	-1.63462
H	3.19170	-2.82561	-0.48373

29

CBX/Neutral Phenylthiol - Reactant

I	0.66027	-0.33843	1.85320
S	1.84292	1.86519	-1.01599
N	3.87464	-0.81821	1.25208
C	2.74969	-0.64253	1.45461
O	-1.49169	-0.21634	1.87753
C	-2.12583	-0.71739	0.84885
O	-3.31904	-0.73592	0.69483
C	-1.18680	-1.28316	-0.19875
C	0.18294	-1.21988	-0.01926
C	1.11879	-1.66183	-0.93856
H	2.19204	-1.57802	-0.76401
C	0.61369	-2.22339	-2.11447
H	1.31439	-2.58694	-2.86736
C	-0.76306	-2.32762	-2.32957
H	-1.13175	-2.77566	-3.25304
C	-1.66352	-1.85591	-1.37839
H	-2.74537	-1.90317	-1.51505
C	0.08643	1.81671	-1.27207
C	-0.37486	1.31507	-2.49363
C	-1.74375	1.17950	-2.71709
C	-2.66155	1.54483	-1.73352
C	-0.83435	2.19317	-0.28673
C	-2.20111	2.06016	-0.52276
H	0.34099	1.03346	-3.26845
H	-2.09283	0.78000	-3.67098
H	-3.73169	1.42003	-1.89987
H	-0.48665	2.58376	0.67216
H	-2.90972	2.32873	0.26170
H	1.83955	2.79308	-0.04003

29

CBX/Neutral Phenylthiol - TS

I	1.39187	-1.22773	0.47030
S	1.88864	2.20629	0.21552
N	3.44672	0.61323	-1.47320
C	2.62189	0.65512	-0.64091
O	-0.91677	-1.74218	1.77208
C	-1.88042	-1.36784	1.06963
O	-3.04861	-1.14377	1.38506
C	-1.52316	-1.06407	-0.41140
C	-0.22946	-0.91893	-0.88201
C	0.08667	-0.59794	-2.20114
H	1.12227	-0.51059	-2.53252
C	-0.96596	-0.40164	-3.09397
H	-0.74567	-0.15572	-4.13397
C	-2.28752	-0.53777	-2.66086
H	-3.10774	-0.39410	-3.36620
C	-2.55677	-0.86045	-1.33498
H	-3.57369	-0.95979	-0.95051
C	0.15397	2.04693	0.50518
C	-0.67768	2.47515	-0.53546
C	-2.05400	2.35586	-0.37458
C	-2.57983	1.82790	0.80615
C	-0.35848	1.51969	1.69691
C	-1.73642	1.42668	1.84310
H	-0.25711	2.87781	-1.45910
H	-2.71675	2.66020	-1.18500
H	-3.65507	1.68847	0.91723
H	0.29776	1.15285	2.48760
H	-2.15584	0.95824	2.73284
H	2.32334	1.89464	1.45650

29

CBX/Neutral Phenylthiol - Product

I	-2.74853	-0.24424	-0.08666
S	0.38013	1.86740	-1.46508
N	-0.73088	3.11134	0.85046
C	-0.26880	2.59717	-0.07765
O	-0.32157	-1.39321	-2.00292
C	0.19703	-2.05599	-0.96370
O	0.78813	-3.08217	-1.13317
C	0.10804	-1.41002	0.40330
C	-0.90716	-0.58212	0.90570
C	-0.78456	0.01122	2.16376
H	-1.57144	0.66938	2.53174
C	0.34108	-0.23767	2.94504
H	0.42634	0.23615	3.92394
C	1.33524	-1.09738	2.48281
H	2.21145	-1.31121	3.09602
C	1.21235	-1.67466	1.22592
H	1.97929	-2.34367	0.83394
C	1.87280	1.13241	-0.79497
C	2.44699	1.53401	0.40918
C	3.61747	0.90883	0.83703
C	4.20494	-0.09864	0.07354
C	2.45012	0.12665	-1.57454
C	3.61922	-0.48747	-1.13125
H	1.98404	2.31517	1.01413
H	4.06933	1.21527	1.78167
H	5.11871	-0.58410	0.41816
H	1.97789	-0.19691	-2.50432
H	4.06272	-1.28343	-1.73055
H	-0.73616	-0.55966	-1.73459

35

CDBX/Phenylthiol Anion - Reactant

I	0.10770	-0.09058	0.78096
S	1.04367	2.66483	1.40156
N	3.09901	-1.06436	1.99024
C	2.07240	-0.69411	1.59992
O	-1.82279	-0.09558	-0.12887
C	-2.55491	-1.26282	0.01246
C	-1.59425	-2.46057	0.08986
C	-0.27237	-2.21240	0.45224
C	0.66182	-3.23322	0.58947
H	1.68977	-3.01112	0.88167
C	0.26247	-4.54968	0.34954
H	0.98806	-5.35948	0.44567
C	-1.05633	-4.82498	-0.00993
H	-1.36938	-5.85437	-0.19512
C	-1.97868	-3.78665	-0.13447
H	-3.01164	-4.01058	-0.41083
C	1.85969	2.95768	-0.12039
C	2.89773	2.12394	-0.59194
C	3.53657	2.37377	-1.80438
C	3.17627	3.46904	-2.59160
C	1.51060	4.05886	-0.93314
C	2.15723	4.31091	-2.13943
H	3.20442	1.27428	0.02280
H	4.33337	1.70275	-2.13565
H	3.67962	3.66326	-3.54079
H	0.70660	4.71139	-0.58729
H	1.85671	5.17404	-2.73961
C	-3.38582	-1.22817	1.30880
C	-3.47751	-1.37614	-1.20611
H	-4.14702	-2.24805	-1.15248
H	-4.08768	-0.46369	-1.25831
H	-2.86857	-1.43731	-2.11843
H	-3.98717	-2.14134	1.43857
H	-2.71718	-1.12547	2.17668
H	-4.05001	-0.35210	1.28045

35

CDBX/Phenylthiol Anion - TS

I	-0.41199	-0.71146	0.57219
S	2.07811	1.25751	0.17783
N	1.86044	-0.99524	-1.74633
C	1.41342	-0.45224	-0.79458
O	-2.28129	-1.23927	1.78980
C	-2.73190	-2.51798	1.70100
C	-2.04405	-3.25788	0.52968
C	-0.98921	-2.65162	-0.13556
C	-0.31037	-3.24710	-1.19844
H	0.51130	-2.72182	-1.69102
C	-0.71324	-4.51896	-1.60565
H	-0.19851	-5.00249	-2.43801
C	-1.76405	-5.16550	-0.95340
H	-2.07584	-6.16270	-1.27127
C	-2.41947	-4.53896	0.10366
H	-3.24039	-5.05140	0.61167
C	2.13232	2.33858	-1.21202
C	2.76682	1.95763	-2.40708
C	2.82219	2.84132	-3.48288
C	2.27114	4.12031	-3.38742
C	1.56235	3.61960	-1.12961
C	1.64178	4.50456	-2.20246
H	3.18133	0.95147	-2.47799
H	3.30977	2.52640	-4.40835
H	2.32817	4.81114	-4.23093
H	1.05369	3.90722	-0.20759
H	1.19820	5.49906	-2.11513
C	-2.41492	-3.29832	2.99684
C	-4.25495	-2.50742	1.45634
H	-4.69956	-3.51370	1.39772
H	-4.72659	-1.95570	2.28266
H	-4.45890	-1.96581	0.52180
H	-2.76742	-4.34228	2.97205
H	-1.32666	-3.29368	3.15748
H	-2.88815	-2.77400	3.84049

35
CDBX/Phenylthiol Anion - Product

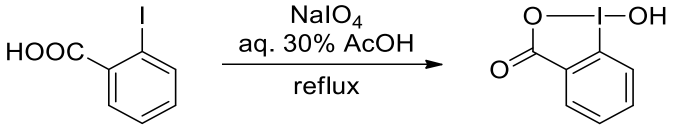
I	-2.34514	0.67036	-3.10119
S	1.13979	-0.48657	-1.91337
N	1.93440	1.65043	-3.62750
C	1.59857	0.79436	-2.92325
O	-3.27704	-1.28582	-1.17534
C	-2.75548	-0.98555	-0.02183
C	-1.89864	0.35961	-0.00859
C	-1.66527	1.14978	-1.13121
C	-0.90208	2.32336	-1.07482
H	-0.73532	2.89726	-1.98868
C	-0.34794	2.74348	0.13014
H	0.25272	3.65513	0.16642
C	-0.56213	1.97968	1.27827
H	-0.12744	2.28213	2.23424
C	-1.32075	0.81767	1.19212
H	-1.47165	0.22098	2.09588
C	1.87639	0.04153	-0.37307
C	2.66814	1.18070	-0.22831
C	3.17405	1.50247	1.02976
C	2.89914	0.69772	2.13424
C	1.59329	-0.77214	0.72683
C	2.10914	-0.44025	1.97625
H	2.87263	1.82273	-1.08587
H	3.78494	2.39976	1.14343
H	3.29409	0.96071	3.11677
H	0.93800	-1.63763	0.61292
H	1.87159	-1.07148	2.83408
C	-3.85615	-0.79149	1.07857
C	-1.76775	-2.10741	0.46654
H	-1.26285	-1.93232	1.43472
H	-2.34980	-3.04000	0.52475
H	-1.01826	-2.23892	-0.33198
H	-3.49709	-0.57160	2.09907
H	-4.51942	0.02034	0.74424
H	-4.44529	-1.72123	1.09513

3. General Methods

Technical grade solvents were used for quantitative flash chromatography. HPLC grade solvents purchased from Sigma-Aldrich or freshly distilled solvents were used for flash chromatography for compounds undergoing full characterization. Reaction solvents were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 30 ppm, Karl-Fischer titration). We note; however, that the thiol-alkynylation reaction gives identical results when using HPLC grade THF purchased from Sigma-Aldrich or dried THF from the solvent system. Commercially available reagents were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used without any further purification. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plates and visualized with UV light and permanganate stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H NMR spectra were measured on a Brucker DPX-400 400 MHz spectrometer, all signals are reported in ppm with the corresponding internal solvent peak or TMS as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration; interpretation). ^{13}C NMR spectra were carried out with 1H-decoupling on a Brucker DPX-400 100 MHz. All signals are reported in ppm with the corresponding internal solvent signal or TMS as standard. Infrared spectra were obtained on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, sh = shoulder). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.

4. Preparation of Reagents

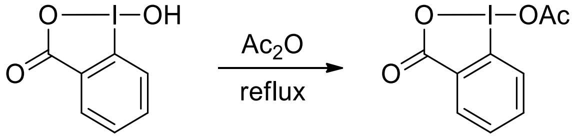
1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (**20**)



19 **20**

Following a reported procedure,[1] $NaIO_4$ (25.8 g, 121 mmol, 1.05 eq.) and 2-iodobenzoic acid (**19**) (28.5 g, 115 mmol, 1.00 eq.) were suspended in 30% (v:v) aq. AcOH (175 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (500 mL) and allowed to cool to room temperature, while protecting it from light. After 1 h, the crude product was collected by filtration. The crystals were washed with ice water (3 x 100 mL) followed by acetone (3 x 100 mL) and then air-dried in the dark affording **20** (29.3 g, 111 mmol, 96.5%) as a white solid. ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 8.04 (s, 1 H, O*H*), 8.01 (dd, 1 H, *J* = 7.6, 1.5 Hz, Ar*H*), 7.96 (ddd, 1 H, *J* = 8.5, 7.2, 1.5 Hz, Ar*H*), 7.84 (dd, 1 H, *J* = 8.2, 0.7 Hz, Ar*H*), 7.70 (td, 1 H, *J* = 7.3, 1.1 Hz, Ar*H*). ^{13}C NMR (100 MHz, (DMSO-*d*$_6$) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m). The characterization data is in accordance with reported literature values.[2]

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (**21**)



20 **21**

Following a reported procedure,[3] 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**20**, 10.3 g, 39.1 mmol, 1.00 eq.) was suspended in acetic anhydride (35 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* affording **21** (10.8 g, 35.3 mmol, 90.2%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24 (dd, 1 H, *J* = 7.6, 1.6 Hz, Ar*H*), 8.00 (dd, 1 H, *J* = 8.3, 1.0 Hz, Ar*H*), 7.92 (ddd, 1 H, *J* = 8.4, 7.2, 1.6 Hz, Ar*H*), 7.71 (td, 1 H, *J* = 7.3, 1.1 Hz, Ar*H*), 2.25 (s, 3 H, COC*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. The values of the NMR spectra are in accordance with reported literature data.[3]

1-Cyano-1,2-benziodoxol-3-(1*H*)-one (**10**)

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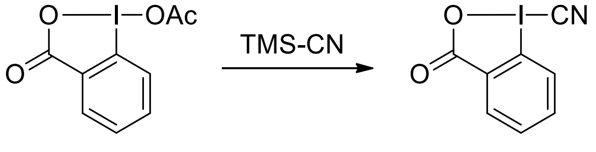
[1] Kraszkiewicz, L.; Skulski, L. *Arkivoc* **2003**, 120.

[2] Brand, J. P.; Charpentier, J.; Waser, J. *Angew. Chem. Int. Ed.* **2009**, *48*, 9346.

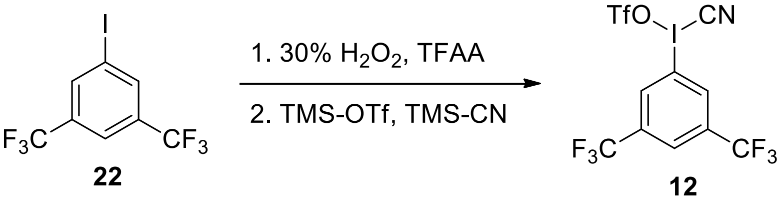
[3] Eisenberger, P.; Gischig, S.; Togni, A. *Chem. Eur. J.* **2006**, *12*, 2579.



21 **10**

Following a reported procedure,[4] 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**21**, 10.5 g, 34.3 mmol, 1.00 eq.) was dissolved under nitrogen in dry dichloromethane (80 mL). To the clear colorless solution was added *via* syringe trimethylsilyl cyanide (TMS-CN, 9.20 mL, 68.6 mmol, 2.00 eq.) over a five minute time period. The reaction mixture was stirred at room temperature and under nitrogen for 72 hours. The resulting thick white suspension was filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **10** (8.89 g, 32.6 mmol, 95.0%) as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.29 (d, 1 H, *J* = 8.3 Hz, Ar*H*), 8.13 (dd, 1 H, *J* = 7.4, 1.7 Hz, Ar*H*), 8.06-7.97 (m, 1 H, Ar*H*), 7.88 (t, 1 H, *J* = 7.3 Hz, Ar*H*). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 166.7, 136.5, 132.0, 131.9, 130.2, 127.8, 117.5, 87.9. IR ν 3157 (w), 3093 (w), 2160 (w), 1629 (s), 1562 (m), 1439 (m), 1321 (s), 1298 (s), 1148 (m), 839 (m), 747 (s). The characterization data is in accordance with reported literature values.[4]

3,5-Di(trifluoromethyl)phenyl(cyano)iodonium triflate (**12**)



22 **12**

Following a reported procedure,[5] to a solution consisting of trifluoroacetic anhydride (TFAA, 20 mL) and dichloromethane (25 mL) was added dropwise at -50 °C aq. 30 wt% hydrogen peroxide (4.0 mL). After 10 minutes of stirring at -50 °C, a solution consisting of 1-iodo-3,5-bis(trifluoromethyl)benzene (**22**) (1.02 g, 3.00 mmol, 1.00 eq.) and dichloromethane (5.0 mL) was added dropwise. The reaction mixture was gradually warmed to 15 °C over a 14 hour time period. Next, the mixture was concentrated *in vacuo*, affording the corresponding trifluoroacetate derivative (1.64 g, 2.90 mmol, 97%) as a white solid. The intermediate was dissolved in dry dichloromethane (10 mL) without additional purification and trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 524 µL, 2.90 mmol, 1.00 eq.), followed by trimethylsilyl cyanide (TMS-CN, 388 µL, 2.90 mmol, 1.00 eq.), were added dropwise at room temperature. The resulting white suspension was diluted with dry dichloromethane (5.0 mL) and stirred at room temperature for 60 minutes, after which it was filtered. The white solid was washed with dichloromethane (2 x 10 mL), pentane (2 x 10 mL) and dried *in vacuo* to afford the title compound **12** (1.46 g, 2.83 mmol, 98%) as a white solid. ^{1}H NMR (CD_3CN, 400 MHz): δ 8.97 (s, 2 H, Ar*H*), 8.45 (s, 1 H, Ar*H*). ^{19}F NMR (CD_3CN, 376 MHz): δ -63.6, -79.3. The values of the NMR spectra are in accordance with reported literature data.[5]

1-Acetoxy-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**31**)

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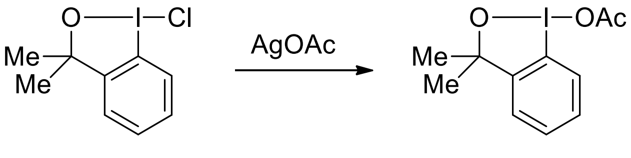
[4] Akai, S.; Okuno, T.; Egi, M.; Takada, T.; Tohma, H.; Kita, Y. *Heterocycles* **1996**, *42*, 47.

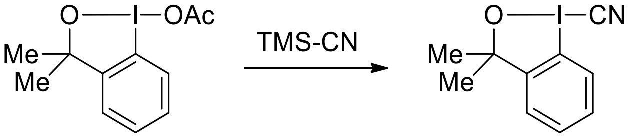
[5] Zhdankin, V. V.; Scheuller, M. C.; Stang, P. J. *Tetrahedron Lett.* **1993**, *34*, 6853.



23 **24**

Following a reported procedure,[3] 1-chloro-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole[6] (**23**, 3.10 g, 10.5 mmol, 1.00 eq.) and silver acetate (1.83 g, 11.0 mmol, 1.05 eq.) were suspended under nitrogen in dry acetonitrile (30 mL). The mixture was stirred in the dark at room temperature for 15 hours. Filtration of the precipitated silver chloride followed by solvent removal *in vacuo* yielded compound **24** (2.98 g, 9.31 mmol, 89%) as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.79 (dd, 1 H, *J* = 8.0, 1.3 Hz, Ar*H*), 7.52-7.41 (m, 2 H, Ar*H*), 7.17 (dd, 1 H, *J* = 7.4, 1.6 Hz, Ar*H*), 2.10 (s, 3 H, $COCH_3$), 1.52 (s, 6 H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.4, 149.4, 130.5, 130.0, 129.9, 126.3, 115.8, 84.6, 29.3, 21.6. The characterization data is in accordance with reported literature values.[3]

1-Cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (11)



24 **11**

To a solution consisting of 1-acetoxy-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**24**, 2.00 g, 6.25 mmol, 1.00 eq.) and dry dichloromethane (15 mL) was added dropwise trimethylsilyl cyanide (TMS-CN, 1.71 mL, 12.5 mmol, 2.00 eq.) at room temperature under nitrogen. The clear colorless solution was stirred at room temperature for 20 hours. Solvent removal afforded a white solid, which was suspended in pentane (10 mL), filtered and dried *in vacuo* affording pure compound **11** (1.73 g, 6.03 mmol, 96%) as a white solid. R_f (pentane:EtOAc 7:3) = 0.54. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05 (d, 1 H, *J* = 8.3 Hz, Ar*H*), 7.62 (t, 1 H, *J* = 7.3 Hz, Ar*H*), 7.58-7.49 (m, 1 H, Ar*H*), 7.33 (d, 1 H, *J* = 7.5 Hz, Ar*H*), 1.48 (s, 6 H, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.1, 131.7, 131.0, 128.3, 126.9, 111.6, 98.0, 80.4, 30.3. IR ν 2974 (w), 2925 (w), 2139 (w), 1461 (m), 1436 (m), 1251 (m), 1160 (s), 1003 (w), 954 (s), 869 (m), 761 (s). The characterization data is in accordance with reported literature values.[7]

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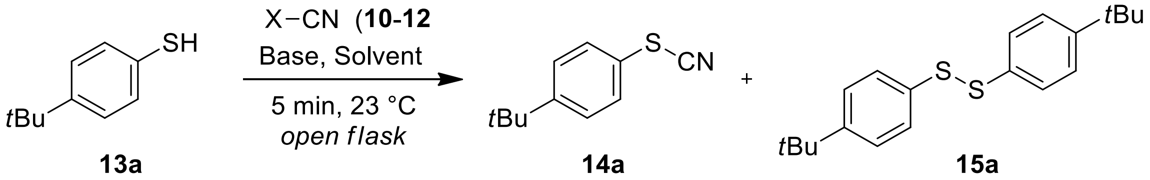
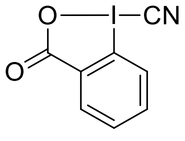
[6] This commercially available compound can also be synthesized following the practical procedure by Matousek, V.; Pietrasiak, E.; Schwenk, R.; Togni, A. *J. Org. Chem.* **2013**, *78*, 6763.

[7] Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Mismash, B.; Woodward, J. K.; Simonsen, A. J. *Tetrahedron Lett.* **1995**, *36*, 7975.

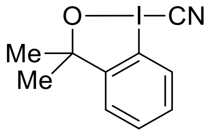
5. Cyanation Reaction

5.1 Reaction Optimization with 1-(tert-Butyl)-4-Thiocyanatobenzene

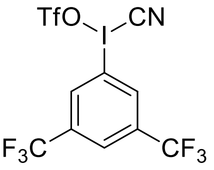




10



11



12

The following general procedure was utilized to optimize the thiol-cyanation reaction. A 25 mL round bottom flask was charged with a magnetic stir bar, 1-(*tert*-butyl)-4-thiol (**13a**, 83.0 mg, 0.500 mmol, 1.00 eq.) and the indicated solvent (5.0 mL). To this solution was added base (0.525 mmol, 1.05 eq.), followed by the cyano source (**10-12**, 0.550 mmol, 1.10 eq.). The resulting reaction mixture was stirred with an open flask for 5 minutes at room temperature followed by solvent removal under reduced pressure. The crude product was purified by flushing it dissolved in minimum amounts of THF through a small plug of silica gel using pentane:EtOAc 99:1 as mobile phase. The desired cyanation product (**14a**) and disulfide side-product(**15a**) were isolated as analytically pure products. It took 20 minutes of stirring at room temperature with an open flask for the control experiment (entry 5) with no added base to go to completion. For this entry, the 2-iodobenzoic acid side product **21** was also isolated by switching the mobile phase to pentane:EtOAc 10:1 and 1% acetic acid once the disulfide (**15a**) and cyanation product (**14a**) eluted off the column.

1-(*tert*-Butyl)-4-thiocyanatobenzene (**14a**) was obtained as a colorless oil. R$_f$ (pentane) = 0.38. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50-7.43 (m, 4 H, Ar*H*), 1.33 (s, 9 H, *t*Bu). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.4, 130.5, 127.4, 120.6, 111.0, 34.9, 31.2. IR ν 2965 (m), 2906 (w), 2870 (w), 2158 (w), 1490 (m), 1400 (w), 1365 (w), 1269 (w), 1116 (m), 1011 (w), 827 (s). HRMS (ESI) $C_{11}H_{13}NNaS^+$ $[M+Na]^+$ calc. = 214.0661; $[M+Na]^+$ obs. = 214.0656.

1,2-Bis(4-(*tert*-butyl)phenyl)disulfane (**15a**) was obtained as a light yellow solid. R$_f$ (pentane) = 0.58. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48-7.42 (m, 4 H, Ar*H*), 7.37-7.31 (m, 4 H, Ar*H*), 1.31 (s, 18 H, *t*Bu). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.6, 134.1, 127.8, 126.3, 34.7, 31.4. IR ν 2963 (s), 2903 (w), 2866 (w), 1487 (m), 1397 (w), 1364 (w), 1269 (w), 1116 (w), 1012 (w), 823 (s), 737 (w). The values of the NMR spectra are in accordance with reported literature data.[8]

2-Iodobenzoic acid (**19**) (68.7 mg, 0.277 mmol) was obtained as a white solid. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 13.3 (bs, 1 H, CO_2H), 7.97 (dd, 1 H, *J* = 8.0, 1.1 Hz, Ar*H*), 7.71 (dd, 1 H, *J* = 7.7, 1.8 Hz, Ar*H*), 7.47 (td, 1 H, *J* = 7.6, 1.2 Hz, Ar*H*), 7.22 (td, 1 H, *J* = 7.7, 1.8 Hz,

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[8] Hayashi, M.; Okunaga, K.; Nishida, S.; Kawamura, K.; Eda, K. *Tetrahedron Lett.* **2010**, *51*, 6734.

Ar*H*). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 168.2, 140.6, 136.9, 132.5, 130.1, 128.2, 94.2. The values of the NMR spectra are in accordance with reported literature data.[9]

Table S3. Results of the thiol-cyanation optimization study.

Entry	Cyanating Reagent	Base	Solvent	Isolated Yield **14a**	Isolated Yield **15a**
1	**10**	NEt_3	THF	40%	60%
2	**10**	TMG	THF	79%	20%
3	**10**	TBD	THF	74%	26%
4	**10**	DBU	THF	>95%	<5%
5	**10**	DBU	MeOH	64%	35%
6	**10**	DBU	CH_3CN	86%	12%
7	**10**	-	THF	<10%	90%
8	**12**	DBU	THF	17%	81%
9	**11**	DBU	THF	>95%	<5%

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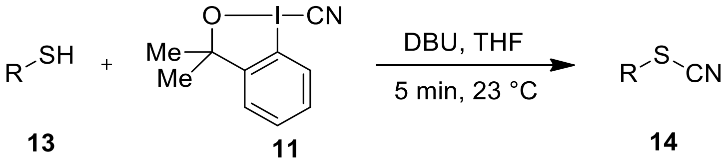
[9] Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. *Chem. Eur. J.* **2012**, *18*, 2931.

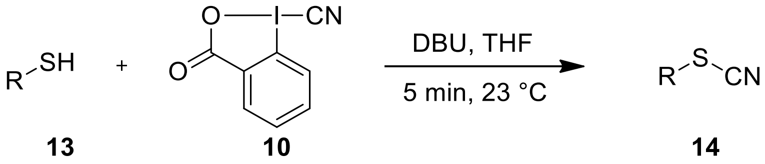
5.2 General Procedures for Cyanation

General Procedure A (GPA): for thiols with CDBX (11)



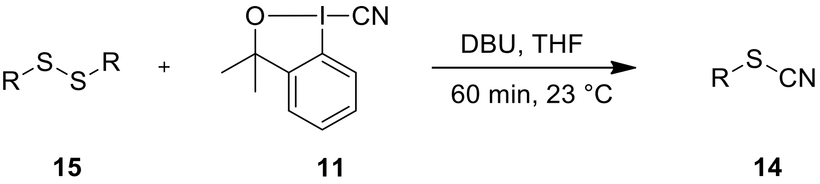
A 25 mL round bottom flask was charged with a magnetic stirring bar, thiol derivative (0.500 mmol, 1.00 eq.) and THF (5.0 mL). To this solution was added 1,8-diazabicycloundec-7-ene (DBU, 79.0 µL, 0.525 mmol, 1.05 eq.), followed by 1-cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (CDBX (**11**), 158 mg, 0.550 mmol, 1.10 eq.). In case DBU addition yielded a THF-insoluble thiolate, CDBX was added prior to DBU. An additional equivalent of DBU (total amount: 153 µL, 1.03 mmol. 2.05 eq.) was added for carboxylic acid containing substrates. The resulting reaction mixture was stirred in an open flask for 5 minutes at room temperature (unless otherwise stated). The reaction was quenched with 5% aq. citric acid (10 mL). The aq. mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was further purified as indicated below.

General Procedure B (GPB): for thiols with CBX (10)



A 25 mL round bottom flask was charged with a magnetic stirring bar, thiol derivative (0.500 mmol, 1.00 eq.) and THF (5.0 mL). To this solution was added 1,8-diazabicycloundec-7-ene (DBU, 79.0 µL, 0.525 mmol, 1.05 eq.), followed by 1-cyano-1,2-benziodoxol-3-(1*H*)-one (CBX (**10**), 150 mg, 0.550 mmol, 1.10 eq.). In case DBU addition yielded a THF-insoluble thiolate, CBX was added prior to DBU. An additional equivalent of DBU (total amount: 153 µL, 1.03 mmol. 2.05 eq.) was added for carboxylic acid containing substrates. The resulting reaction mixture was stirred in an open flask for 5 minutes at room temperature (unless otherwise stated). The reaction was quenched with 5% aq. citric acid (10 mL), extracted and further purified as indicated below.

General procedure C: For disulfides with CDBX (11).

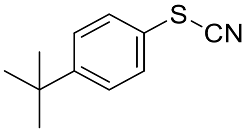


A 25 mL round bottom flask was charged with a magnetic stirring bar, disulfide derivative (0.250 mmol, 1.00 eq.) and THF (5.0 mL). To this solution was added 1,8-diazabicycloundec-

7-ene (DBU, 79.0 µL, 0.525 mmol, 2.10 eq.), followed by 1-cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (CDBX, **11**, 158 mg, 0.550 mmol, 2.20 eq.). The resulting reaction mixture was stirred in an open flask for 60 minutes at room temperature. The reaction was quenched with 5% aq. citric acid (10 mL), extracted and further purified by flash chromatography over silica gel.

5.3 Scope of the Cyanation Reaction

1-(*tert*-Butyl)-4-thiocyanatobenzene (14a)

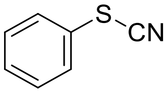


Following general procedure GPA with thiol **13a** (86 mg, 0.50 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 99:1 as mobile phase affording **14a** (91.8 mg, 0.480 mmol, 96%) as a colorless oil.

Following general procedure GPC with disulfide **15a** (83 mg, 0.25 mmol, 1.0 equiv.), the obtained crude oil was purified by flash chromatography using pentane:EtOAc 99:1 as mobile phase affording **14a** (88 mg, 0.46 mmol, 92 %) as a colorless oil.

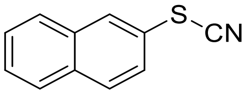
R*f* (pentane) = 0.38. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.50-7.43 (m, 4 H, Ar*H*), 1.33 (s, 9 H, *t*Bu). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 153.4, 130.5, 127.4, 120.6, 111.0, 34.9, 31.2. IR ν 2965 (m), 2906 (w), 2870 (w), 2158 (w), 1490 (m), 1400 (w), 1365 (w), 1269 (w), 1116 (m), 1011 (w), 827 (s). HRMS (ESI) $C_{11}H_{13}NNaS^+$ $[M+Na]^+$ calc. = 214.0661; $[M+Na]^+$ obs. = 214.0656.

Thiocyanatobenzene (14b)



Following general procedure GPA with thiol **13b** (55.6 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 40:1 as mobile phase affording **14b** (60.9 mg, 0.450 mmol, 90%) as a colorless oil. R*f* (pentane:EtOAc 95:5) = 0.57. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.56-7.49 (m, 2 H, Ar*H*), 7.47-7.38 (m, 3 H, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 130.3, 130.1, 129.6, 124.4, 110.6. IR ν 3063 (w), 2158 (m), 1582 (w), 1479 (m), 1444 (m), 1021 (w), 911 (w), 740 (s). The values of the NMR spectra are in accordance with reported literature data.[10]

2-Thiocyanatonaphthalene (14c)



Following general procedure GPA with thiol **13c** (81.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was purified by flushing it dissolved in minimum amounts of THF through a small plug of silica gel using using pentane:EtOAc 99:1 as mobile phase affording **14c** (87.7 mg, 0.473 mmol, 95%) as a colorless oil. R*f* (pentane:EtOAc 95:5) = 0.54. ^{1}H NMR (CDCl$_3$,

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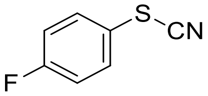
[10] Sun, N.; Zhang, H.; Mo, W. M.; Hu, B. X.; Shen, Z. L.; Hu, X. Q. *Synlett* **2013**, *24*, 1443.

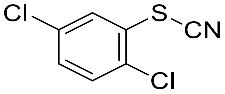
400 MHz): δ 8.01 (d, 1 H, *J* = 2.0 Hz, Ar*H*), 7.93-7.77 (m, 3 H, Ar*H*), 7.62-7.50 (m, 3 H, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 133.7, 133.1, 130.4, 129.9, 128.0, 127.8, 127.7, 127.6, 126.3, 121.3, 110.8. IR ν 3057 (w), 2157 (m), 1503 (m), 857 (m), 813 (s), 745 (s). The values of the characterization data are in accordance with reported literature data.[10]

1-Fluoro-4-thiocyanatobenzene (14d)



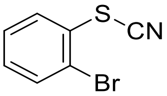
Following general procedure GPA with thiol **13d** (66.8 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was purified by flushing it dissolved in minimum amounts of THF through a small plug of silica gel using using pentane:EtOAc 99:1 as mobile phase affording **14d** (72.3 mg, 0.472 mmol, 94%) as a colorless oil. R$_f$ (pentane:EtOAc 95:5) = 0.49. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.62-7.49 (m, 2 H, Ar*H*), 7.21-7.08 (m, 2 H, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 163.7 (d, *J* = 250 Hz), 133.3 (d, *J* = 8.8 Hz), 119.3 (d, *J* = 3.5 Hz), 117.7 (d, *J* = 23 Hz), 110.7. IR ν 3099 (w), 2159 (m), 1591 (m), 1491 (s), 1402 (w), 1232 (s), 1161 (m), 1082 (w), 1013 (w), 830 (s). The values of the NMR spectra are in accordance with reported literature data.[10]

1,4-Dichloro-2-thiocyanatobenzene (14e)



Following general procedure GPA with thiol **13e** (91.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 50:1 as mobile phase affording **14e** (97.6 mg, 0.478 mmol, 96%) as a white solid. R$_f$ (pentane) = 0.27. Melting point = 81.6-84.9 °C. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.66 (d, 1 H, *J* = 2.3 Hz, Ar*H*), 7.37 (d, 1 H, *J* = 8.6 Hz, Ar*H*), 7.30 (dd, 1 H, *J* = 8.6, 2.3 Hz, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 134.5, 131.2, 130.6, 130.3, 128.9, 126.7, 108.4. IR ν 3083 (w), 3068 (w), 2164 (m), 1565 (w), 1448 (s), 1372 (m), 1252 (w), 1100 (m), 1032 (s), 865 (m), 825 (s). HRMS (APPI) $C_7H_2Cl_2NS^+$ $[M]^+$ calc. = 201.92900; $[M]^+$ obs. = 201.9299. The above melting point is in accordance with a reported literature value.[11]

1-Bromo-2-thiocyanatobenzene (14f)



Following general procedure GPA with thiol **13f** (100 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was purified by flushing it dissolved in minimum amounts of THF through a small plug of silica gel using pentane:EtOAc 50:1 as mobile phase affording **14f** (105 mg, 0.489 mmol, 98%) as a clear colorless oil. R$_f$ (pentane:EtOAc 95:5) = 0.75. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.70 (dd, 1 H, *J* = 8.0, 1.5 Hz, Ar*H*), 7.60 (dd, 1 H, *J* = 8.0, 1.4 Hz, Ar*H*), 7.42 (ddd, 1 H, *J* = 8.0, 7.5, 1.4 Hz, Ar*H*), 7.25 (ddd, 1 H, *J* = 8.0, 7.4, 1.5 Hz, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 133.6, 130.2, 129.5, 129.1, 127.2, 121.8, 109.6. IR ν 2943 (w), 2864 (w), 2161 (w), 2094 (w), 1555 (w), 1451 (s), 1432 (m), 1262 (w), 1018 (m), 883 (w), 856 (w), 748 (s). The values of the characterization data are in accordance with reported literature data.[10]

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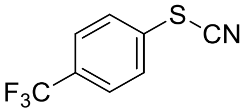
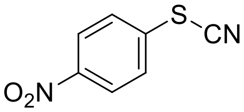
[11] Pilgram, K.; Phillips, D. D. *J. Org. Chem.* **1965**, *30*, 2388.

1-Thiocyanato-4-(trifluoromethyl)benzene (14g)



Following general procedure GPA with thiol **13g** (91.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was purified by flushing it dissolved in minimum amounts of THF through a small plug of silica gel using pentane:EtOAc 99:1 as mobile phase affording **14g** (89.2 mg, 0.439 mmol, 88%) as a white solid. R$_f$ (pentane:EtOAc 95:5) = 0.52. Melting point = 31.0-31.3°C. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 7.70 (d, 2 H, *J* = 8.4 Hz, Ar*H*), 7.63 (d, 2 H, *J* = 8.4 Hz, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 131.5 (q, *J* = 33 Hz), 129.7, 129.2, 127.2 (q, *J* = 3.8 Hz), 123.5 (q, *J* = 270 Hz), 109.1. IR ν 2162 (w), 1610 (w), 1407 (w), 1324 (s), 1170 (m), 1126 (s), 1088 (m), 1064 (s), 1013 (m), 831 (m). The values of the characterization data are in accordance with reported literature data.[10]

1-Nitro-4-thiocyanatobenzene (14h)

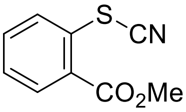


Following general procedure GPA with thiol **13h** (78.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by two consecutive flash chromatography's using pentane:EtOAc 20:1 and 15:1 as mobile phase affording **14h** (83.2 mg, 0.462 mmol, 92%) as a white solid.

Following general procedure GPC with disulfide **15h** (77 mg, 0.25 mmol, 1.0 equiv.), the obtained crude oil was purified by flash chromatography using pentane:EtOAc 99:1 as mobile phase affording **14h** (68 mg, 0.38 mmol, 75 %) as a white solid.

R$_f$ (pentane:EtOAc 9:1) = 0.44. Melting point = 133.6-133.8 °C ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.34-8.26 (m, 2 H, Ar*H*), 7.71-7.64 (m, 2 H, Ar*H*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 148.0, 133.5, 128.8, 125.2, 108.2. IR ν 3107 (w), 2163 (w), 1604 (w), 1579 (w), 1523 (s), 1477 (w), 1343 (s), 1084 (w), 845 (m), 738 (m). The values of the characterization data are in accordance with reported literature data.[12]

Methyl 2-thiocyanatobenzoate (14i)



Following general procedure GPA with thiol **13i** (87.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 49:1 as mobile phase affording **14i** (91.0 mg, 0.471 mmol, 94%) as a white solid. R$_f$ (pentane:EtOAc 95:5) = 0.67. Melting point = 75.0-76.0 °C. ^{1}H NMR (CDCl$_3$, 400 MHz): δ 8.10 (dd, 1 H, *J* = 7.8, 1.6 Hz, Ar*H*), 7.88 (dd, 1 H, *J* = 8.2, 1.1 Hz, Ar*H*), 7.62 (ddd, 1 H, *J* = 8.2, 7.4, 1.6 Hz, Ar*H*), 7.40 (td, 1 H, *J* = 7.6, 1.1 Hz, Ar*H*), 3.94 (s, 3 H, CO$_2$C*H$_3$*). ^{13}C NMR (CDCl$_3$, 100 MHz): δ 166.5, 134.2, 131.7, 130.9, 127.8, 127.6, 126.1, 111.6, 53.0. IR ν 2961 (w), 2154 (w), 1700 (s), 1436 (m), 1309 (s), 1290 (s),

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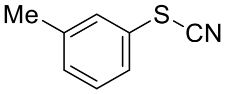
[12] Bangher, A.; Guy, R. G.; Pichot, Y.; Sillence, J. M.; Steel, C. J.; Swinbourne, F. J.; Tamiatti, K. *Spectrochim. Acta Mol. Biomol. Spectros.* **1995**, *51*, 1703.

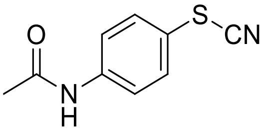
1269 (s), 1117 (m), 1057 (m), 739 (s). The values of the characterization data are in accordance with reported literature data.[13]

1-Methyl-3-thiocyanatobenzene (14j)



Following general procedure GPA with thiol **13j** (63.4 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 99:1 as mobile phase affording **14j** (69.5 mg, 0.466 mmol, 93%) as a colorless oil. R_f (pentane:EtOAc 95:5) = 0.63. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.27 (m, 3 H, Ar*H*), 7.24-7.17 (m, 1 H, Ar*H*), 2.37 (s, 3 H, C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.5, 130.5, 130.4, 130.0, 127.1, 124.0, 110.8, 21.3. IR ν 2923 (w), 2158 (m), 1596 (w), 1478 (m), 849 (w), 776 (s). The values of the NMR spectra are in accordance with reported literature data.[10]

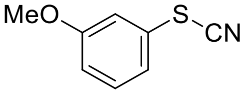
N-(4-Thiocyanatophenyl)acetamide (14k)



Following general procedure GPA with thiol **13k** (85.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 2:1 to 1:1 as mobile phase affording **14k** (87.6 mg, 0.456 mmol, 91%) as a white solid. R_f (EtOAc:pentane 7:3) = 0.49. Melting point = 190.6-192.4 °C. ^{1}H NMR (THF-*d*$_8$, 400 MHz): δ 9.29 (bs, 1 H, N*H*), 7.76-7.68 (m, 2 H, Ar*H*), 7.53-7.43 (m, 2 H, Ar*H*), 2.04 (s, 3 H, C*H*$_3$). ^{13}C NMR (THF-*d*$_8$, 100 MHz): δ 169.0, 142.6, 132.8, 121.3, 118.0, 111.3, 24.3. IR ν 3250 (w), 3179 (w), 3101 (w), 3057 (w), 2152 (w), 1675 (m), 1610 (m), 1588 (s), 1538 (s), 1492 (m), 1396 (m), 1370 (m), 1318 (s), 1265 (w), 840 (m), 771 (w). HRMS (ESI) $C_9H_8N_2NaOS^+$ $[M+Na]^+$ calc. = 215.0250; $[M+Na]^+$ obs. = 215.0255.

In addition, 2-(2-iodophenyl)propan-2-ol (132 mg, 0.505 mmol, 92% based on 0.550 mmol of starting material **11**) was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.95 (dd, 1 H, *J* = 7.8, 1.4 Hz, Ar*H*), 7.62 (dd, 1 H, *J* = 7.9, 1.7 Hz, Ar*H*), 7.31 (ddd, 1 H, *J* = 8.0, 7.3, 1.4 Hz, Ar*H*), 6.88 (td, 1 H, *J* = 7.6, 1.7 Hz, Ar*H*), 3.07 (bs, 1 H, O*H*), 1.75 (s, 6 H, C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.5, 142.7, 128.6, 128.1, 126.8, 93.3, 73.6, 29.8. The values of the NMR data are in accordance with reported literature data.[14]

1-Methoxy-3-thiocyanatobenzene (14l)



Following general procedure GPA with thiol **13l** (71.5 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was purified by flushing it dissolved in minimum amounts of THF through a small plug of silica gel using pentane:EtOAc 60:1 as mobile phase affording **14l** (77.6 mg, 0.470 mmol, 94%) as a colorless oil. R_f (pentane:EtOAc 95:5) = 0.43. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33 (t, 1 H, *J* = 8.1 Hz, Ar*H*), 7.08 (ddd, 1 H, *J* = 7.8, 1.8, 0.9 Hz, Ar*H*), 7.04 (t, 1 H, *J* = 2.1 Hz, Ar*H*), 6.93 (ddd, 1 H, *J* = 8.4, 2.5, 0.9 Hz, Ar*H*), 3.83 (s, 3 H, OC*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.7, 131.1, 125.4, 122.0, 115.6, 115.2, 110.5, 55.7. IR ν 2941

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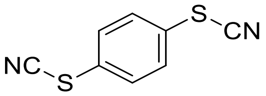
[13] Zang, H.; Breydo, L.; Mitra, K.; Dannaldson, J.; Gates, K. S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1511.

[14] Powers, D. C.; Lee, E.; Ariafard, A.; Sanford, M. S.; Yates, B. F.; Canty, A. J.; Ritter, T. *J. Am. Chem. Soc.* **2012**, *134*, 12002.

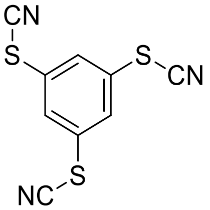
(w), 2838 (w), 2159 (w), 1594 (s), 1483 (s), 1289 (m), 1251 (s), 1036 (s), 855 (m), 775 (m). The values of the characterization data are in accordance with reported literature data.[10]

1,4-Dithiocyanatobenzene (14m)



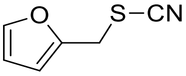
The reaction was performed using general procedure GPB with dithiol **13m** (73.3 mg, 0.500 mmol, 1.0 equiv.). As the starting material contained two thiol functionalities, the reaction was carried out using 2.10 eq. DBU (158 µL, 1.05 mmol) and 2.20 eq. 1-cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**10**, 316 mg, 1.10 mmol). The crude oil was dissolved in minimum amounts of THF and purified by two consecutive flash chromatography's using pentane:EtOAc 15:1 and 10:1 as mobile phase affording **14m** (83.8 mg, 0.436 mmol, 87%) as a white solid. R_f (pentane:EtOAc 9:1) = 0.38. Melting point = 109.0-109.8. °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (s, 4 H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 130.9, 126.7, 109.2. IR ν 2161 (m), 1669 (w), 1632 (w), 1478 (w), 1394 (w), 1007 (w), 809 (s). The values of the characterization data are in accordance with reported literature data.[12]

1,3,5-Trithiocyanatobenzene (14n)



The reaction was performed using general procedure GPB with dithiol **13n** (89 mg, 0.500 mmol, 1.0 equiv.). As the starting material contained three thiol functionalities, the reaction was carried out using 3.15 eq. DBU (237 µL, 1.58 mmol) and 3.30 eq. 1-cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**10**, 474 mg, 1.65 mmol). The crude oil was dissolved in minimum amounts of THF and purified by two consecutive flash chromatography's using pentane:EtOAc 9:1 and 7:1 as mobile phase affording **14n** (97.3 mg, 0.390 mmol, 78%) as a white solid. R_f (pentane:EtOAc 7:3) = 0.57. Melting point = 112.1-114.3 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66 (s, 3 H, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 130.4, 129.0, 107.8. IR ν 3057 (m), 2167 (m), 1567 (s), 1421 (m), 1125 (w), 848 (m), 782 (w). HRMS (ESI) $C_9H_4N_3S_3$ $[M+H]^+$ calc. = 249.9562; $[M+H]^+$ obs. = 249.9564.

2-(Thiocyanatomethyl)furan (14o)



Following general procedure GPB with thiol **13o** (57.0 mg, 0.500 mmol, 1.0 equiv.), the obtained crude oil was purified by flash chromatography using pentane:EtOAc 95: to 9:1 as mobile phase affording **14o** (61 mg, 0.47 mmol, 88%) as a yellow oil. R_f (Pentane:EtOAc 9:1) = 0.45. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45 (dd, 1H, *J* = 1.8, 0.8 Hz, C*H*O), 6.44 (dd, 1H, *J* = 3.2, 0.5 Hz, Ar*H*), 6.38 (dd, 1H, *J* = 3.4, 2.0 Hz, Ar*H*), 4.21 (s, 2H, C*H*$_2$S).^{13}C NMR ($CDCl_3$, 100 MHz): δ. 147.05, 143.95, 111.59, 111.09, 110.65, 30.98. IR ν 2361 (w), 2341 (w), 2155 (m), 2082 (w), 1500 (w), 1249 (w), 1153 (m), 1014 (s), 940 (m), 746 (s).

The values of the ^{1}HNMR data are in accordance with reported literature data[15]

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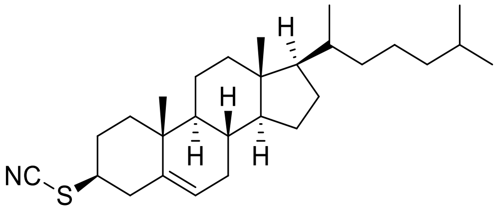
[15] Maeda, H.; Kawaguchi, T.; Masui, M.; Ohmori, H. *Chem. Pharm. Bull.* **1990**, *38*, 1389.

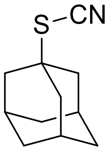
Cholest-5-en-3β-yl thiocyanate (14p)



Following general procedure GPB with thiol **13p** (201 mg, 0.500 mmol, 1.0 equiv.), the crude solid was purified by flash chromatography using pentane:EtOAc 9:1 as mobile phase affording **14p** (211 mg, 0.477 mmol, 97%) as white crystals. R_f (Pentane:EtOAc 95:5) = 0.55. Melting point = 125.0-126.2°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.43-5.39 (m, 1H, CH_{sp2}), 3.08 (tt, 1H, *J* = 12.4, 4.2 Hz, C*H*S), 2.59 – 2.48 (m, 1H), 2.44 (ddd, 1H, *J* = 13.6, 4.5, 2.3 Hz), 2.08 – 1.93 (m, 4H), 1.90-1.76 (m, 2H), 1.62-1.04 (m, 18H), 1.02 (s, 3H, CH_3), 1.01-0.93 (m, 2H), 0.91 (d, 3H, *J* = 6.5 Hz, CH_3), 0.87 (d, 3H, *J* = 1.8 Hz, CH_3-*iPr*), 0.85 (d, 3H, *J* = 1.7 Hz, CH_3-*iPr*), 0.67 (s, 3H, CH_3).^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.9, 123.1, 111.2, 56.6, 56.1, 50.0, 48.1, 42.2, 39.7, 39.6, 39.5, 39.3, 36.4, 36.2, 35.8, 31.8, 31.78, 31.73, 29.9, 28.2, 28.0, 24.2, 23.8, 22.8, 22.5, 20.9, 19.2, 18.7, 11.8. IR ν 2930 (s), 2865 (s), 2153 (w), 1465 (m), 1380 (w), 823 (w).

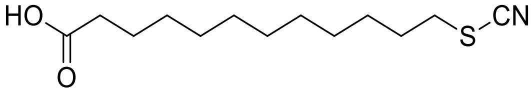
The values of the NMR spectra and physical data are in accordance with reported literature data.[16]

1-Thiocyanatoadamantane (14q)



Following general procedure GPB with thiol **13q** (84.0 mg, 0.500 mmol, 1.0 equiv.), the crude solid was purified by flash chromatography using pentane:EtOAc 99:1 to 95:5 as mobile phase affording **14q** (96.0 mg, 0.497 mmol, 99%) as a white solid. R_f (Pentane:EtOAc 9:1) = 0.7. Melting point = 66.0-67.0°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.16 (s, 3H, C*H*), 2.08- 2.03 (m, 6H, CH_2), 1.78-1.65 (m, 6H, CH_2).^{13}C NMR ($CDCl_3$, 100 MHz): δ. 110.9, 54.0, 43.6, 35.4, 30.3. IR ν 2911 (s), 2854 (m), 2143 (w), 1453 (w), 1301 (w), 1035 (s), 819 (w).HRMS (ESI) $C_{11}H_{15}NNaS^+$ $[M+Na]^+$ calc. = 216.0817; $[M+Na]^+$ obs. = 216.0816. The values of the NMR spectra and physical data are in accordance with reported literature data.[17]

12-Thiocyanatododecanoic acid (14r)



Following general procedure GPB with thiol **13r** (121 mg, 0.500 mmol, 1.0 equiv.), the aq. mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude oil was purified by two consecutive flash chromatography's using pentane:EtOAc 20:1 and 1% acetic acid as mobile phase affording **14r** (111 mg, 0.432 mmol, 86%) as a white solid. R_f (pentane:EtOAc 4:1, bromocresol green staining) = 0.49. Melting point = 32.1-33.8 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 11.1 (bs, 1 H, CO_2H), 2.94 (t, 2 H, *J* = 7.3 Hz, CH_2SCN), 2.34 (t, 2 H, *J* = 7.5 Hz, CH_2CO_2H), 1.81 (p, 2 H, *J* = 7.4 Hz, CH_2CH_2SCN), 1.62 (p, 2 H, *J* = 7.5 Hz, $CH_2CH_2CO_2H$),

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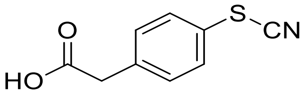
[16] Morzycki, J.W. *et al. Steroids* **2014**, *82*, 60.

[17] Ando, T.; Clark, J.H. ; Cork, D.G. ; Fujita, M. ; Kimura, T. *J. Org. Chem.* **1987**, *52*, 681.

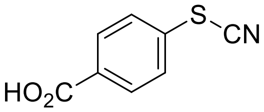
1.43 (p, 2 H, *J* = 7.2 Hz, CH_2), 1.38-1.21 (m, 12 H, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz)[18]: δ 180.3, 112.6, 34.2, 30.0, 29.5, 29.4, 29.3, 29.1, 29.0, 28.1, 24.8. IR ν 3458 (w), 2931 (s), 2857 (m), 2155 (s), 1711 (m), 1462 (w), 1274 (w), 1054 (m), 730 (w). HRMS (ESI) $C_{13}H_{24}NO_2S$ $[M+H]^+$ calc. = 258.1522; $[M+H]^+$ obs. = 258.1522.

2-(4-Thiocyanatophenyl)acetic acid (14s)



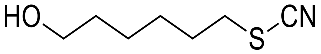
Following general procedure GPA with thiol **13s** (87.0 mg, 0.500 mmol, 1.0 equiv.), the crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 8:1 to 7:1 with 1% acetic acid as mobile phase affording **14s** (87.2 mg, 0.451 mmol, 90%) as a white solid. R_f (pentane:EtOAc 7:3 with 1% acetic acid) = 0.34. Melting point = 105.2-106.8 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ 11.5 (bs, 1 H, CO_2H), 7.50 (d, 2 H, *J* = 7.9 Hz, Ar*H*), 7.36 (d, 2 H, *J* = 8.0 Hz, Ar*H*), 3.68 (s, 2 H, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.2, 135.1, 131.4, 130.4, 123.5, 110.5, 40.5. IR ν 2918 (w), 2153 (w), 1691 (s), 1420 (m), 1249 (m), 911 (m), 810 (m), 739 (w). HRMS (ESI) $C_9H_7NNaO_2S^+$ $[M+Na]^+$ calc. = 216.0090; $[M+Na]^+$ obs. = 216.0088. In addition, 2-(2-iodophenyl)propan-2-ol (130 mg, 0.496 mmol, 90% based on 0.550 mmol of starting material **11**) was isolated as a colorless oil.

4-Thiocyanatobenzoic acid (14t)



Following general procedure GPA with thiol **13t** (78.0 mg, 0.500 mmol, 1.0 equiv.), the crude solid was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 7:1 with 1% acetic acid as mobile phase affording **14t** (81.6 mg, 0.455 mmol, 91%) as a white solid. R_f (pentane:EtOAc 7:3 with 1% acetic acid) = 0.54. Melting point = 223.9-225.8 °C. ^1H NMR (THF-d_8, 400 MHz): δ 11.6 (bs, 1 H, CO_2H), 8.08 (d, 2 H, *J* = 8.2 Hz, Ar*H*), 7.65 (d, 2 H, *J* = 8.2 Hz, Ar*H*). ^{13}C NMR (THF-d_8, 100 MHz): δ 166.7, 132.6, 132.2, 131.9, 129.3, 109.8. IR ν 2942 (w), 2673 (w), 2561 (w), 2164 (w), 1683 (s), 1595 (s), 1426 (m), 1323 (m), 1297 (s), 1188 (m), 847 (m), 759 (s). HRMS (ESI) $C_8H_4NO_2S^-$ $[M-H]^-$ calc. = 177.9963; $[M-H]^-$ obs. = 177.9954.

6-Thiocyanatohexan-1-ol (14u)



Following general procedure GPB with thiol **13u** (68.5 mg, 0.500 mmol, 1.0 equiv.), the aq. mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were washed with sat. aq. $NaHCO_3$ (3 x 10 mL) dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude oil was purified by flash chromatography using pentane:EtOAc 3:2 as mobile phase affording **14u** (70.2 mg, 0.441 mmol, 88%) as a colorless oil. R_f (pentane:EtOAc 1:1, $KMnO_4$ staining) = 0.40. ^1H NMR ($CDCl_3$, 400 MHz): δ 3.58 (t, 2 H, *J* = 6.5 Hz, $HOCH_2$), 2.92 (t, 2 H, *J* = 7.2 Hz, CH_2SCN), 2.17 (bs, 1 H, O*H*), 1.80 (p, 2 H, *J* = 7.3 Hz, CH_2CH_2SCN), 1.54 (p, 2 H, *J* = 6.7 Hz, $HOCH_2CH_2$), 1.49-1.32 (m, 4 H, CH_2CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 112.5, 62.4, 33.9, 32.3, 29.8, 27.7, 25.1. IR ν 3382 (w), 2936 (s), 2860 (m), 2155 (s), 1462 (w), 1423 (w), 1055 (s), 729 (w). HRMS (ESI) $C_7H_{13}NNaOS$ $[M+Na]^+$ calc. = 182.0610; $[M+Na]^+$ obs. = 182.0612.

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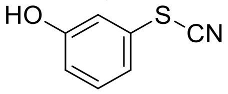
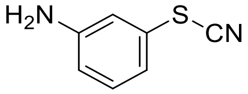
[18] Several signals were not resolved at 100 MHz.

3-Thiocyanatophenol (14v)



Following general procedure GPA with thiol **13v** (65.7 mg, 0.500 mmol, 1.0 equiv.), the crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 9:1 as mobile phase affording **14v** (69.0 mg, 0.456 mmol, 91%) as a colorless oil. R_f (pentane:EtOAc 4:1) = 0.60. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29 (t, 1 H, *J* = 8.0 Hz, Ar*H*), 7.09-7.01 (m, 2 H, Ar*H*), 6.91 (ddd, 1 H, *J* = 8.3, 2.4, 0.9 Hz, Ar*H*), 6.68 (bs, 1 H, O*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.4, 131.4, 124.7, 121.9, 117.2, 116.6, 111.3. IR ν 3370 (w), 2162 (w), 1601 (m), 1586 (s), 1478 (m), 1442 (m), 1319 (w), 1257 (m), 1217 (m), 882 (s), 774 (m). HRMS (ESI) $C_7H_4NOS^-$ $[M-H]^-$ calc. = 150.0014; $[M-H]^-$ obs. = 150.0013.

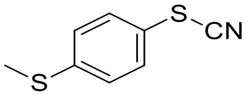
3-Thiocyanatoaniline (14w)



Following general procedure GPA with thiol **13w** (63.9 mg, 0.500 mmol, 1.0 equiv.), the crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 9:1 to 7:1 with 1% triethylamine as mobile phase affording **14w** (67.9 mg, 0.452 mmol, 90%) as a white solid. R_f (pentane:EtOAc 7:3 with 1% triethylamine) = 0.52. Melting point = 50.8-53.4 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.16 (t, 1 H, *J* = 7.9 Hz, Ar*H*), 6.82 (ddd, 1 H, *J* = 7.8, 1.9, 0.9 Hz, Ar*H*), 6.78 (t, 1 H, *J* = 2.0 Hz, Ar*H*), 6.66 (ddd, 1 H, *J* = 8.1, 2.2, 0.9 Hz, Ar*H*), 3.90 (bs, 2 H, N*H*$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 148.2, 130.9, 124.8, 119.3, 115.9, 115.3, 111.0. IR ν 3464 (w), 3372 (w), 3228 (w), 2156 (m), 1624 (s), 1596 (s), 1485 (s), 1447 (w), 1276 (w), 991 (w), 851 (w), 771 (m). HRMS (ESI) $C_7H_7N_2S^+$ $[M+H]^+$ calc. = 151.0324; $[M+H]^+$ obs. = 151.0331.

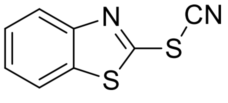
In addition, 2-(2-iodophenyl)propan-2-ol (142 mg, 0.540 mmol, 98% based on 0.550 mmol of starting material **11**) was isolated as a colorless oil.

Methyl(4-thiocyanatophenyl)sulfane (14x)



Following general procedure GPA with thiol **13x** (81.0 mg, 0.500 mmol, 1.0 equiv.), the crude oil was dissolved in minimum amounts of THF and purified by flash chromatography using pentane:EtOAc 99:1 as mobile phase affording **14x** (85.3 mg, 0.471 mmol, 94%) as a colorless oil. R_f (pentane:EtOAc 95:5) = 0.48. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39-7.31 (m, 2 H, Ar*H*), 7.21-7.12 (m, 2 H, Ar*H*), 2.40 (s, 3 H, SC*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.2, 131.3, 127.3, 119.3, 110.8, 15.3. IR ν 2922 (w), 2157 (m), 1736 (m), 1679 (m), 1478 (m), 1438 (m), 1328 (m), 1101 (s), 811 (s). HRMS (APPI) $C_8H_7NS_2$ $[M]^+$ calc. = 181.0020; $[M]^+$ obs. = 181.0015.

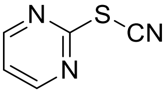
2-Thiocyanatobenzo[d]thiazole (14y)



Following general procedure GPA with thiol **13y** (84 mg, 0.50 mmol, 1.0 equiv.), the crude solid was purified by flash chromatography using pentane:EtOAc 99:1 to 95:5 as mobile phase affording **14y** (82 mg, 0.43 mmol, 85%) as a light-yellow solid. R_f (Pentane:EtOAc 9:1) = 0.5. Melting point = 85.0-86.2°C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.99 (d, 1 H, *J* = 8.1 Hz, Ar*H*), 7.86 (d, 1 H, *J* = 7.9 Hz, Ar*H*), 7.53 (t, 1 H, *J* = 7.7 Hz, Ar*H*), 7.45 (t, 1 H, *J* = 7.6 Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.4, 153.0, 136.5, 127.2, 126.4, 123.2, 121.4, 107.1. IR ν 3053 (w), 2167 (w), 1462 (w), 1421 (s), 1311 (w), 1238 (m), 995 (s), 757 (s). HRMS (ESI) $C_8H_5N_2S_2$ $[M+H]^+$ calc. = 192.9897; $[M+H]^+$ obs. = 192.9894.

The values of the ^{1}H NMR data, IR and melting point are in accordance with reported literature data.[19]

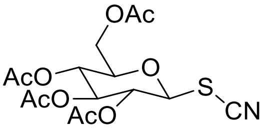
2-Thiocyanatopyrimidine (14z)



Following general procedure GPA with thiol **13z** (57.2 mg, 0.500 mmol, 1.0 equiv.), the crude oil was dissolved in minimum amounts of THF and purified by flash chromatography's using pentane:EtOAc 4:1 as mobile phase affording **14z** (64.5 mg, 0.470 mmol, 94%) as a white solid. R_f (pentane:EtOAc 3:2) = 0.52. Melting point = 112.6-113.0 °C ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.68 (d, 2 H, *J* = 4.7 Hz, Ar*H*), 7.28 (t, 1 H, *J* = 4.8 Hz, Ar*H*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.2, 159.1, 119.9, 107.4. IR ν 2175 (w), 1562 (s), 1380 (s), 1278 (w), 1181 (m), 815 (w), 768 (w), 742 (w). The values of the characterization data are in accordance with reported literature data.[20]

In addition, 2-(2-iodophenyl)propan-2-ol (133 mg, 0.506 mmol, 92% based on 0.550 mmol of starting material **11**) was isolated as a colorless oil.

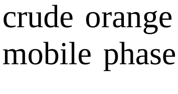
β-Thiocyanato-tetraacetyl-glucopyranoside (14aa)



Following general procedure GPB with thiol **13aa** (164 mg, 0.500 mmol, 1.0 equiv.), the crude oil was purified by flash chromatography using pentane:EtOAc 91 to 8:2 as mobile phase affording **14aa** (167 mg, 0.429 mmol, 95%) as colorless cristals. R_f (Pentane:EtOAc 9:1) = 0.3. Melting point = 133.0-133.5°C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.26 (t, 1 H, *J* = 9.2 Hz, H_3), 5.14 (t, 1 H, *J* = 9.7, H_2) 5.14 (t, 1 H, *J* = 9.7, H_4), 4.90 (d, 1 H, *J* = 9.7 Hz, H_1), 4.27 (dd, 1 H, *J* = 12.6, 4.8 Hz, H_6), 4.19 (dd, 1 H, *J* = 12.7, 2.2 Hz, H_6), 3.83 (ddd, 1 H, *J* = 10.1, 4.8, 2.2 Hz, H_5), 2.11 (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.02 (s, 3 H, CH_3CO). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.4, 169.6, 169.5, 108.3, 83.9, 77.7, 73.4, 71.1, 67.9, 61.9, 21.2, 21.0. IR ν 2948 (w), 2081 (w), 1741 (s), 1370 (m), 1211 (s), 1033 (s), 915 (m), 792 (w).HRMS $C_{15}H_{19}NO_9SNa^+$ $[M+Na]^+$ calc. = 412.0670; $[M+Na]^+$ obs. = 406.0678.

The values of the characterization data are in accordance with reported literature data.[21]

Selenocyanatobenzene (14ab)



Following general procedure GPA with selenol **13ab** (79.0 mg, 0.500 mmol, 1.0 equiv.), the crude orange oil was purified by flash chromatography using pentane:EtOAc 1:0 to 9:1 as mobile phase **14ab** (80 mg, 0.44 mmol, 88%) as red oil. R_f (Pentane:EtOAc 9:1) = 0.7. ^{1}H

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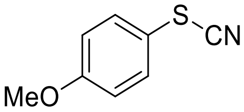
[19] Kaupp, G.; Schmeyers, J.; Boy, J. *Chem. Eur. J.* **1998**, *4*, 2467.

[20] Kim, J. J.; Kweon, D. H.; Cho, S. D.; Kim, H. K.; Jung, E. Y.; Lee, S. G.; Falck, J. R.; Yoon, Y. J. *Tetrahedron* **2005**, *61*, 5889.

[21] Kochetkov, N.K., Klimov, E. M., Malysheva, N. N., Demchenko, A. V. *Carbohydrate. Res.* **1991**, *212*, 77.

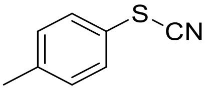
NMR ($CDCl_3$, 400 MHz): δ 7.70-7.57 (m, 2H), 7.49- 7.35 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 132.8, 130.4, 129.8, 121.9, 101.6. HRMS C_7H_5SeN $[M]^+$ calc. = 182.9582 ; $[M]^+$ obs. = 182.9581. The values of the NMR spectra and physical data are in accordance with reported literature data.[22]

1-Methoxy-4-thiocyanatobenzene (14ac)



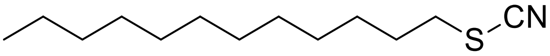
Synthesized following general procedure GPC. The crude oil was purified by flash chromatography using pentane:EtOAc 95:5 to 9:1 as mobile phase **14ac** (55 mg, 0.33 mmol, 66%, 97% purity) as a colorless oil. R_f (Pentane:EtOAc 9:1) = 0.75. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.54 – 7.45 (d, 2H, *J* = 8.7 Hz, Ar*H*), 6.94 (d, 2H, *J* = 8.7 Hz, Ar*H*), 3.82 (s, 2H, C*H₃*O). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 161.3, 133.8, 115.8, 113.8, 111.6, 55.6. IR ν 2361 (w), 2156 (w), 1592 (m), 1494 (s), 1297 (m), 1253 (s), 1179 (m), 1029 (m), 829 (m).
The values of NMR spectra and physical data are in accordance with literature data.[10]

1-Methyl-4-thiocyanatobenzene (14ad)



Synthesized following general procedure GPC. The crude oil was purified by flash chromatography using pentane:EtOAc 95:5 to 9:1 as mobile phase **14ad** (60 mg, 0.40 mmol, 80%) as a colorless oil. R_f (Pentane:EtOAc 9:1) = 0.75. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 (d, 2H, *J* = 8.0 Hz, Ar*H*), 7.17 (d, 2H, *J* = 8.0 Hz, Ar*H*), 2.31 (s, 3H, C*H₃*). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.3, 131.0, 130.8, 120.5, 111.1, 21.2. IR ν 3029 (w), 2925 (w), 2361 (s), 2339 (s), 2157 (m), 1492 (m), 1017 (w), 808 (s).
The values of NMR spectra and physical data are in accordance with literature data.[10]

1-Dodecylthiocyanate (14ae)



Synthesized following general procedure GPC. The crude oil was purified by flash chromatography using pentane:DCM 95:5 to 85:15 as mobile phase. **14ae** (39 mg, 0.17 mmol, 34%) was obtained as a colorless oil. R_f (Pentane:DCM 9:1) = 0.25. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 2.97 (d, 2H, *J* = 7.3 Hz, C*H₂*S), 1.85 (qt, 2H, *J* = 7.3 Hz, C*H₂*CH₂S), 1.51-1.42 (m, 2H, C*H₂*), 1.40 – 1.26 (m, 16H, 8xC*H₂*), 0.91 (t, 3H, *J* = 6.8 Hz, C*H₃*C*H₂*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 112.4, 34.1, 31.9, 29.9, 29.6, 29.5, 29.3, 29.3, 28.9, 27.9, 22.7, 14.1.[23] IR ν 2924 (s), 2855 (m), 2155 (w), 1463 (w), 724 (w).
The values of NMR spectra and physical data are in accordance with literature data.[24]

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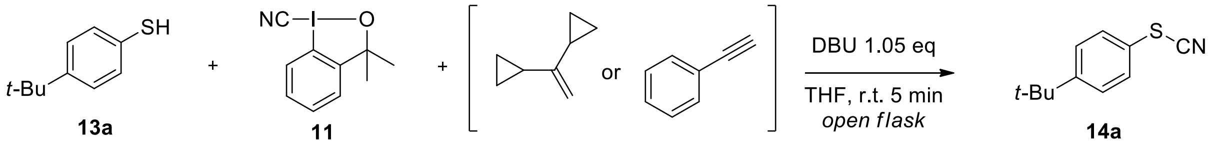
[22] Tomoda, S.; Takeuchi, Y.; Nomura, Y. *Chem. Lett.* **1981**, *10*, 1069.

[23] One aliphatic carbon could not be resolved.

[24] Ciszek, J.W.; Stewart, M.P.; Tour, J.M. *J. Am. Chem. Soc.* **2004**, *126*, 13172.

6. Thiyl radical trapping experiment

1,1 dicylcopropylethene was synthesized according to the literature procedure.[25]



A 25 mL round bottom flask was charged with a magnetic stirring bar, **13a** (0.500 mmol, 1.00 eq.) and THF (5.0 mL). To this solution was added 1,8-diazabicycloundec-7-ene (DBU, 79.0 µL, 0.525 mmol, 1.05 eq.), followed by 1,1-dicyclopropylethene (108 mg, 1.00 mmol, 2.00 eq) or phenylacetylene (102 mg, 1.00 mmol, 2.00 eq) and 1-cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (CDBX (**11**), 158 mg, 0.550 mmol, 1.10 eq.). The resulting reaction mixture was stirred in an open flask for 5 minutes at room temperature. The reaction was concentrated *in vacuo*. The crude product was directly purified by chromatography on silica gel, Pentane:AcOEt 99:1 to afford **14a** as a yellow oil. (89.0 mg, 0.465 mmol, 93%) (95% without radical trap)

No trapped thiyl radical could be recovered or observed.

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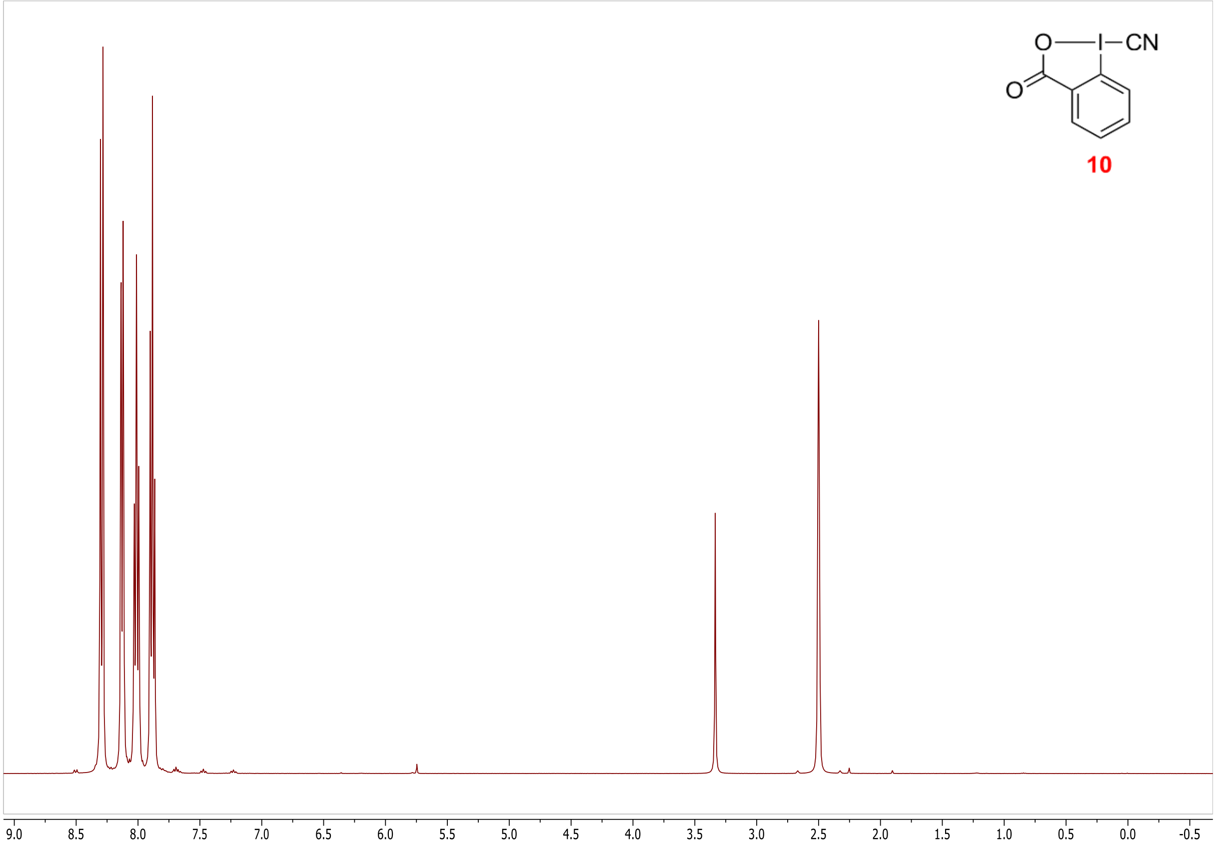
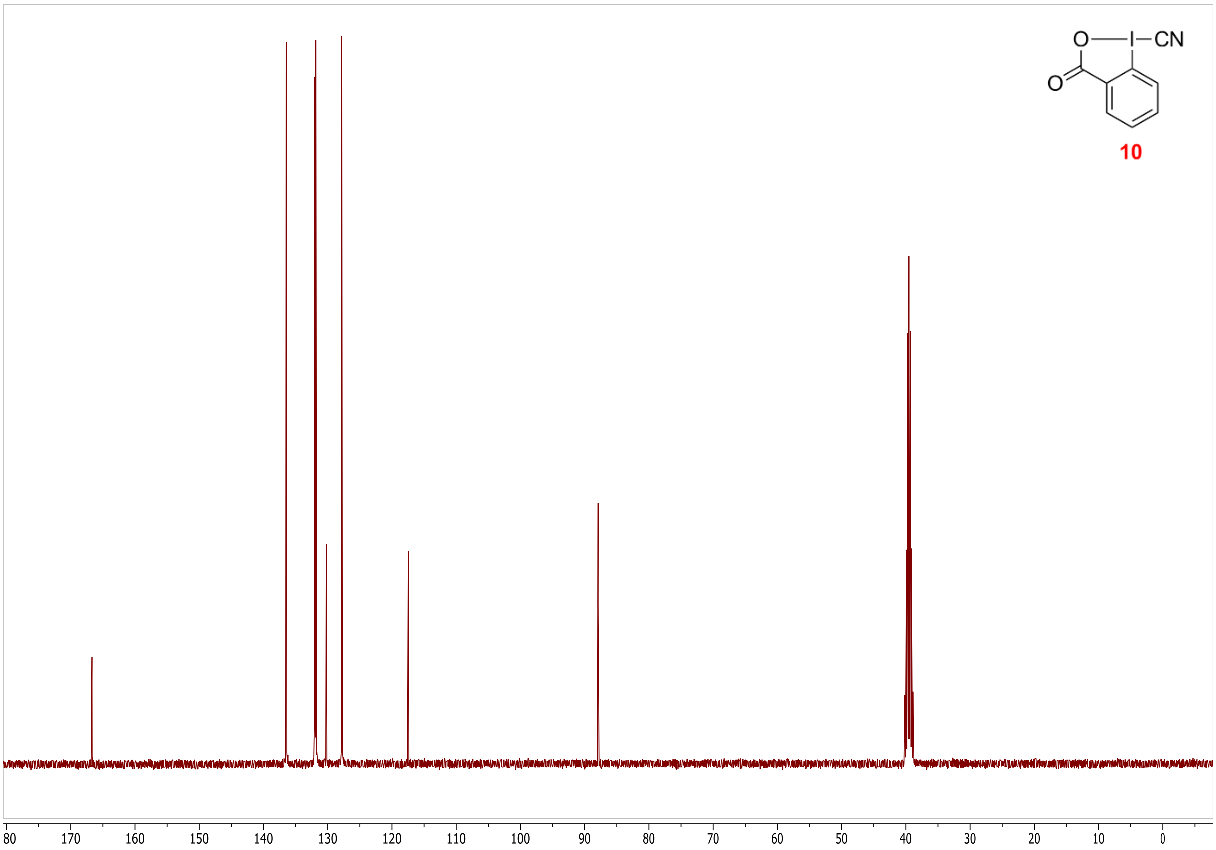
[25] Povie, G. ; Tran, A.-T. ; Bonnaffé, D. ; Habegger, J. ; Le Narvor, D. ; Renaud, P. ; *Ang. Chem. Int. Ed.* **2014,** *53,* 3894.

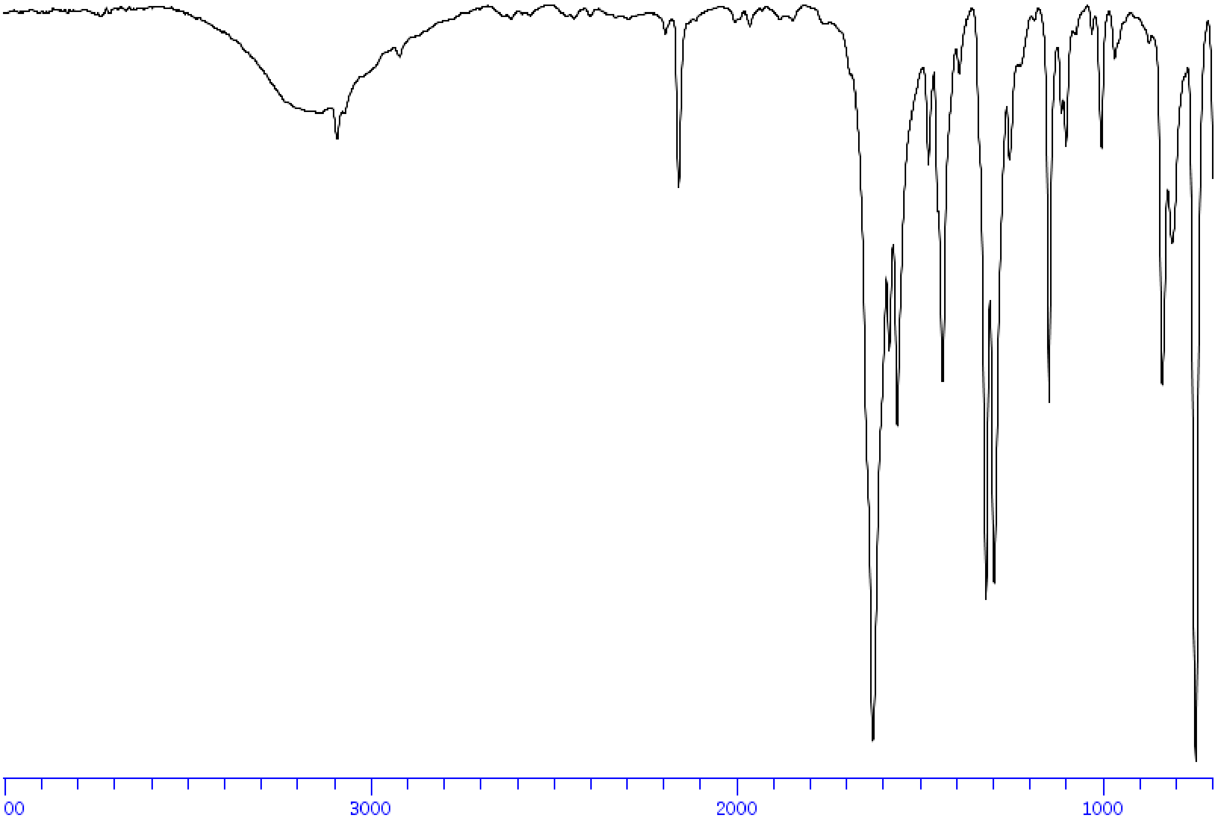
7. Spectra of New Compounds

Shown below are the corresponding ^{1}H ($CDCl_3$, 400MHz), ^{13}C ($CDCl_3$, 100.1MHz) NMR and IR (neat) spectra in this order of the above fully characterized compounds.

1-Cyano-1,2-benziodoxol-3-(1*H*)-one (10)



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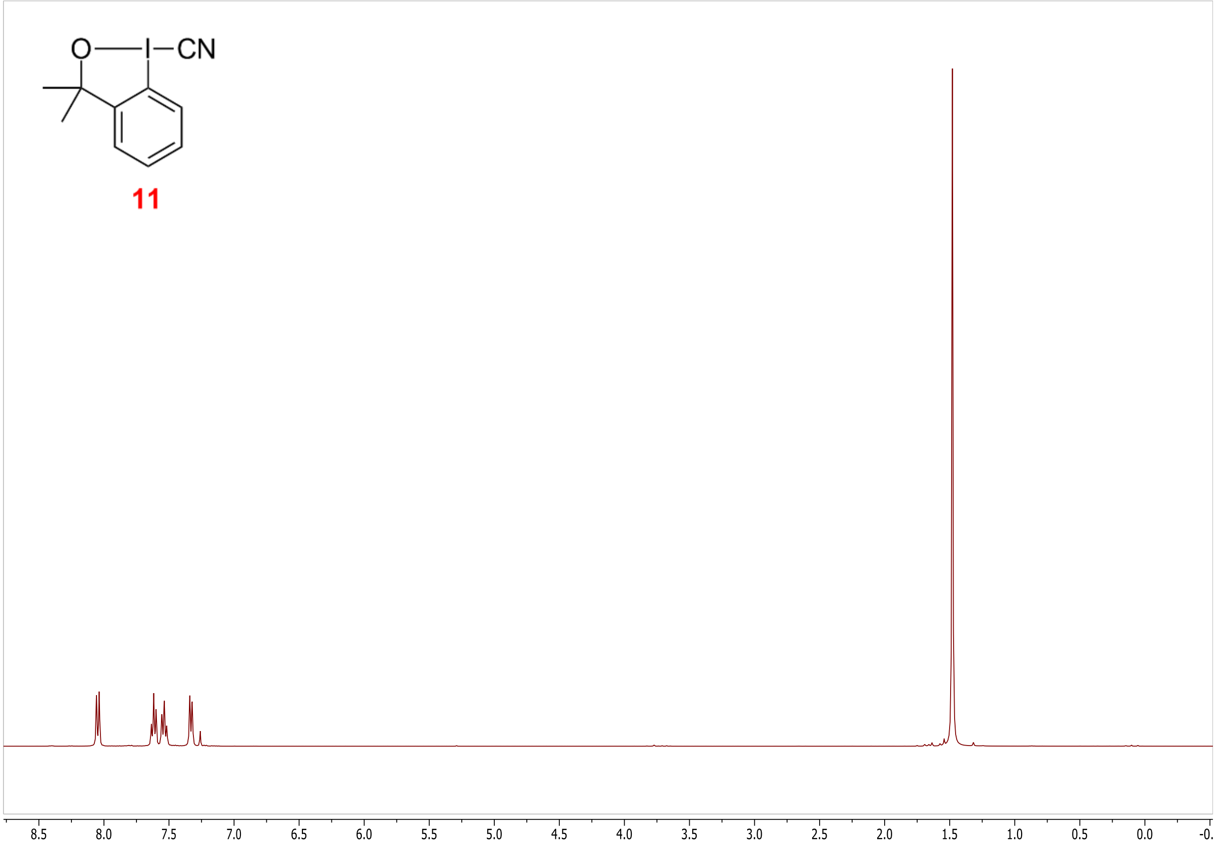
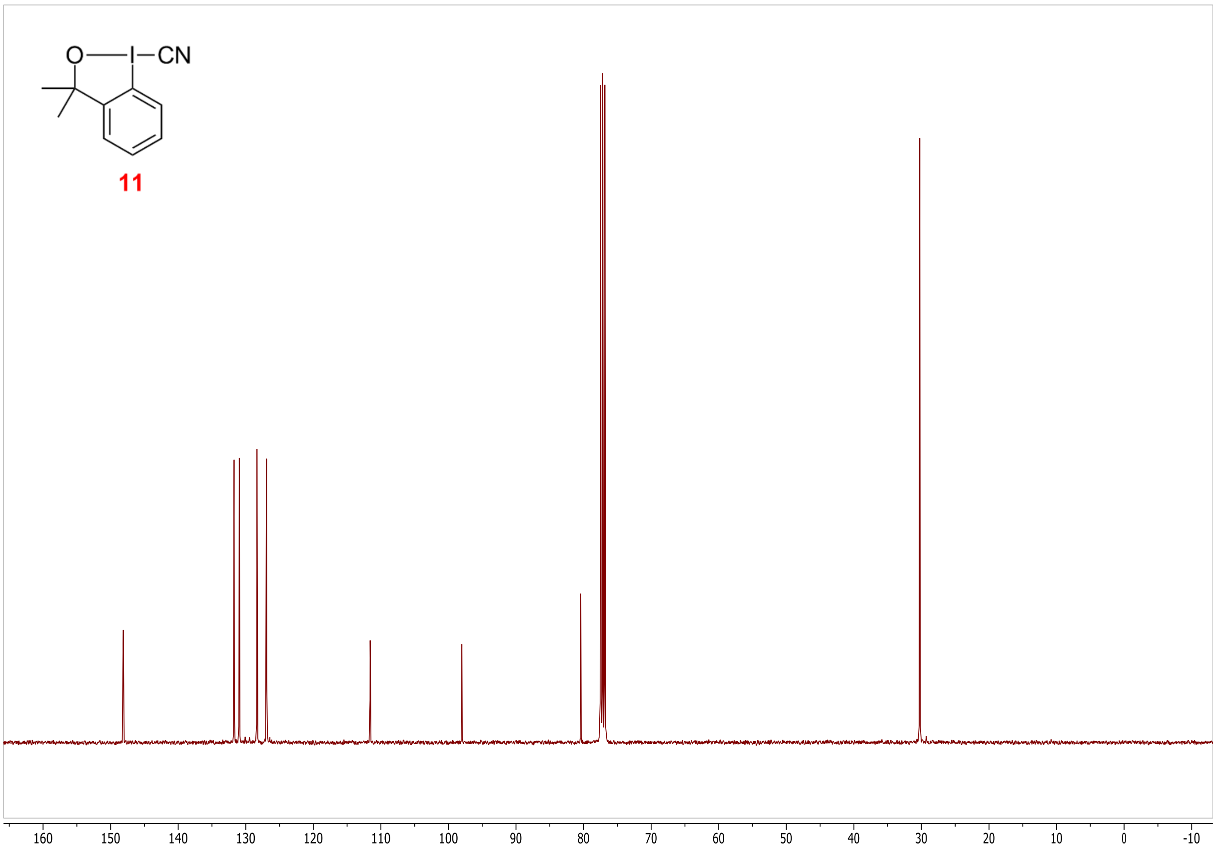
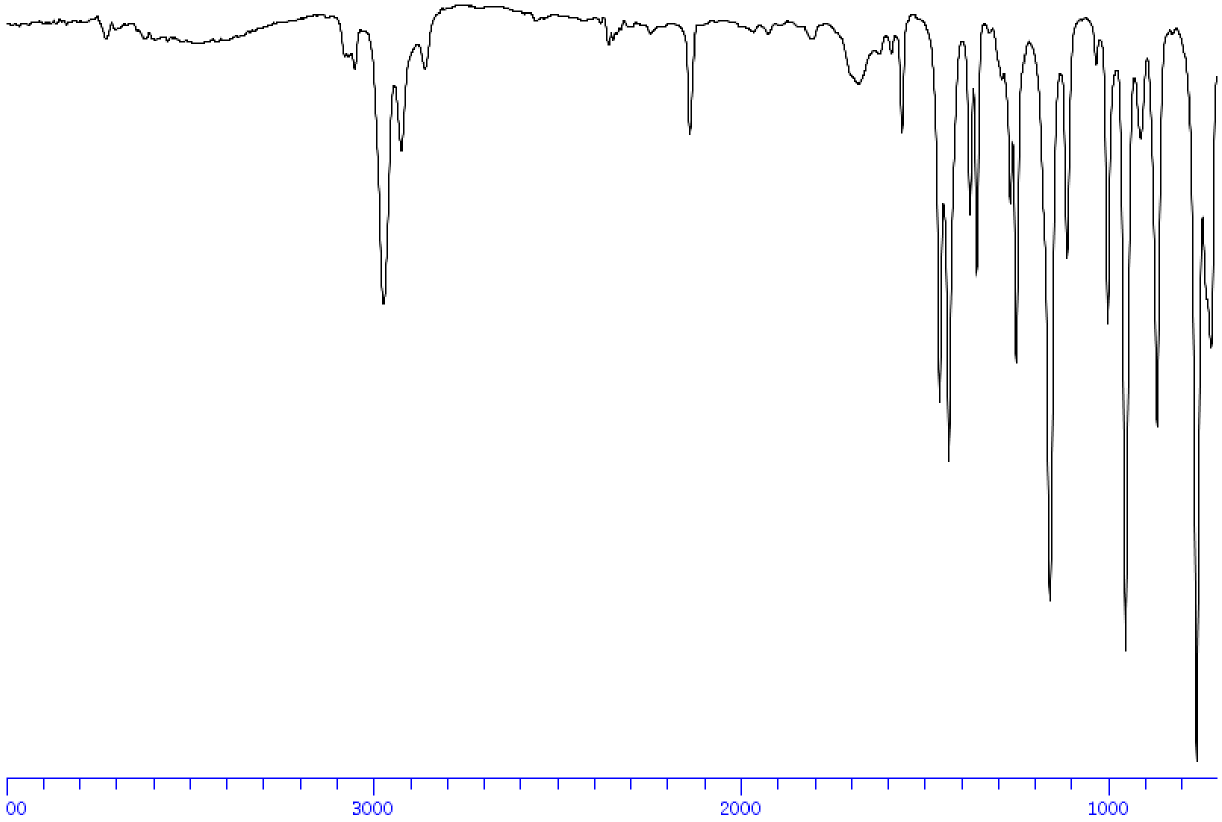
1-Cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (11)



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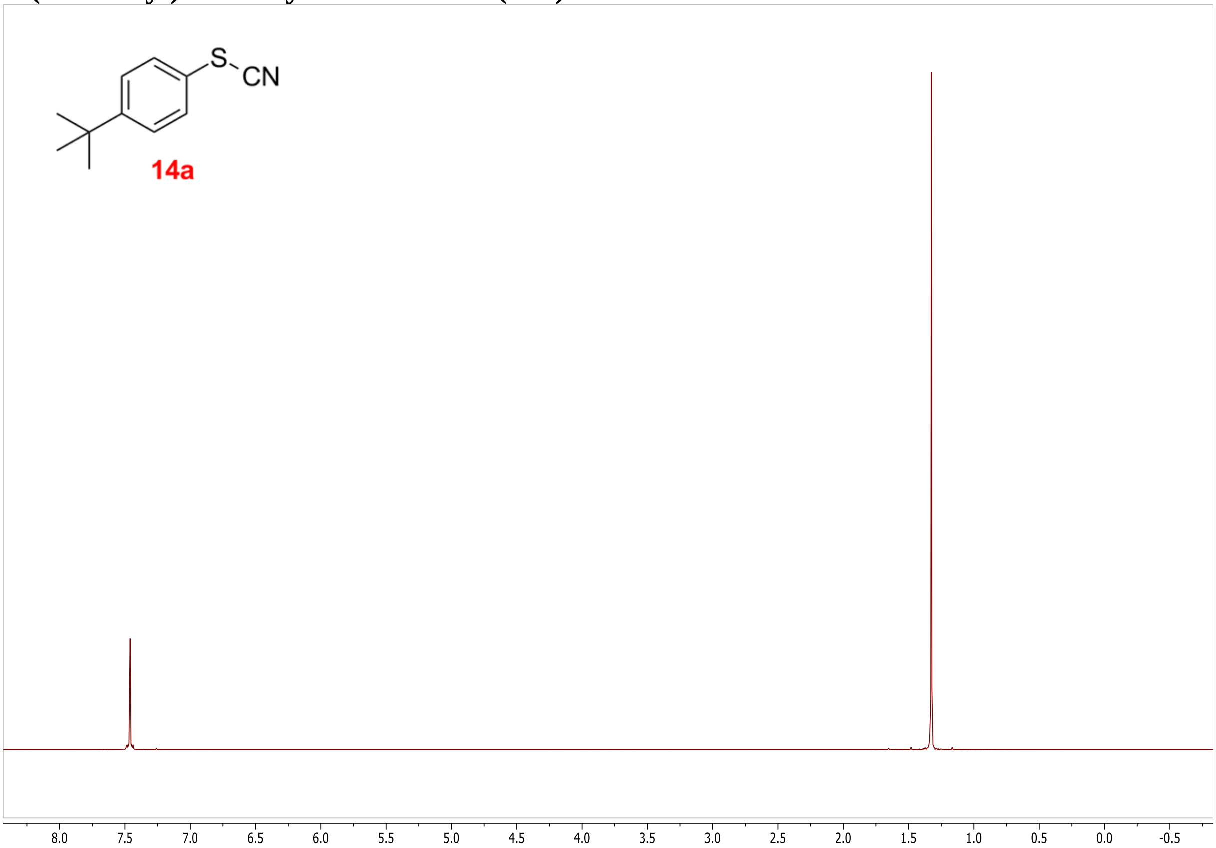
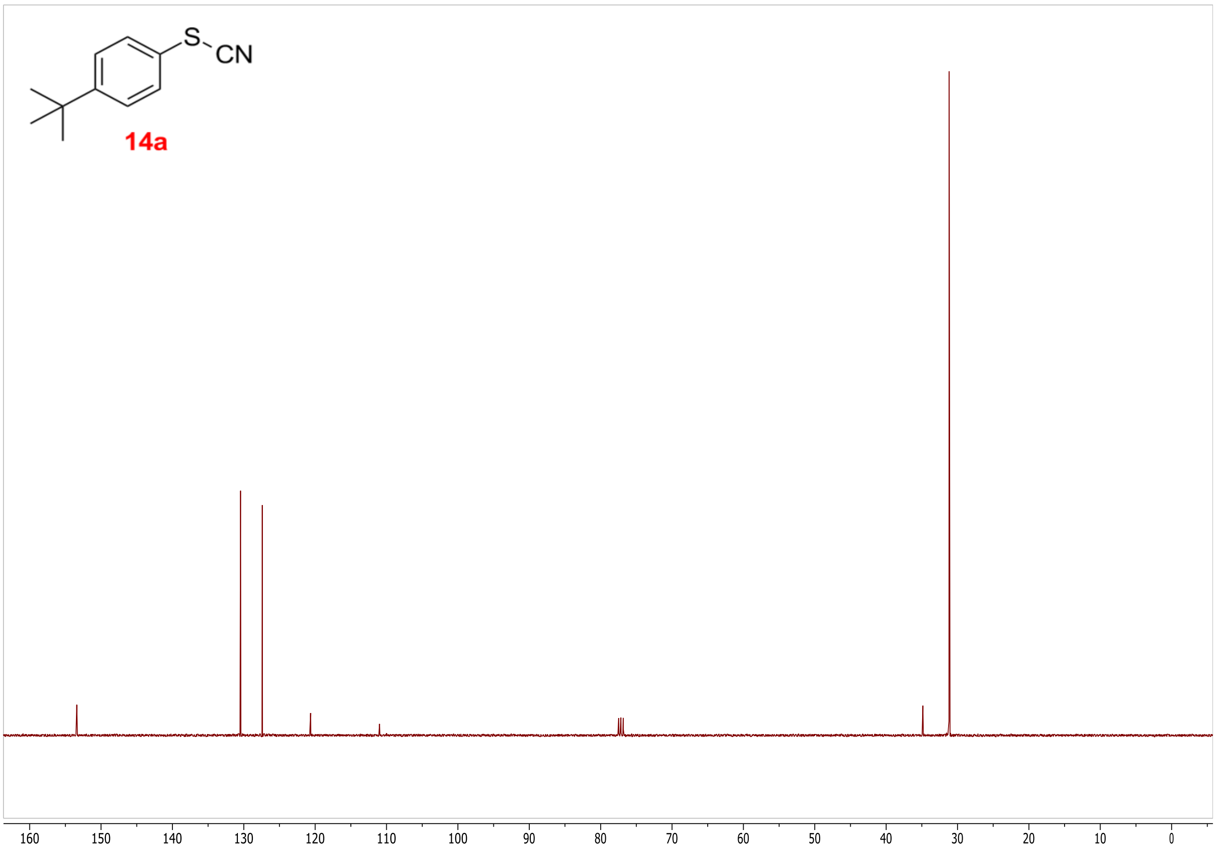
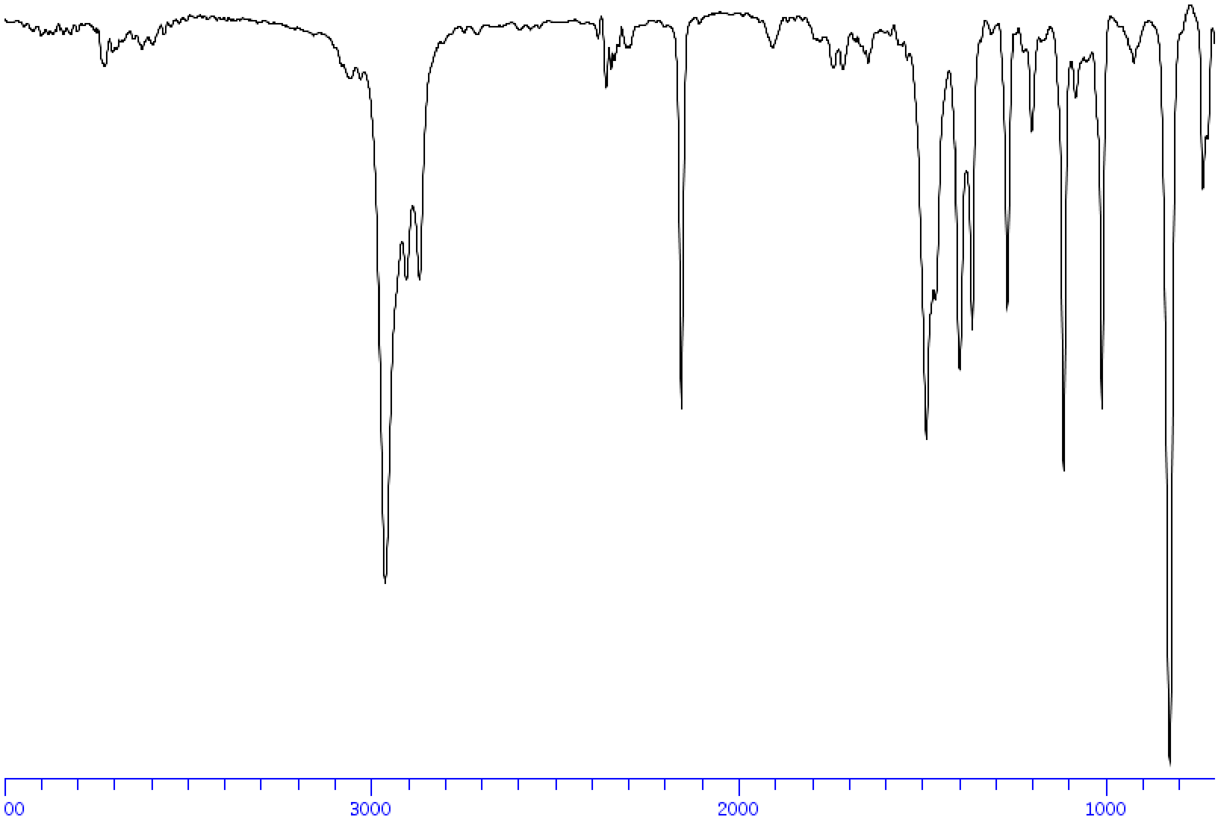
1-(*tert*-Butyl)-4-thiocyanatobenzene (14a)



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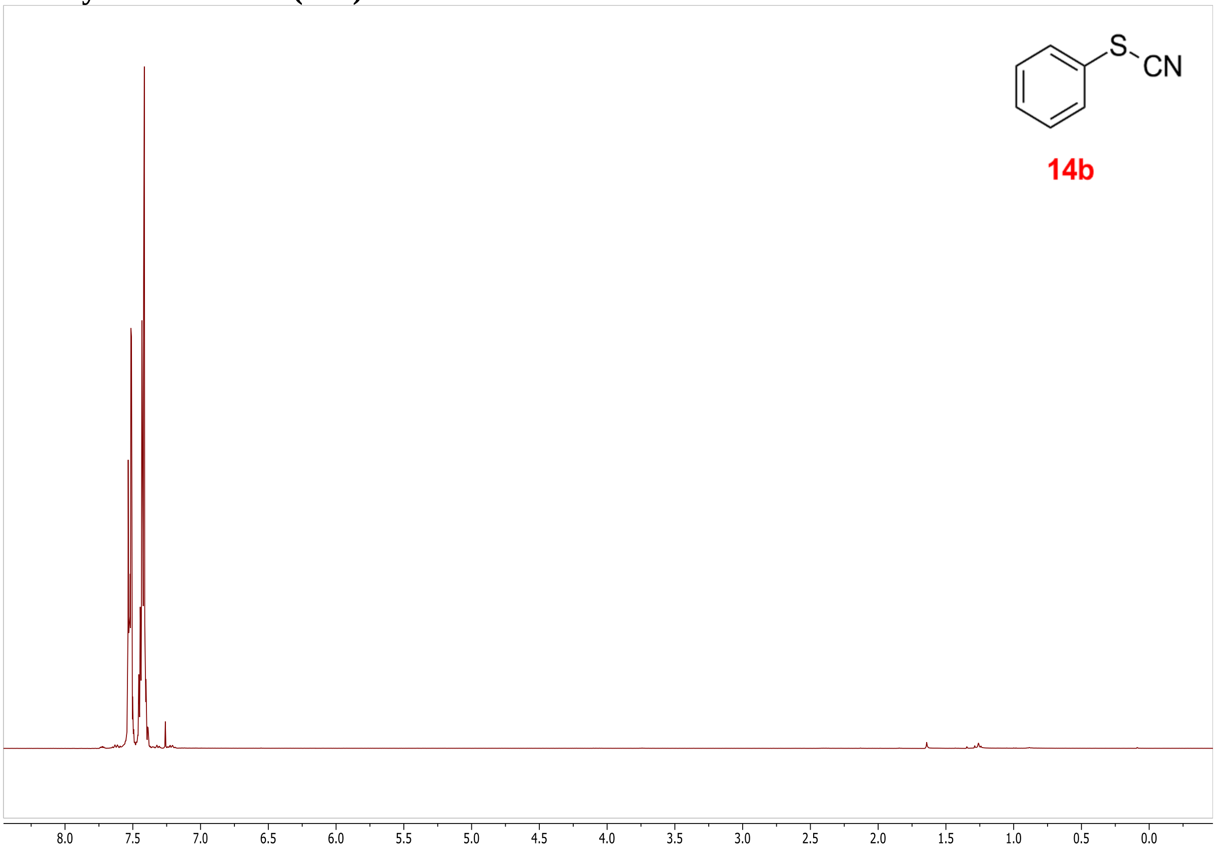
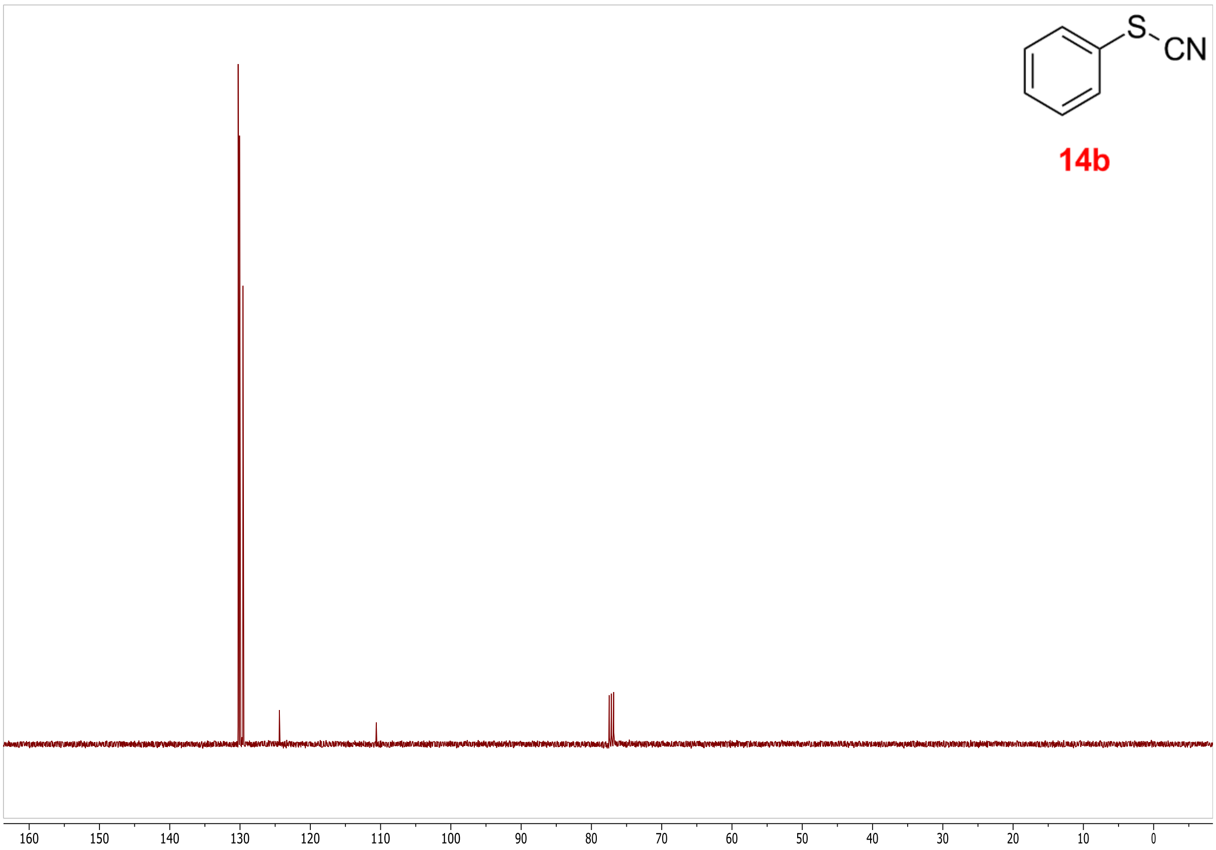
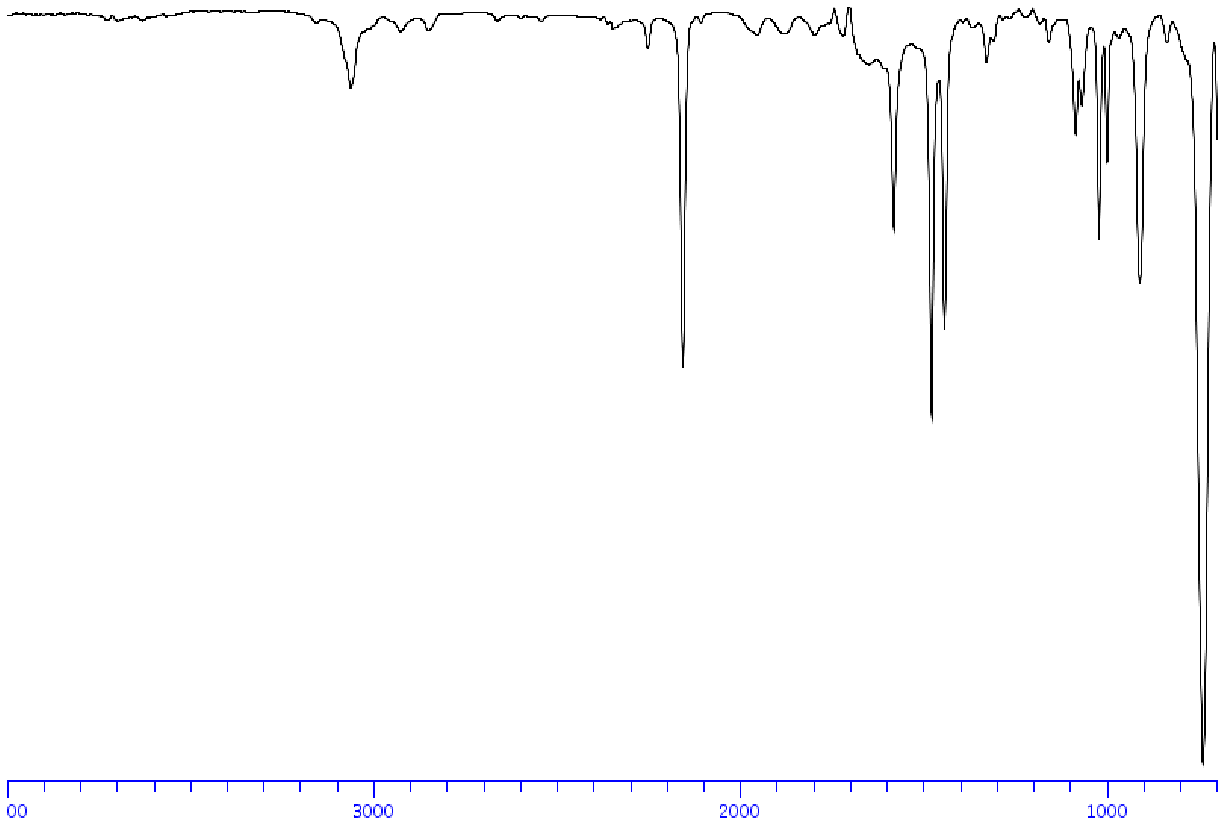
Thiocyanatobenzene (14b)



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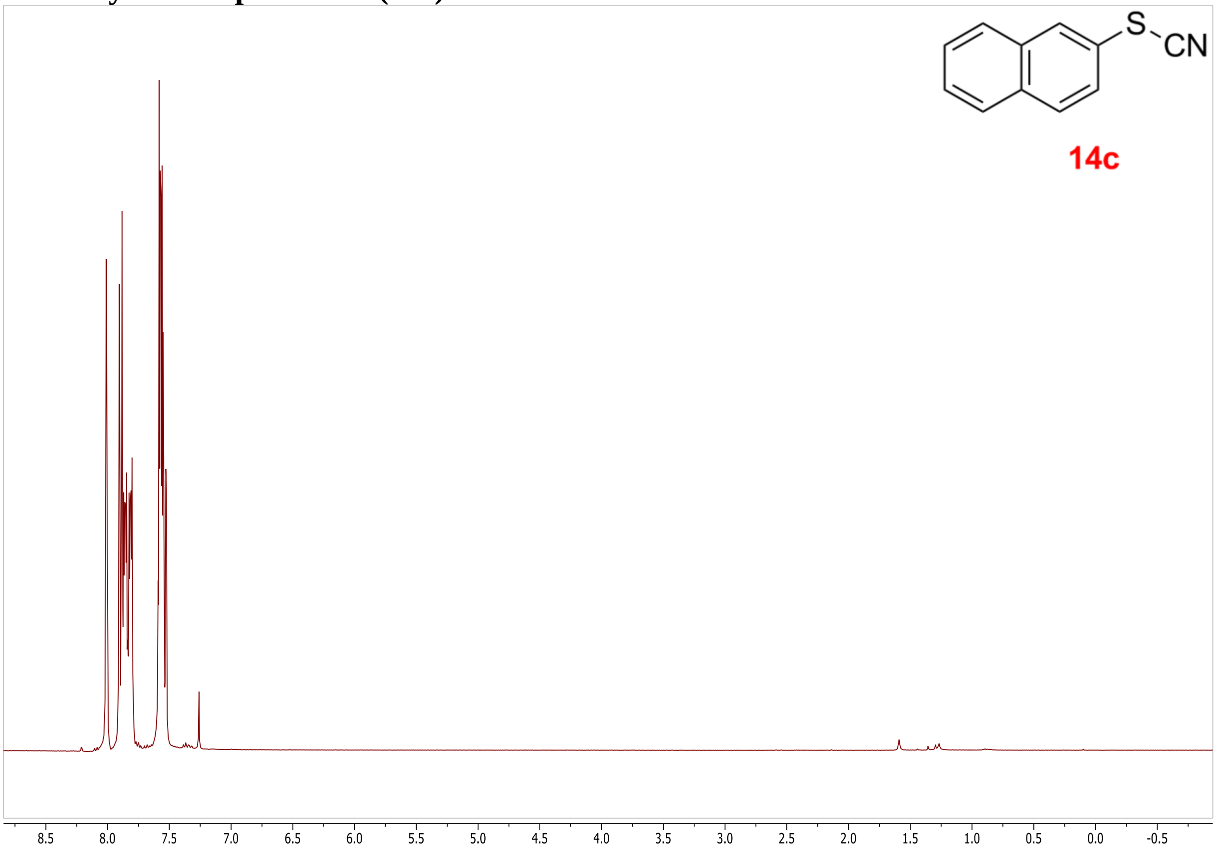
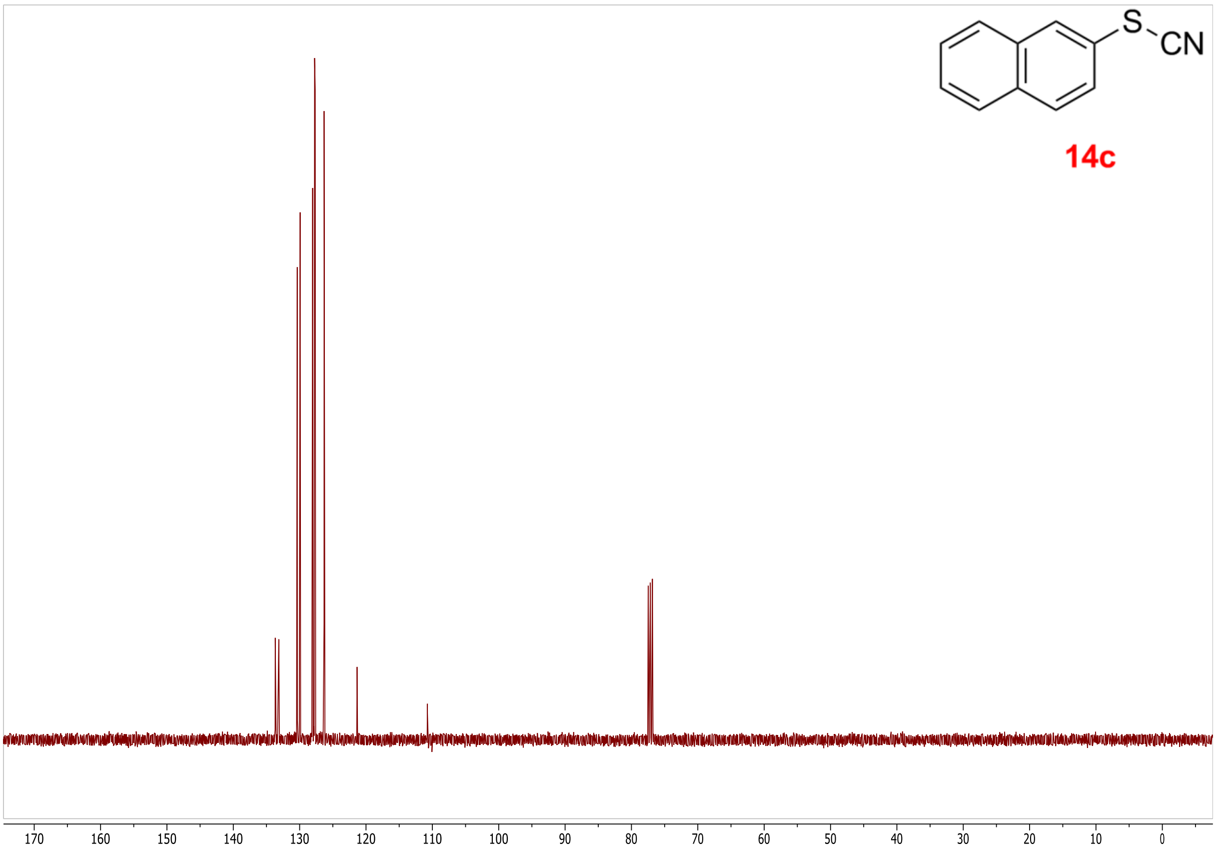
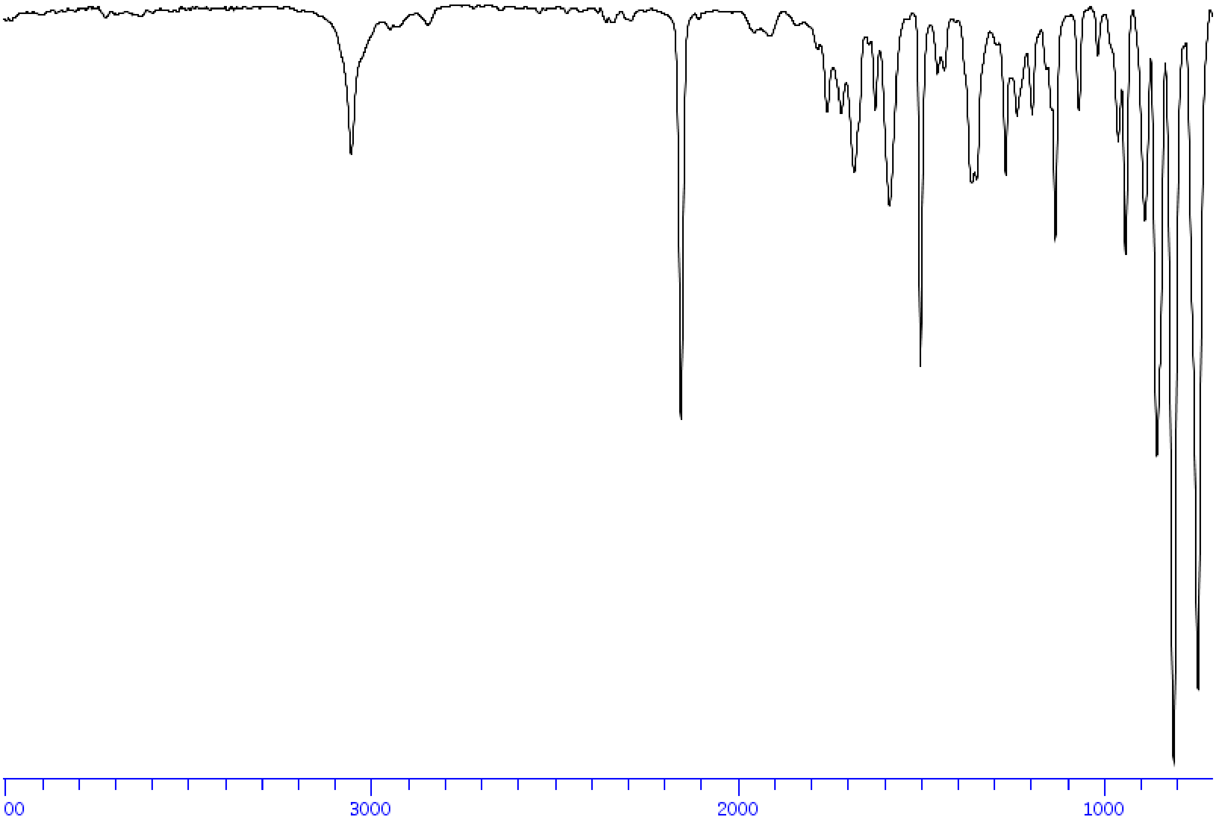
2-Thiocyanatonaphthalene (14c)



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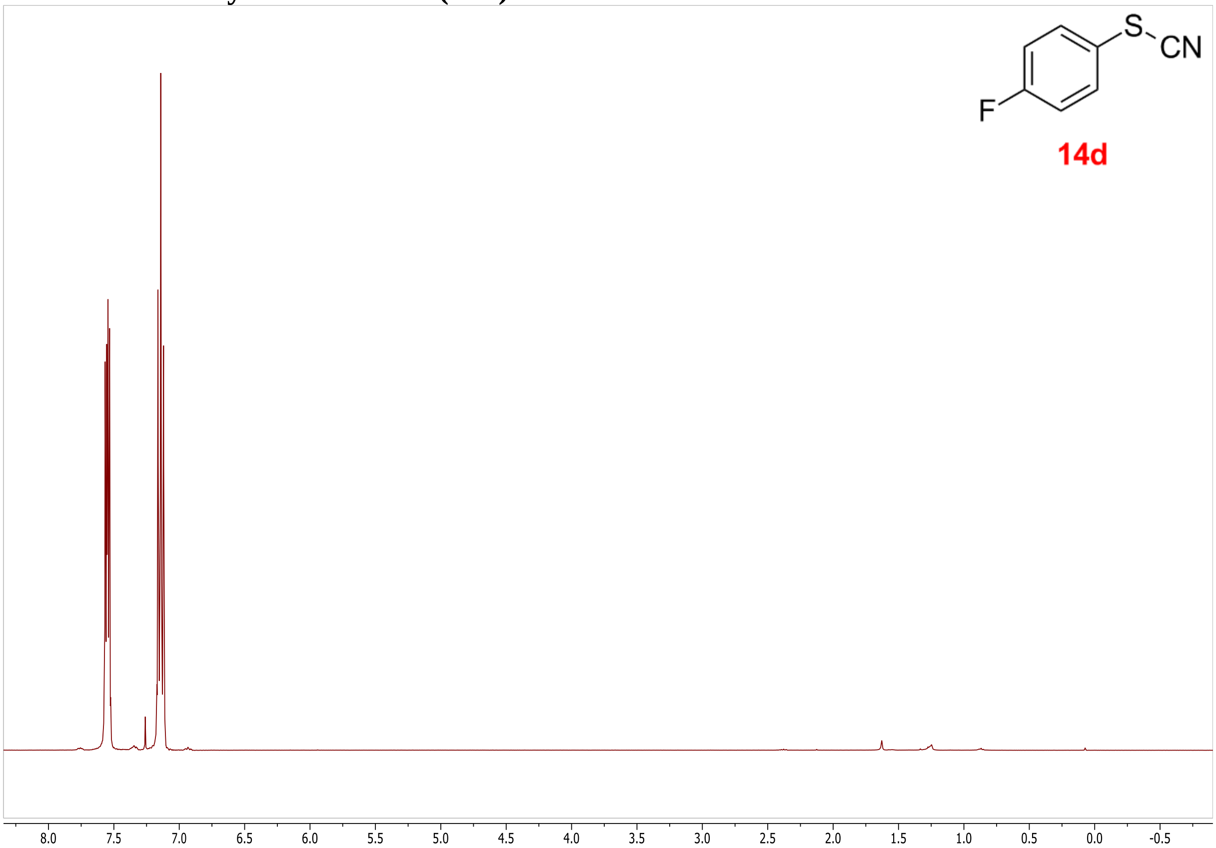
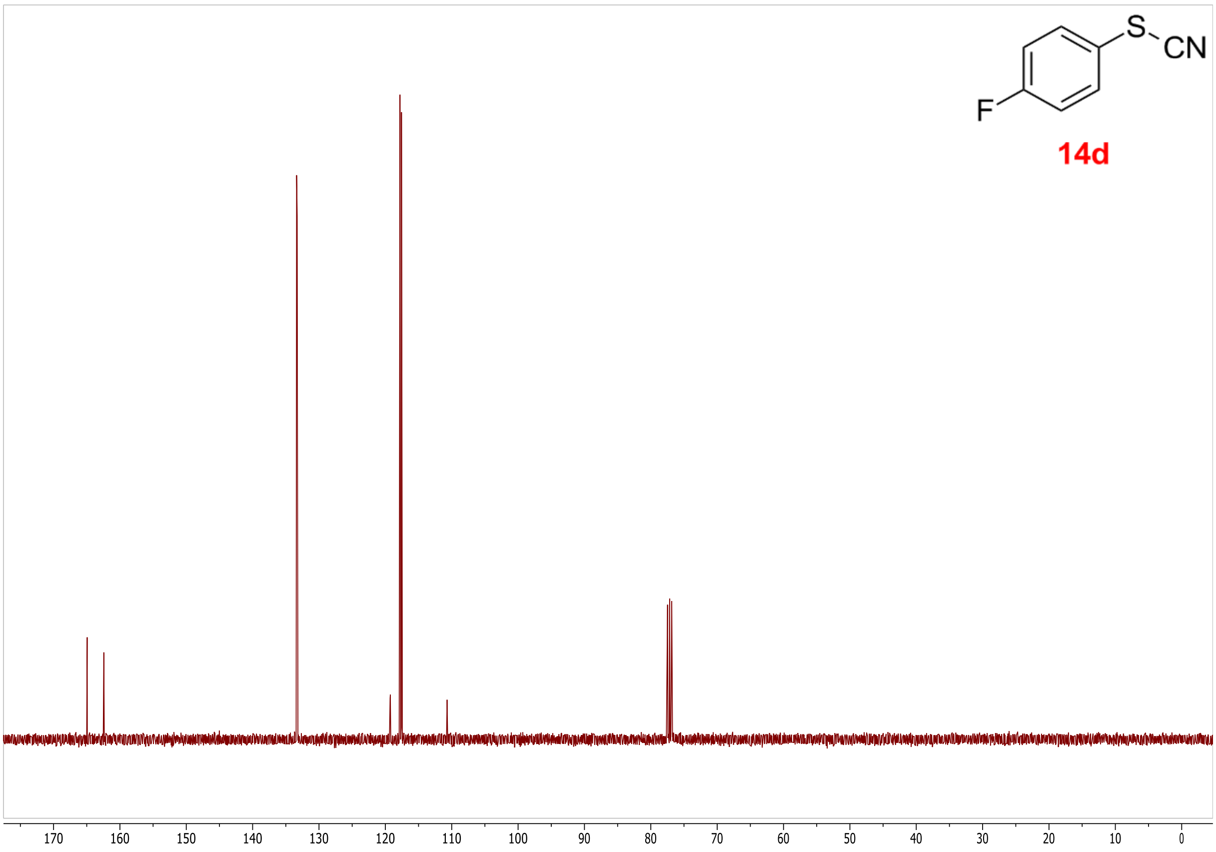
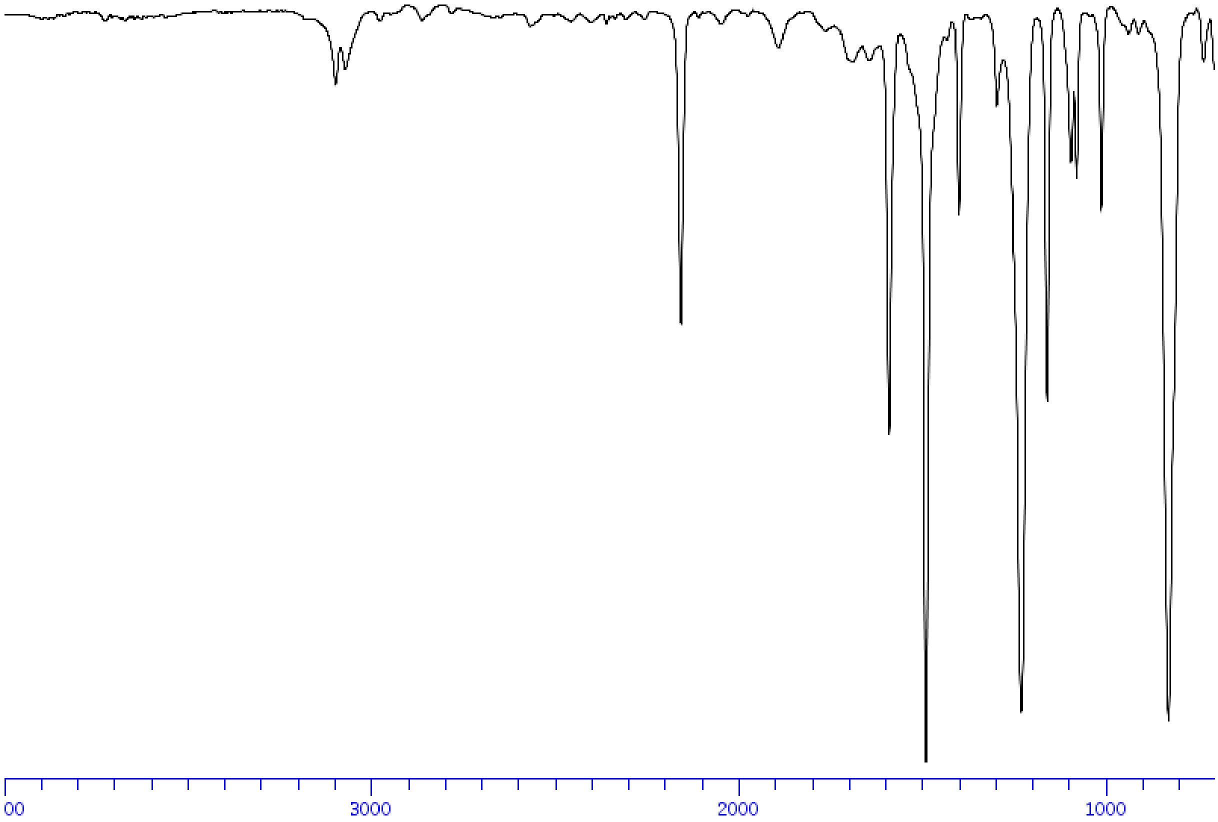
1-Fluoro-4-thiocyanatobenzene (14d)



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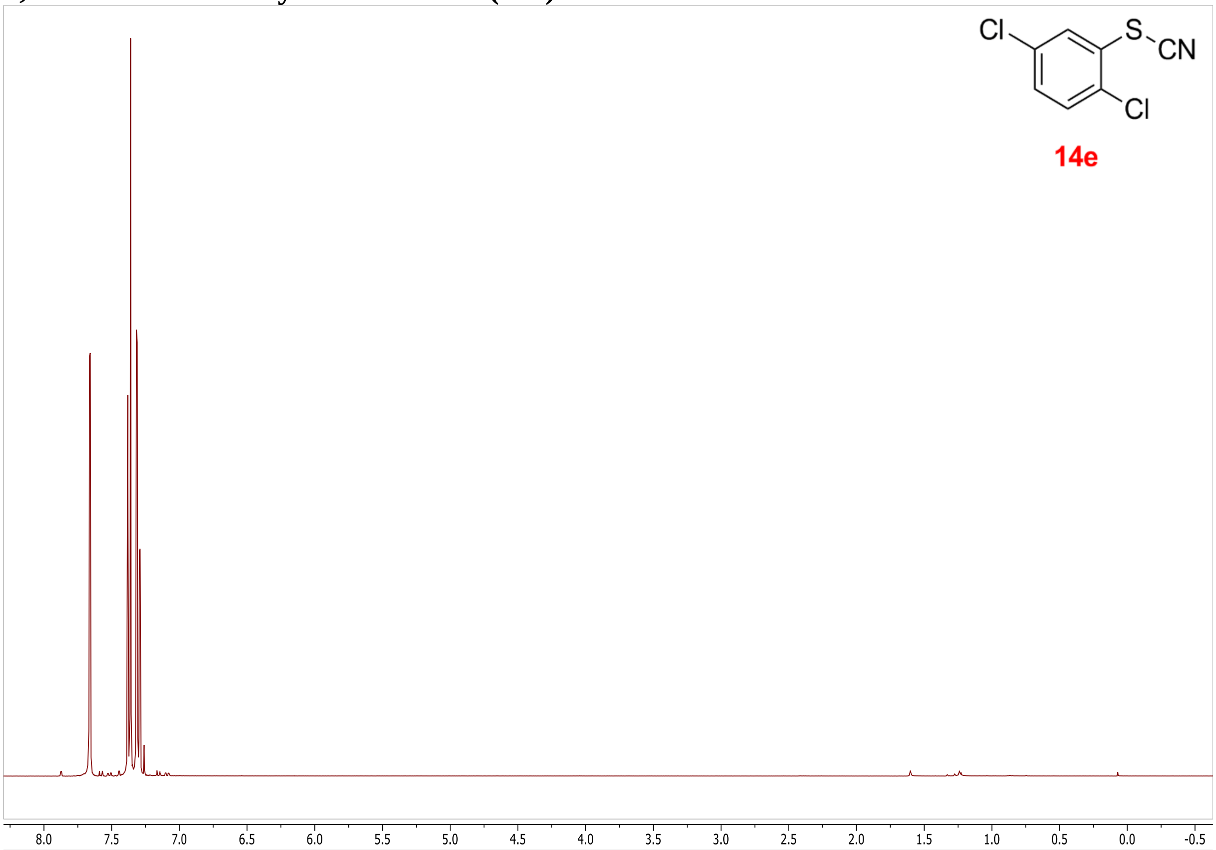
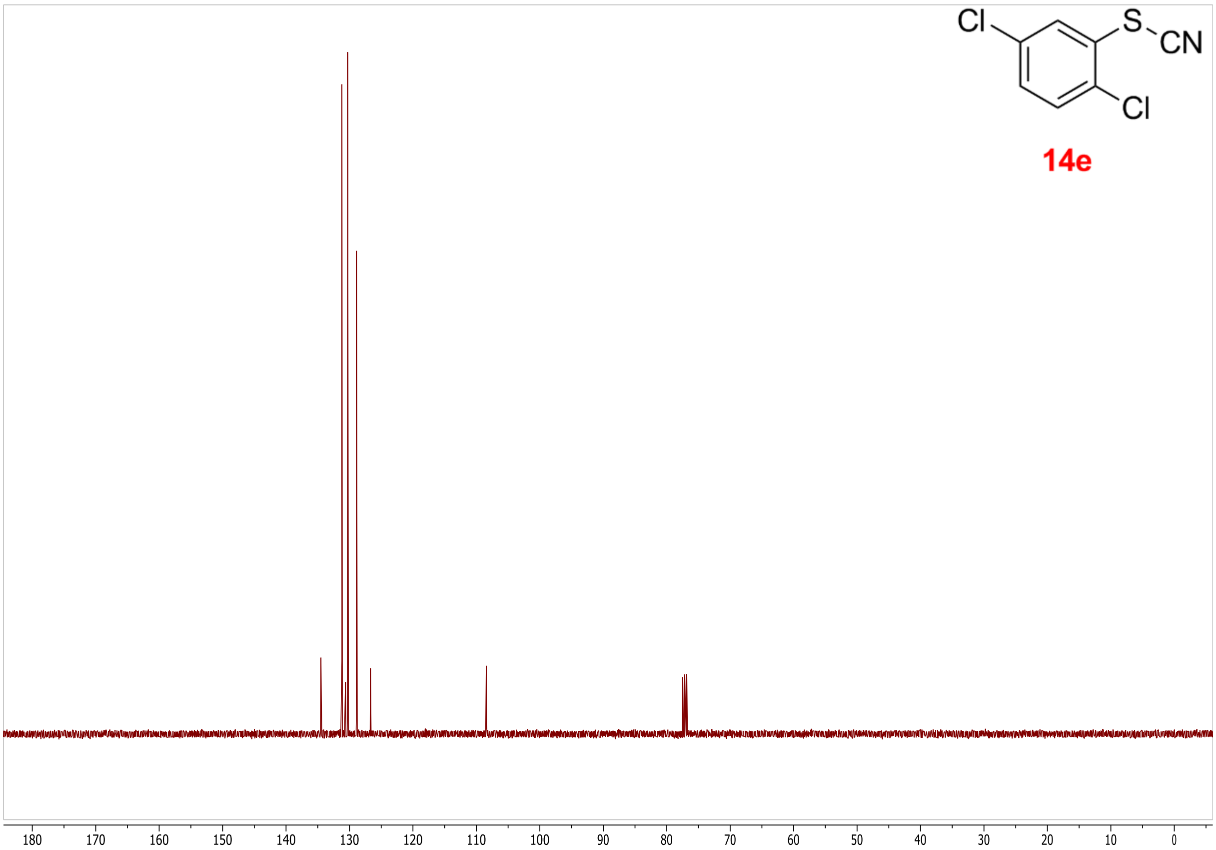
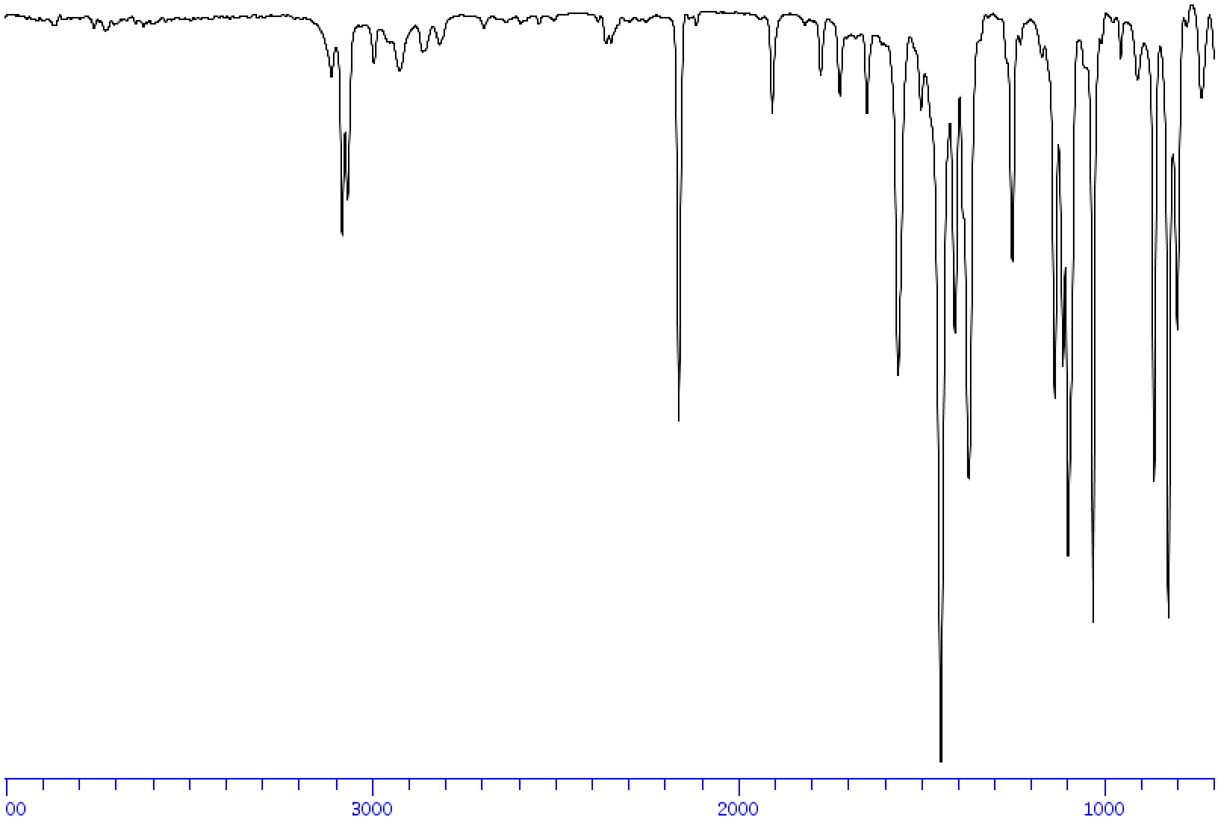
1,4-Dichloro-2-thiocyanatobenzene (14e)



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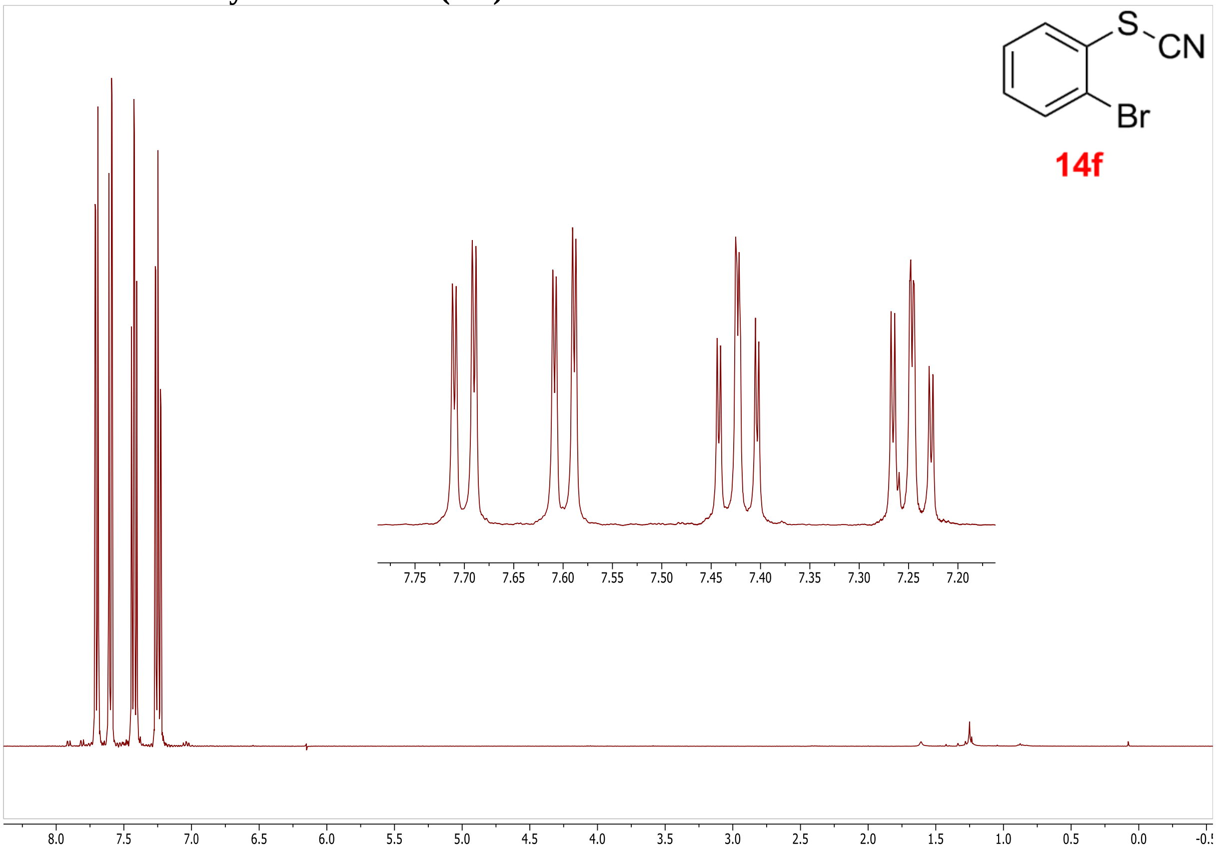
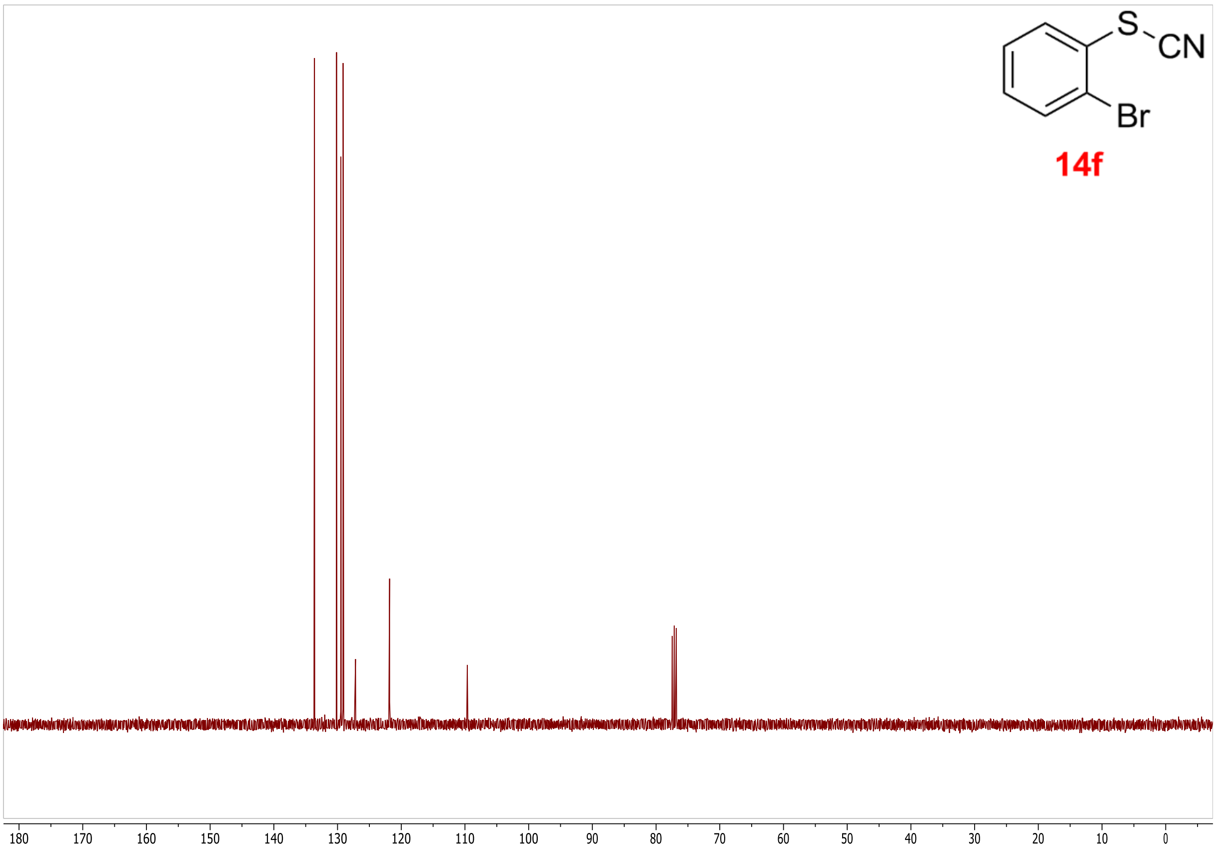
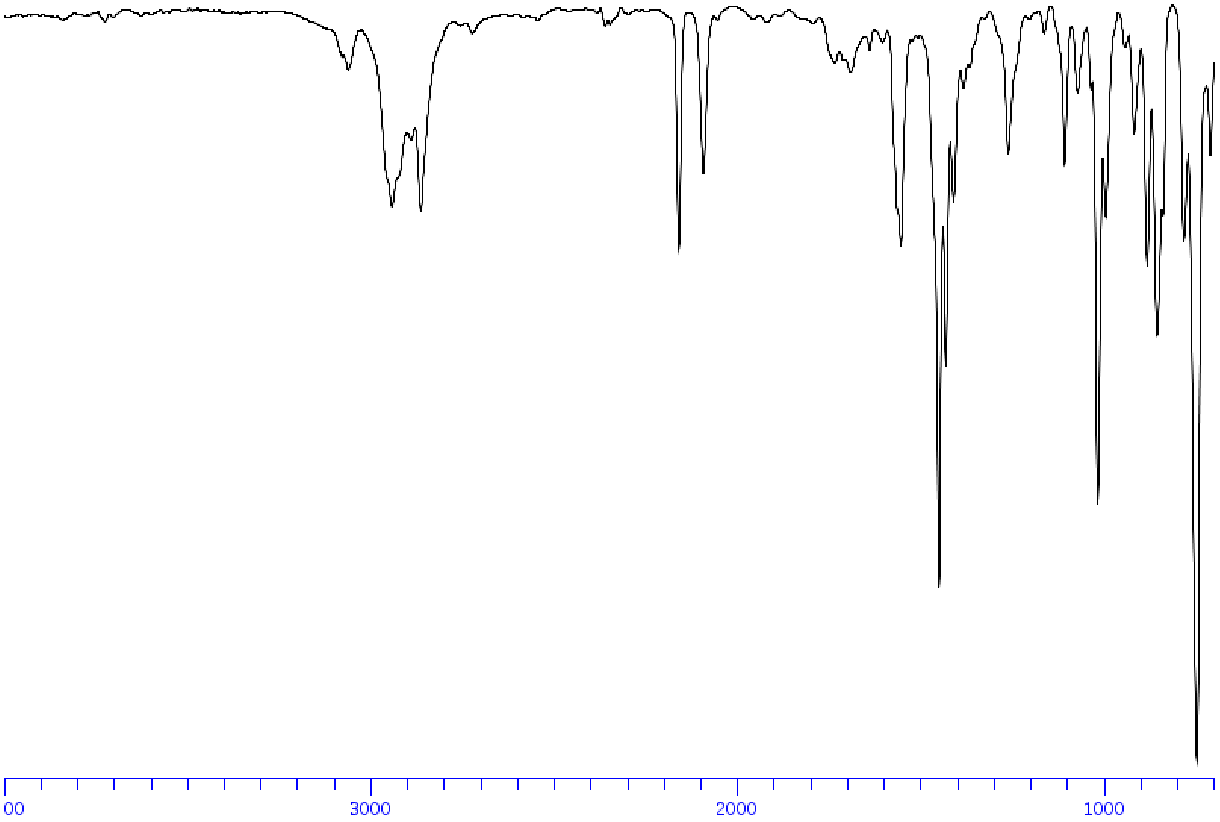
1-Bromo-2-thiocyanatobenzene (14f)



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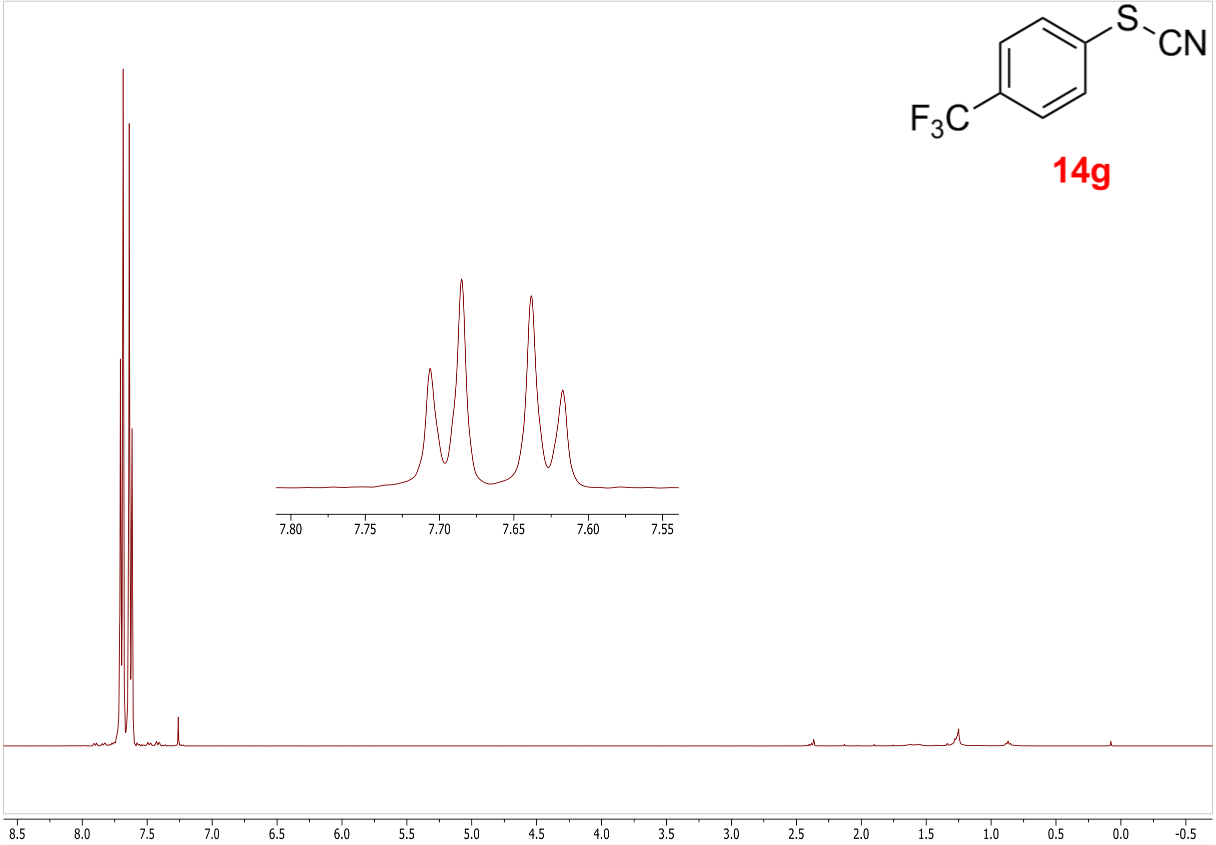
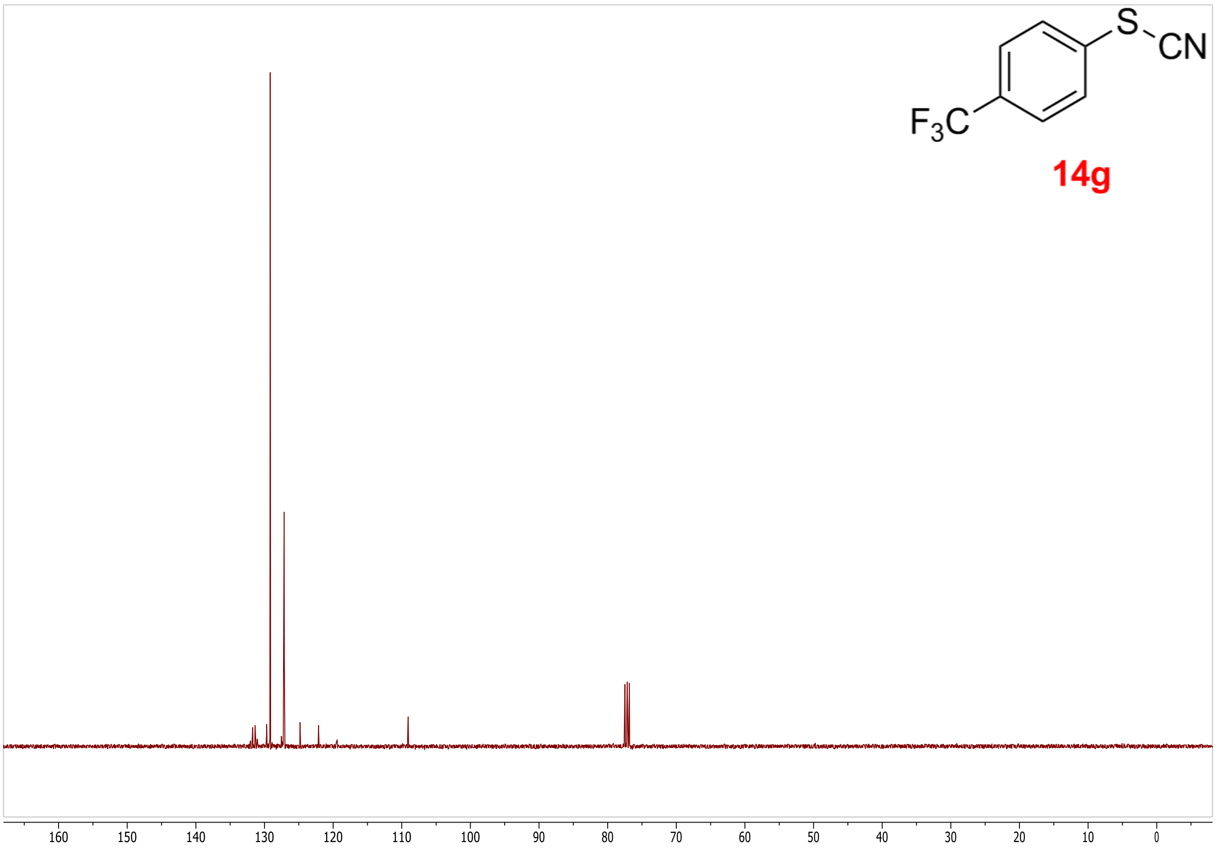
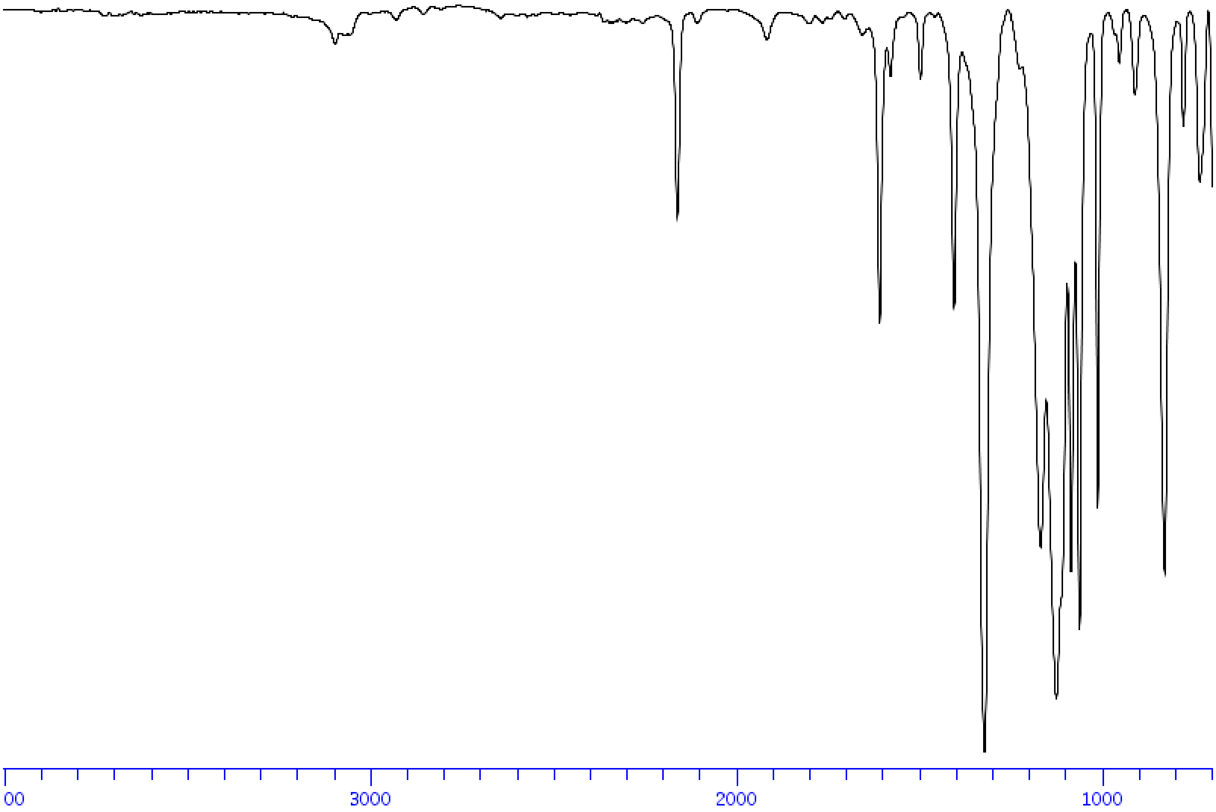
1-Thiocyanato-4-(trifluoromethyl)benzene (14g)



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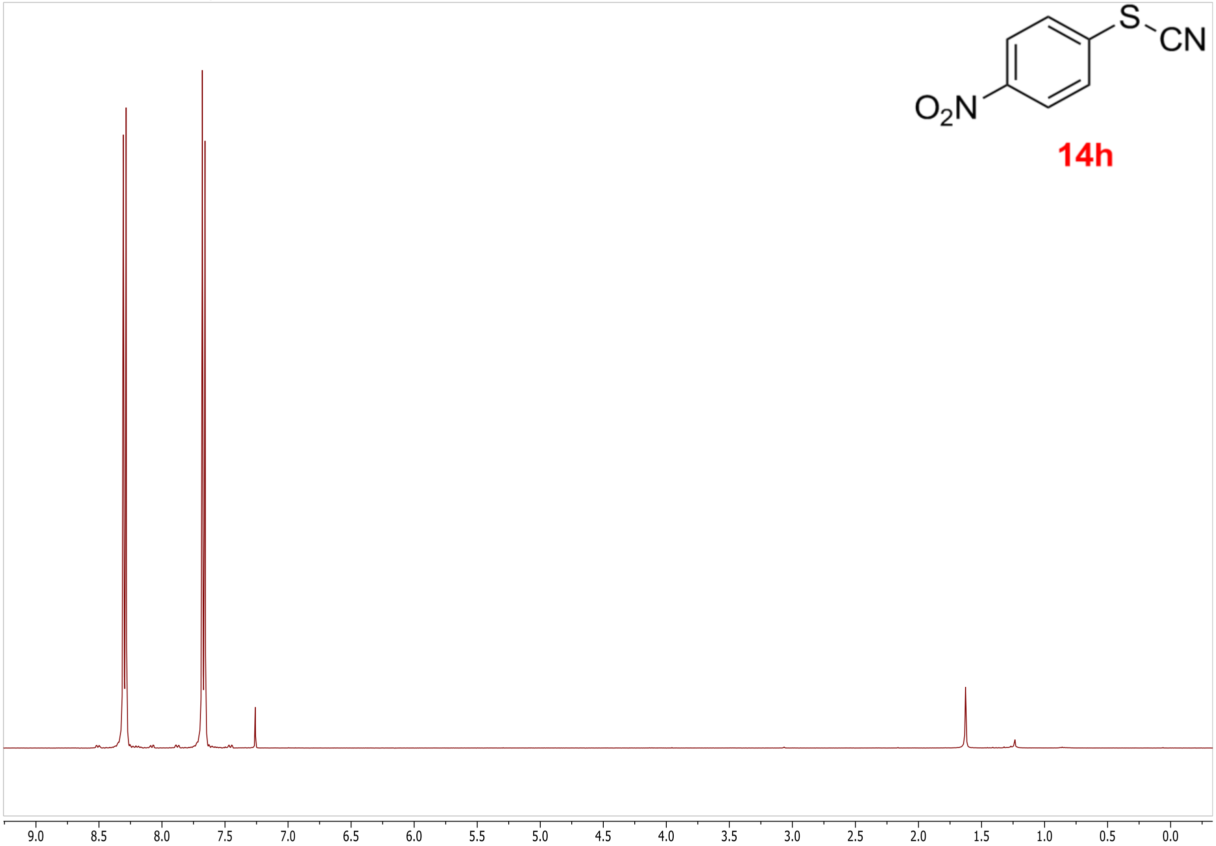
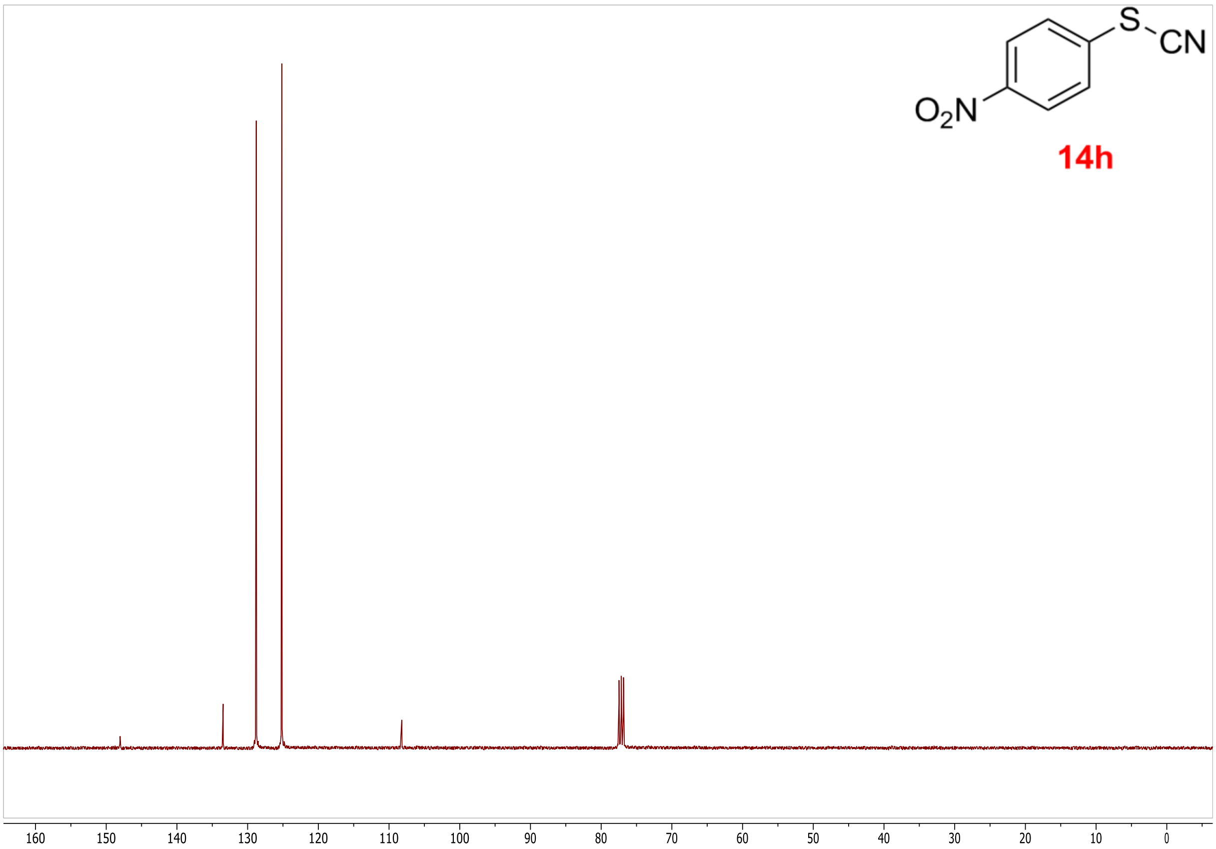
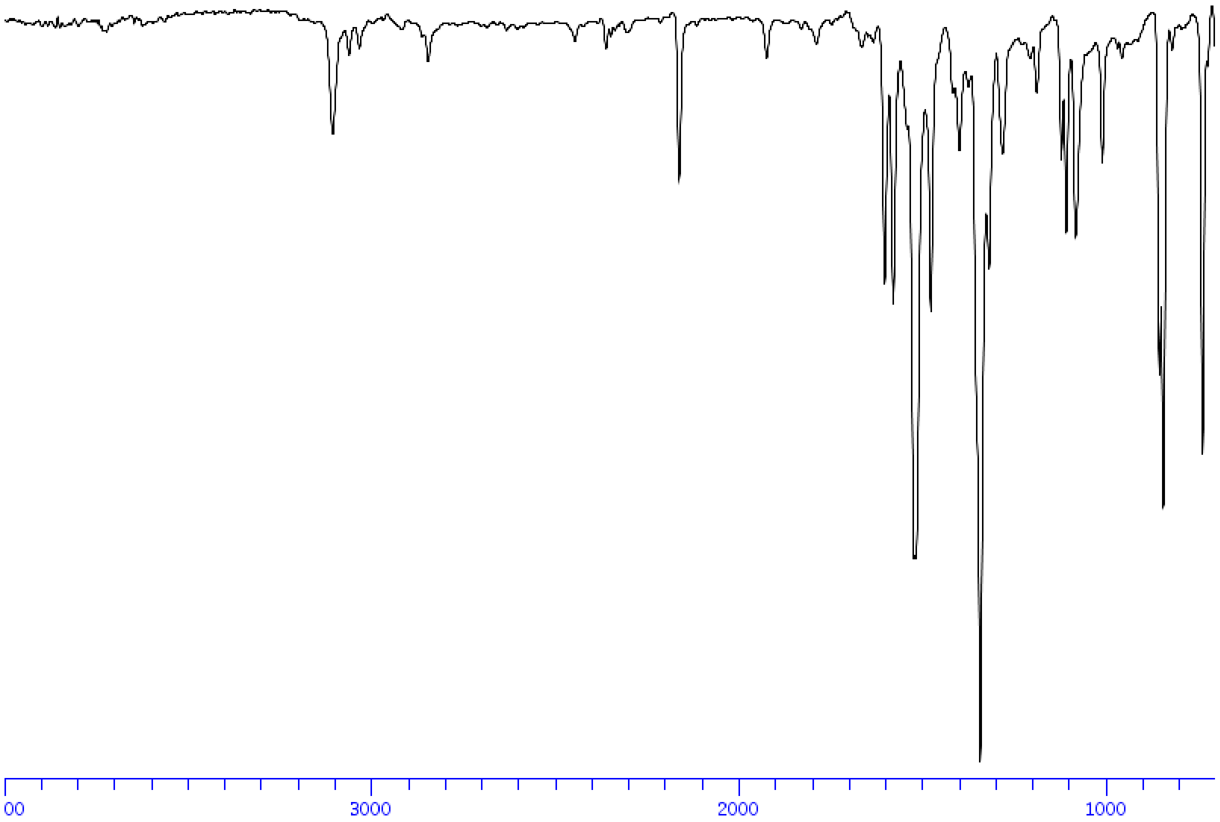
1-Nitro-4-thiocyanatobenzene (14h)



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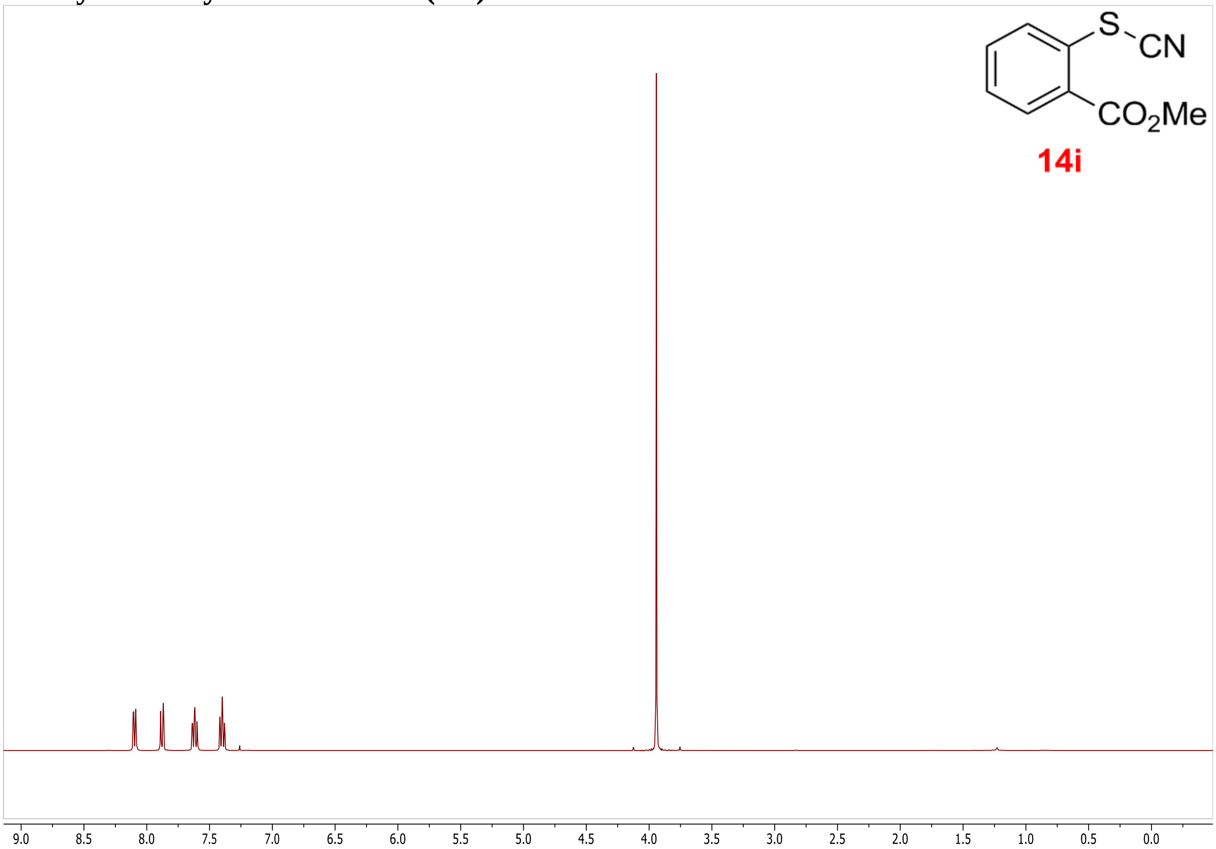
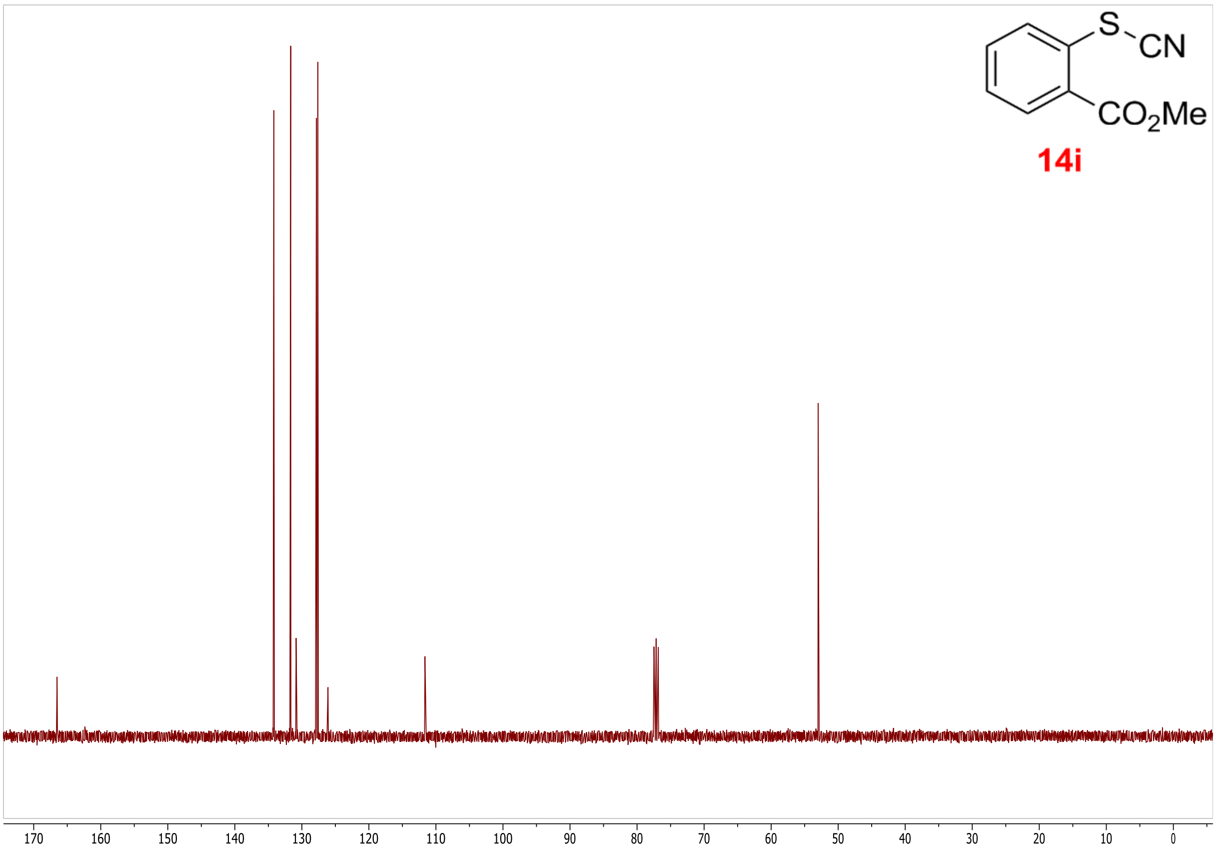
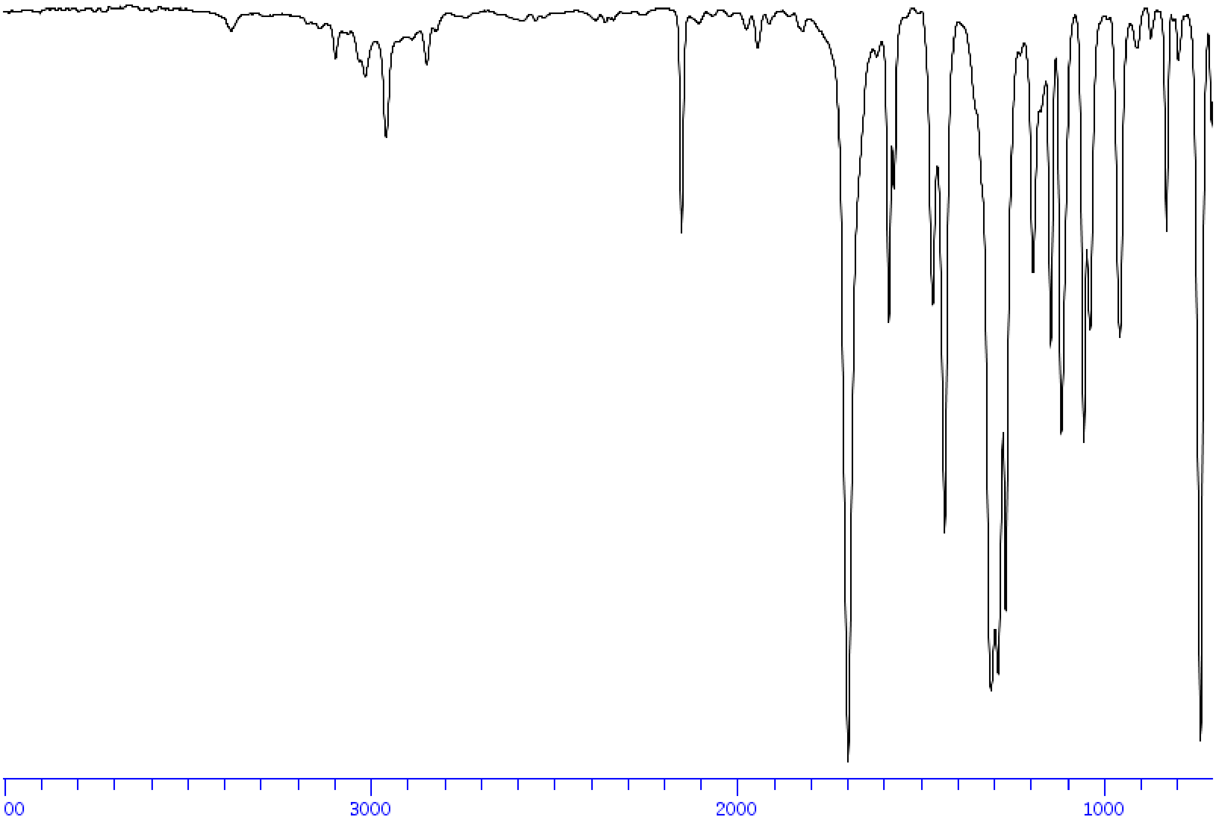
Methyl 2-thiocyanatobenzoate (14i)



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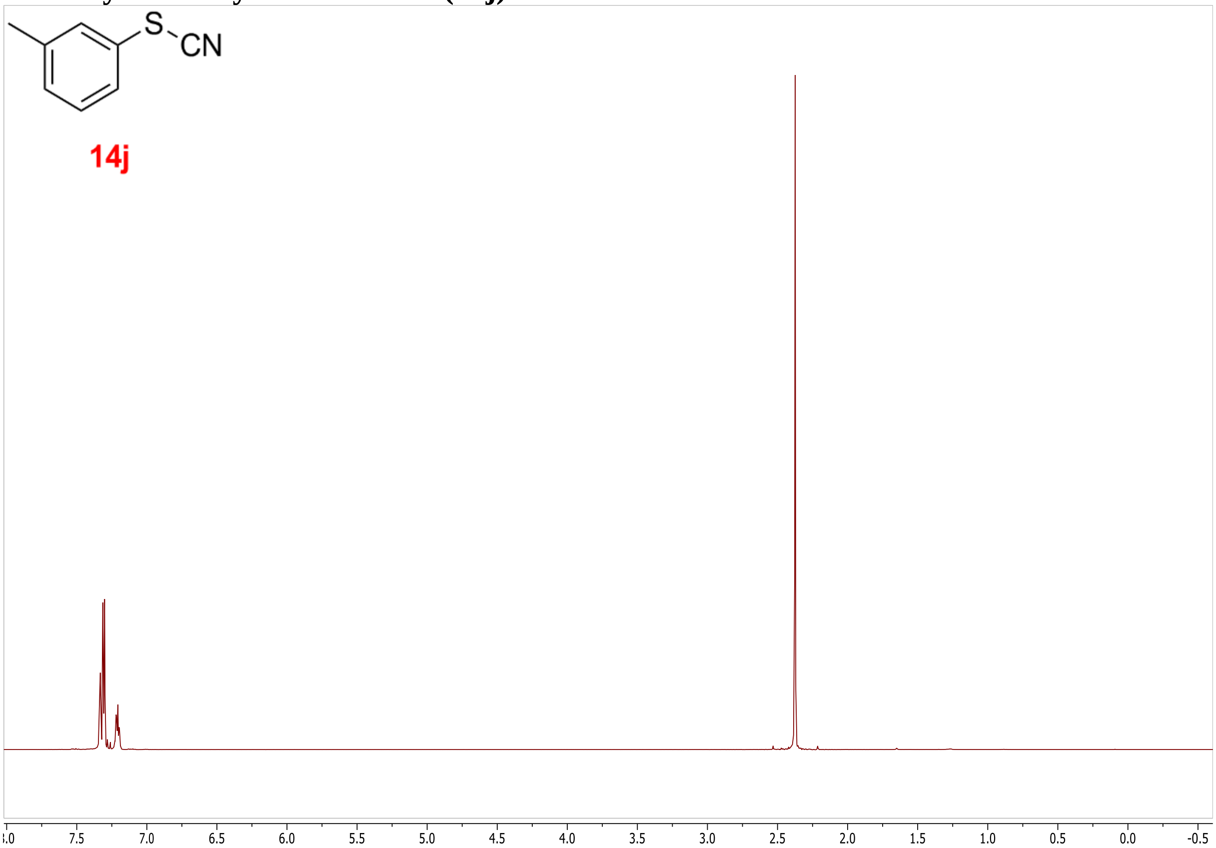
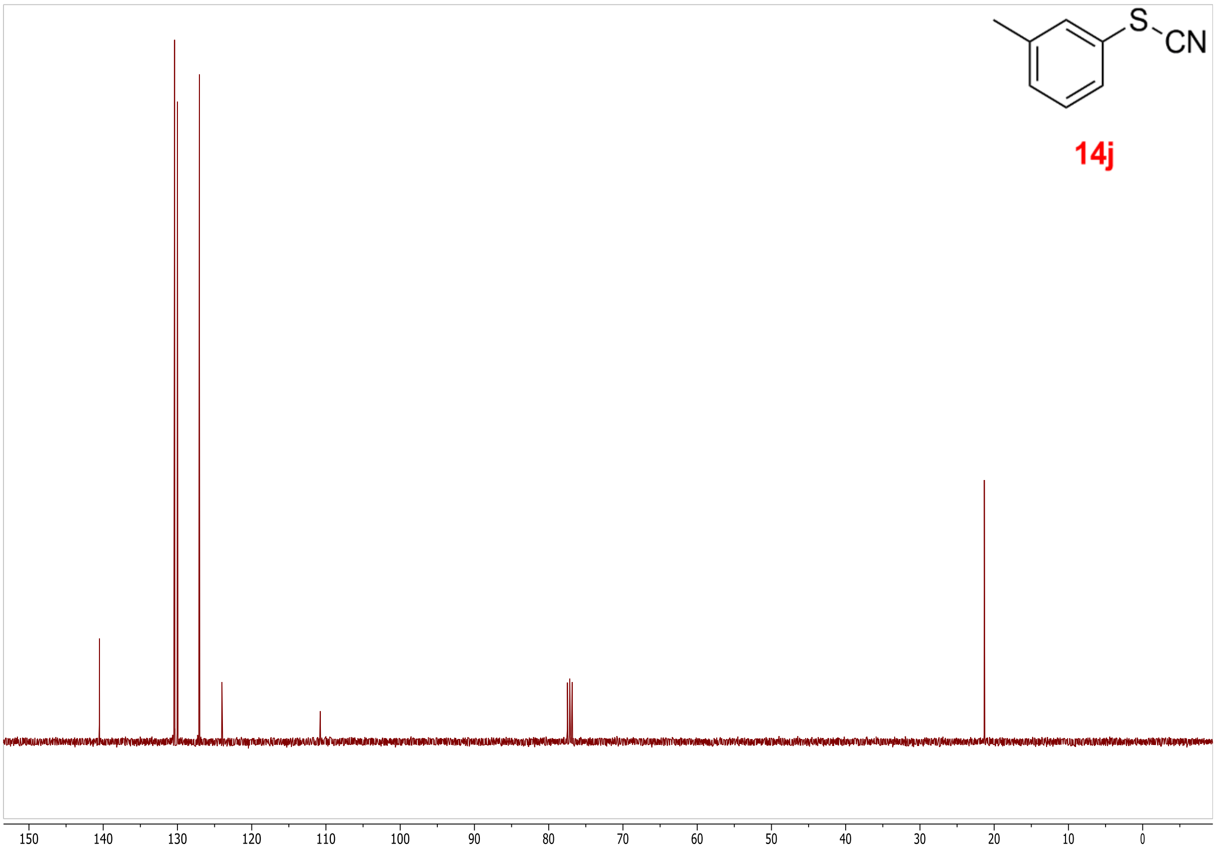
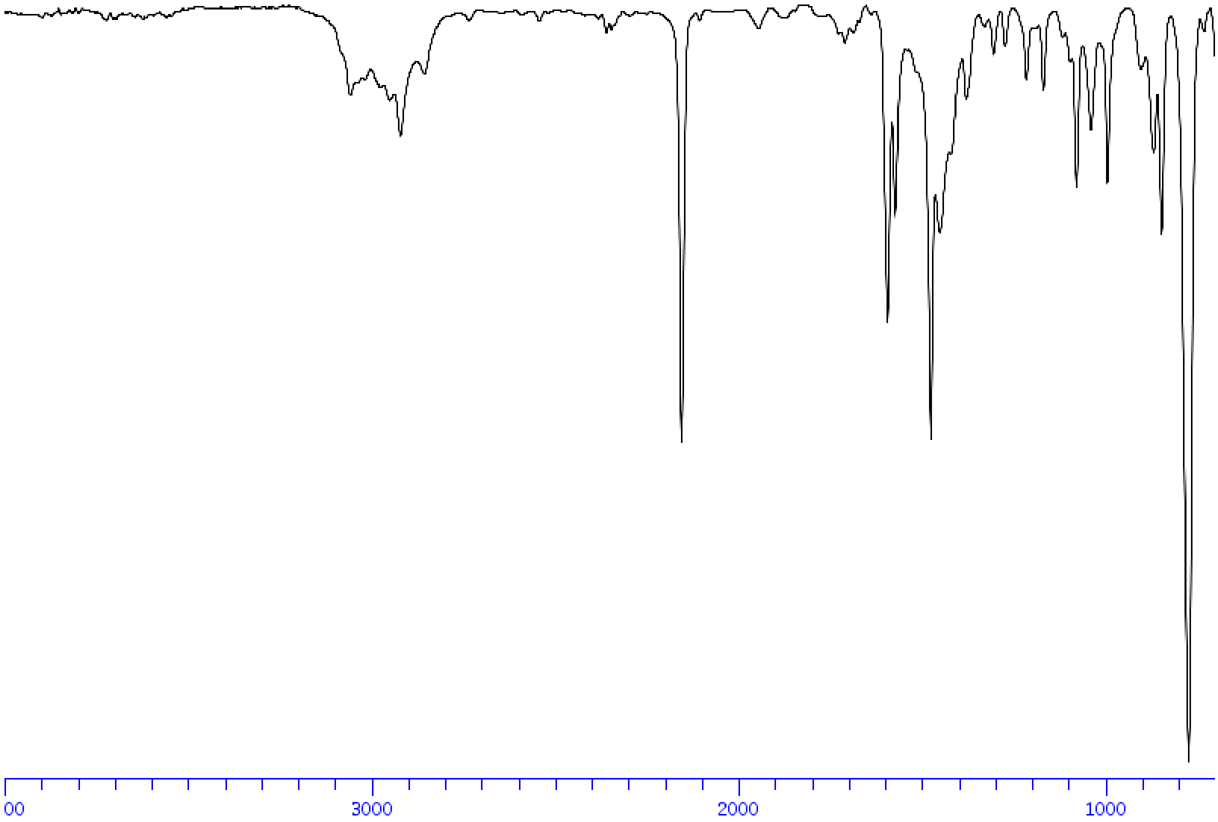
1-Methyl-3-thiocyanatobenzene (14j)



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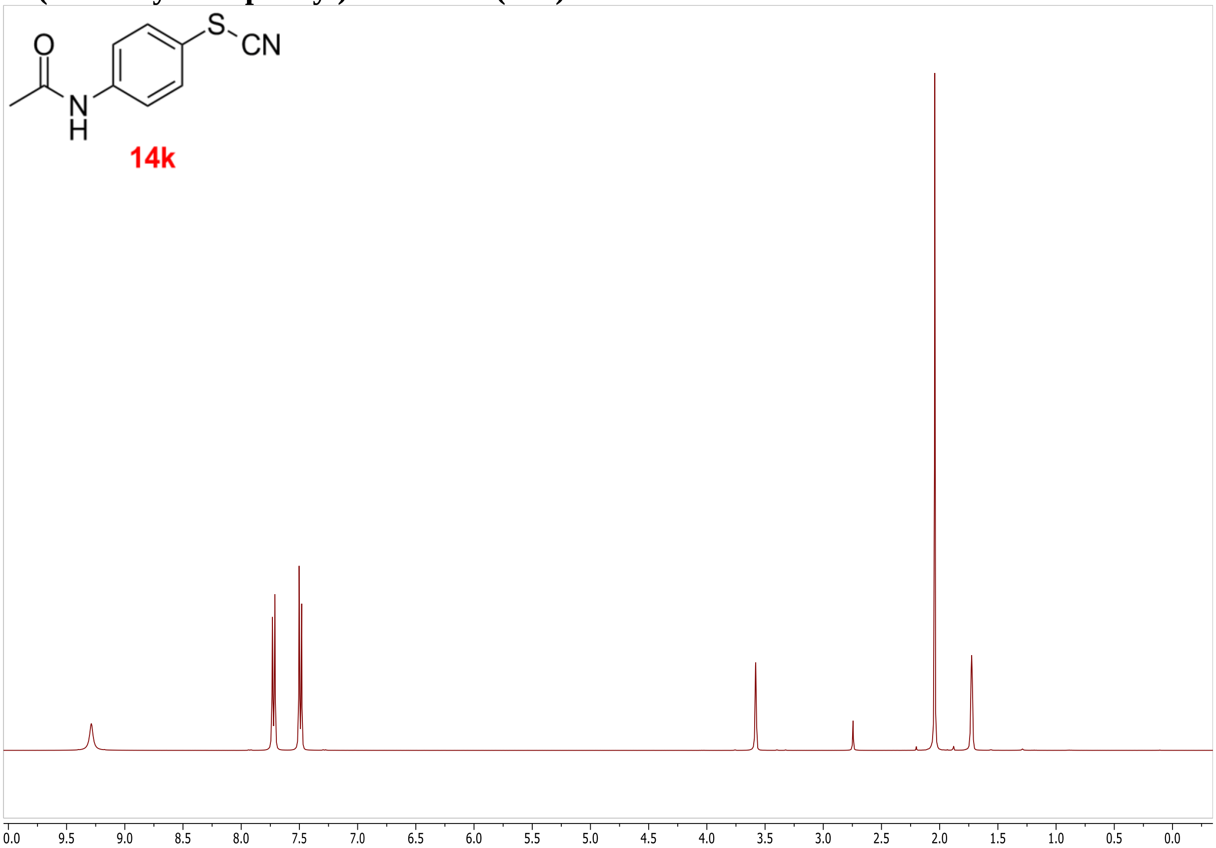
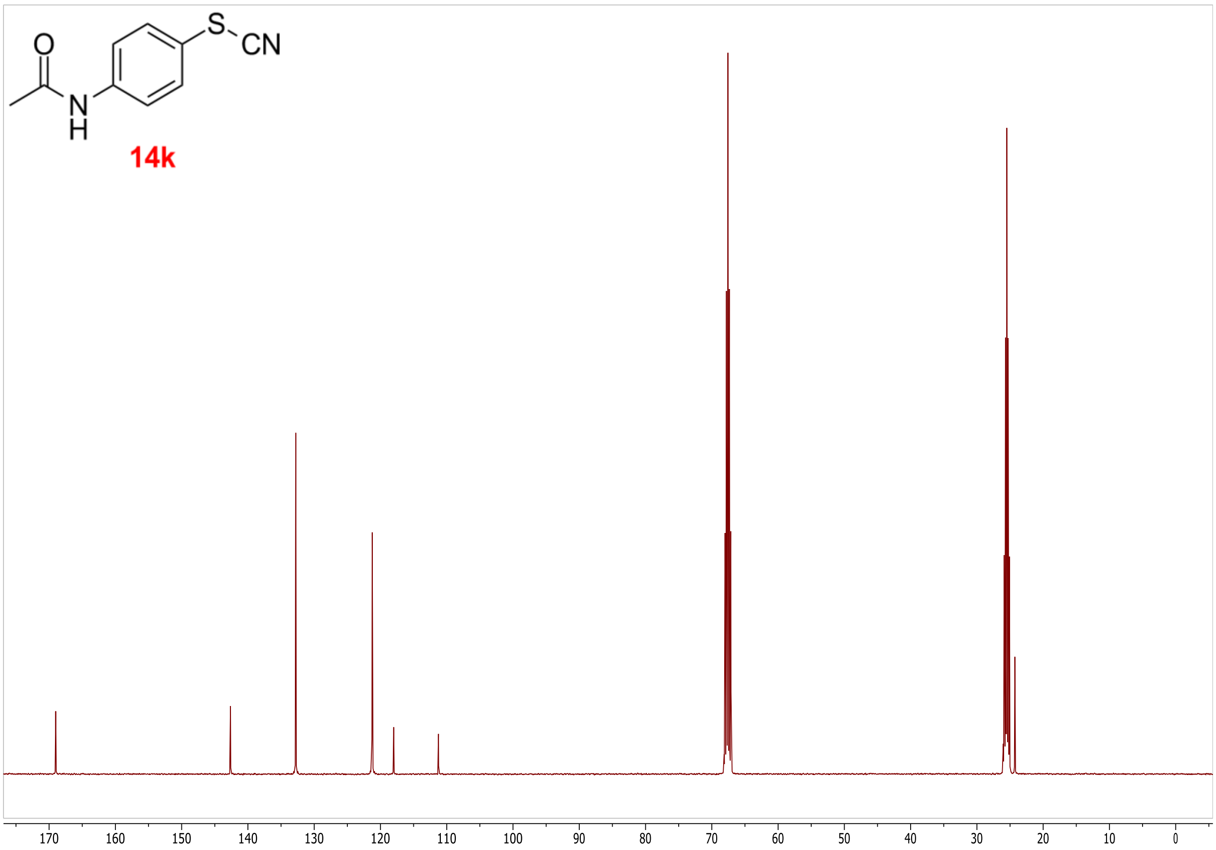
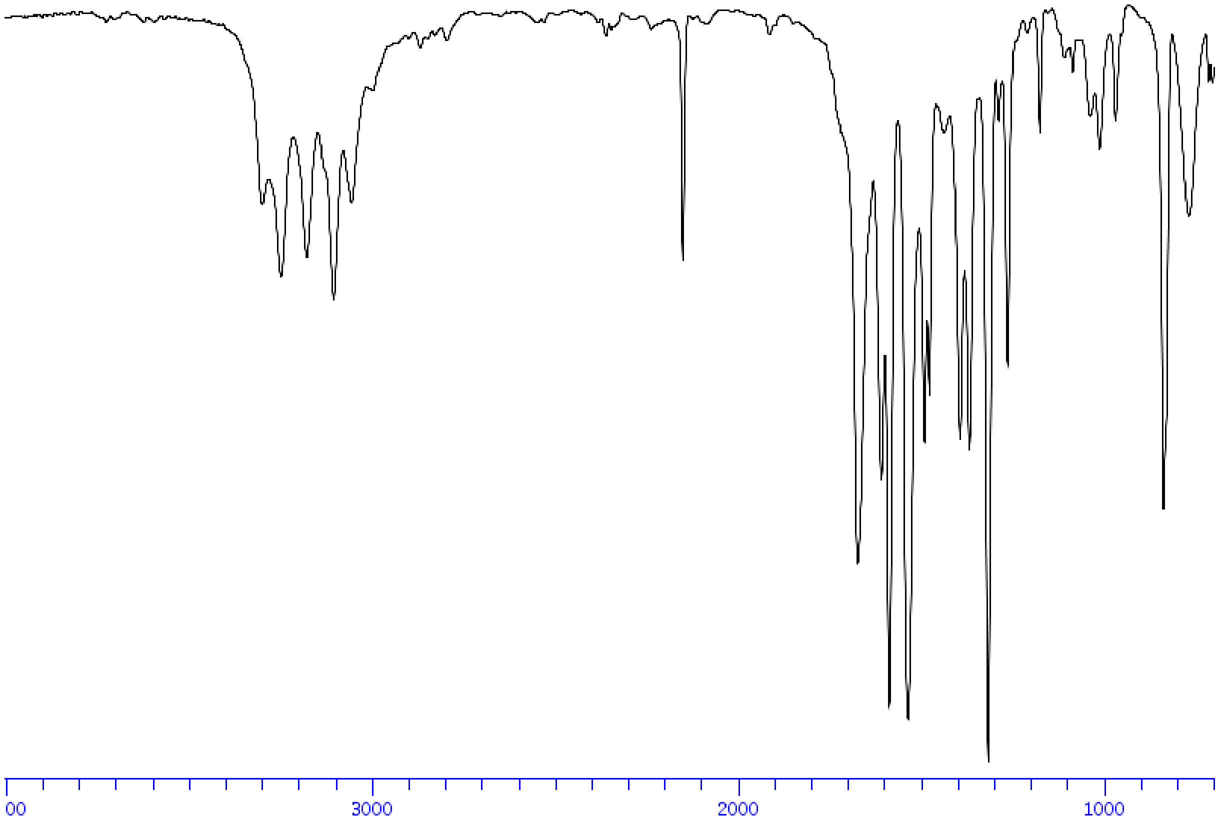
N-(4-Thiocyanatophenyl)acetamide (14k)



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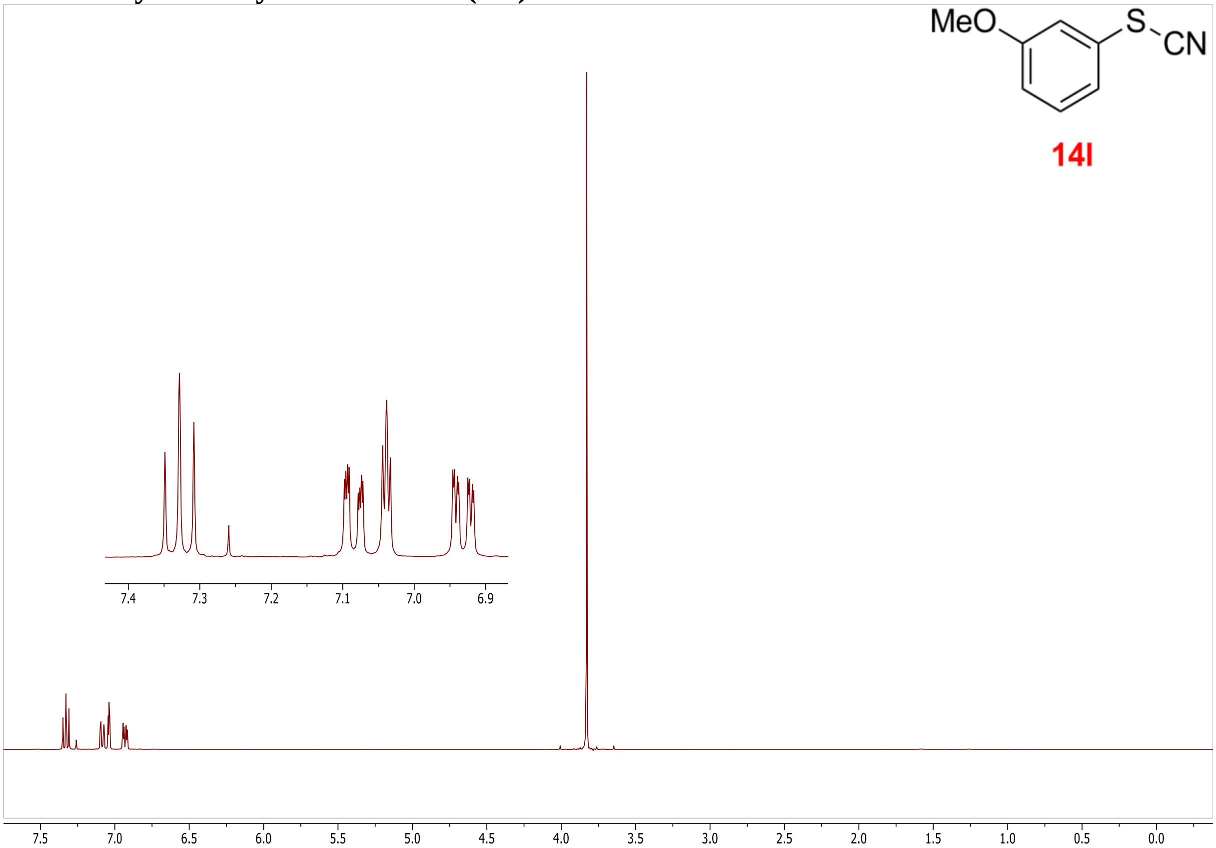
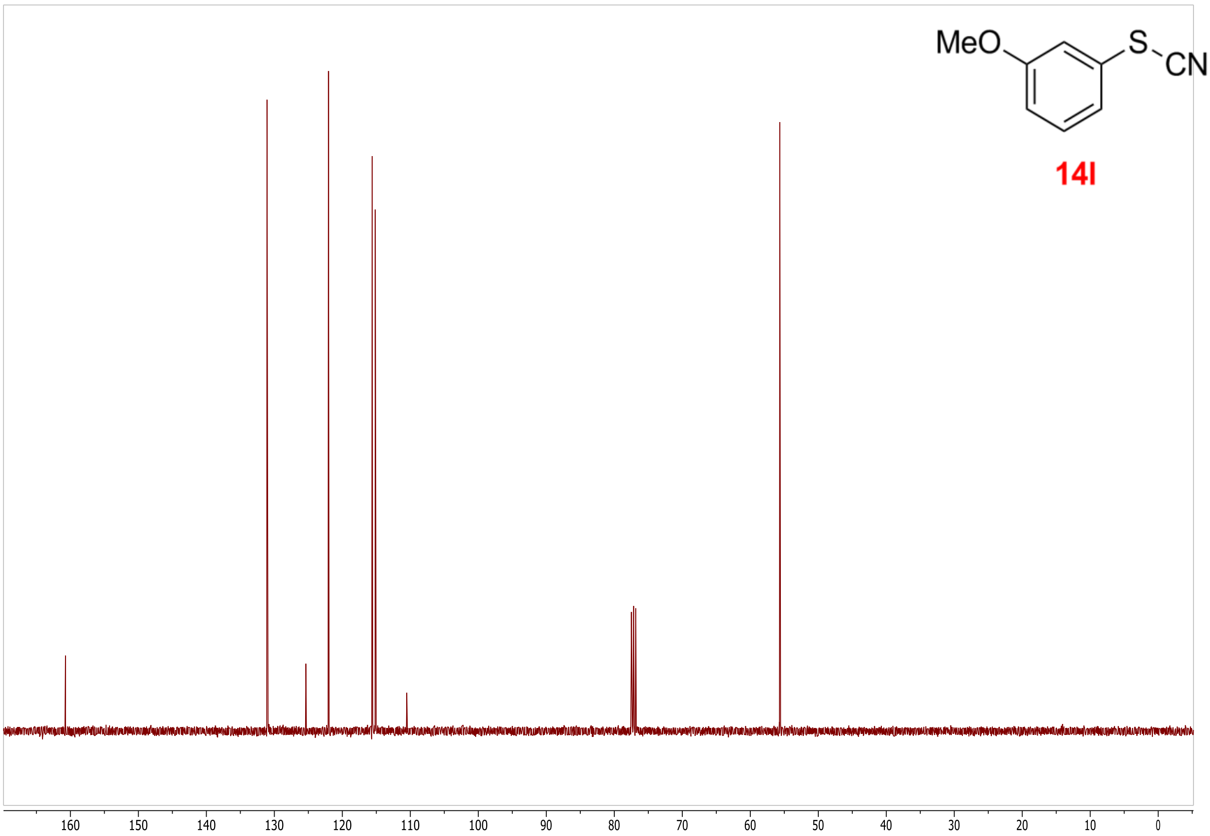
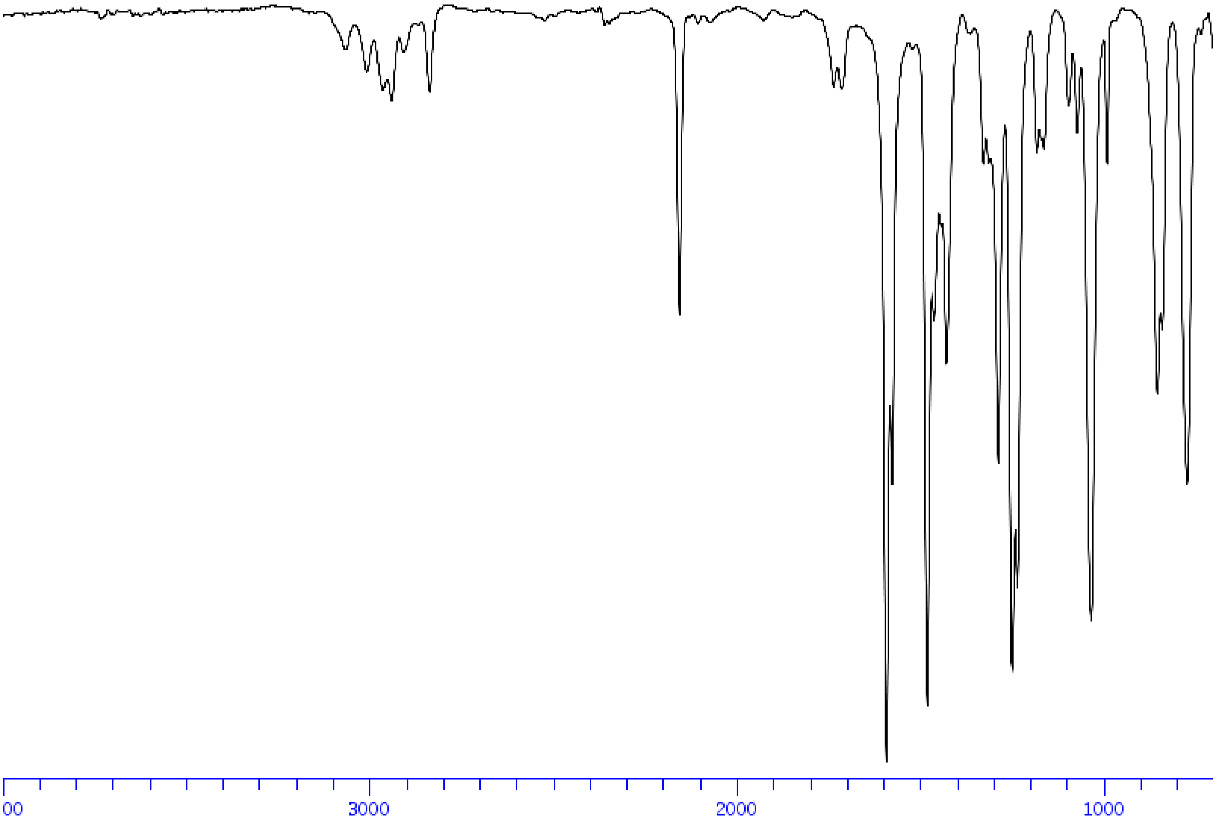
1-Methoxy-3-thiocyanatobenzene (14l)



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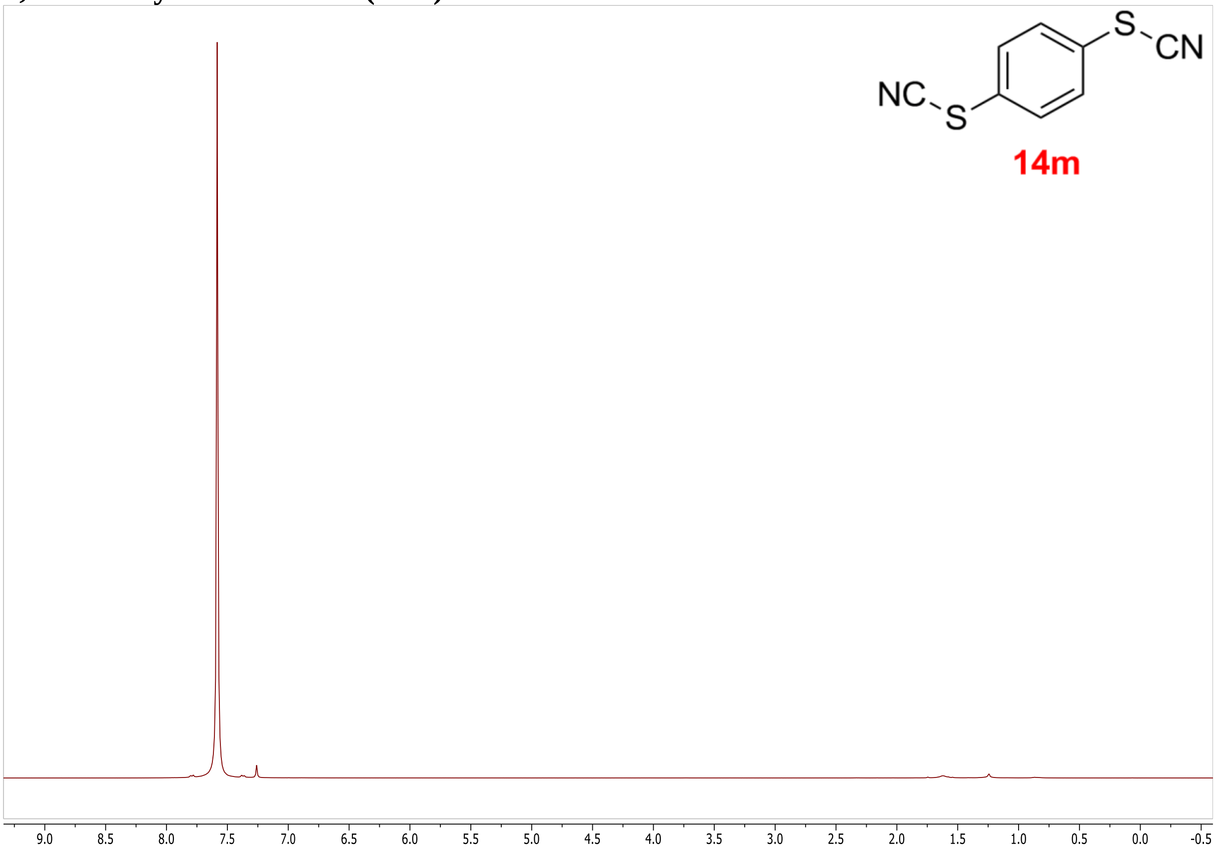
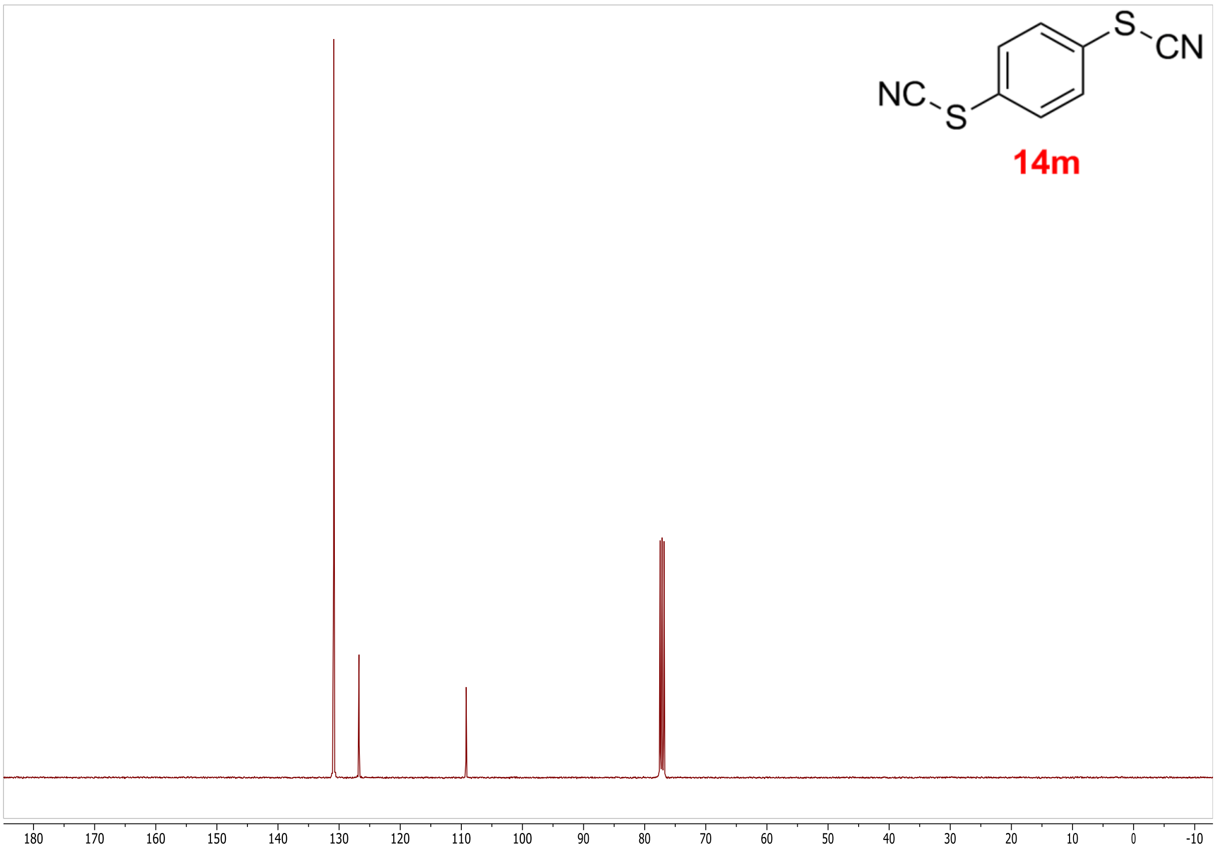
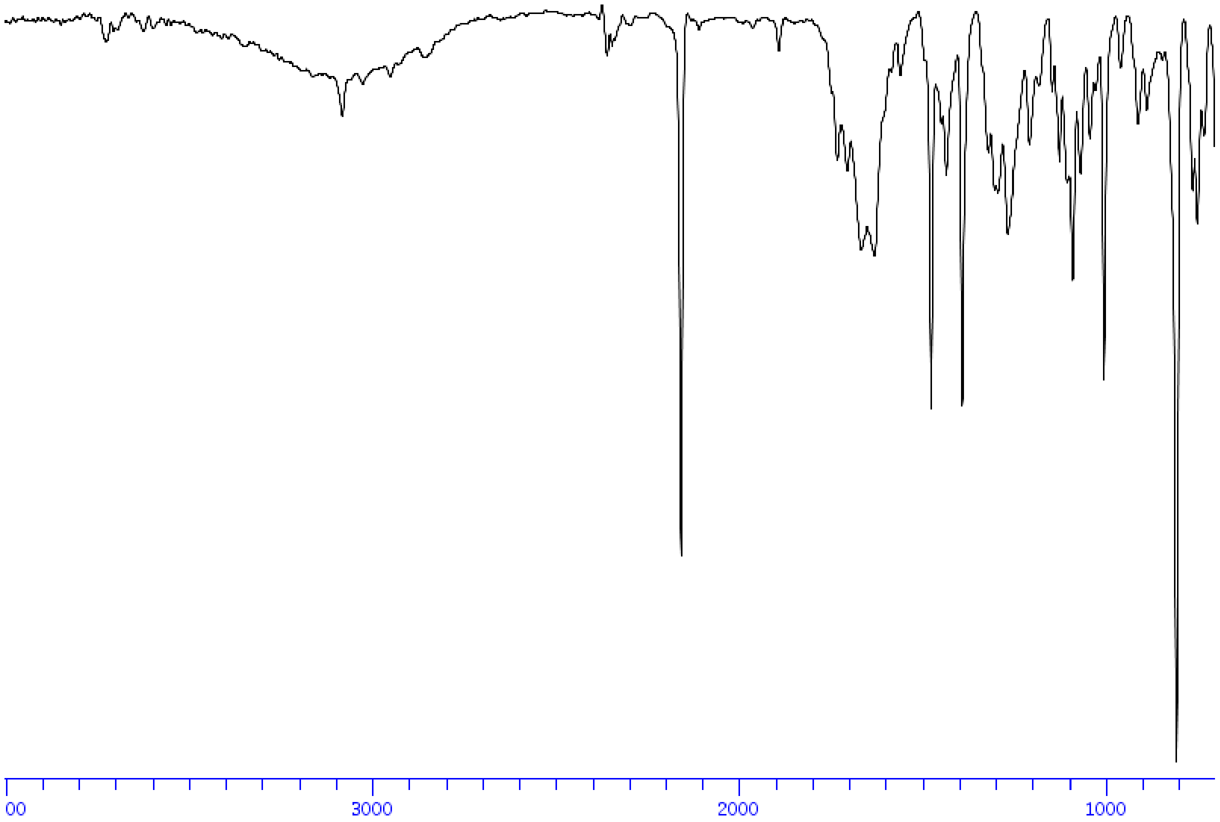
1,4-Dithiocyanatobenzene (14m)



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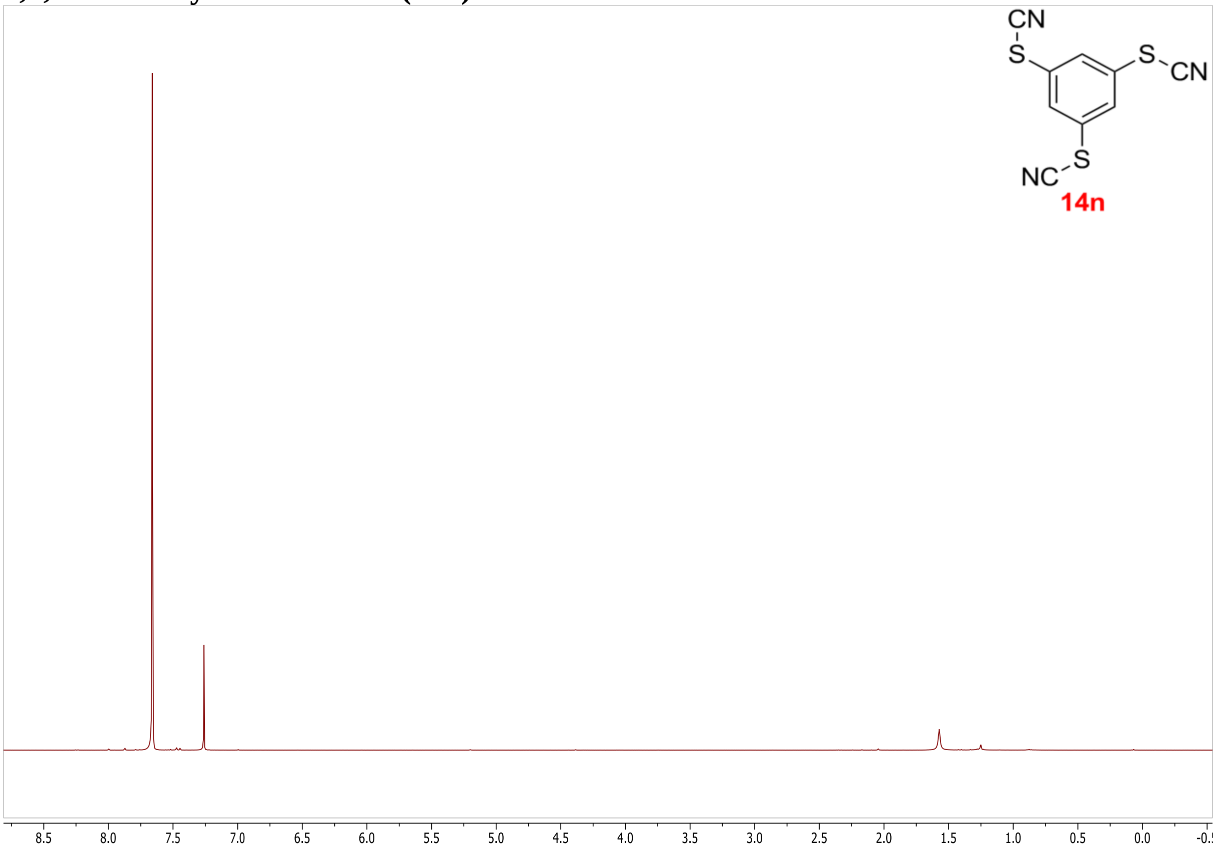
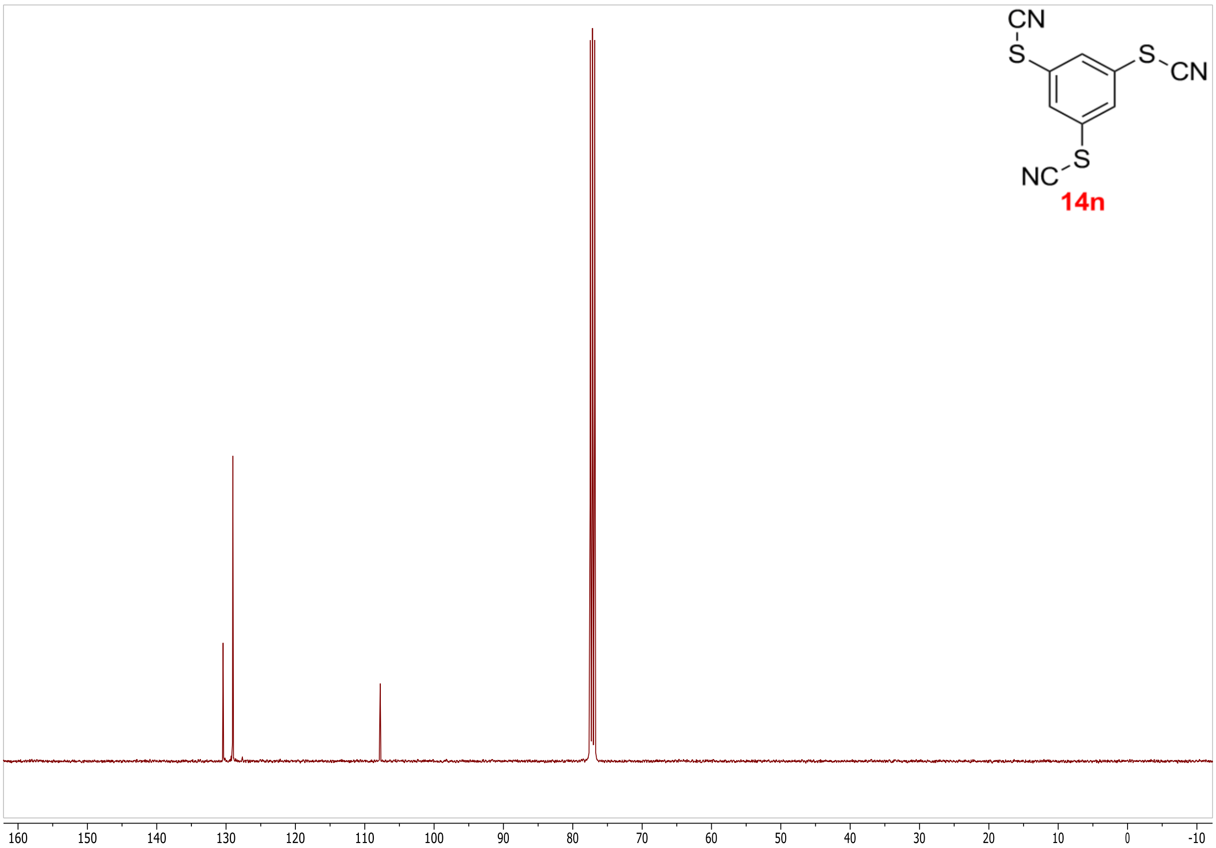
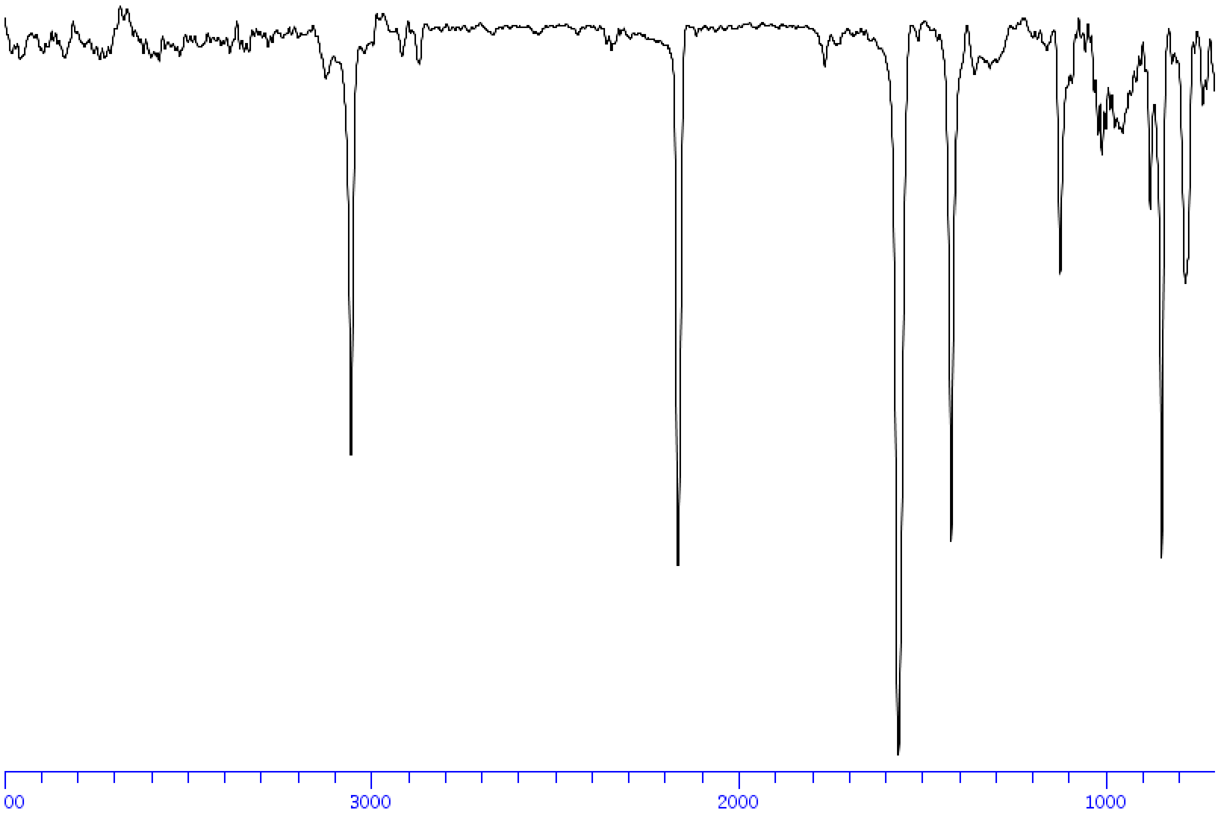
1,3,5-Trithiocyanatobenzene (14n)



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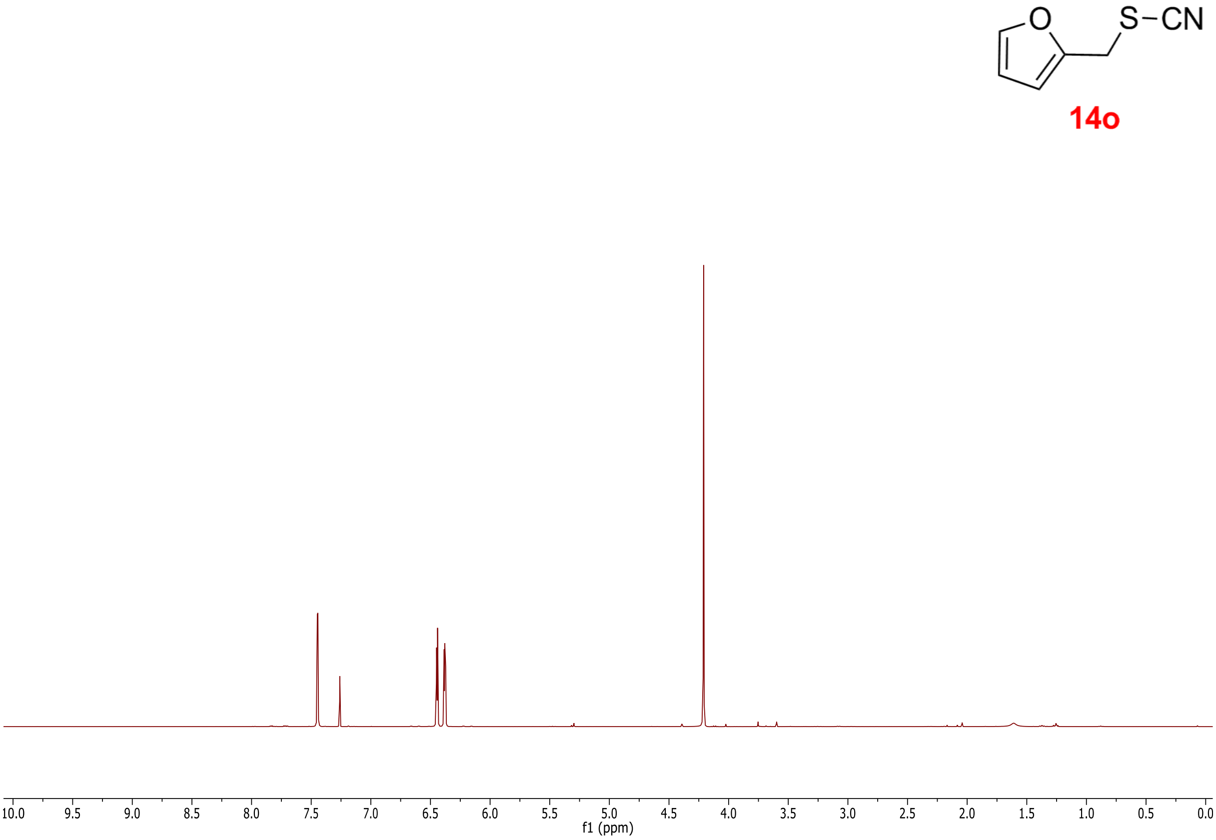
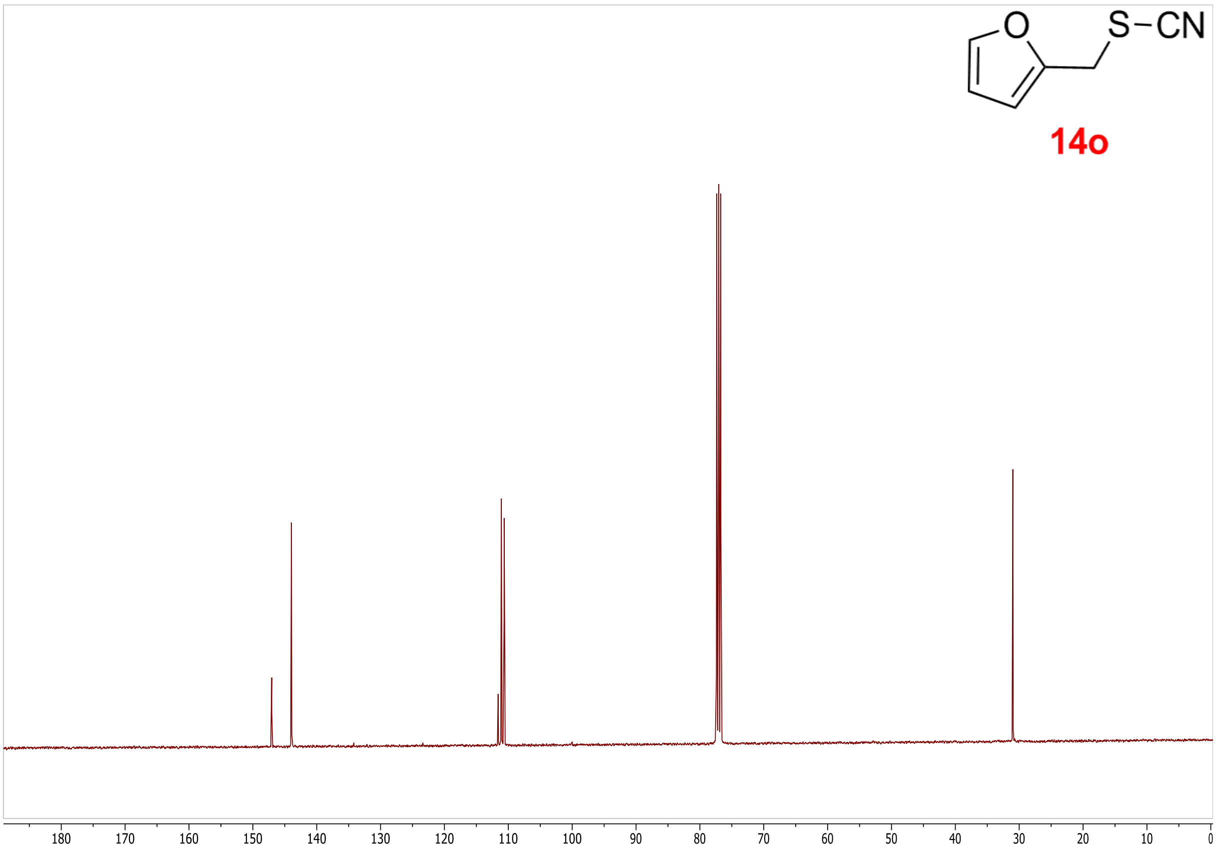
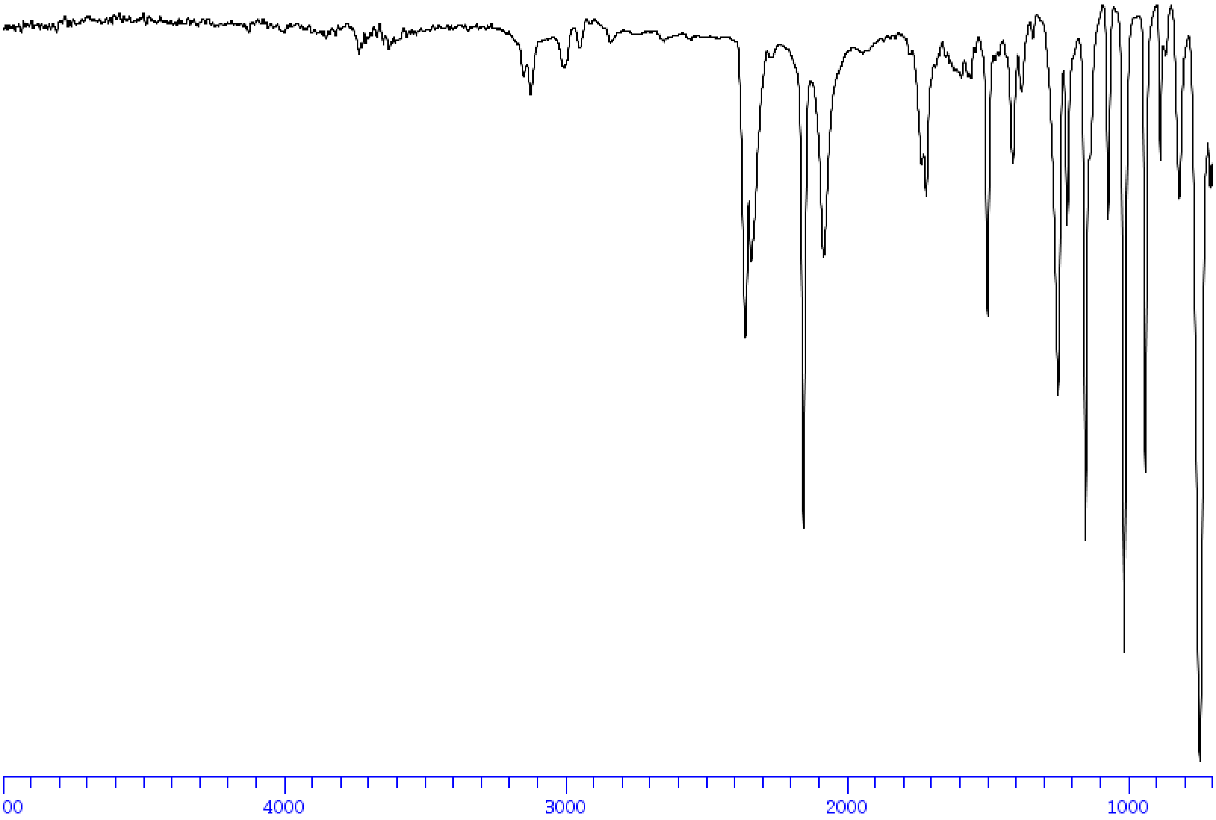
2-(thiocyanatomethyl)furan (14o)



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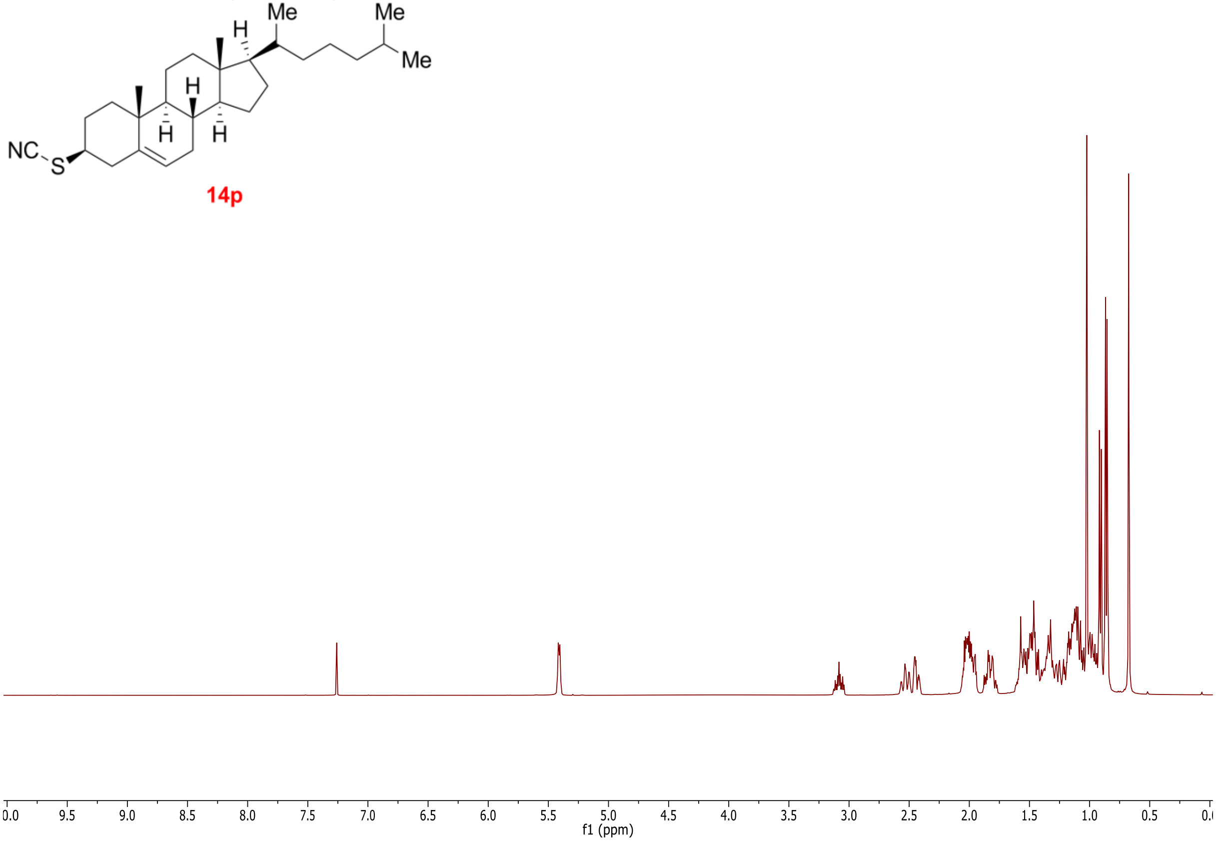
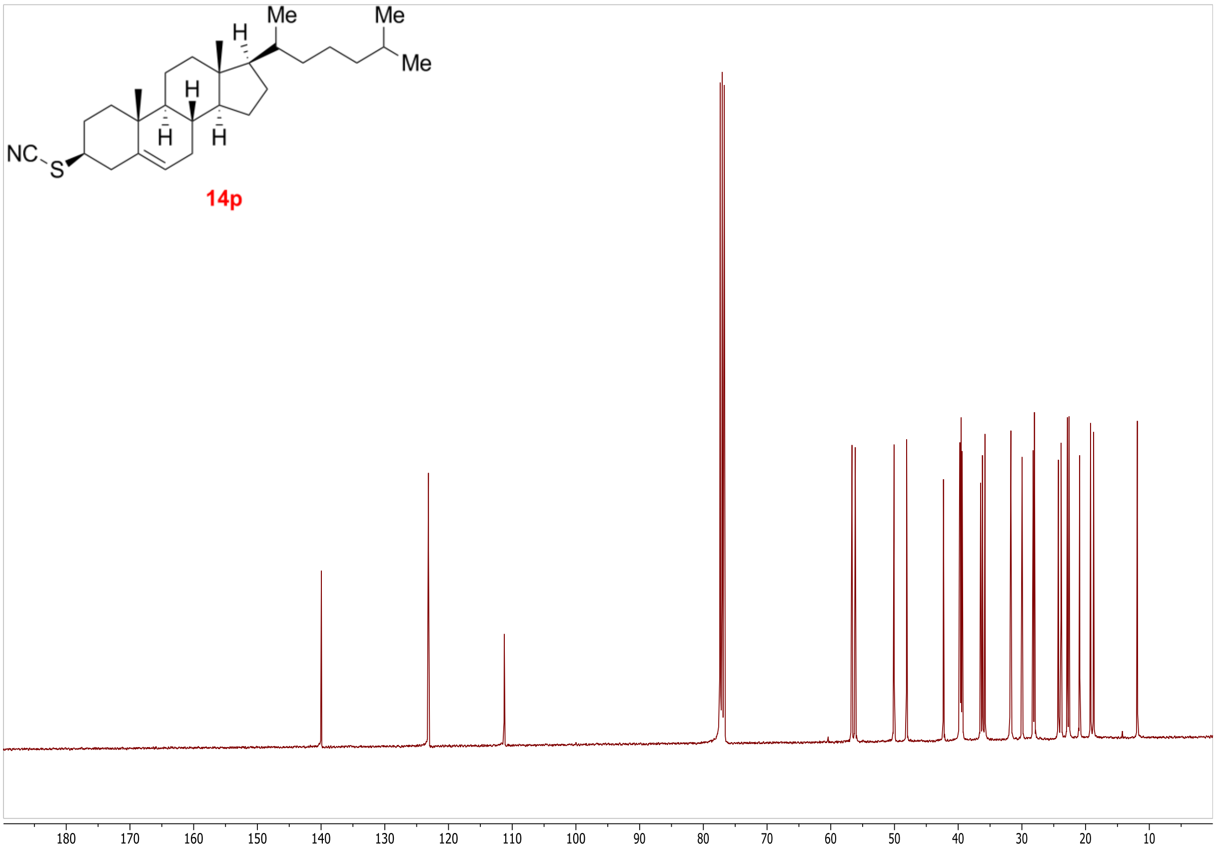
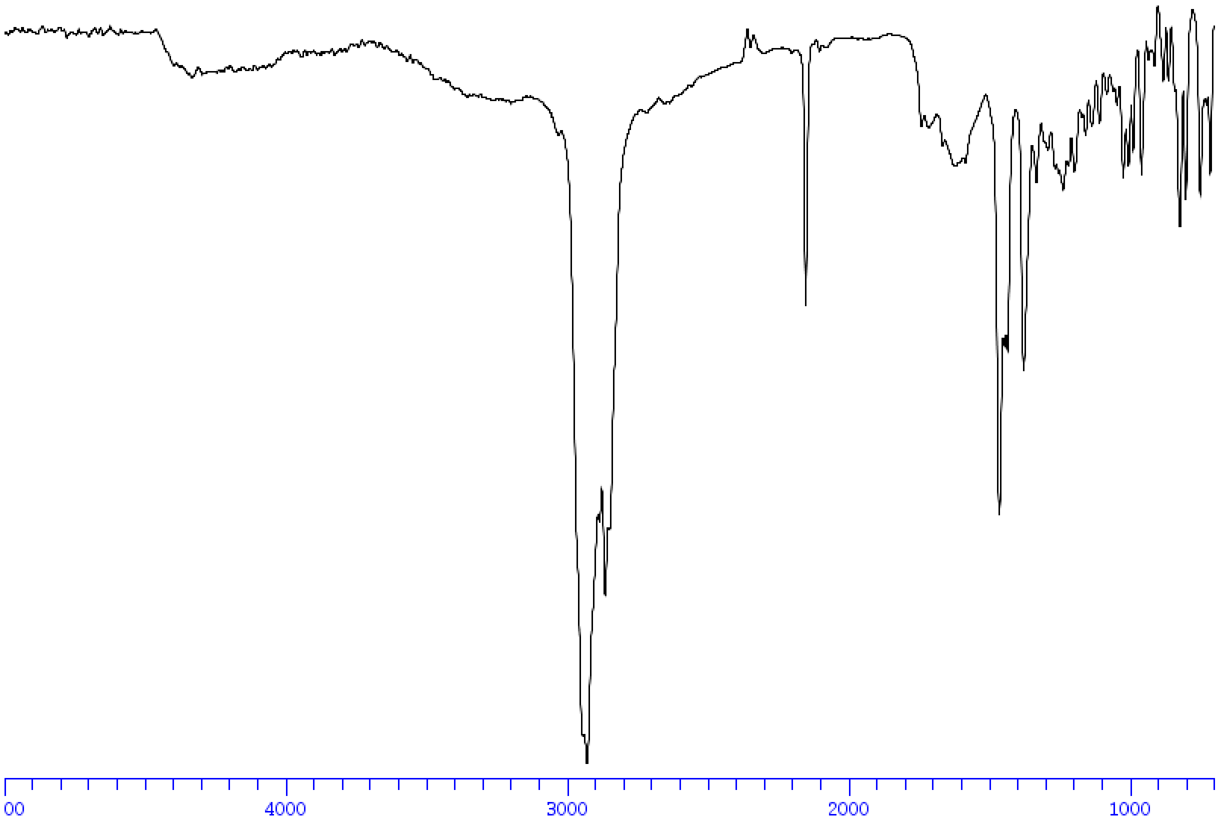
Cholest-5-en-3β-yl thiocyanate (14p)



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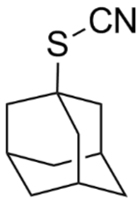
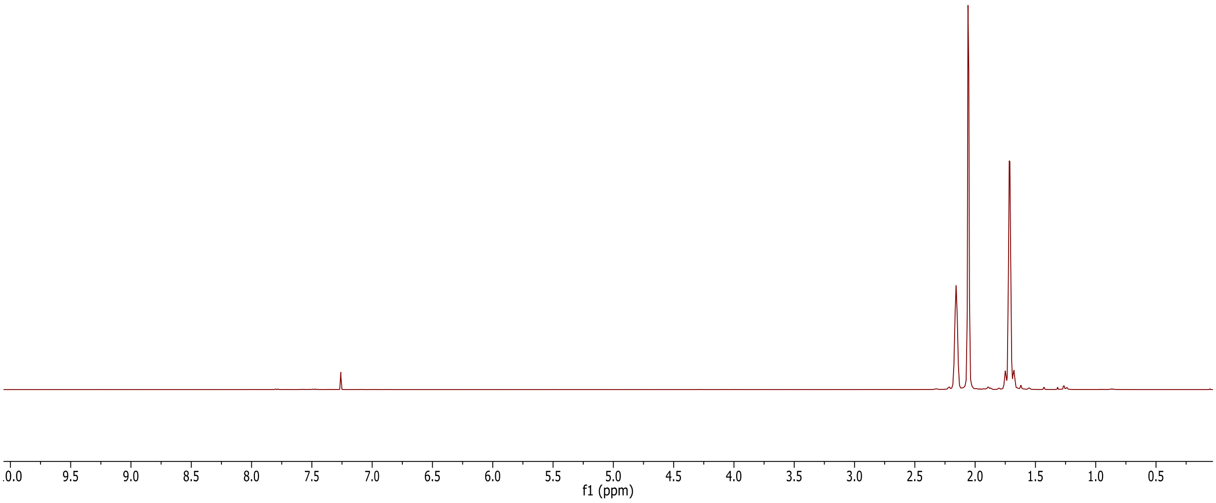
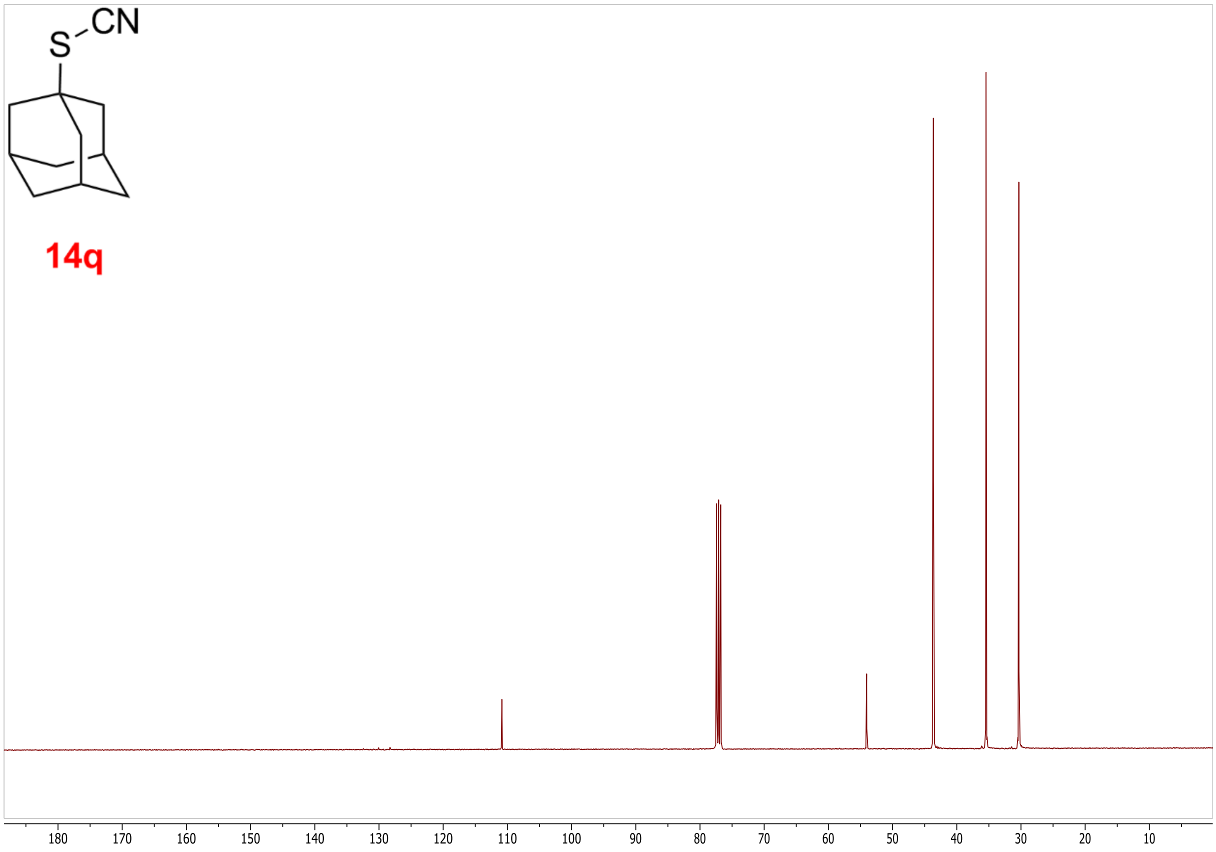
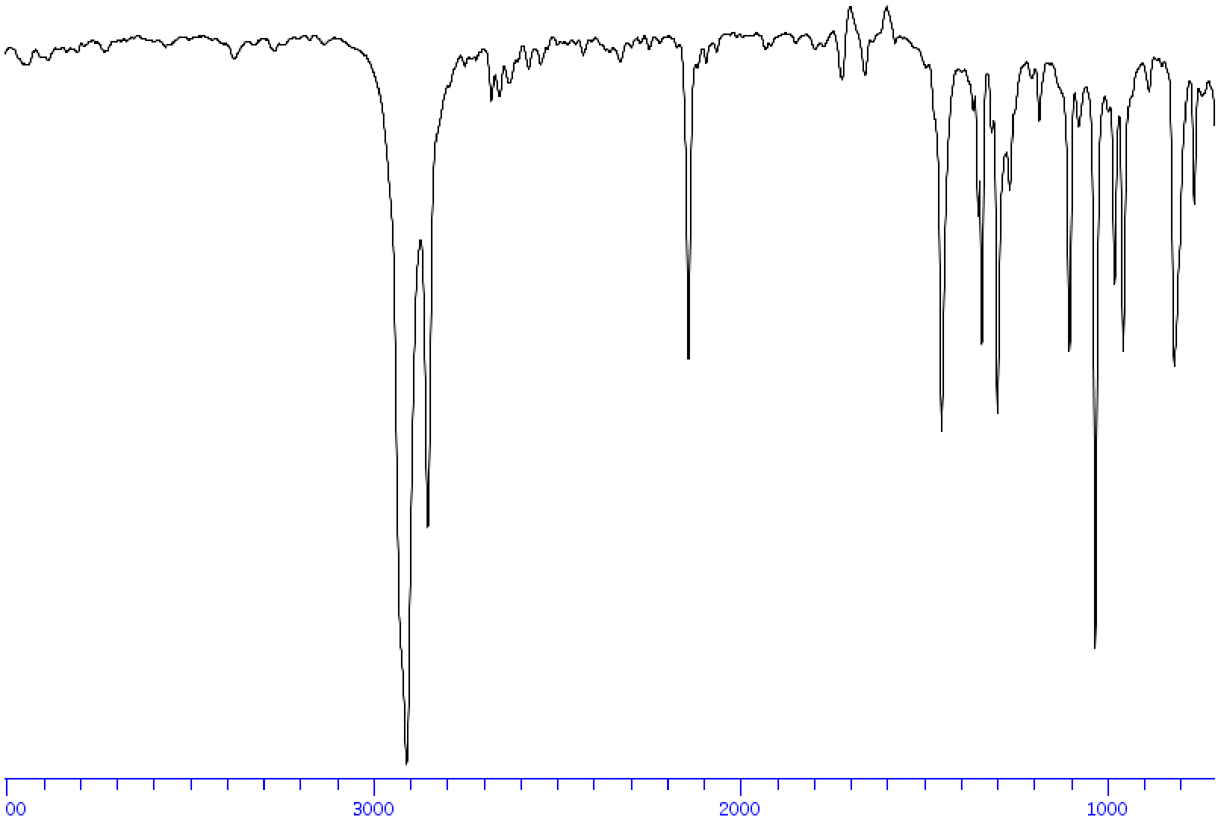
1-thiocyanatoadamantane (14q)



14q



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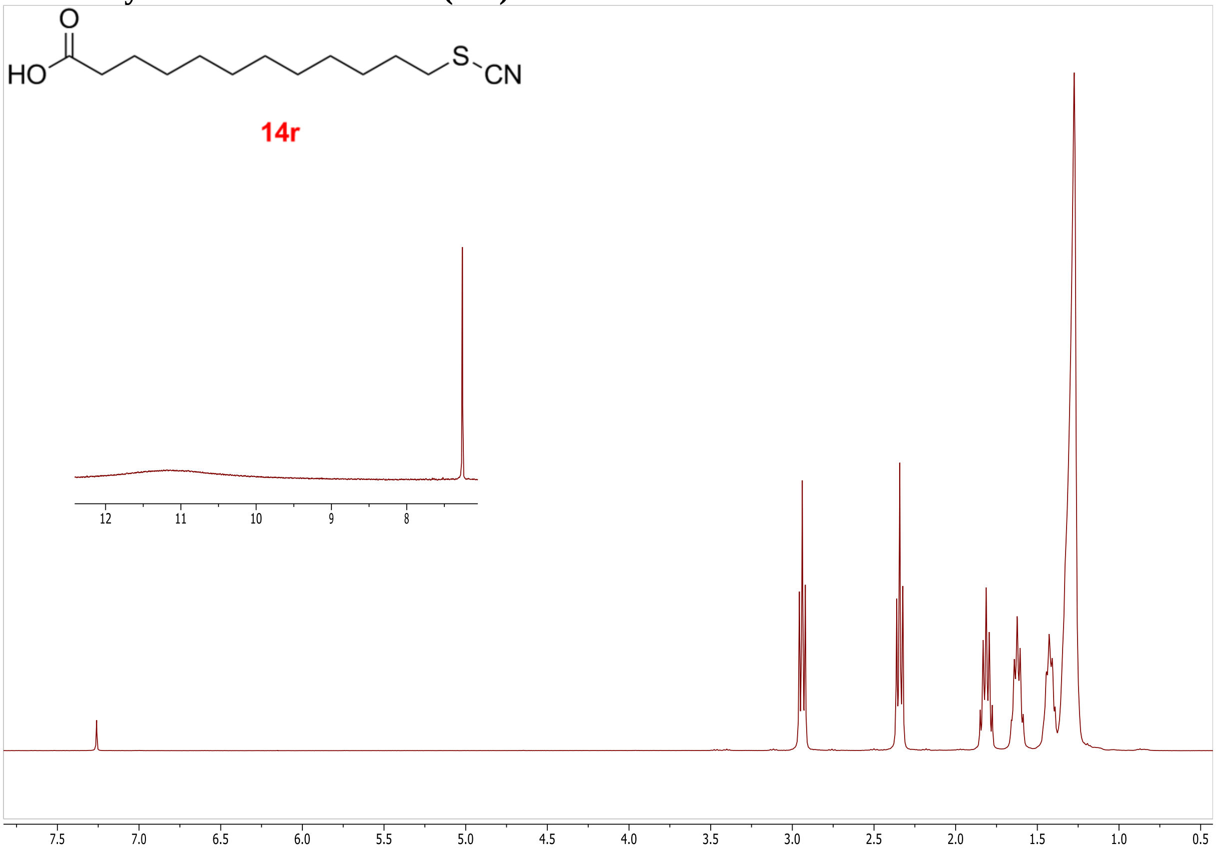
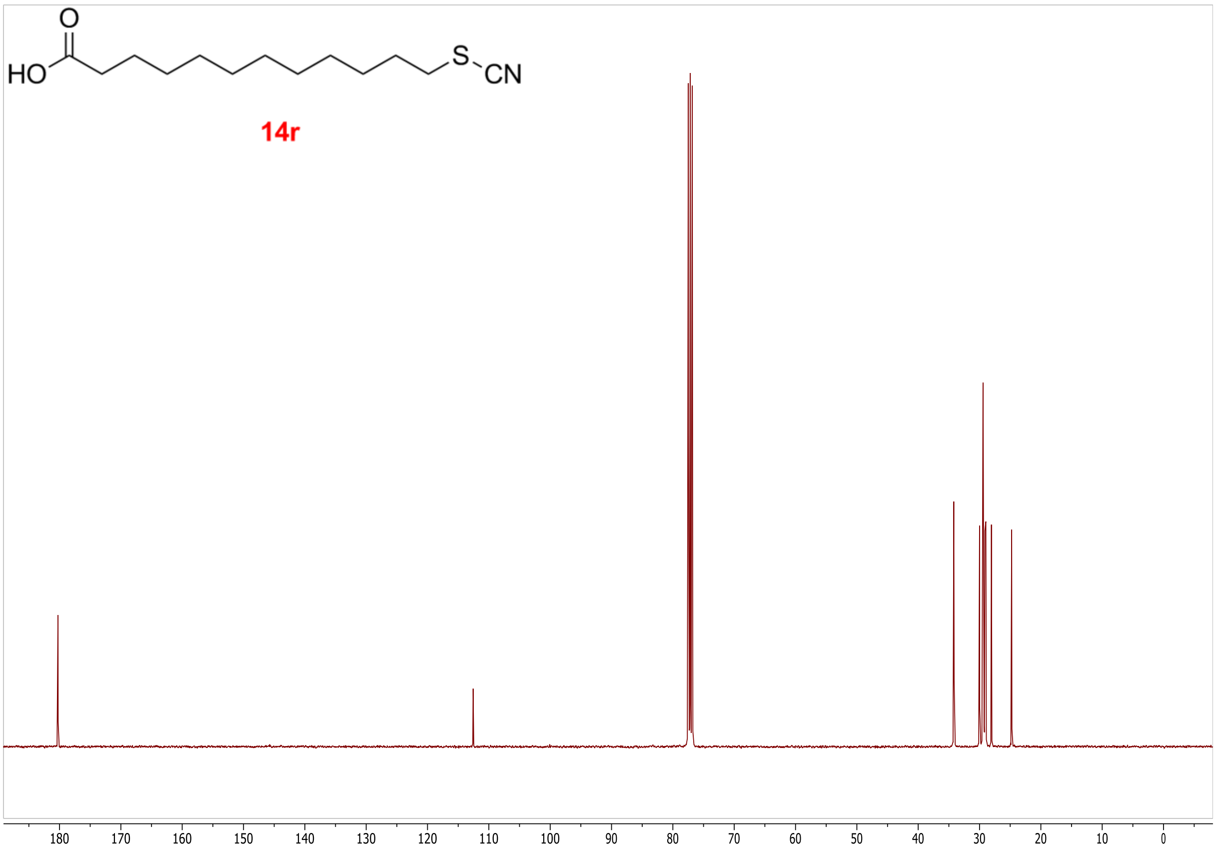
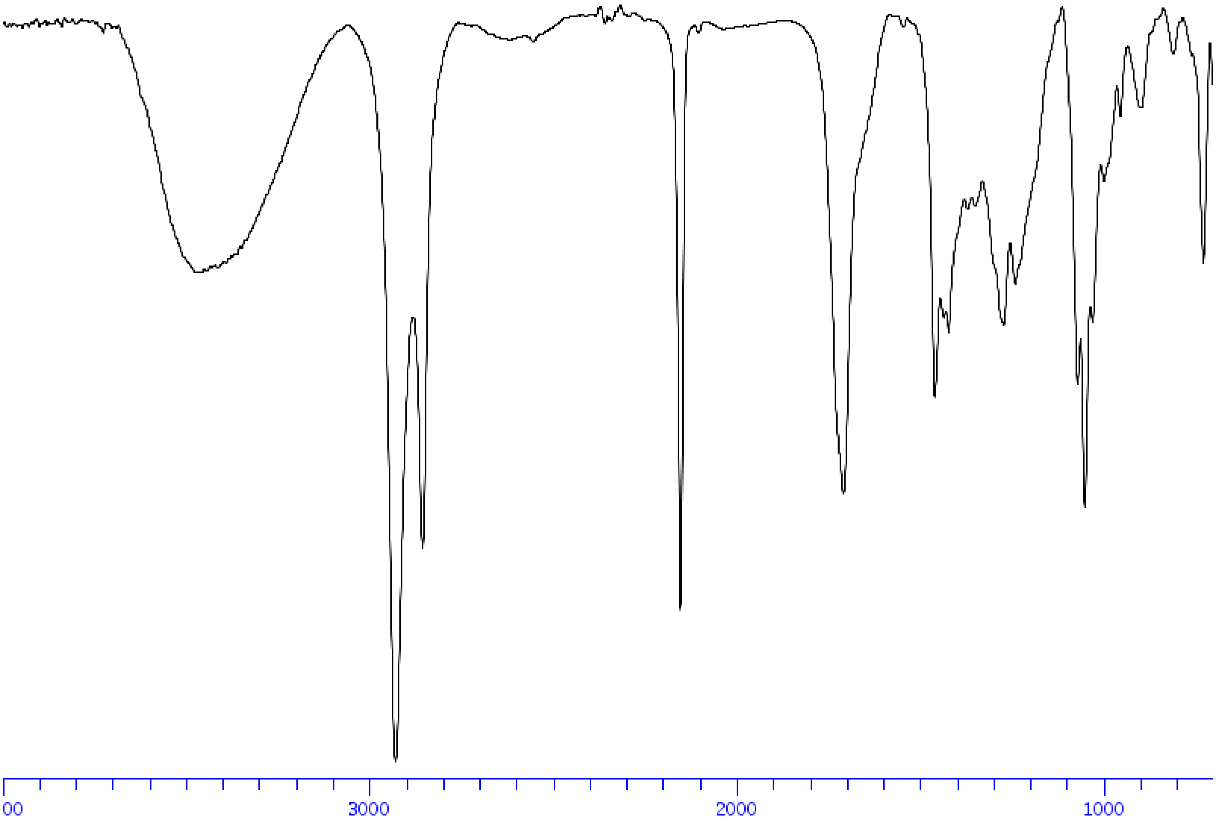
12-Thiocyanatododecanoic acid (14r)



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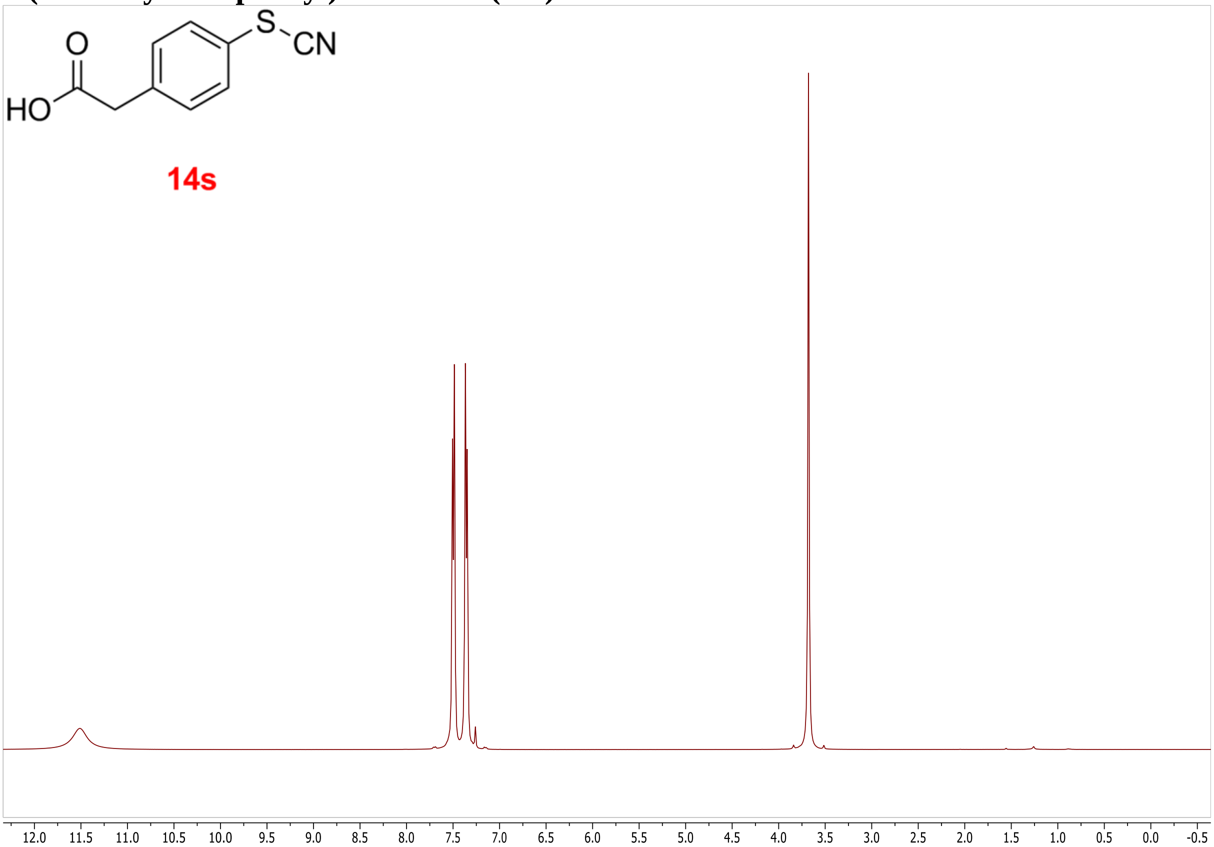
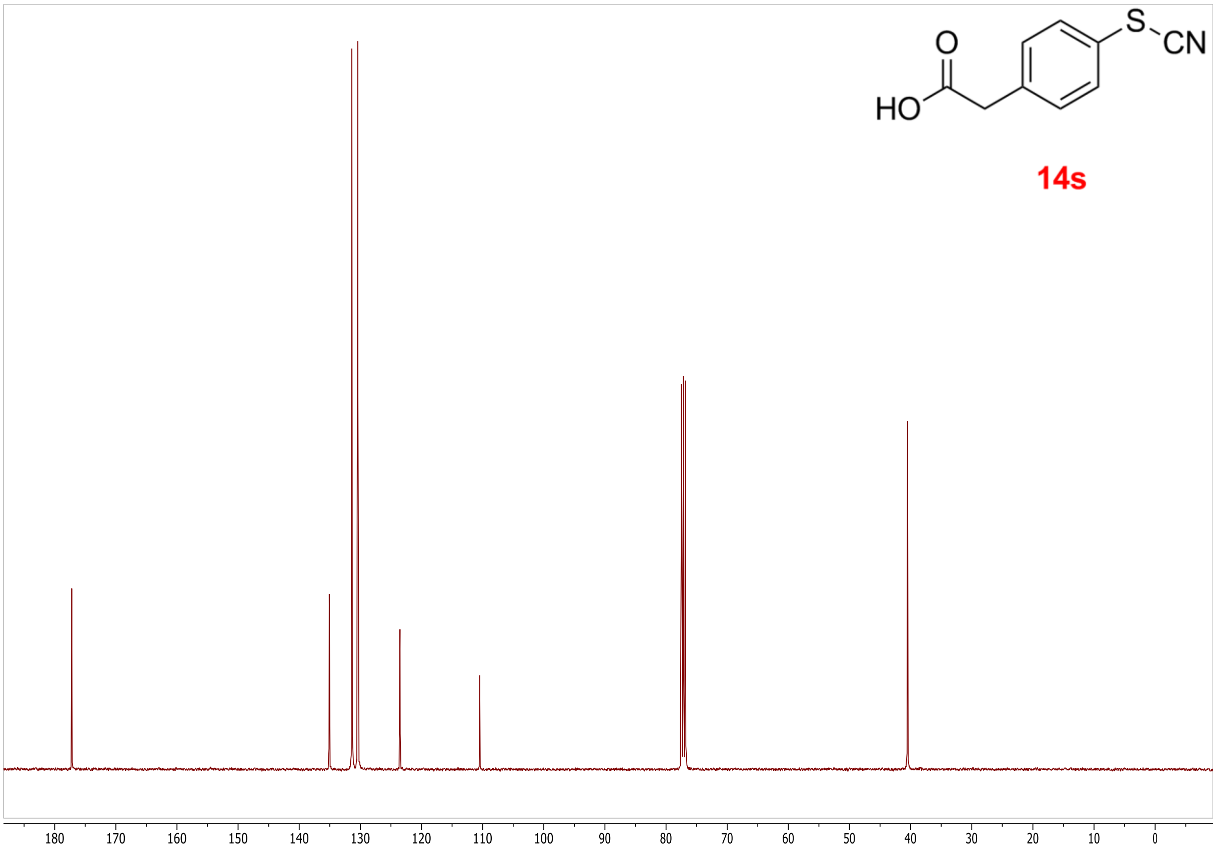
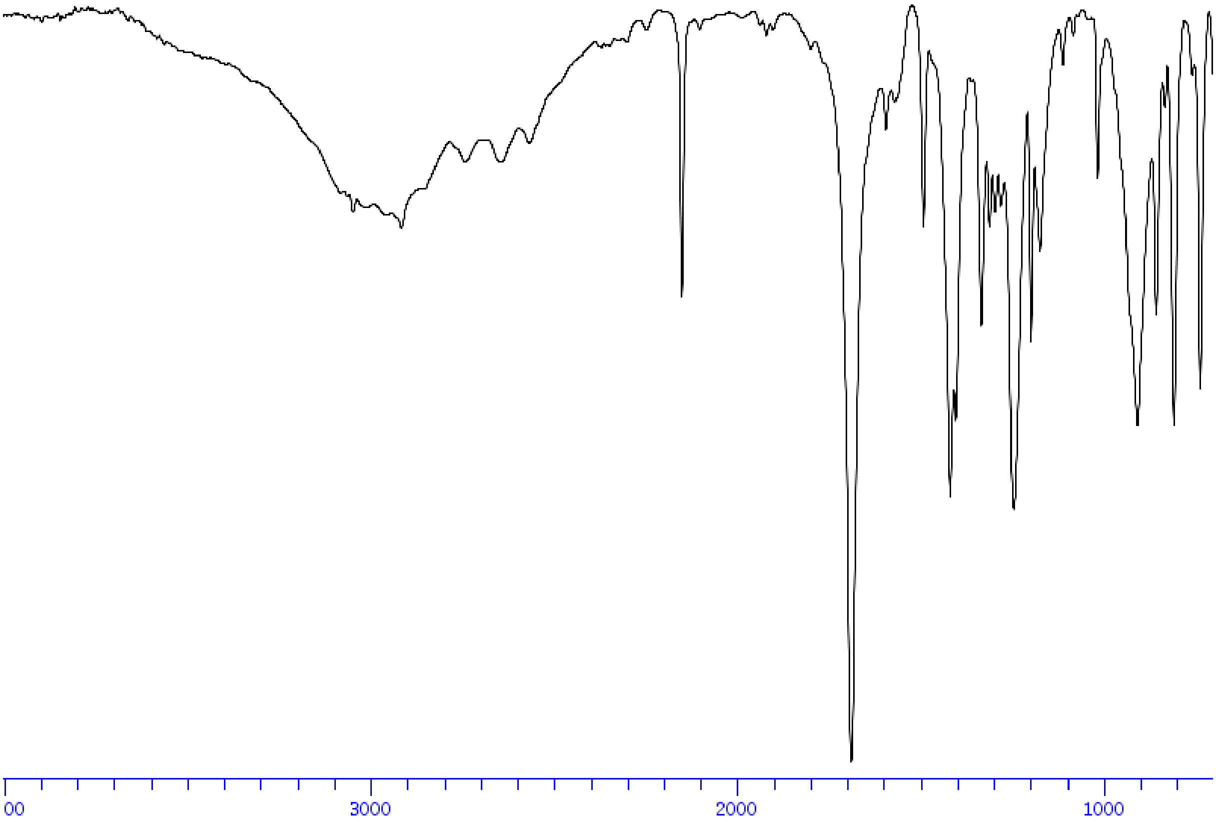
2-(4-Thiocyanatophenyl)acetic acid (14s)



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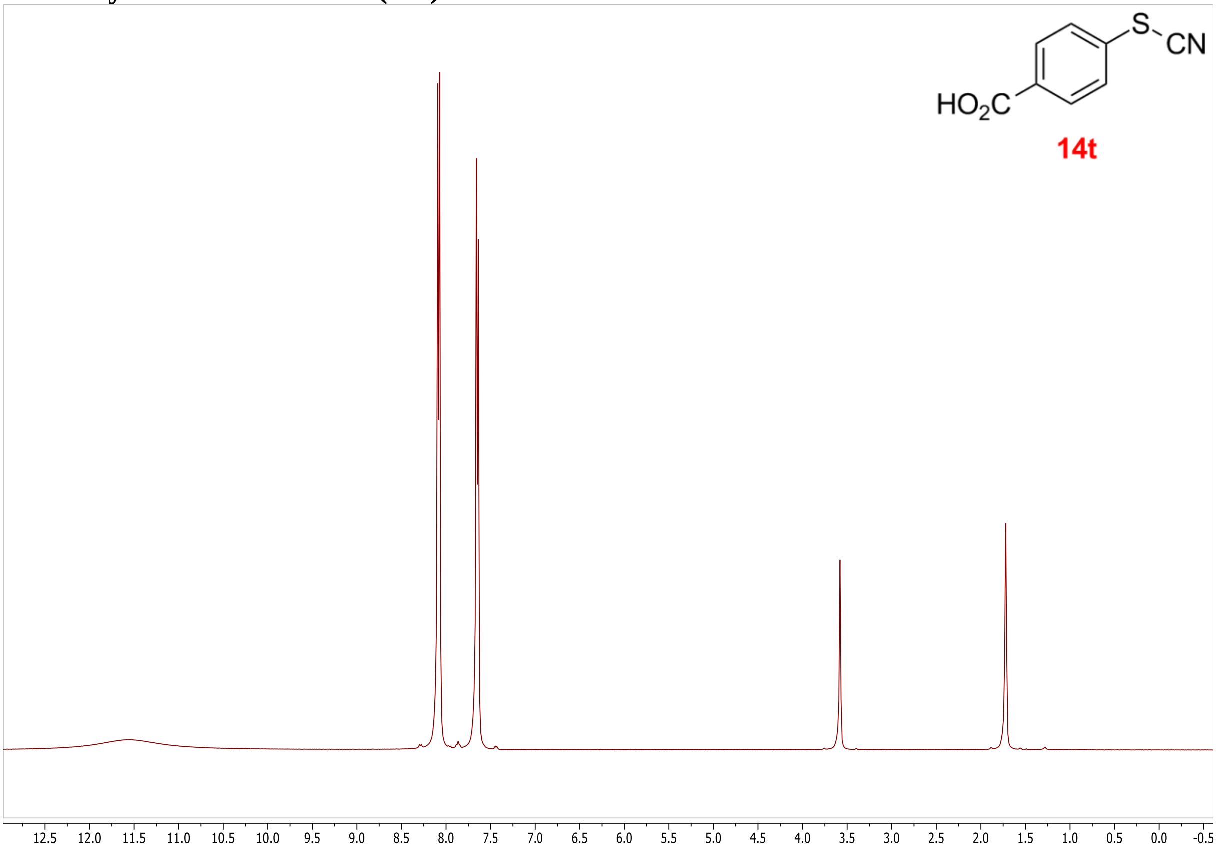
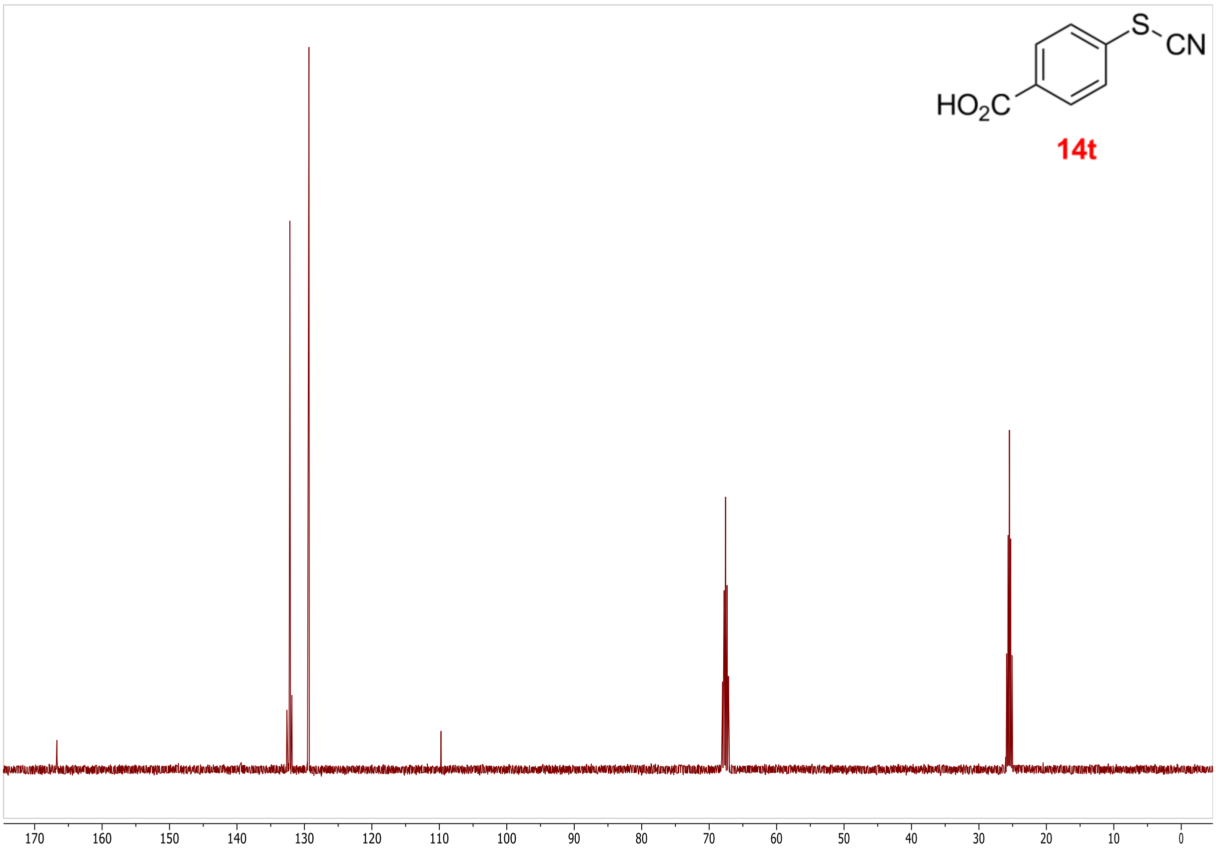
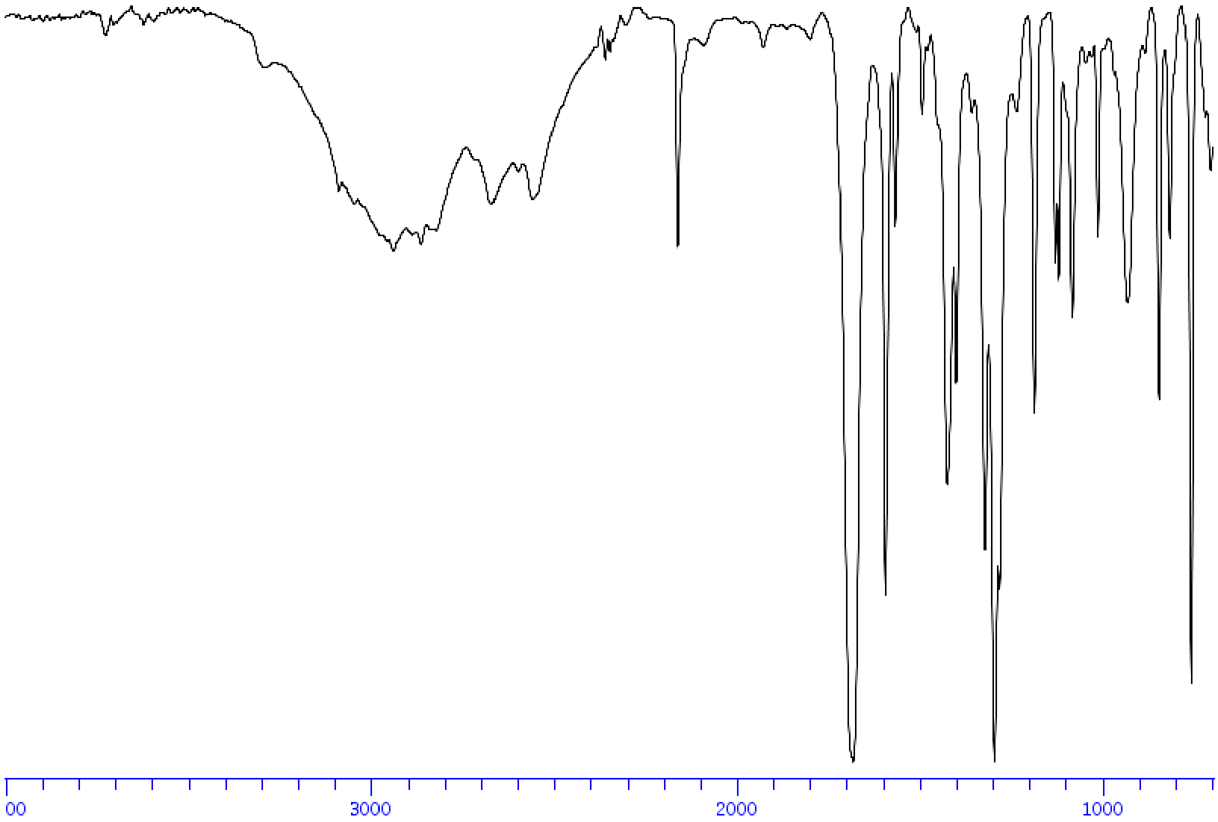
4-Thiocyanatobenzoic acid (14t)



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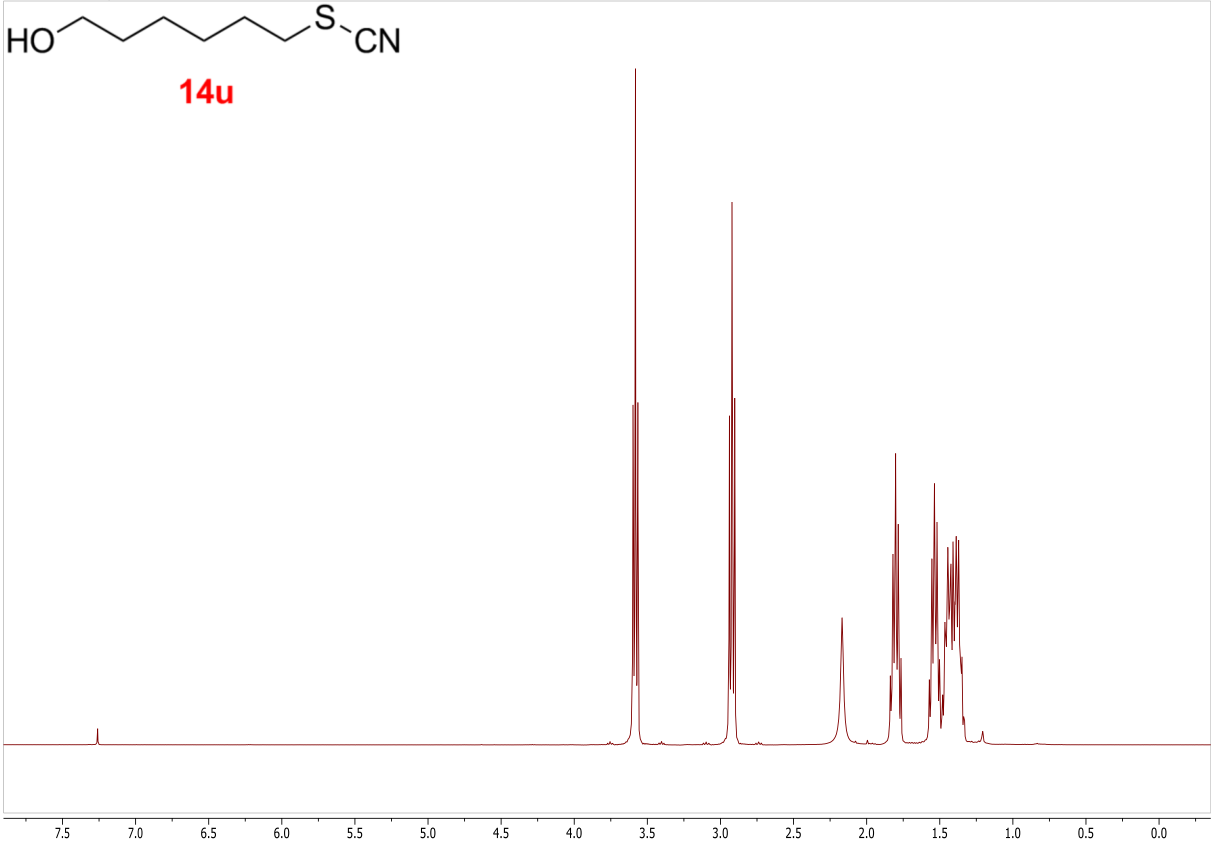
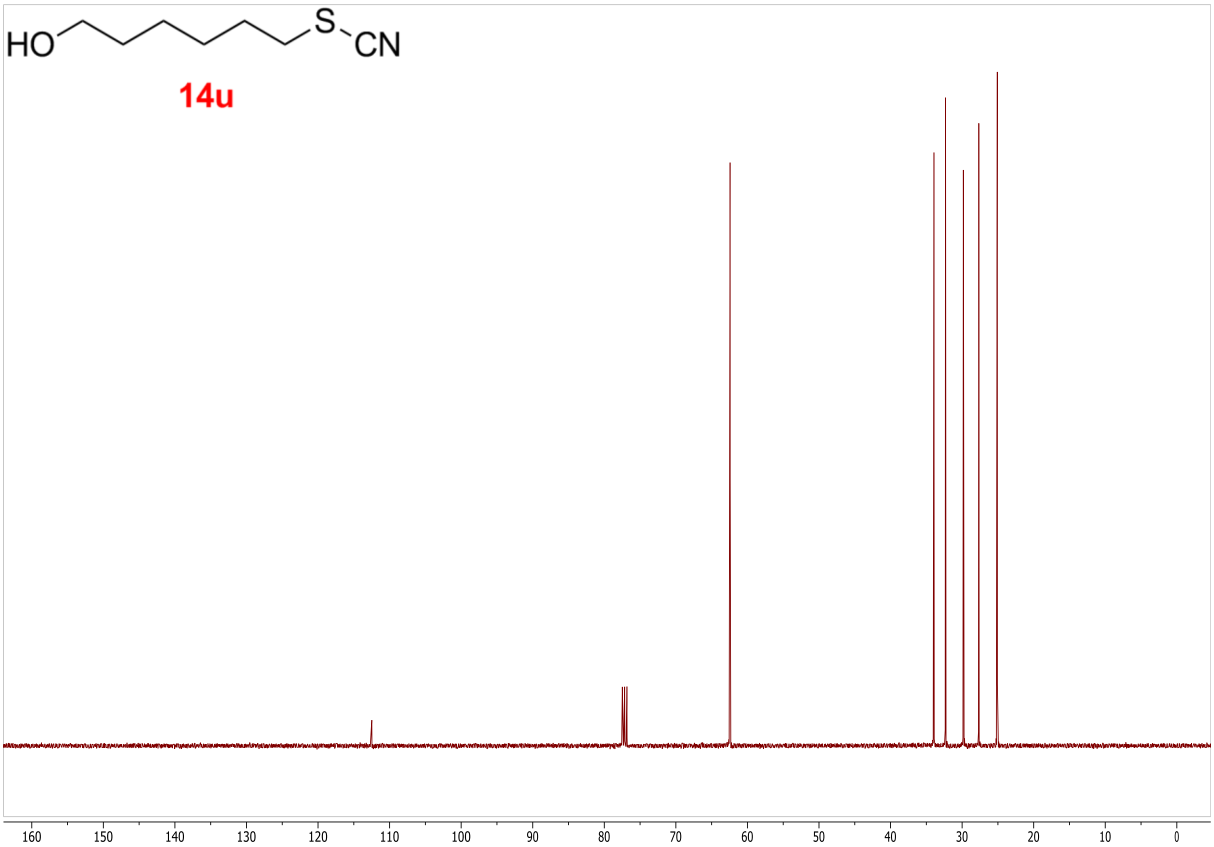
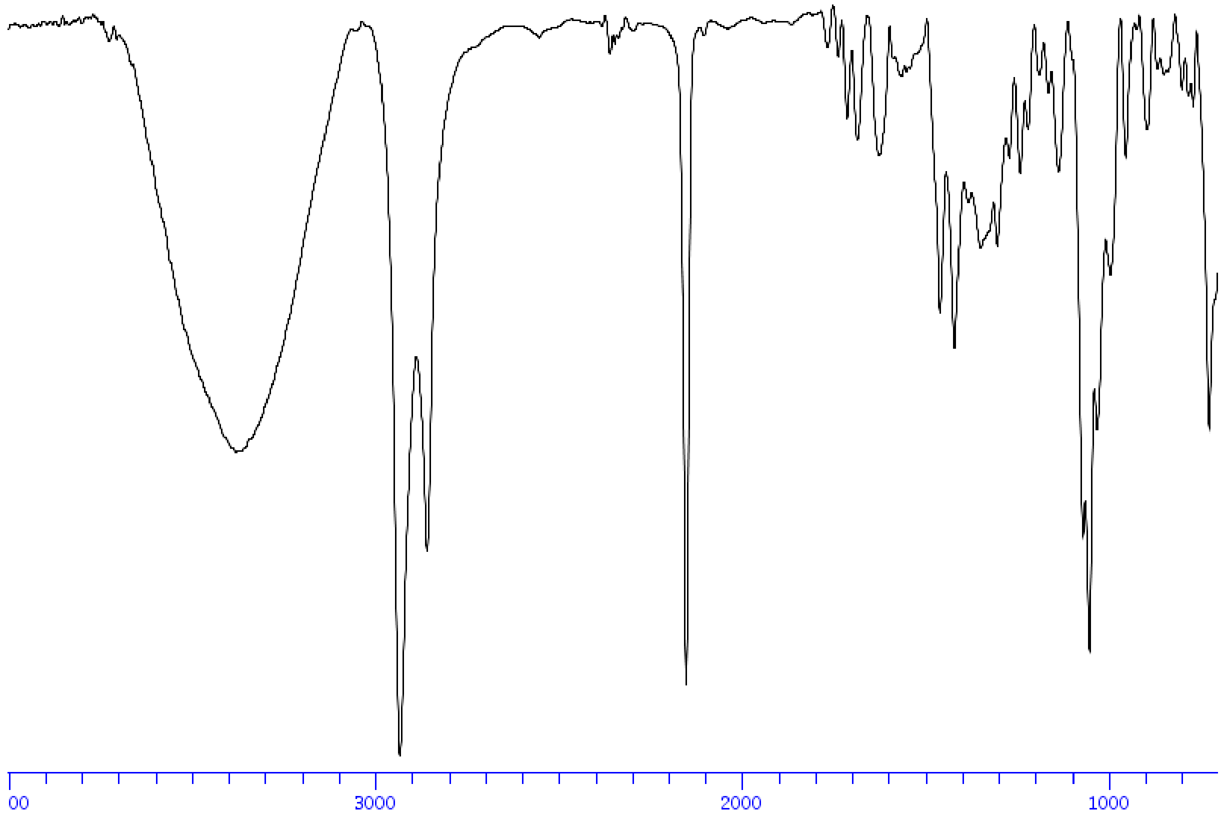
6-Thiocyanatohexan-1-ol (14u)



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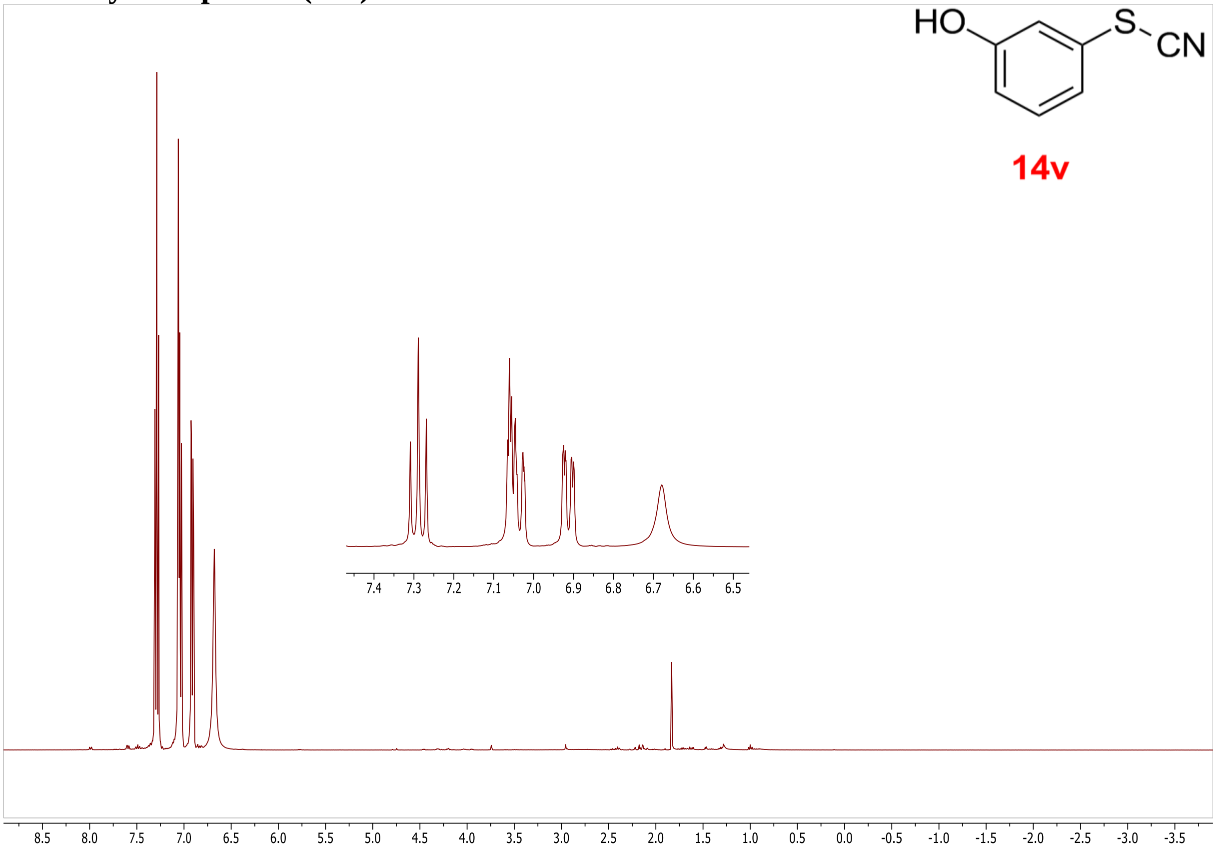
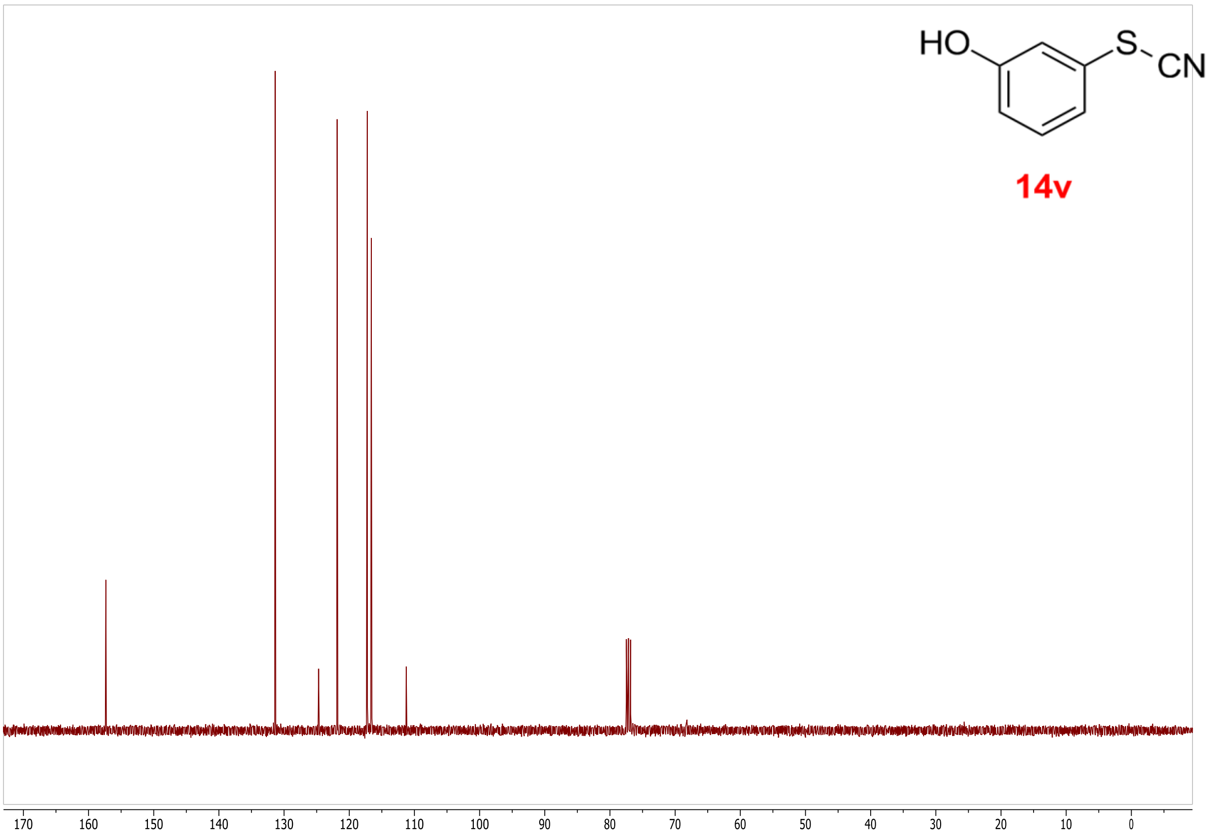
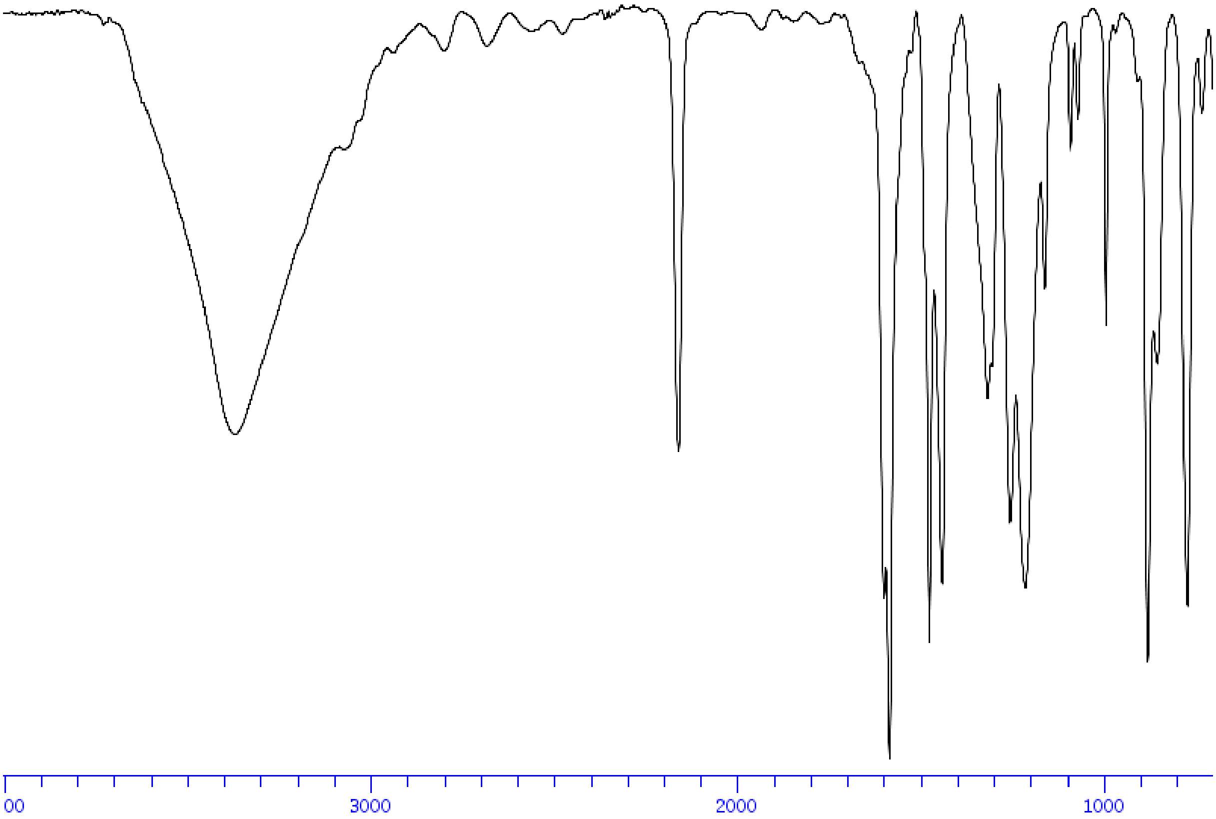
3-Thiocyanatophenol (14v)



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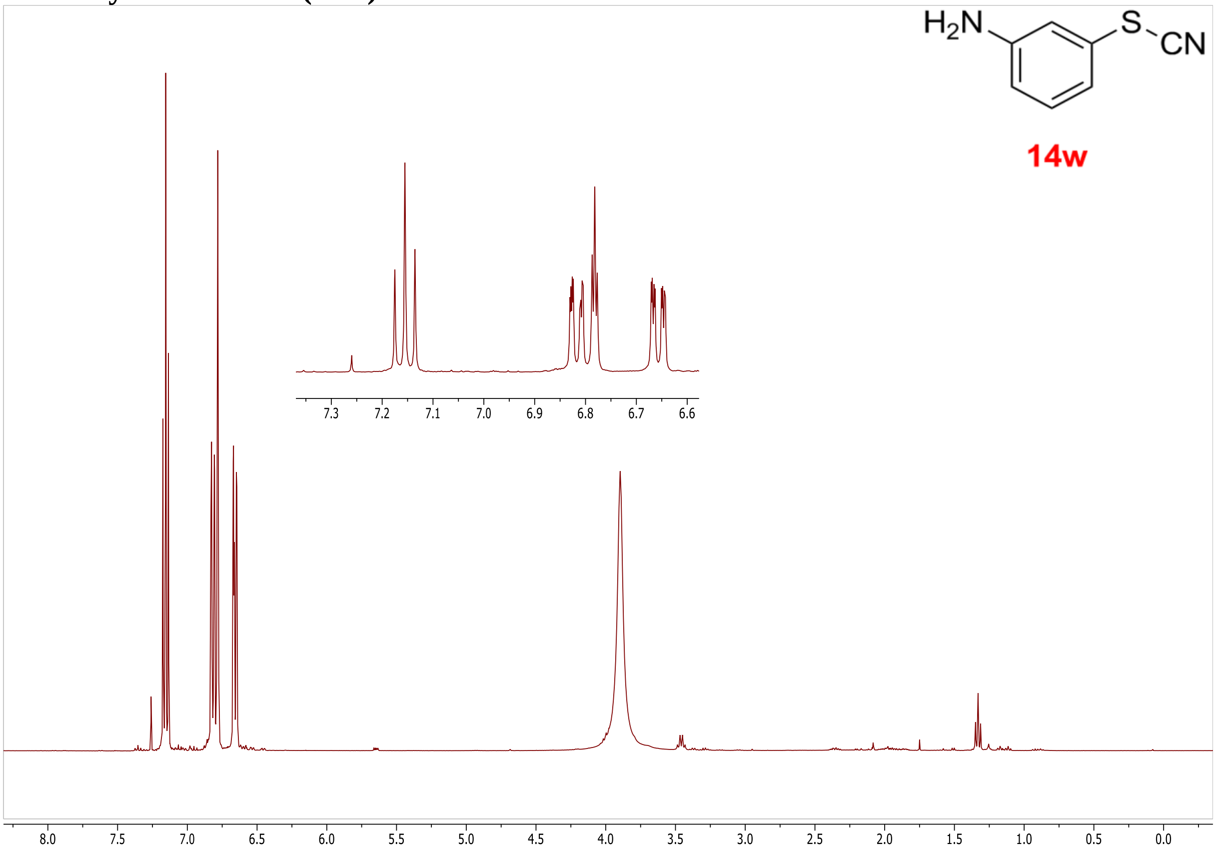
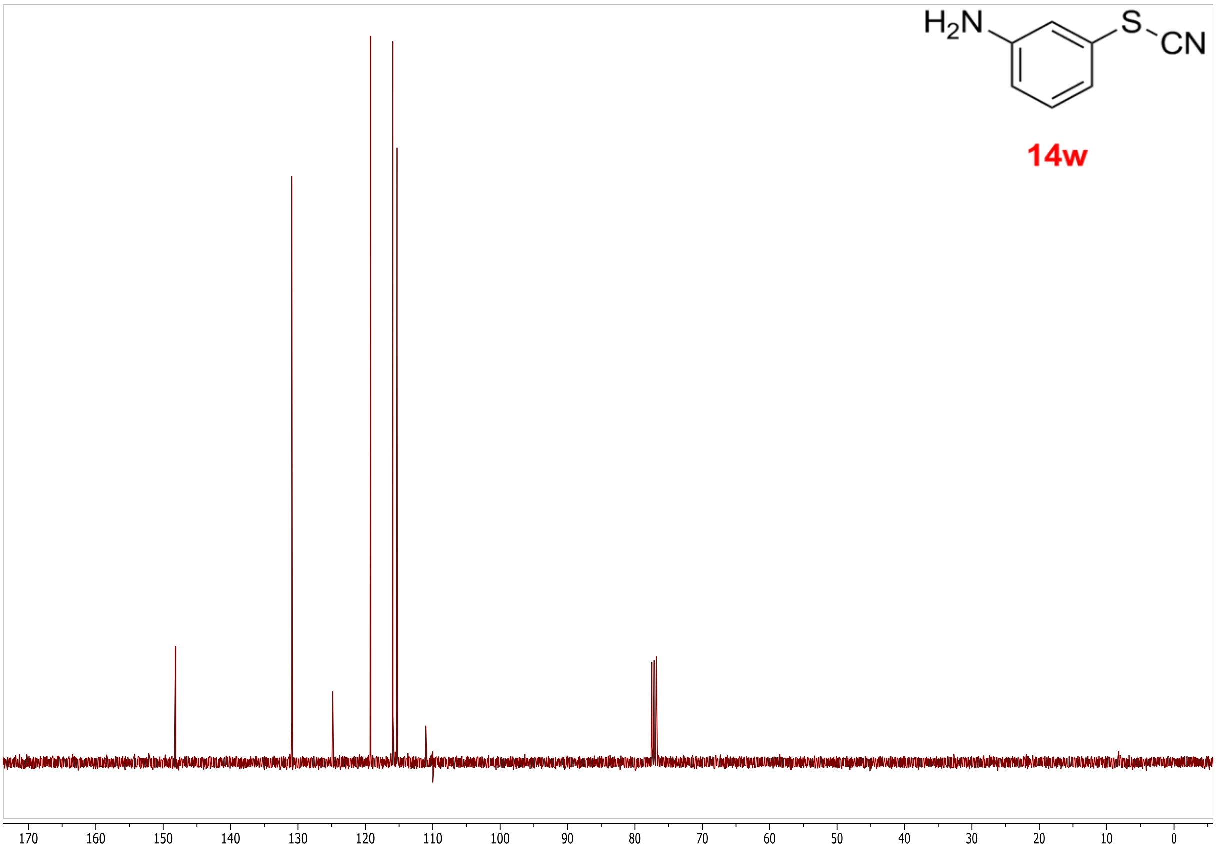
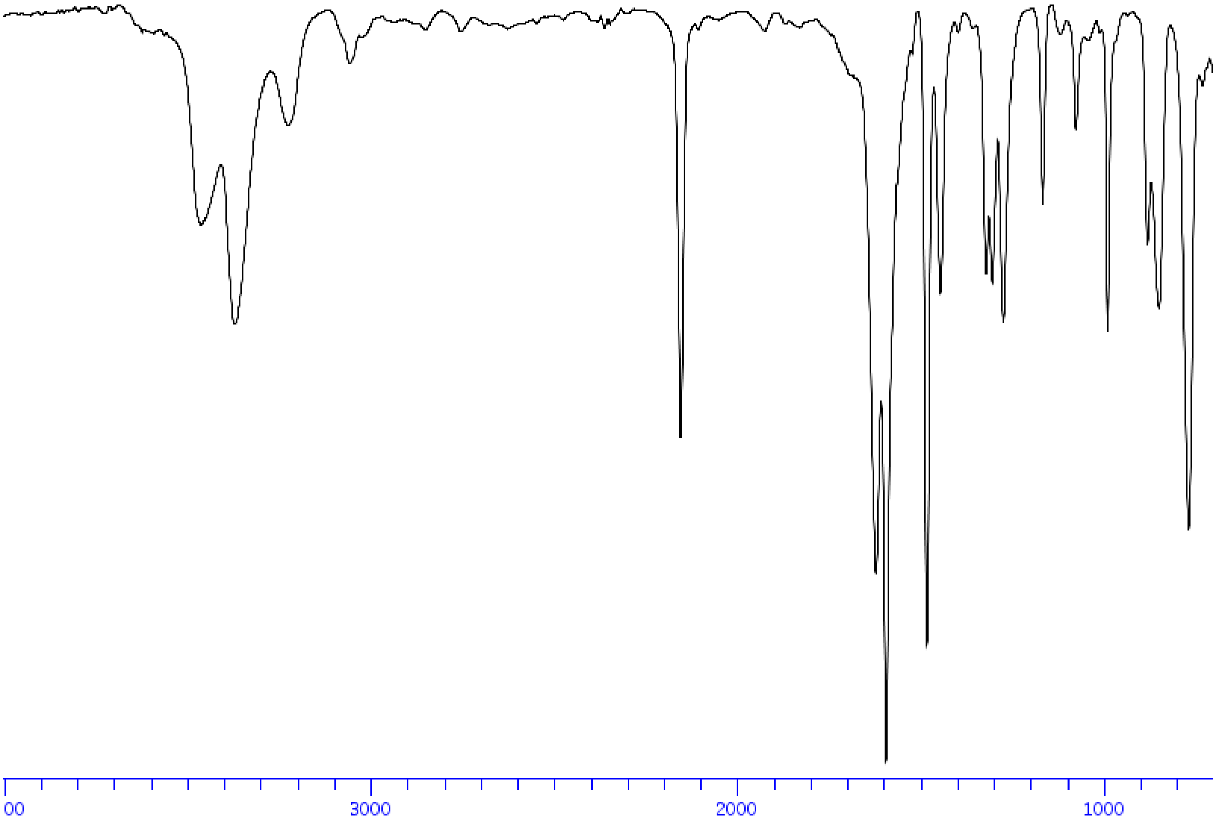
3-Thiocyanatoaniline (14w)



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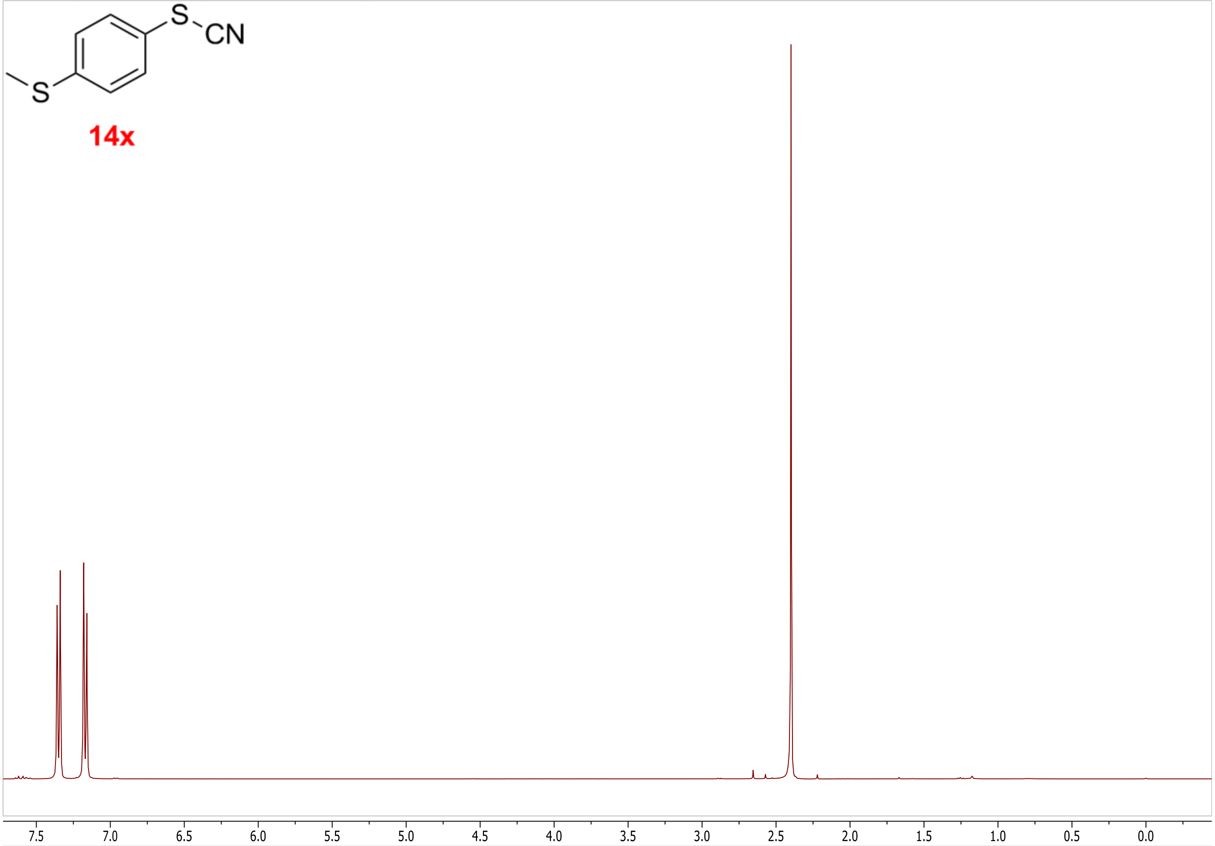
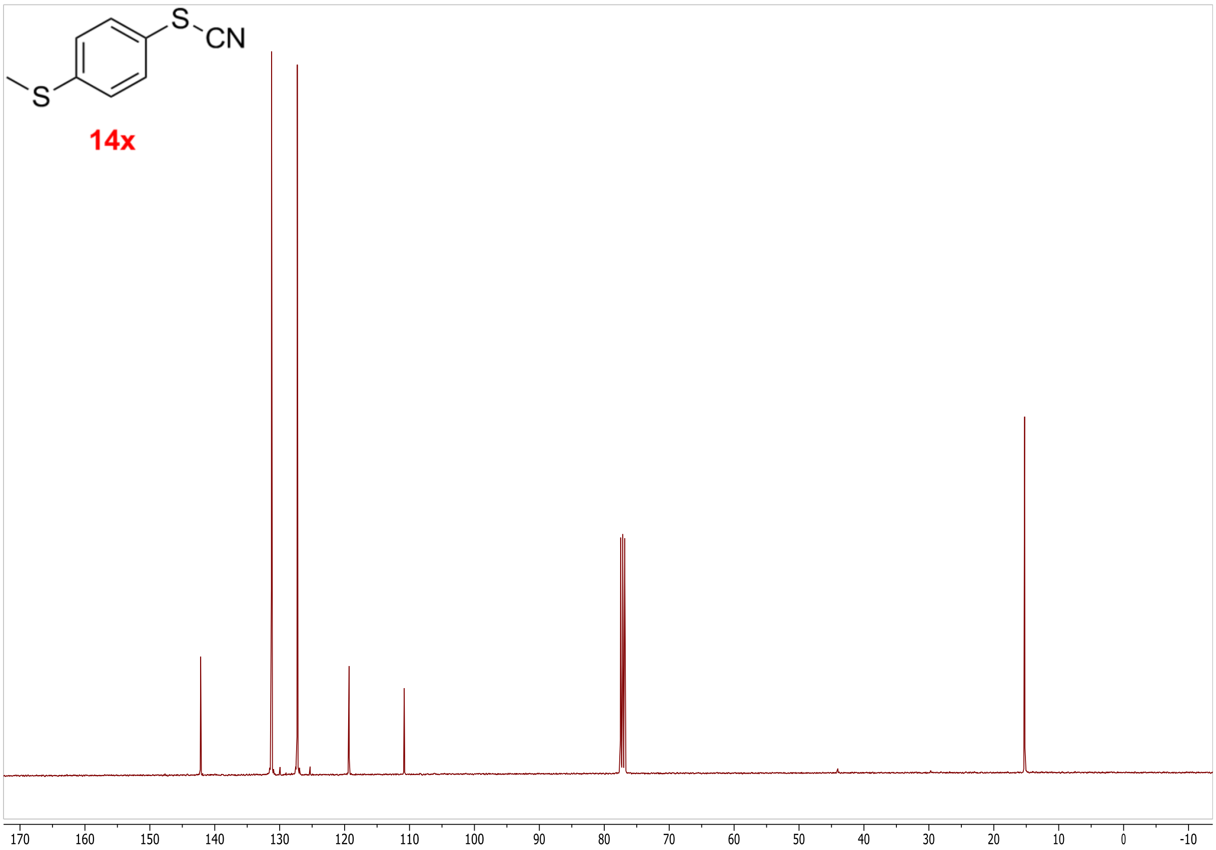
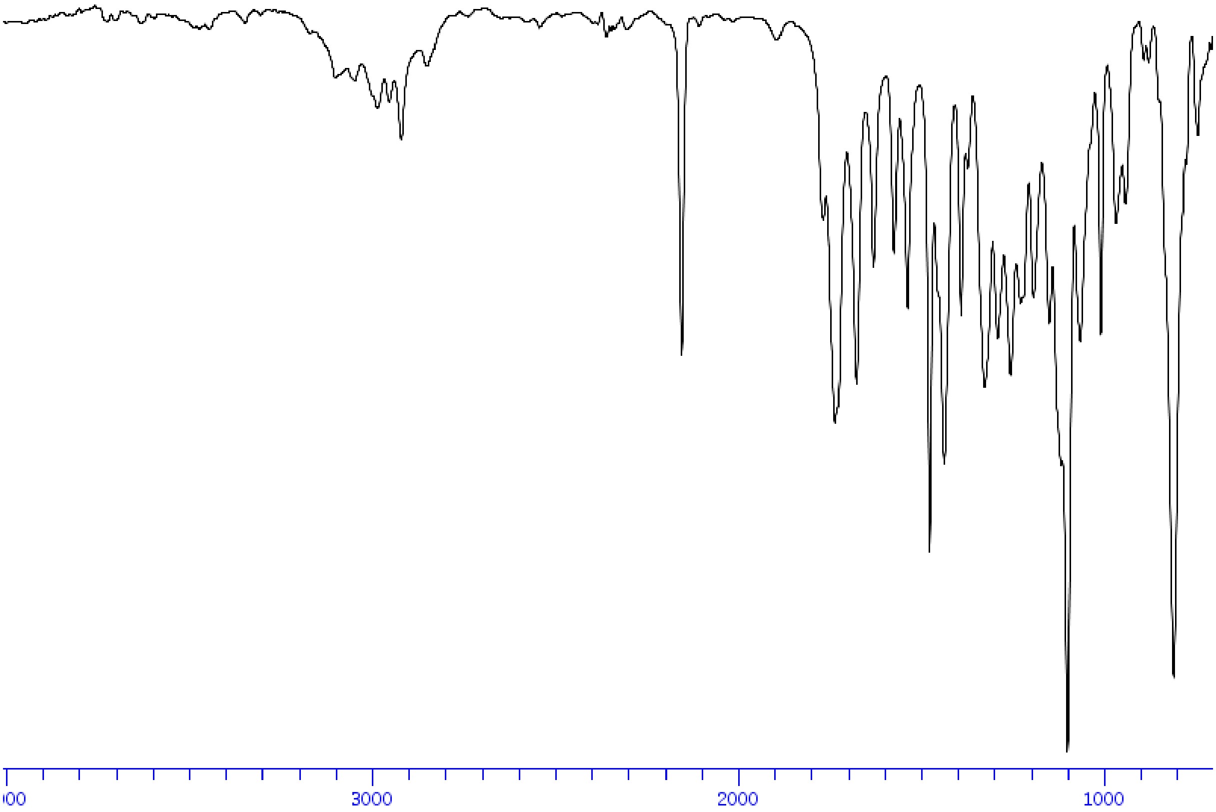
Methyl(4-thiocyanatophenyl)sulfane (14x)



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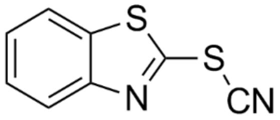
2-thiocyanatobenzo[d]thiazole (14y)



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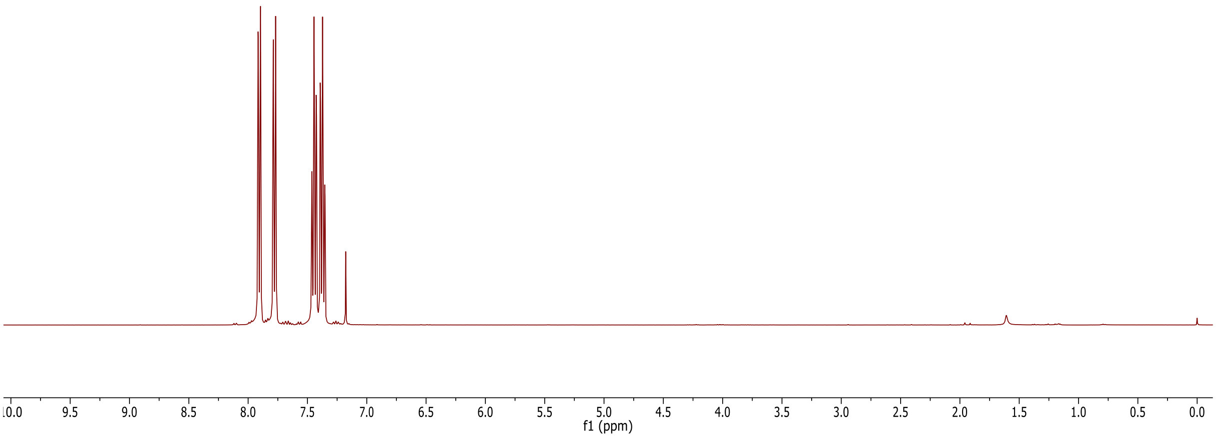

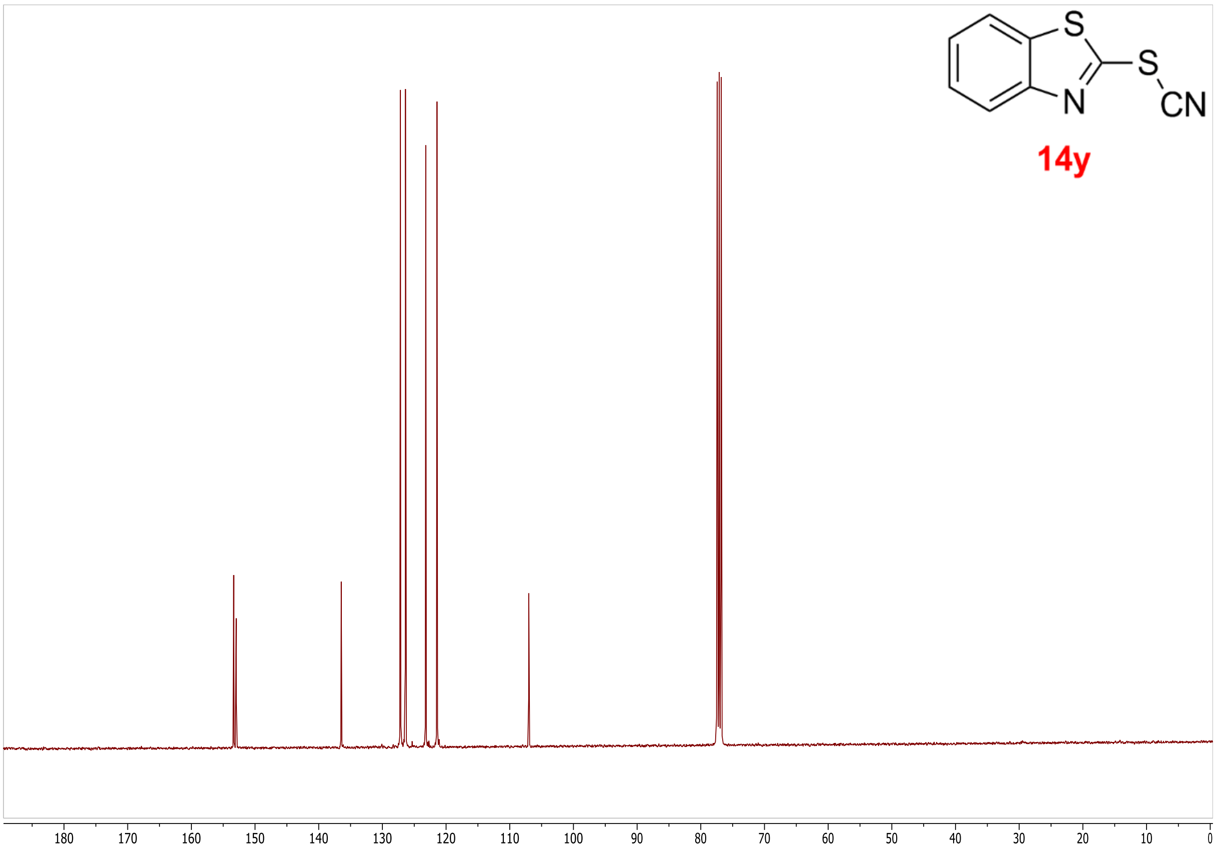

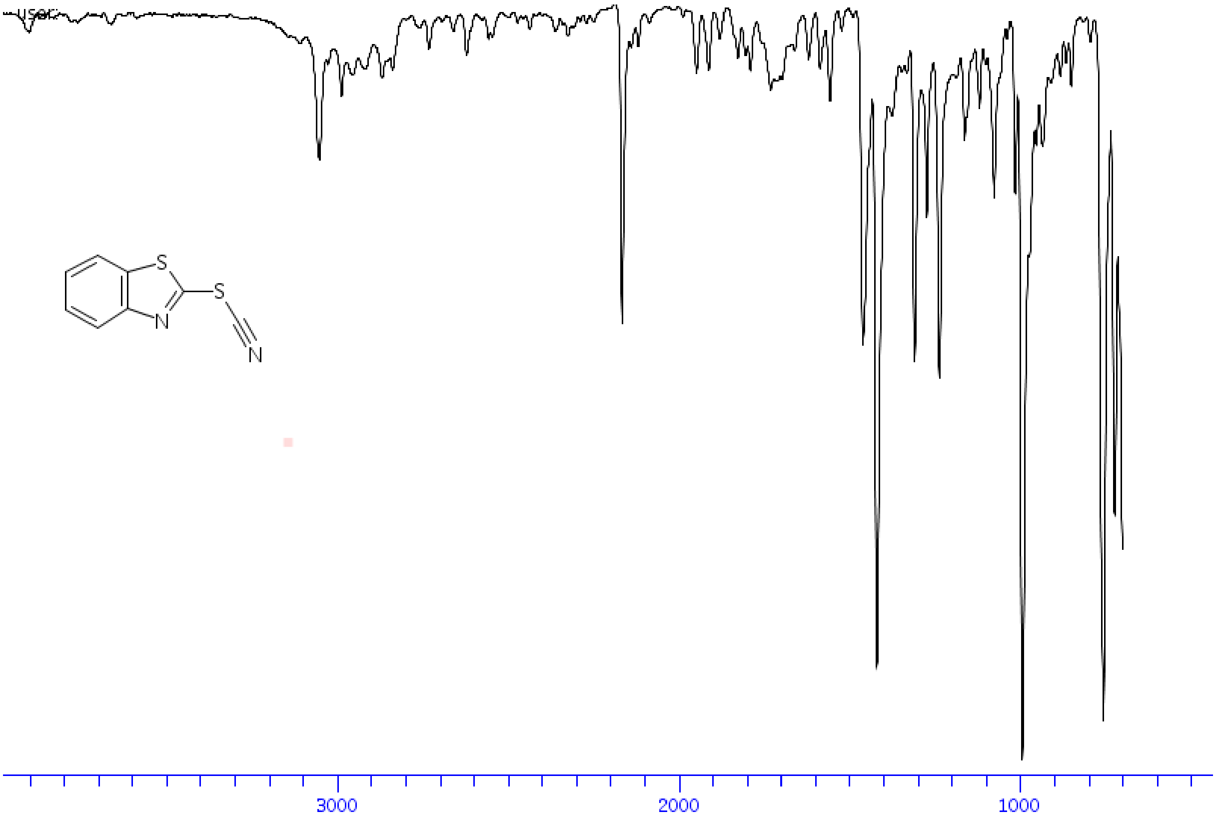
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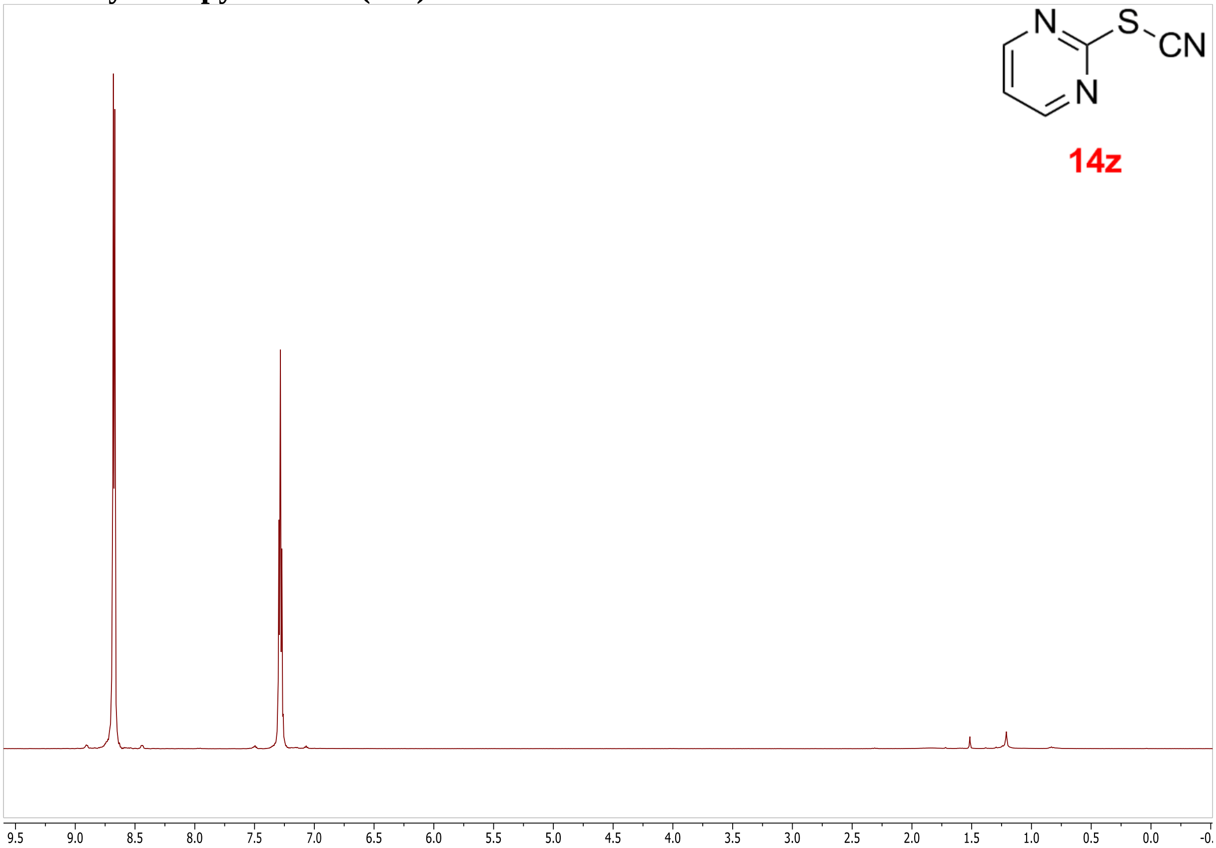
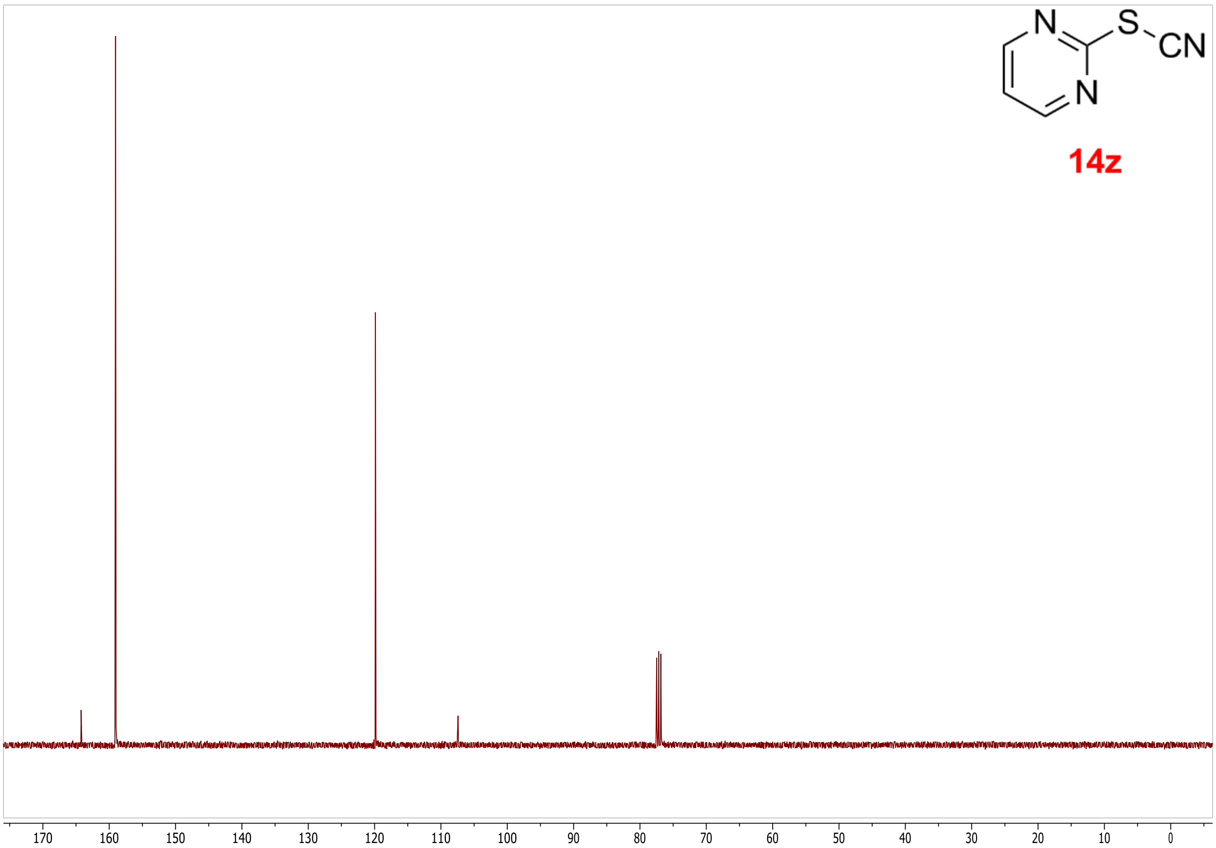
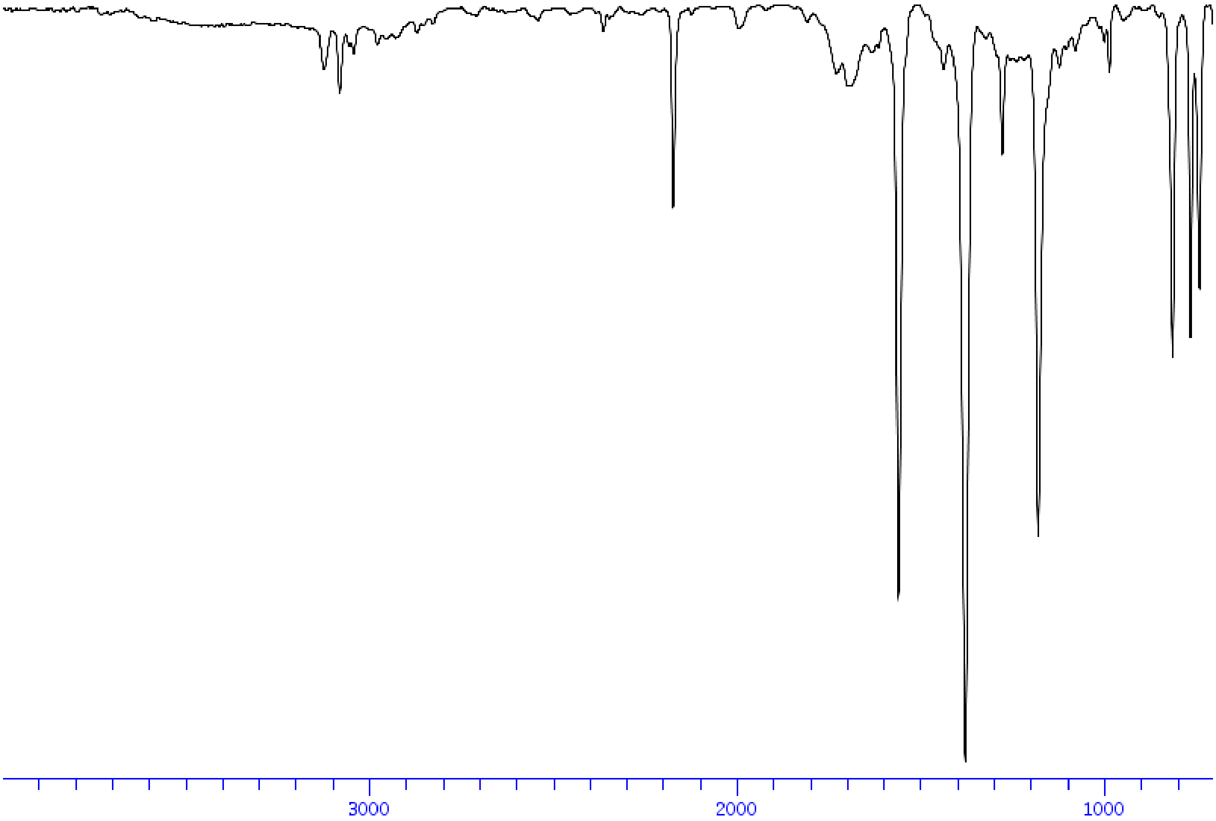
2-Thiocyanatopyrimidine (14z)



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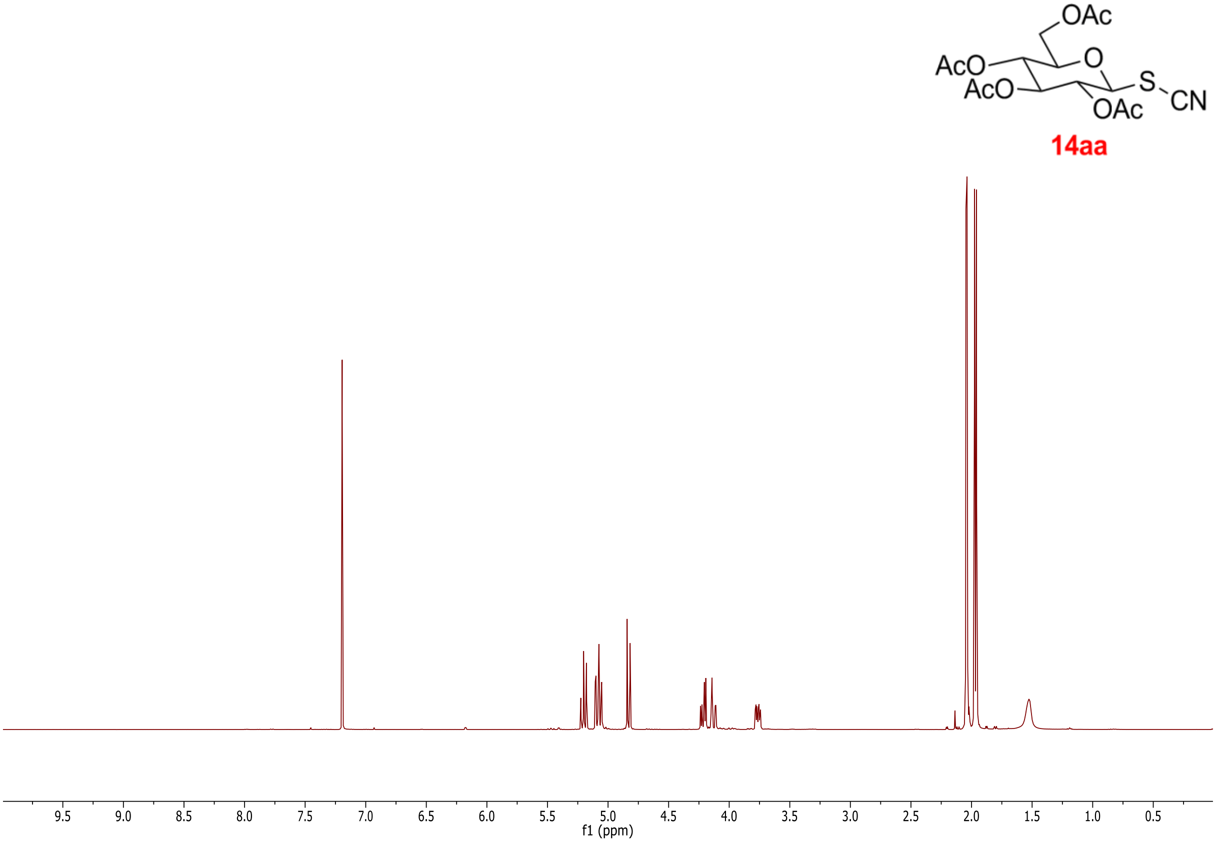
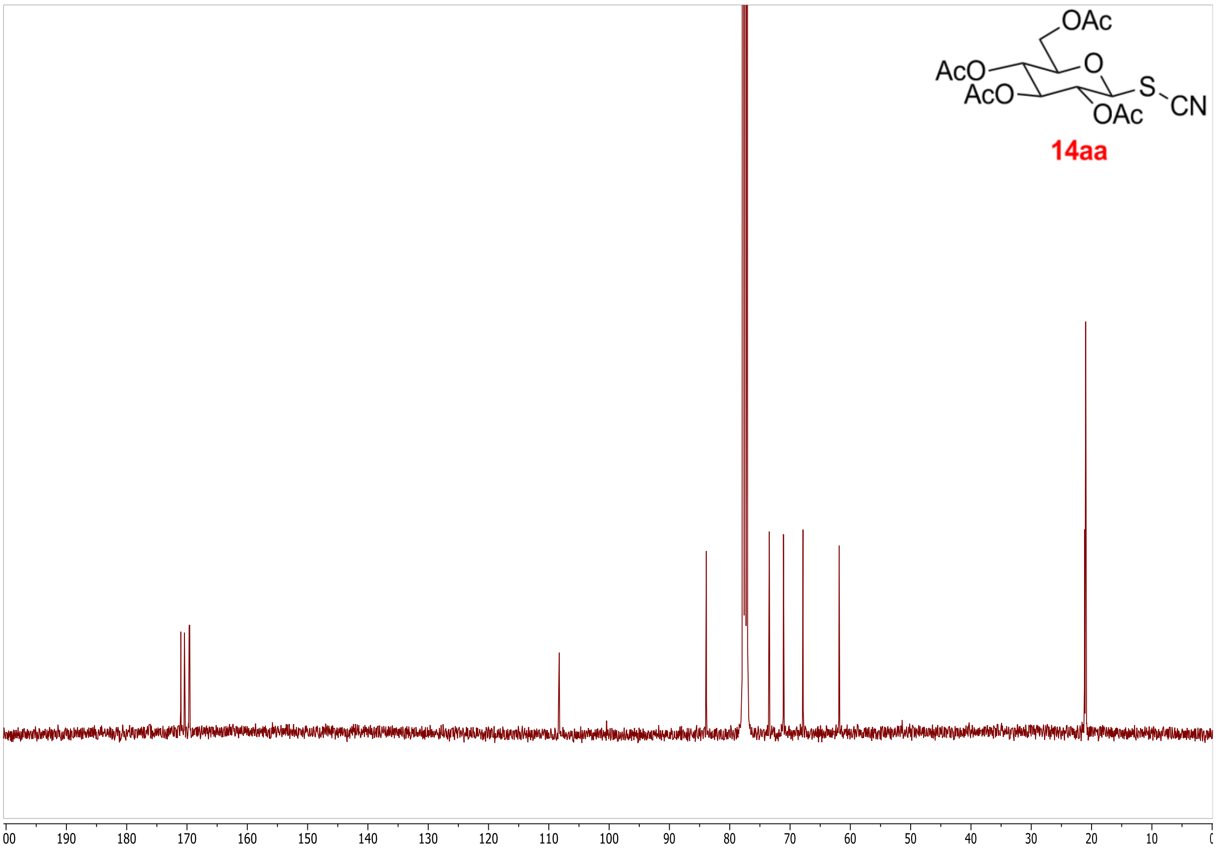
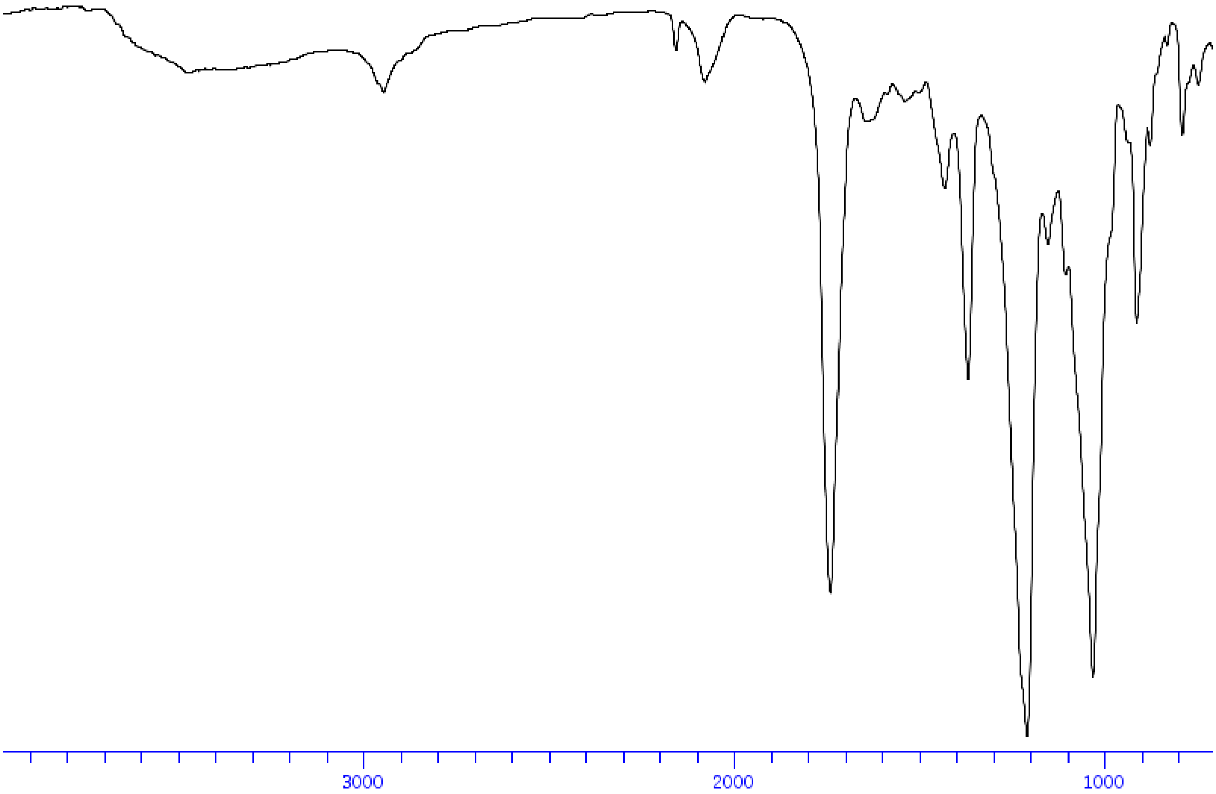
β-thiocyanato-tetraacetyl-glucopyranoside (14aa)



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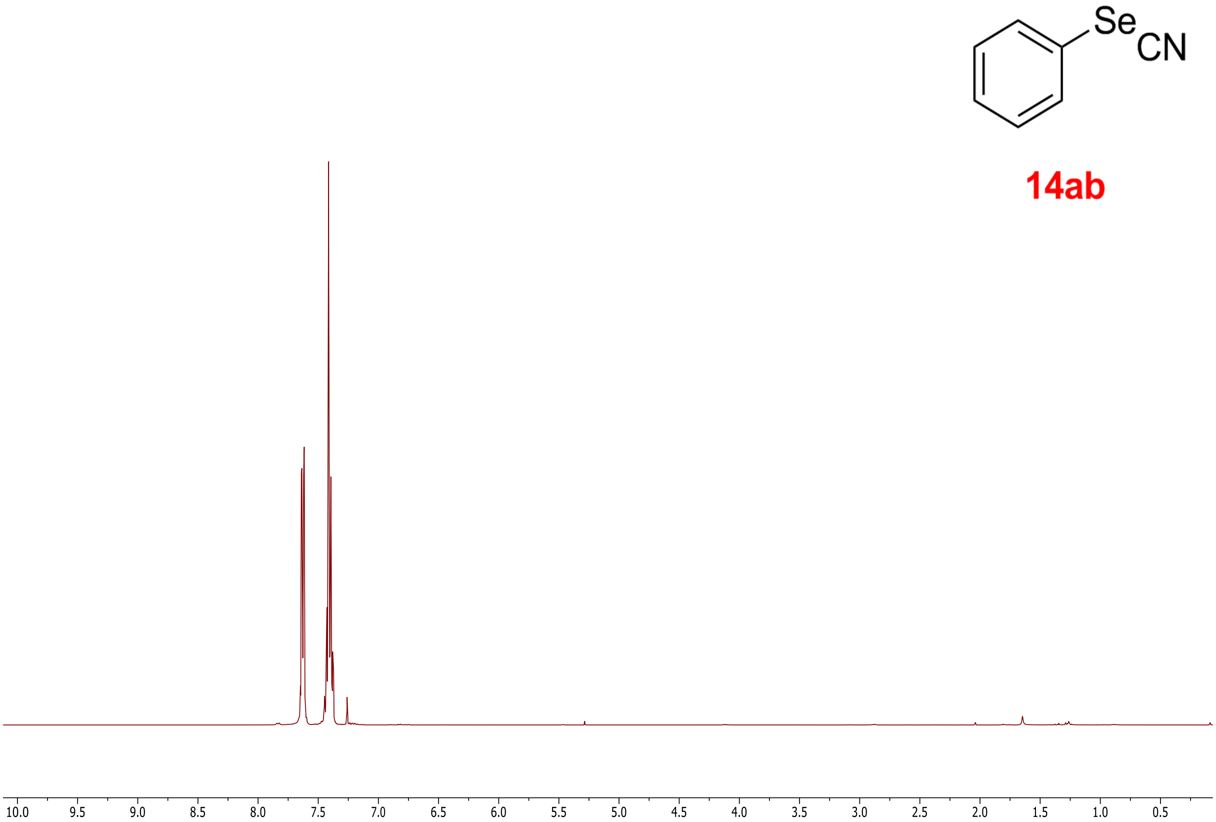
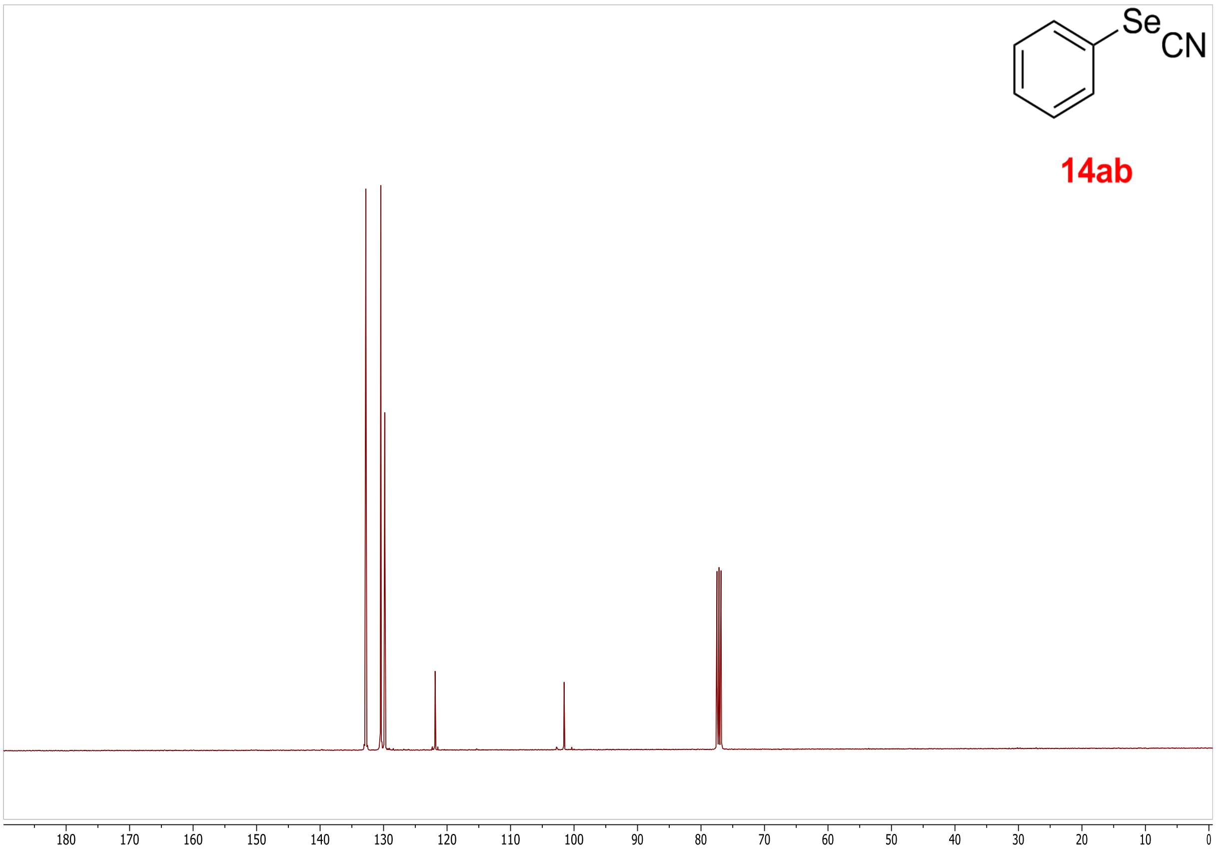
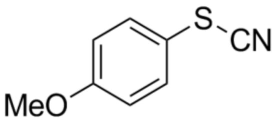
Selenocyanatobenzene (14ab)





1-methoxy-4-thiocyanatobenzene (14ac)



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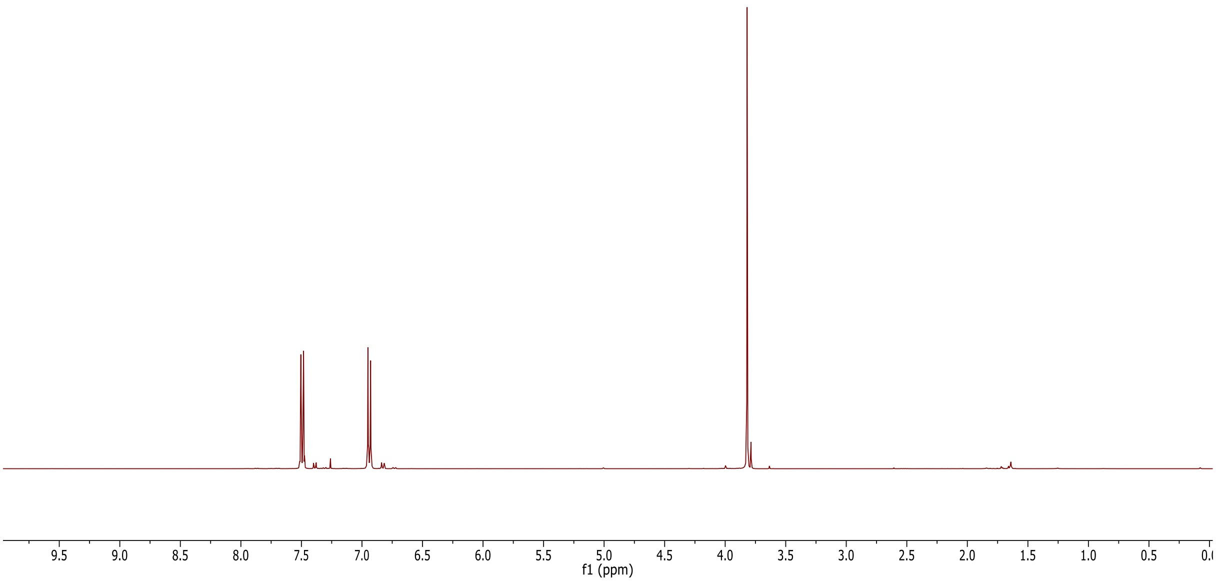

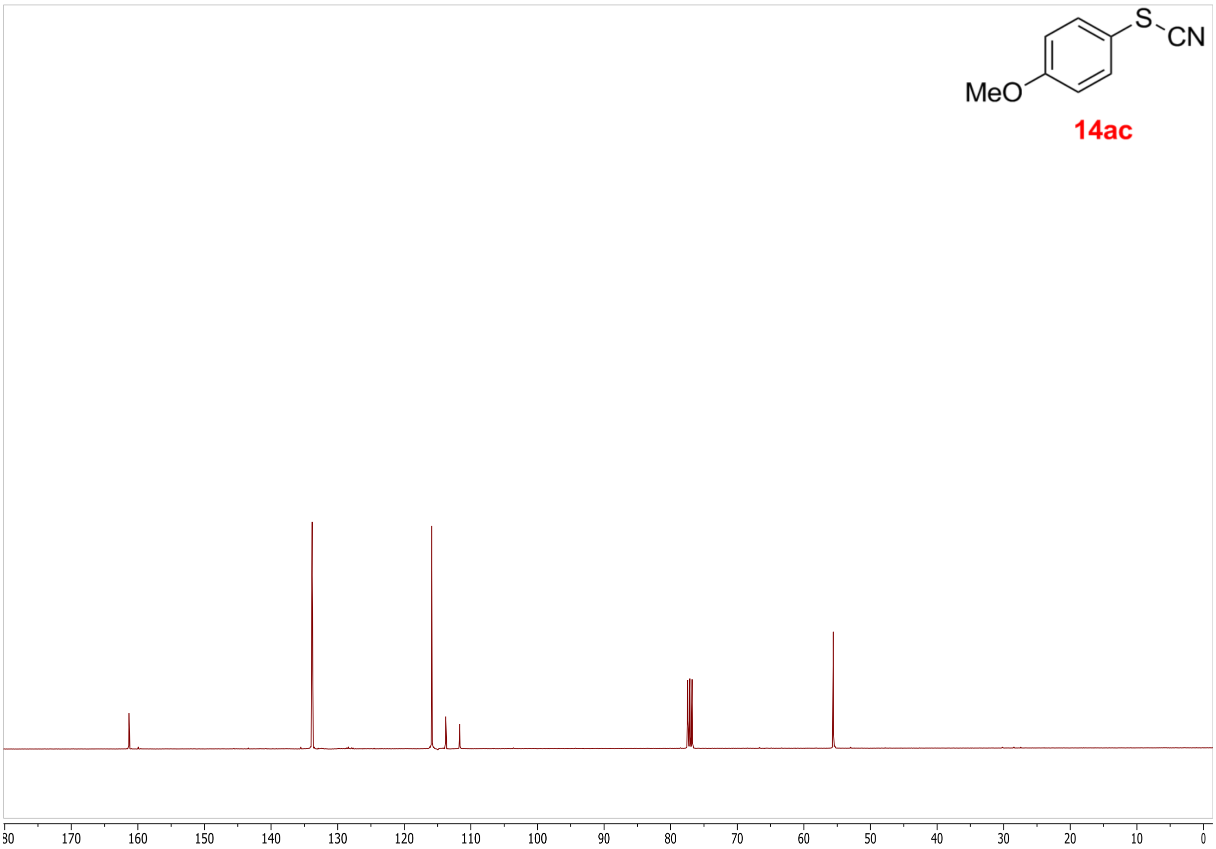

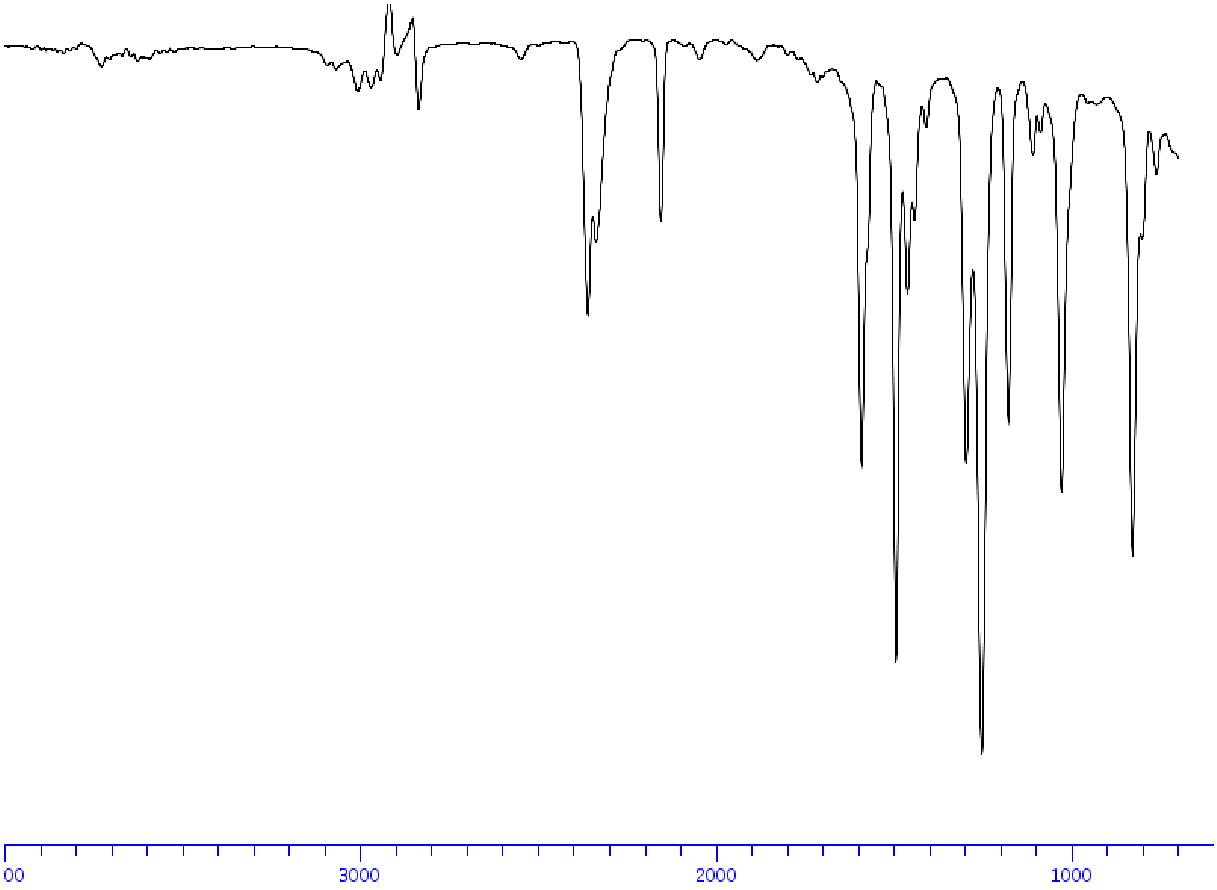
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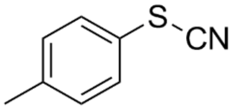
2000
1000

1-methyl-4-thiocyanatobenzene (14ad)



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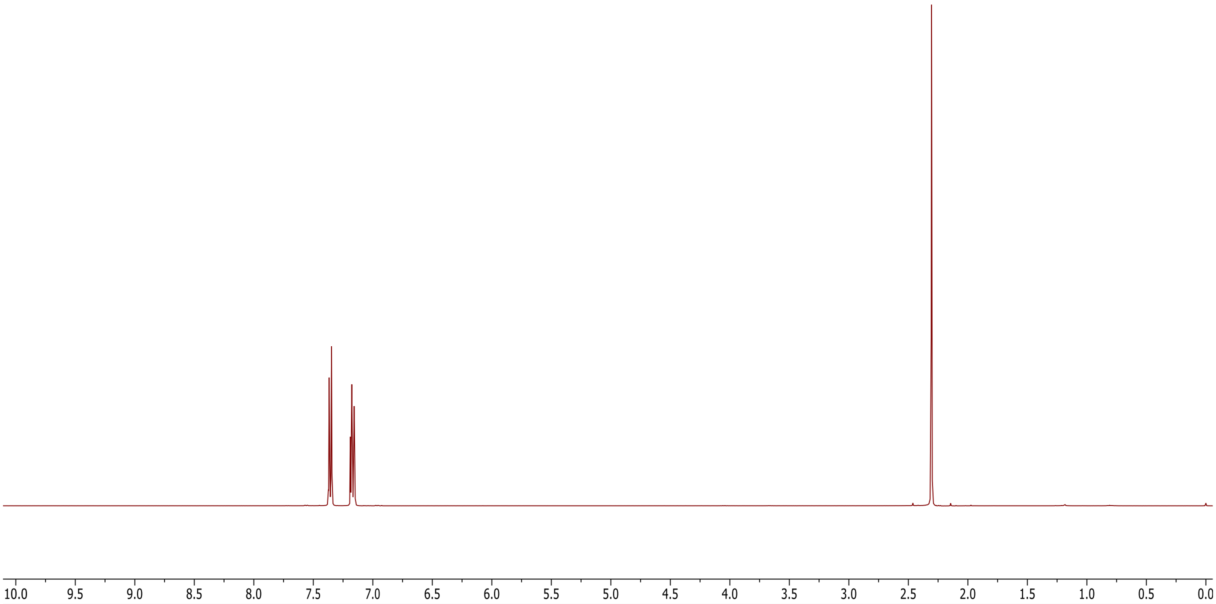

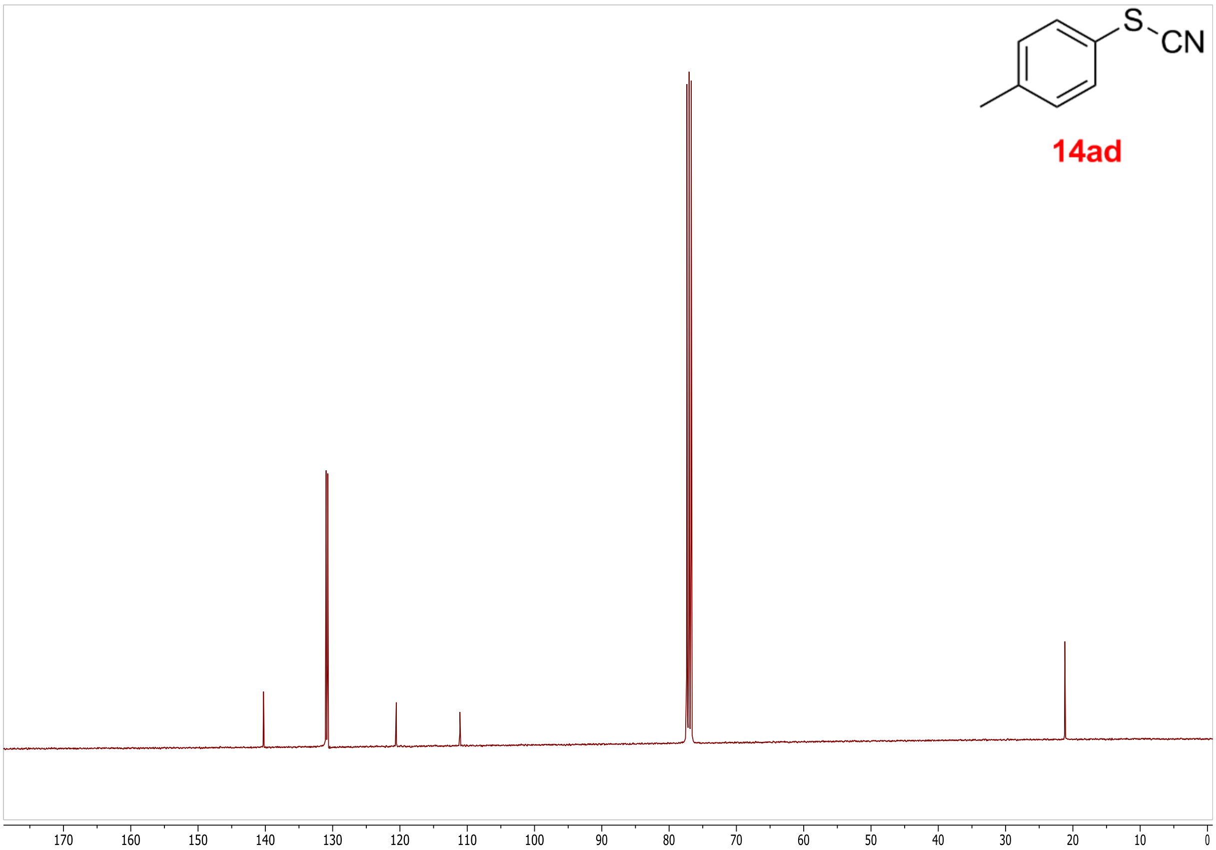

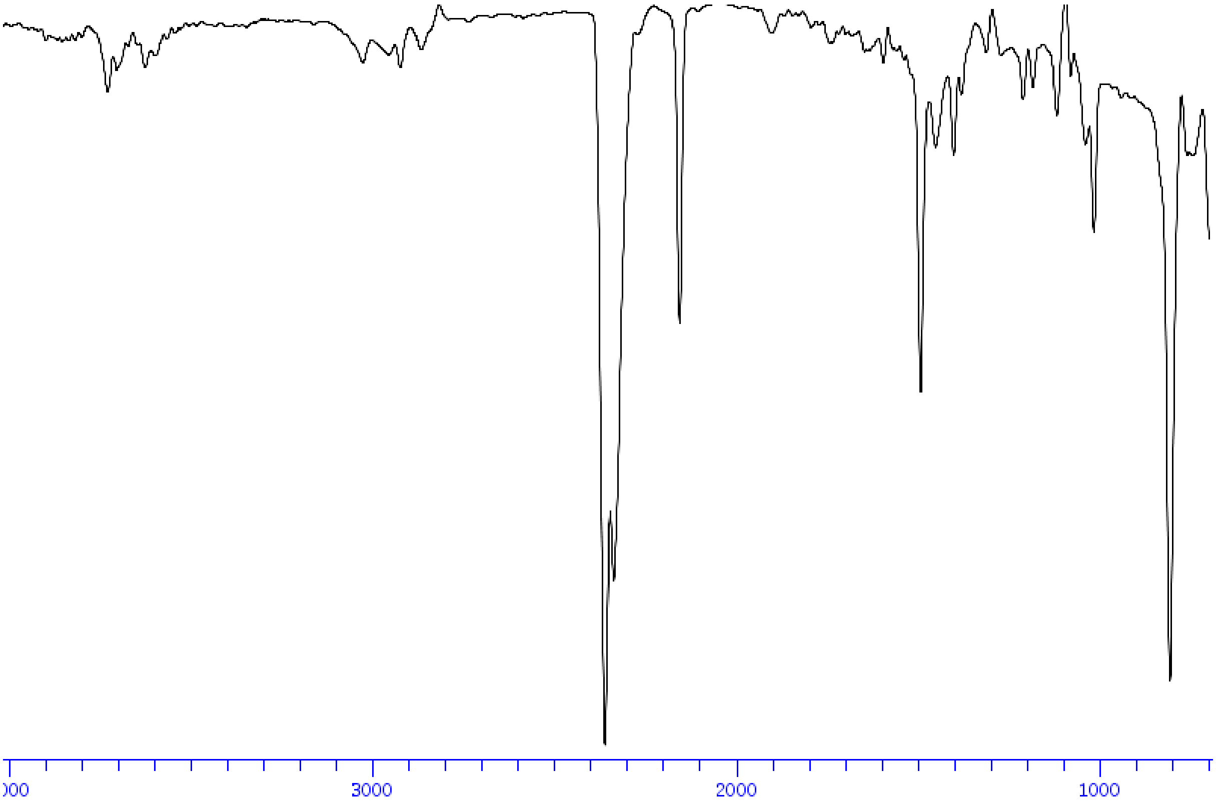
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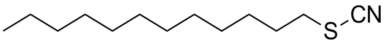
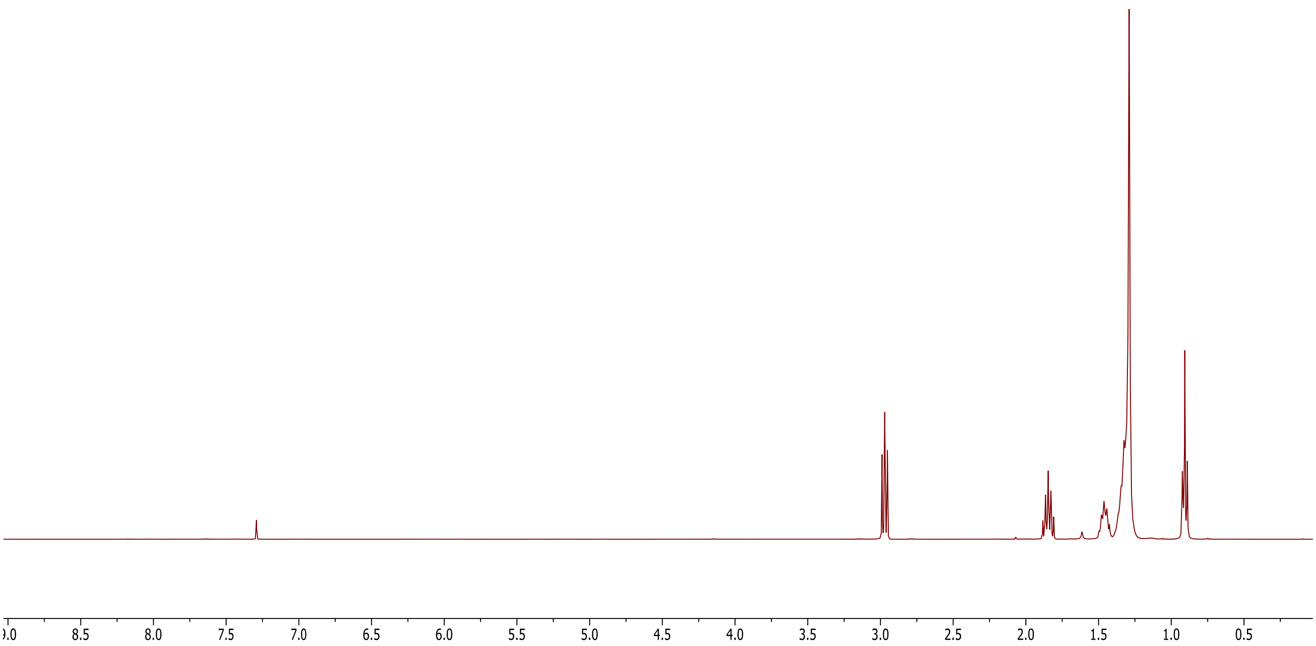
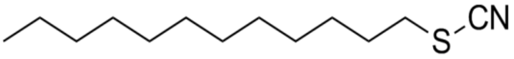
1-dodecylthiocyanate (14ae)

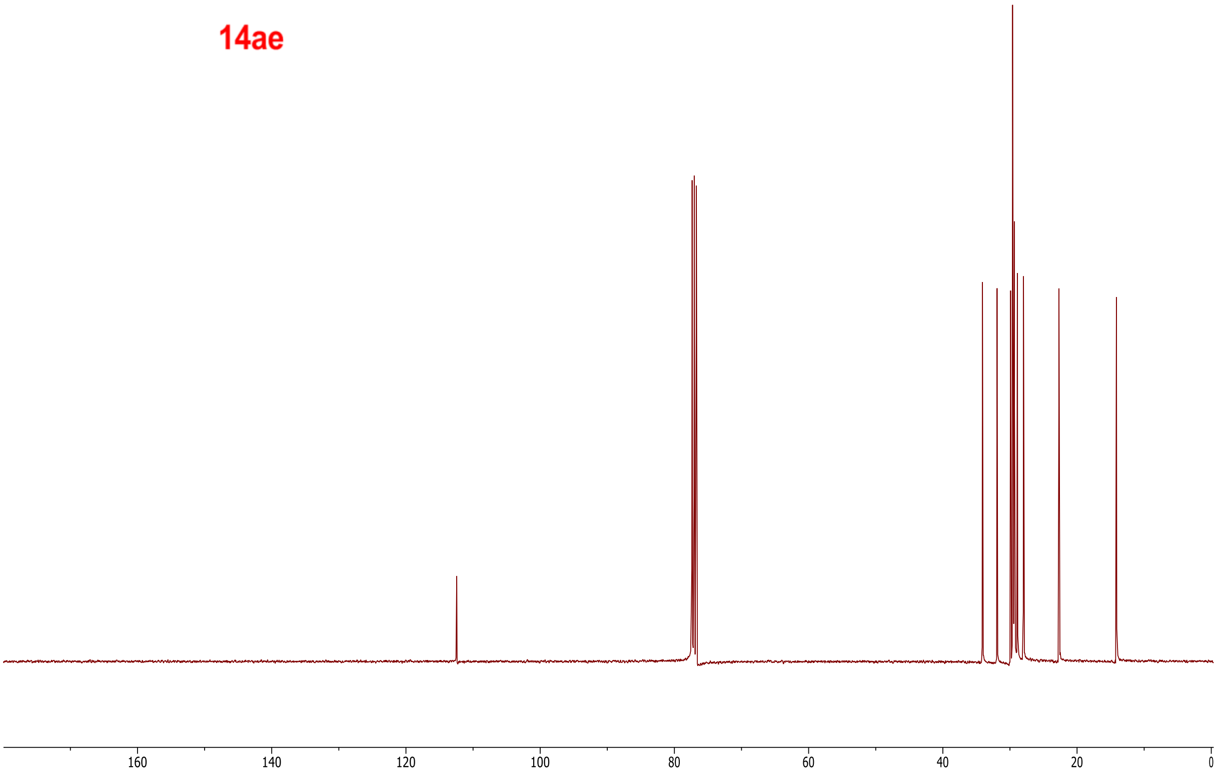


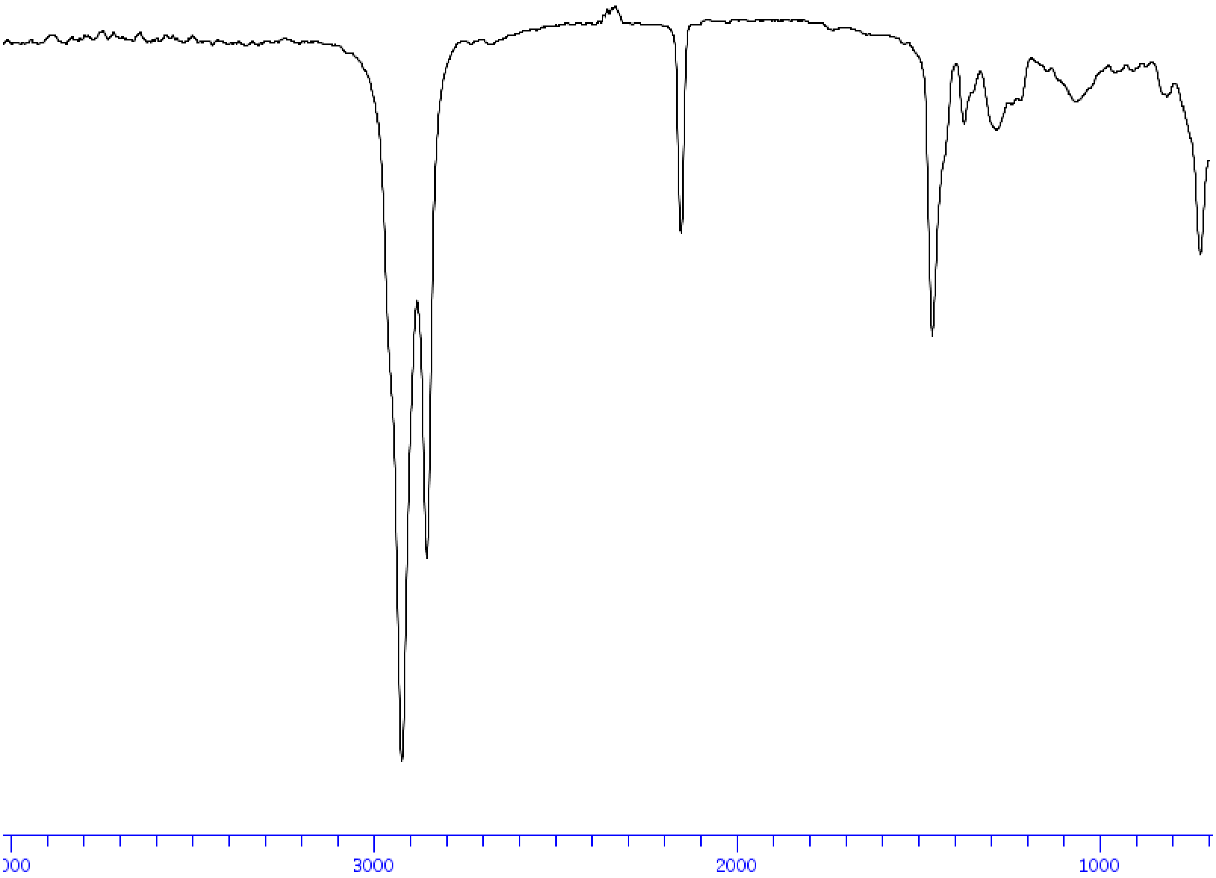
14ae





14ae





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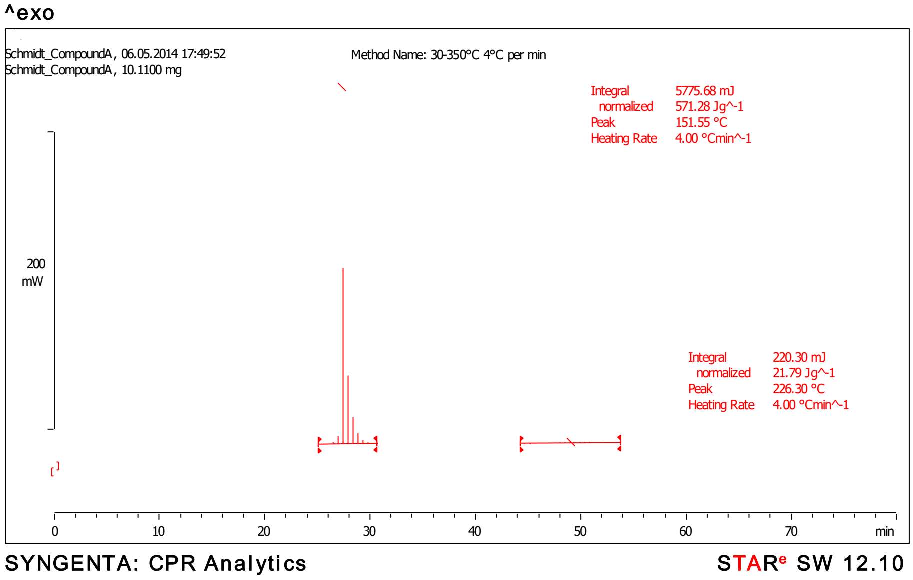
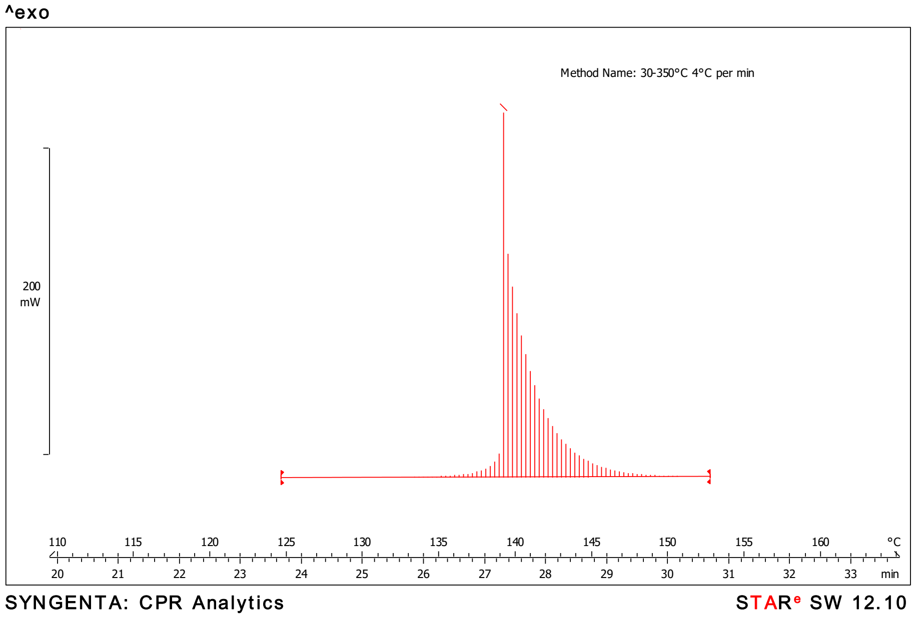
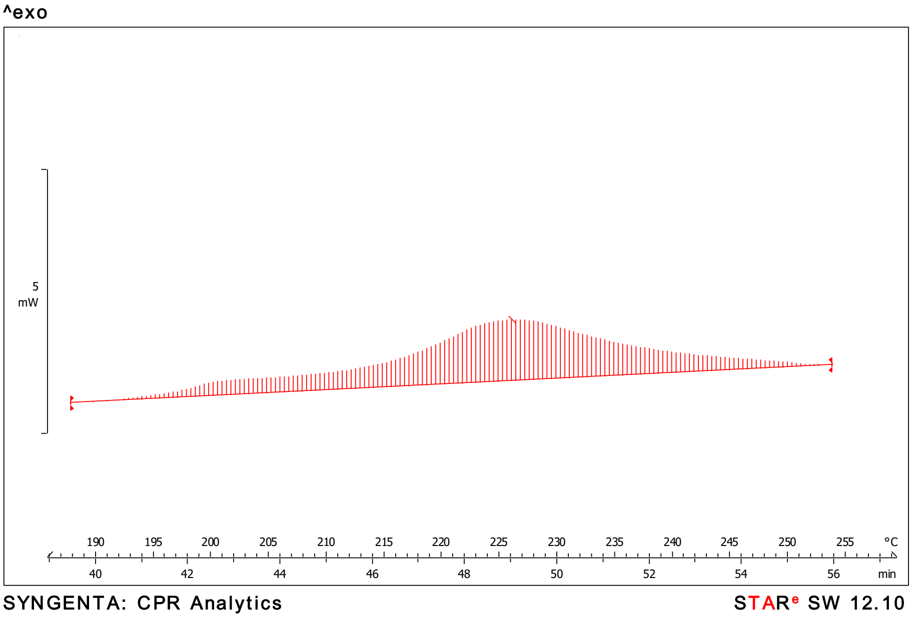
8. DSC Measurements for Compounds (10) and (11)

1-Cyano-1,2-benziodoxol-3-(1*H*)-one (10)







1-Cyano-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (11)