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# An intramolecular Diels–Alder reaction in the synthesis of *N*-aroyl-3a,6-epoxyisoindole-2-carbothioamides

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# SUPPLEMENTARY INFORMATION

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## X-ray diffraction analysis

X-ray diffraction experiments were carried out on an automatic four-circle area-detector diffractometer Bruker KAPPA APEX II (MoKα radiation) [1]. The unit cell constants were refined over the whole data set [2]. The experimental intensities were corrected for absorption using the SADABS program [3]. The structures were solved by the intrinsic phasing method (SHELXT [4]) and refined by the full-matrix least squares method (SHELXL-2018/3 [5]) on $F^2$ for all data in the anisotropic approximation for all non-hydrogen atoms. The H atoms of CH, $CH_2$, and $CH_3$ groups were introduced at geometrically calculated positions with $U_{iso}(H) = 1.2U_{eq}(C)$ for CH, and $CH_2$ groups and $U_{iso}(H) = 1.5U_{eq}(C)$ for $CH_3$ ones. The orientation of $CH_3$ groups was refined. The H atoms of NH groups were located from difference Fourier-maps of electron density and refined with $U_{iso}(H) = 1.2U_{eq}(N)$.

The main crystallographic data and characteristics of X-ray diffraction experiments and structure refinement are given in Table S1. H-Bond parameters for the molecules **6i**, **6x**, **6y** are given in Table S2. The atomic coordinates have been deposited with the Cambridge Crystallographic Data Centre, depositions CCDC 2360331−2360333.

## References

1. Apex2 // Bruker AXS Inc., Madison, Wisconsin, USA (2008).
2. SAINT-Plus (Version 8.40B). Bruker AXS Inc., Madison, Wisconsin, USA (2019).
3. Krause L., Herbst-Irmer R., Sheldrick G. M., Stalke D. *J. Appl. Cryst*. **2015**, *48*, 3−10.
4. Sheldrick G. M. *Acta Crystallogr*. **2015**, *A71*, 3−8.
5. Sheldrick G. M. *Acta Crystallogr*. **2015**, *C71*, 3−8.

**Table S1. Crystal data and structure refinement.**

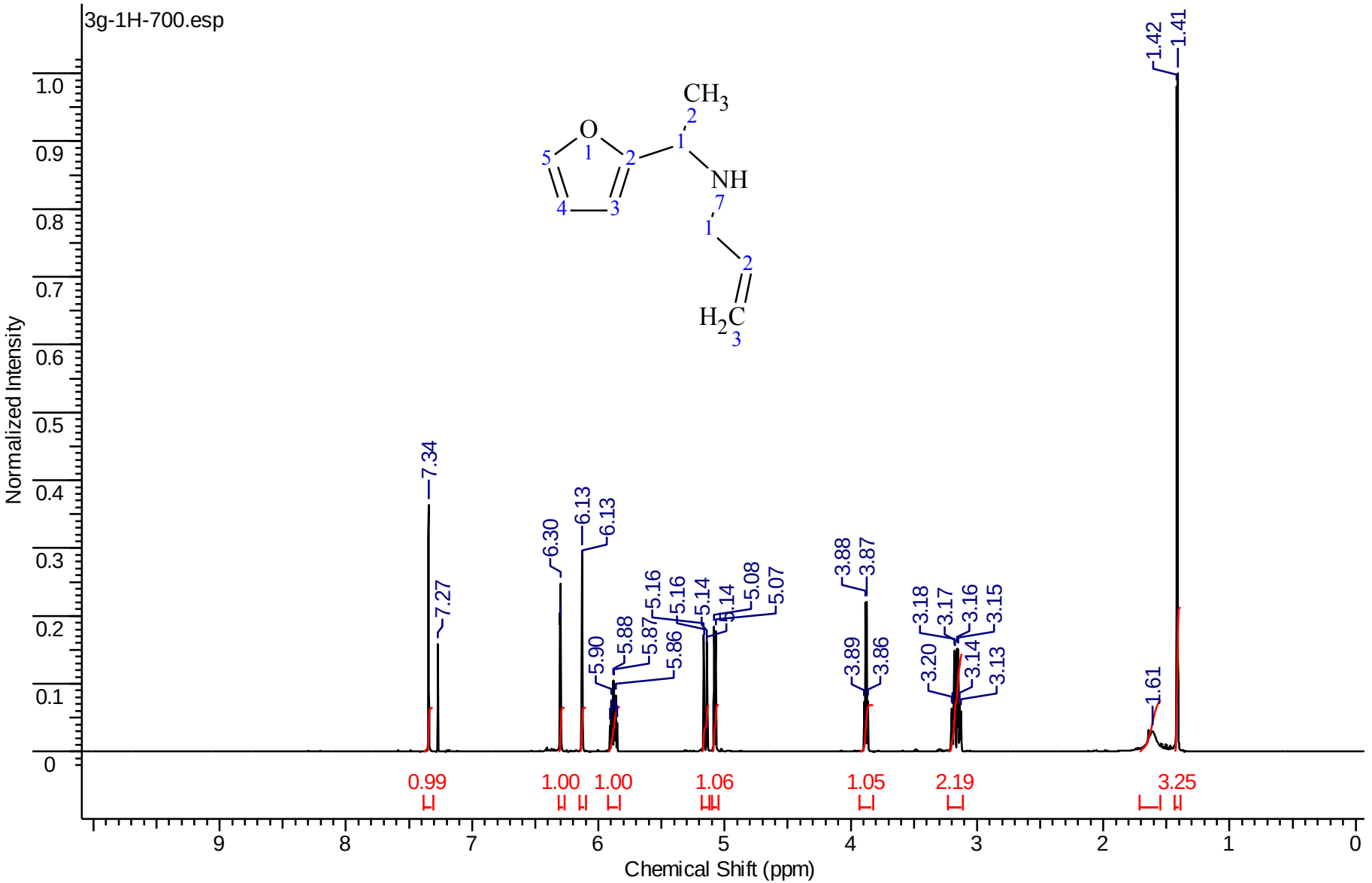
| Identification code | **6i** | **6x** | **6y** |
|---|---|---|---|
| CCDC deposition number | 2360331 | 2360332 | 2360333 |
| Empirical formula | $C_{17}H_{18}N_2O_2S$ | $C_{17}H_{18}N_2O_2S$ | $C_{17}H_{18}N_2O_2S$ |
| Formula weight | 314.39 | 314.39 | 314.39 |
| Temperature/K | 296(2) | 100(2) | 100(2) |
| Crystal system | monoclinic | triclinic | monoclinic |
| Space group | $P2_1/c$ | $P\bar{1}$ | $C2/c$ |
| a/Å | 13.3828(3) | 8.936(2) | 21.6491(11) |
| b/Å | 12.9545(4) | 9.6702(11) | 9.8034(4) |
| c/Å | 10.0160(3) | 10.3466(11) | 14.7286(6) |
| α/° | 90 | 113.935(6) | 90 |
| β/° | 109.345(2) | 100.530(9) | 102.071(2) |
| γ/° | 90 | 100.584(9) | 90 |
| Volume/Å$^3$ | 1638.41(8) | 769.6(2) | 3056.8(2) |
| $Z$ | 4 | 2 | 8 |
| $\rho_{calc}$g/cm$^3$ | 1.275 | 1.357 | 1.366 |
| μ/mm$^{-1}$ | 0.206 | 0.219 | 0.221 |
| $F$(000) | 664.0 | 332.0 | 1328.0 |
| Crystal size/mm$^3$ | 0.46 × 0.26 × 0.18 | 0.32 × 0.3 × 0.2 | 0.4 × 0.32 × 0.26 |
| Radiation | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 6.936 to 59.992 | 6.8 to 69.996 | 8.306 to 59.994 |
| Index ranges | $-18 \le h \le 18$, $-18 \le k \le 18$, $-14 \le l \le 14$ | $-14 \le h \le 14$, $-15 \le k \le 15$, $-16 \le l \le 16$ | $-30 \le h \le 30$, $-13 \le k \le 11$, $-20 \le l \le 20$ |
| Reflections collected | 20720 | 17925 | 16101 |
| Independent reflections | 4762 [$R_{int}$ = 0.0427, $R_{sigma}$ = 0.0374] | 6767 [$R_{int}$ = 0.0289, $R_{sigma}$ = 0.0371] | 4447 [$R_{int}$ = 0.0356, $R_{sigma}$ = 0.0393] |
| Data/restraints/parameters | 4762/0/203 | 6767/0/203 | 4447/0/203 |
| Goodness-of-fit on $F^2$ | 0.994 | 1.028 | 1.037 |
| Final $R$ indexes [$I$>=2σ($I$)] | $R_1$ = 0.0467, $wR_2$ = 0.1007 | $R_1$ = 0.0383, $wR_2$ = 0.0964 | $R_1$ = 0.0434, $wR_2$ = 0.1065 |
| Final R indexes [all data] | $R_1$ = 0.1025, $wR_2$ = 0.1249 | $R_1$ = 0.0501, $wR_2$ = 0.1036 | $R_1$ = 0.0590, $wR_2$ = 0.1147 |
| Largest diff. peak/hole / e Å$^{-3}$ | 0.16/-0.25 | 0.55/-0.26 | 0.51/-0.28 |

**Table S2.** H-Bond parameters.

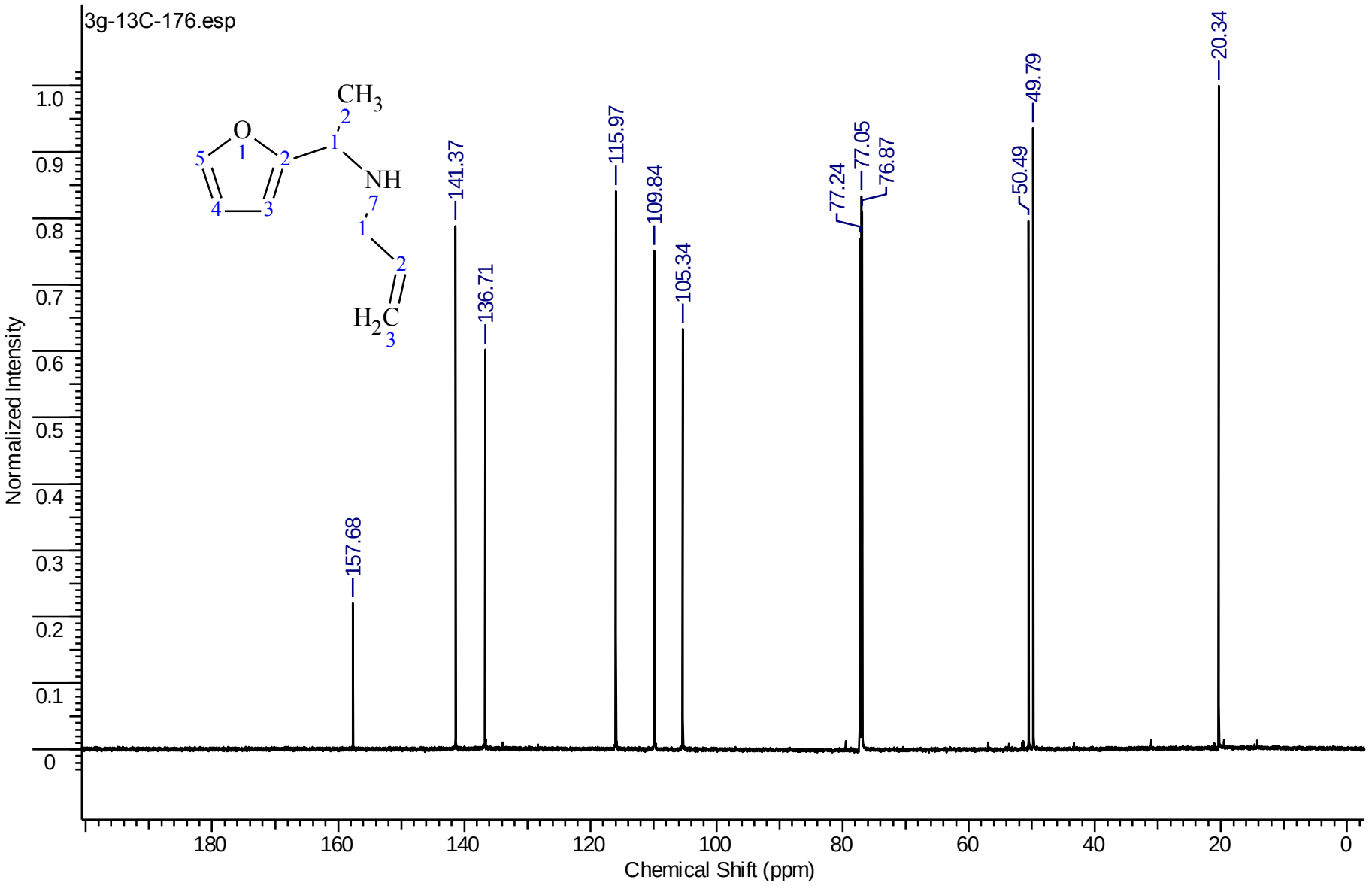
| D-H···A | d(D-H)/Å | d(H···A)/Å | d(D···A)/Å | D-H···A/° | Symmetry transformation for A |
|---|---|---|---|---|---|
| **6i** | | | | | |
| N1-H1···O1 | 0.812(19) | 2.075(19) | 2.8574(17) | 161.6(18) | *x*, 1.5- *y*, 0.5+*z* |
| **6x** | | | | | |
| N1-H1···O8 | 0.829(14) | 2.140(14) | 2.9603(10) | 170.1(13) | 1-*x*, 1-*y*, 1-*z* |
| C1-H1B···O1 | 0.99 | 2.26 | 2.9463(13) | 125 | |
| **6y** | | | | | |
| N1-H1···S1 | 0.75(2) | 2.80(2) | 3.5421(14) | 172.7(18) | 1-*x*, 2-*y*, 1-*z* |

**Copies of NMR spectra**

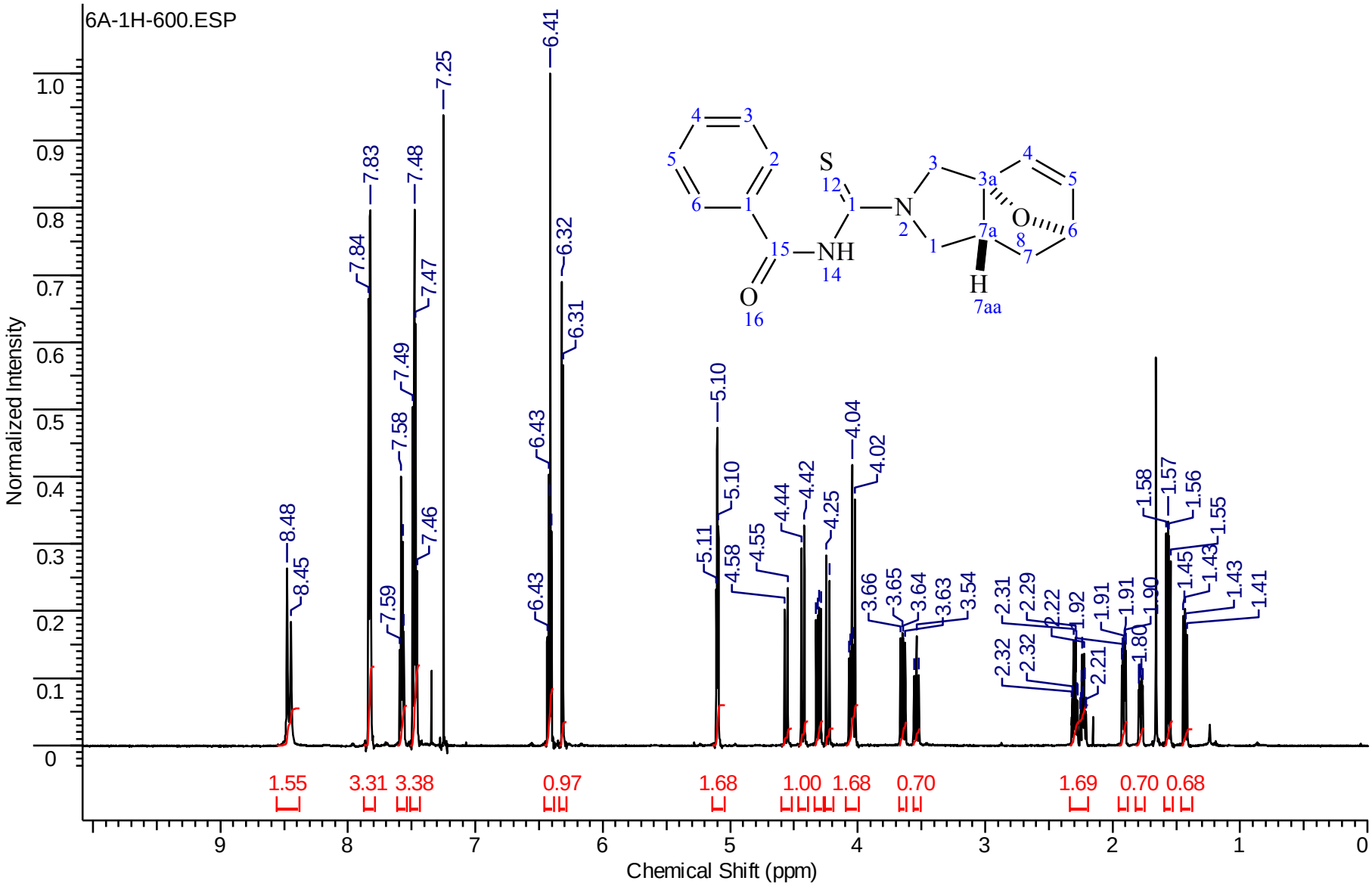
***N*-[1-(2-Furyl)ethyl]prop-2-en-1-amine (3g). $^{1}$H NMR (700.2 MHz, $CDCl_3$)**



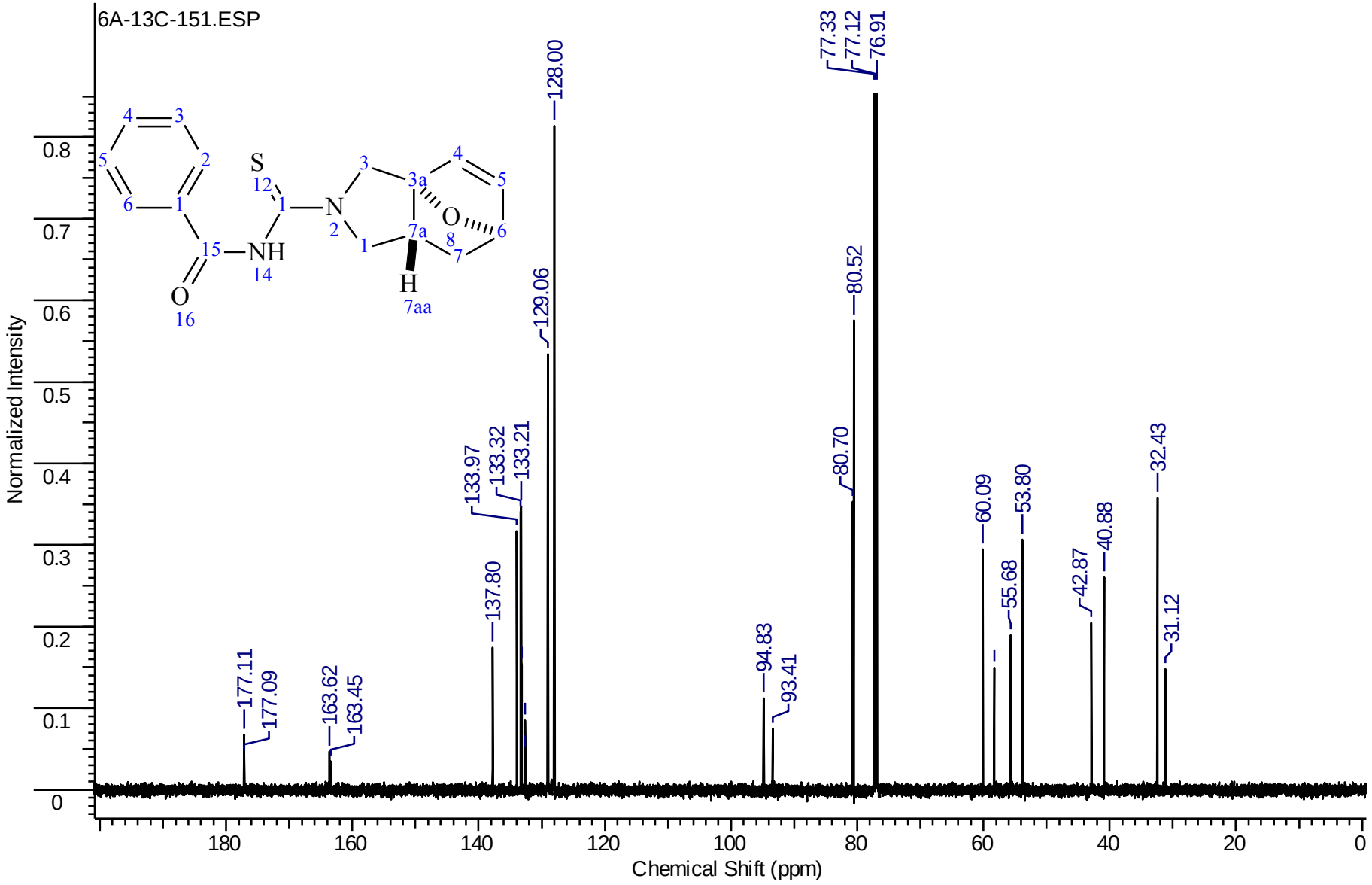
**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**



**_N_-[(3a_RS_,6_RS_,7a_RS_)-1,6,7,7a-Tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]benzamide (6a). $^{1}$H NMR (600.2 MHz, $CDCl_3$)**

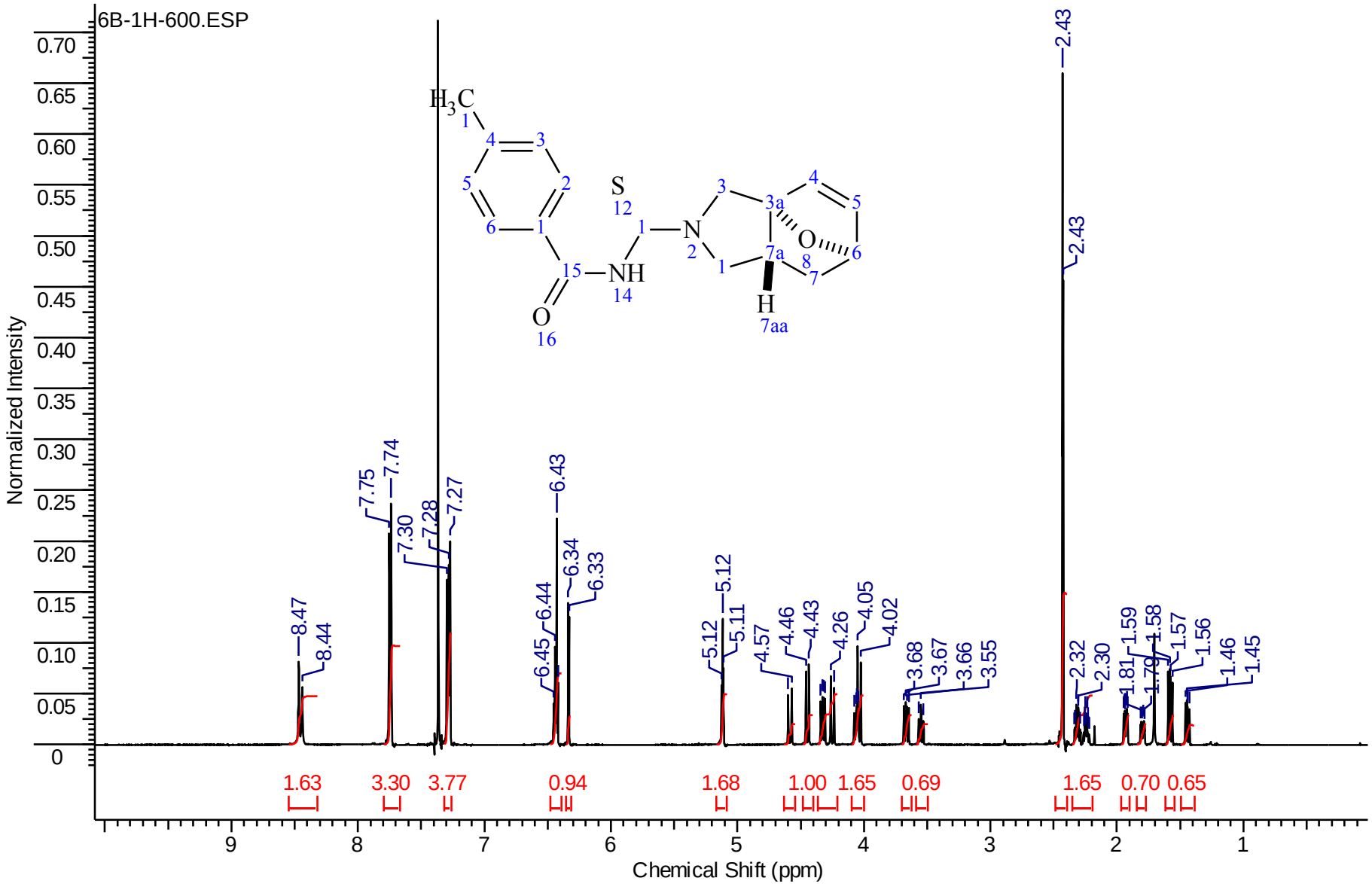


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

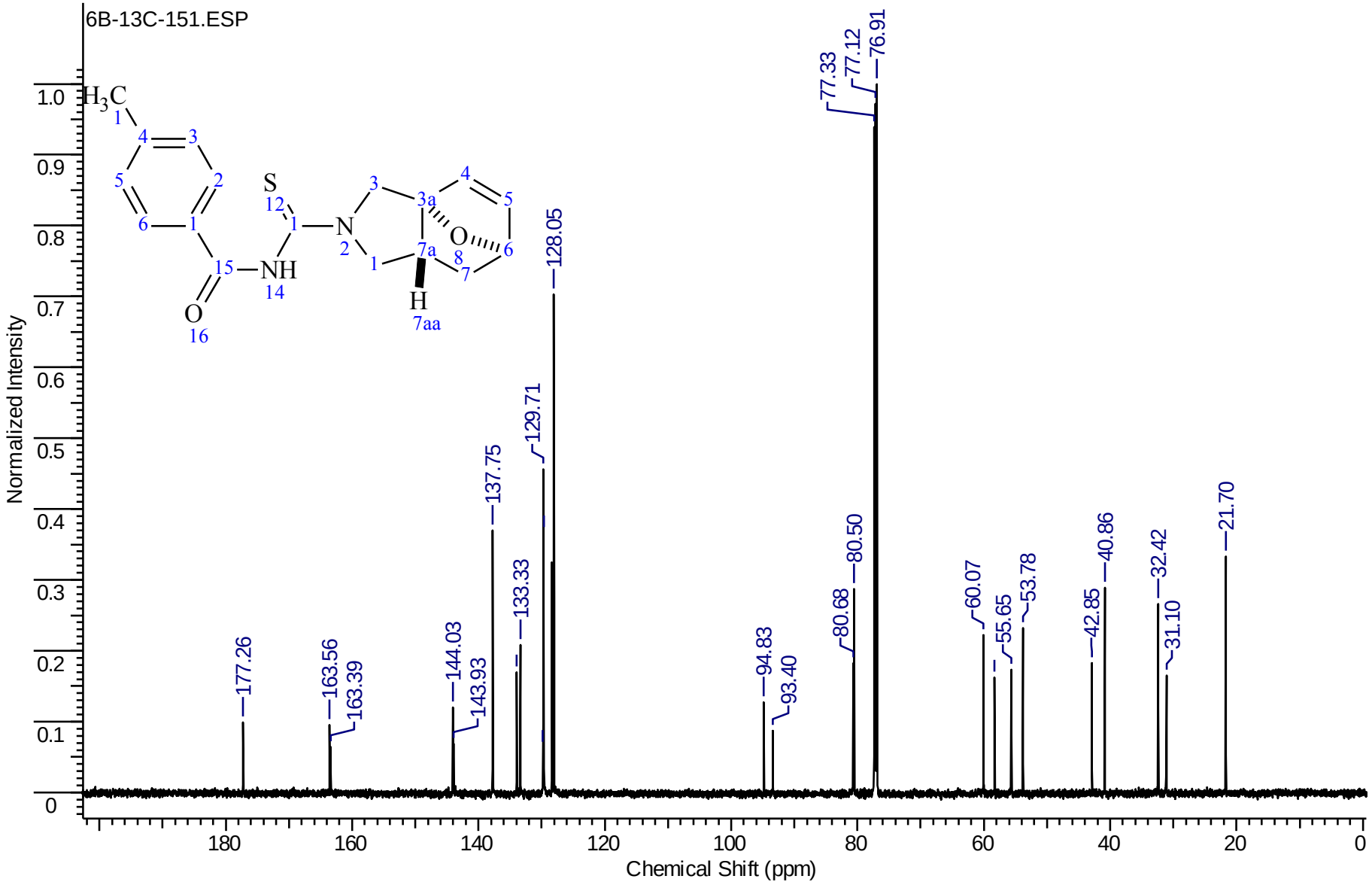


**4-Methyl-*N*-[(3a*RS*,6*RS*,7a*RS*)-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]benzamide (6b).**

**$^1$H NMR (600.2 MHz, $CDCl_3$)**

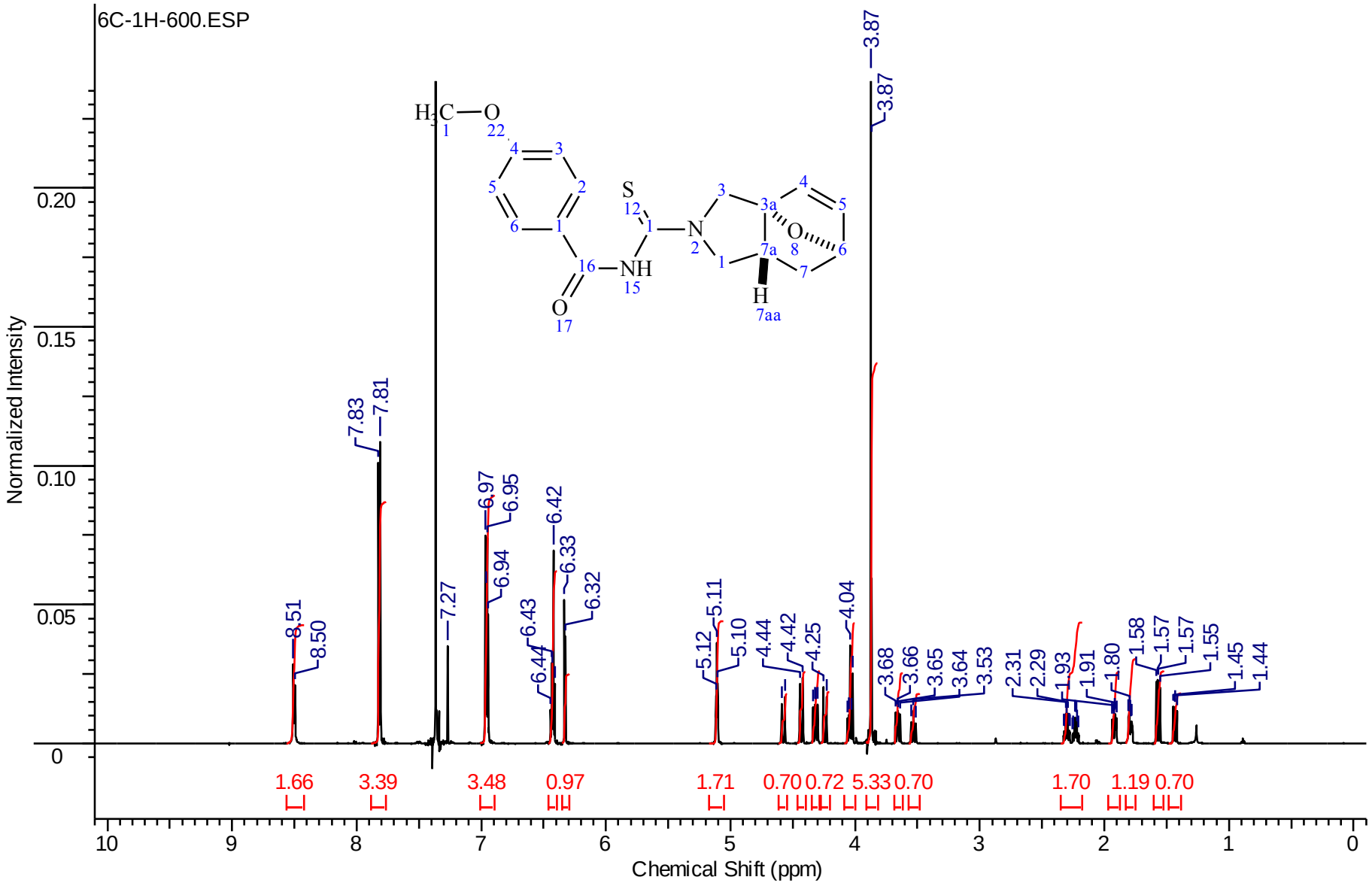


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

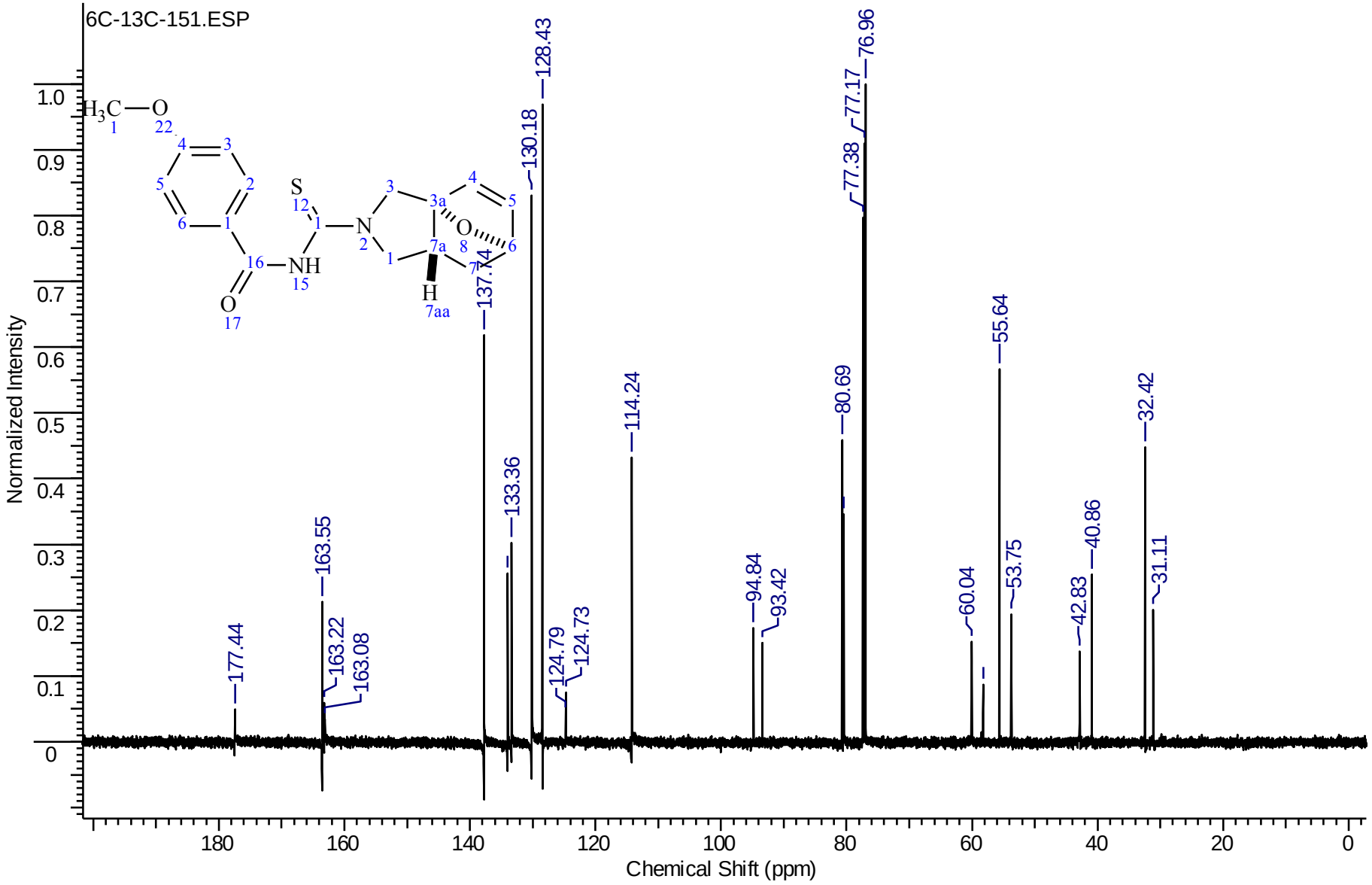


**4-Methoxy-*N*-[(3a*RS*,6*RS*,7a*RS*)-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]benzamide (6c).**

**$^1$H NMR (600.2 MHz, $CDCl_3$)**

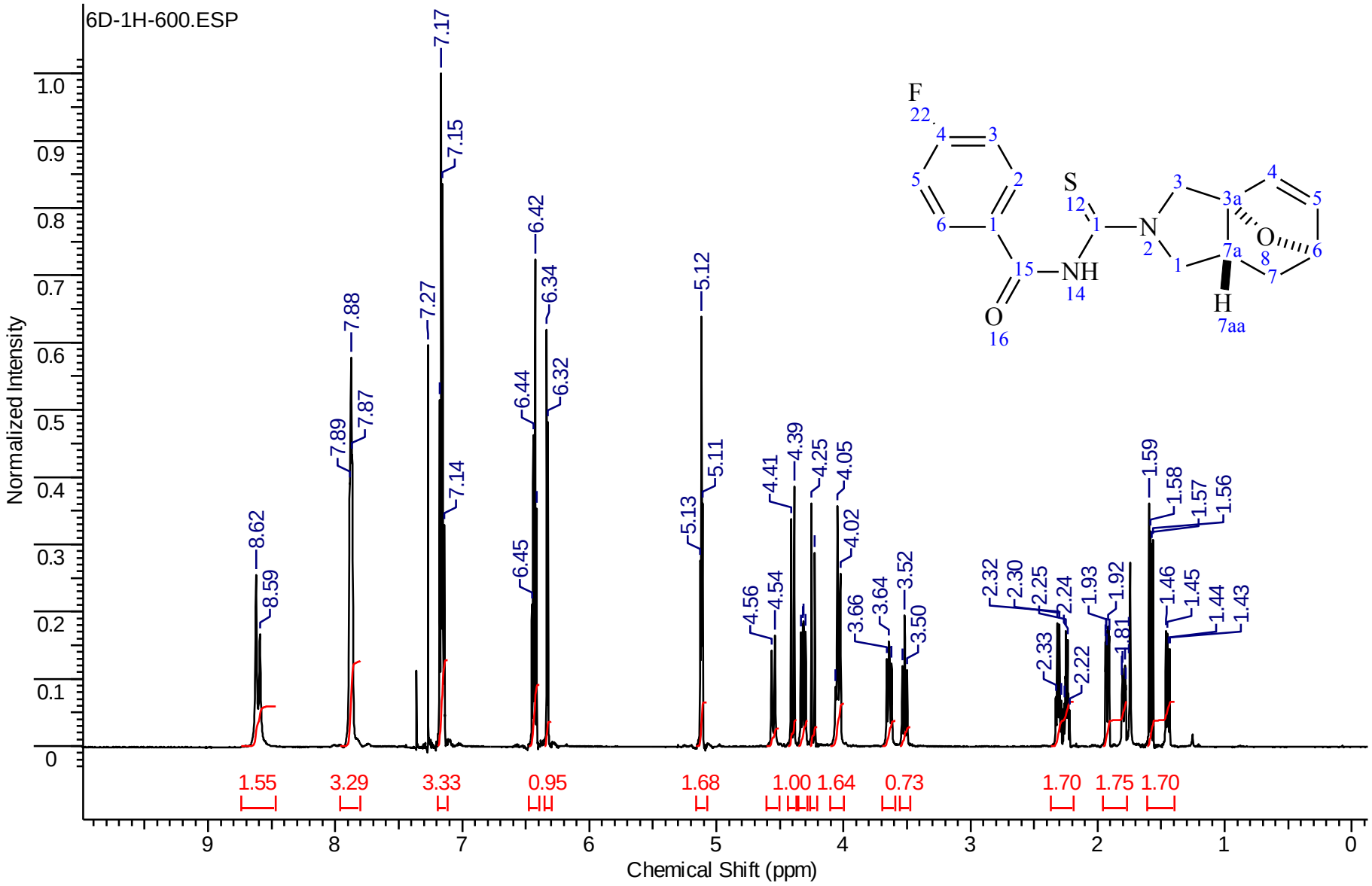


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

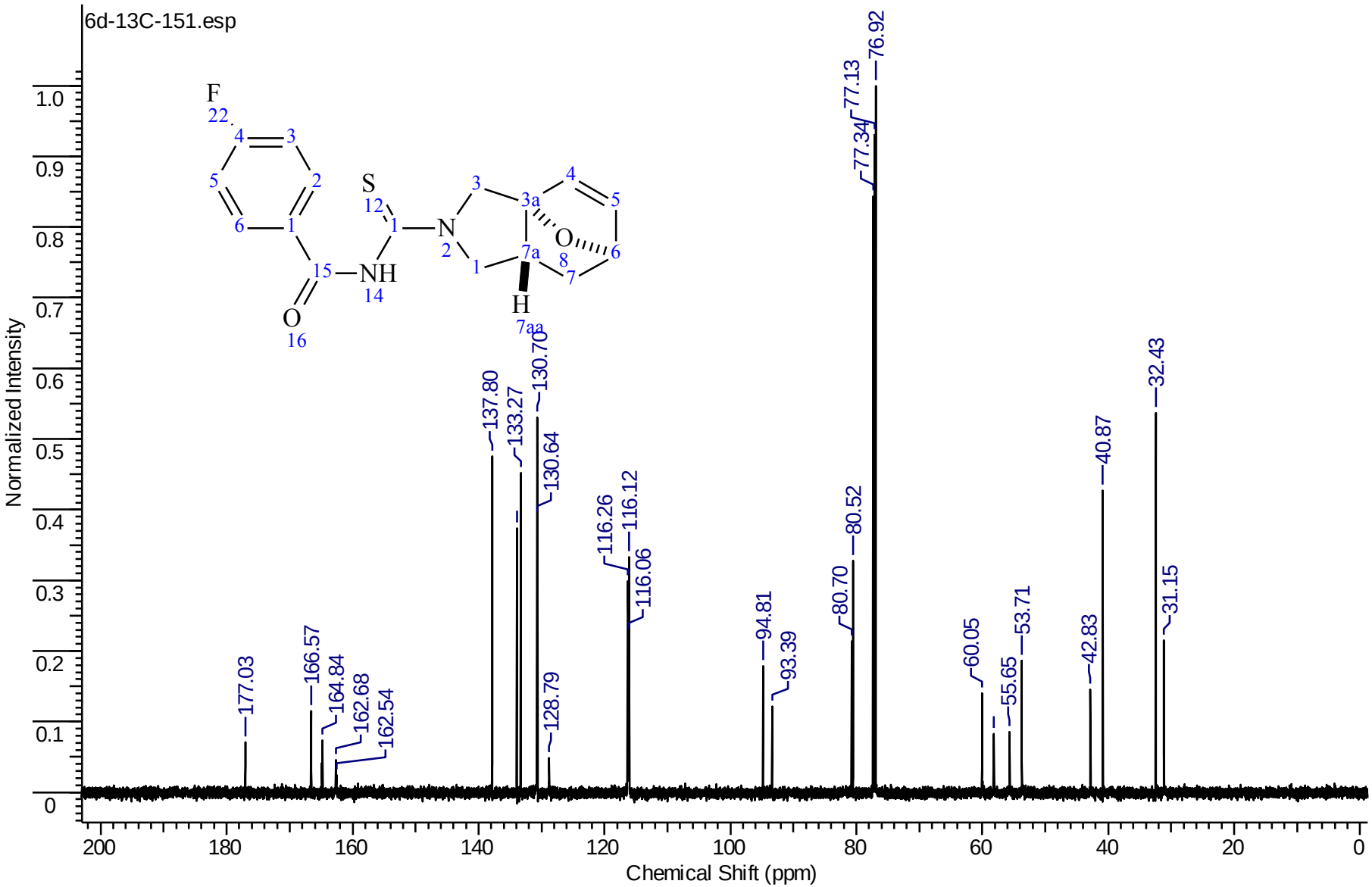


**4-Fluoro-*N*-[(3a*RS*,6*RS*,7a*RD*)-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]benzamide (6d).**

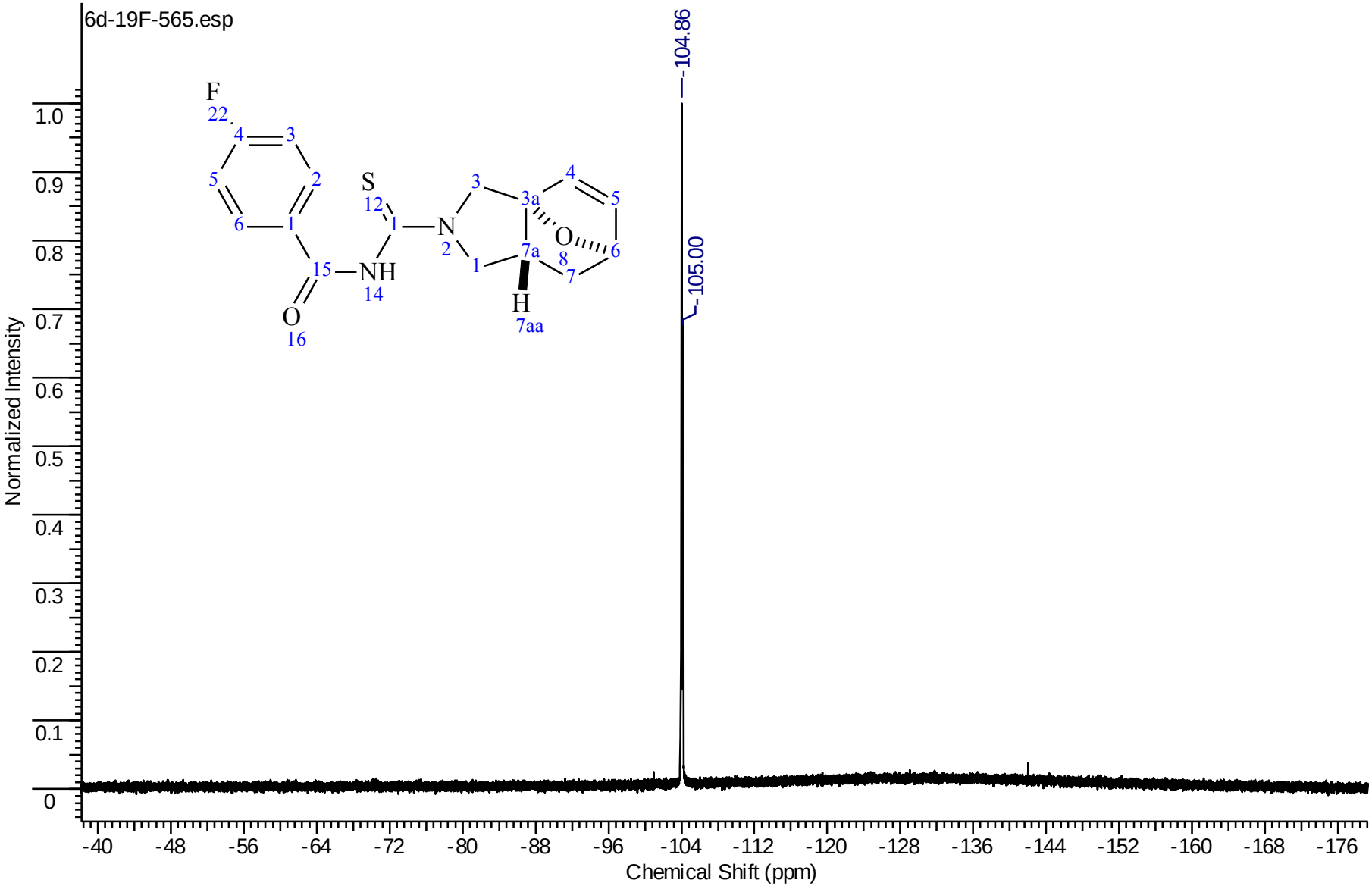
**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**



**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

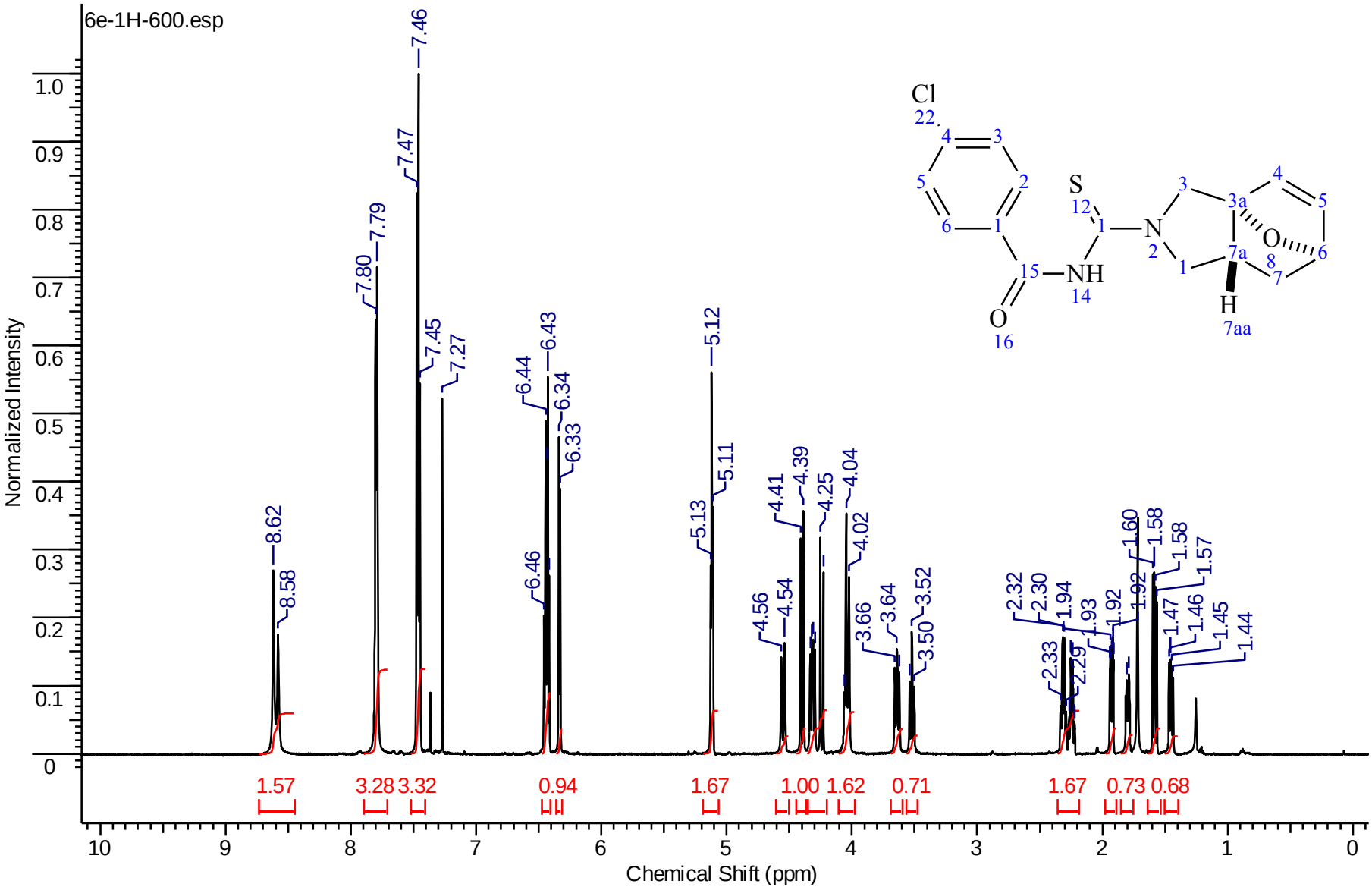


**$^{19}$F NMR (564.7 MHz, $CDCl_3$)**

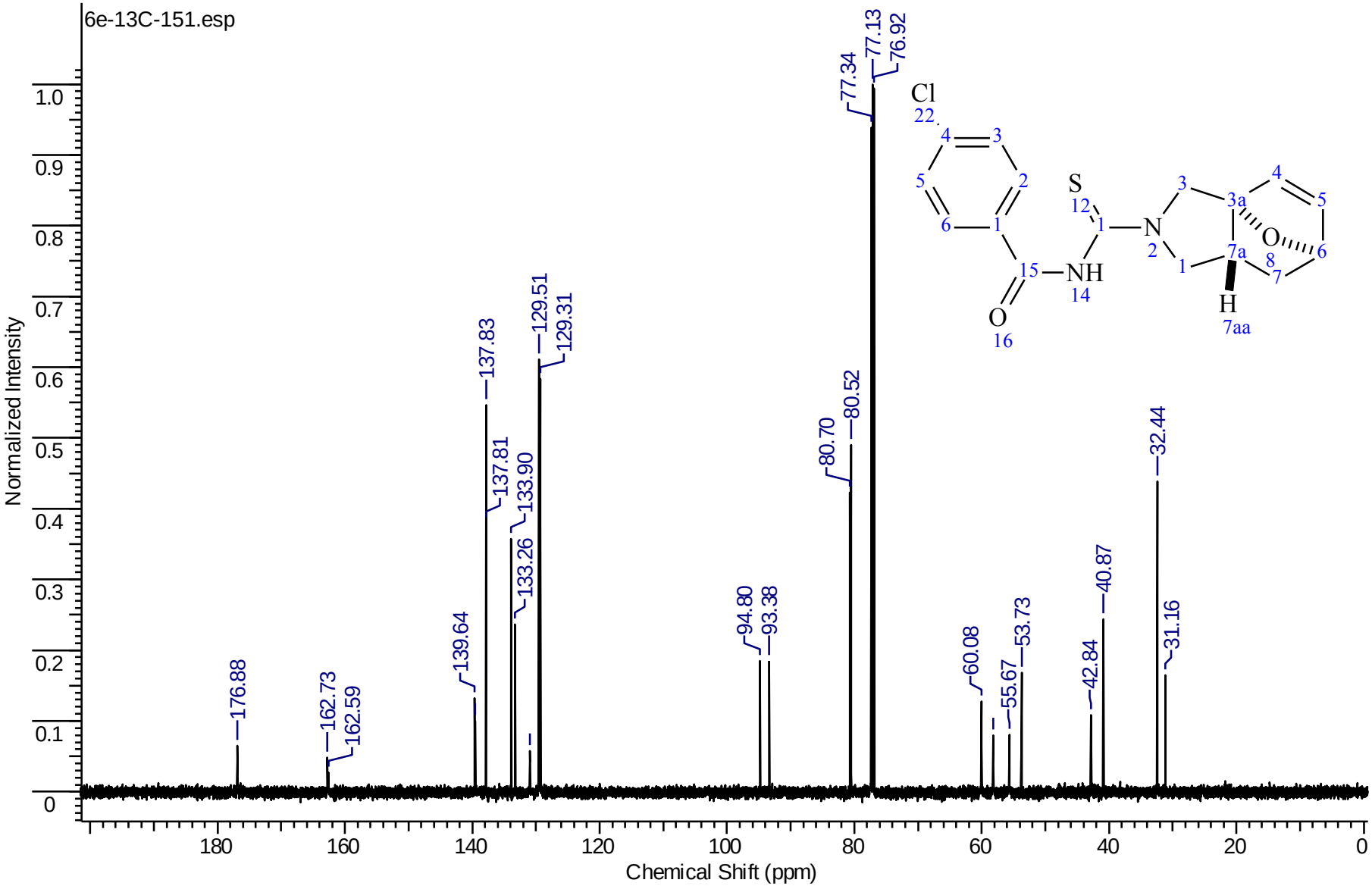


**4-Chloro-*N*-[(3a*RS*,6*RS*,7a*RS*)-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]benzamide (6e).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

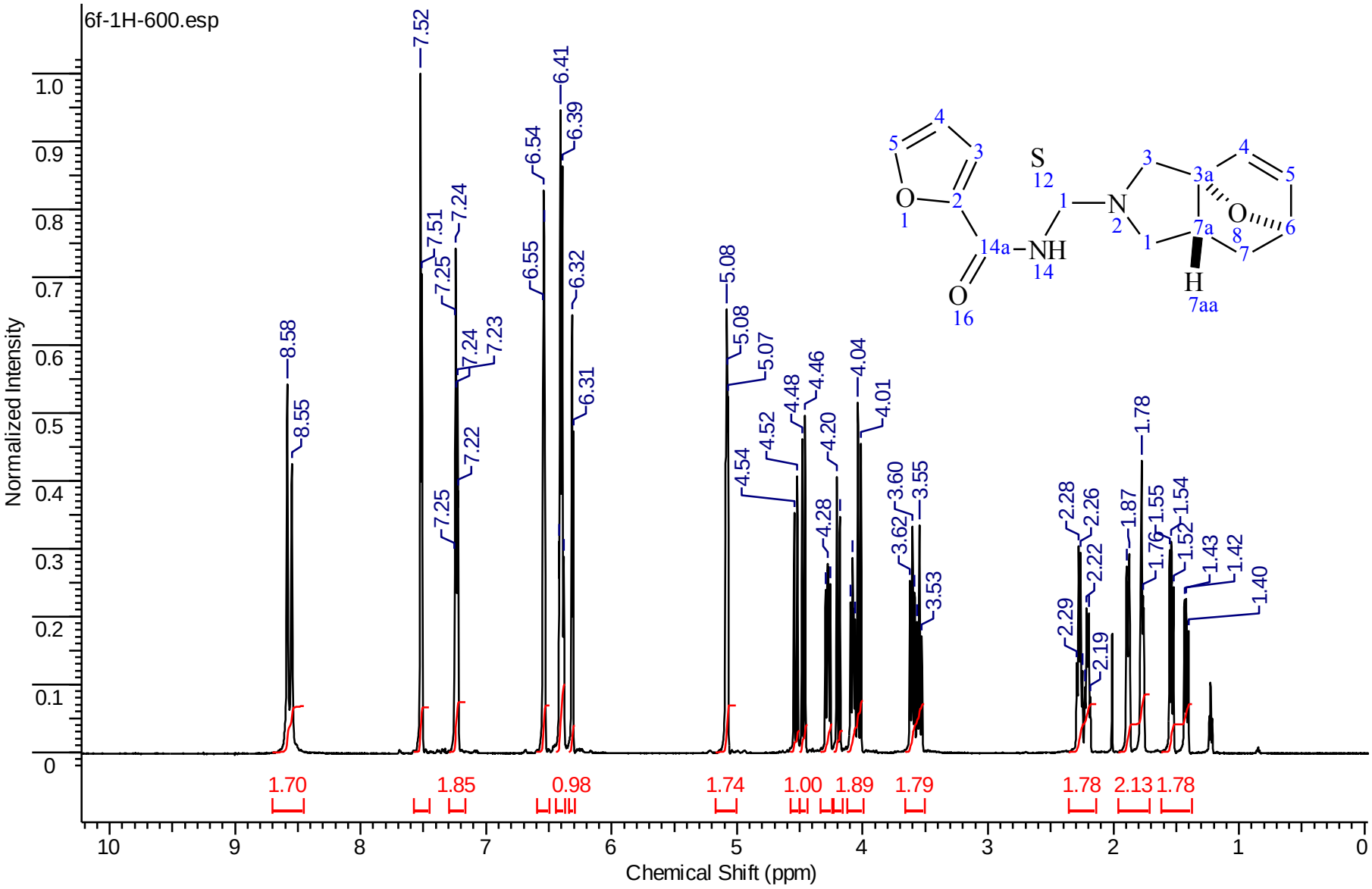


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

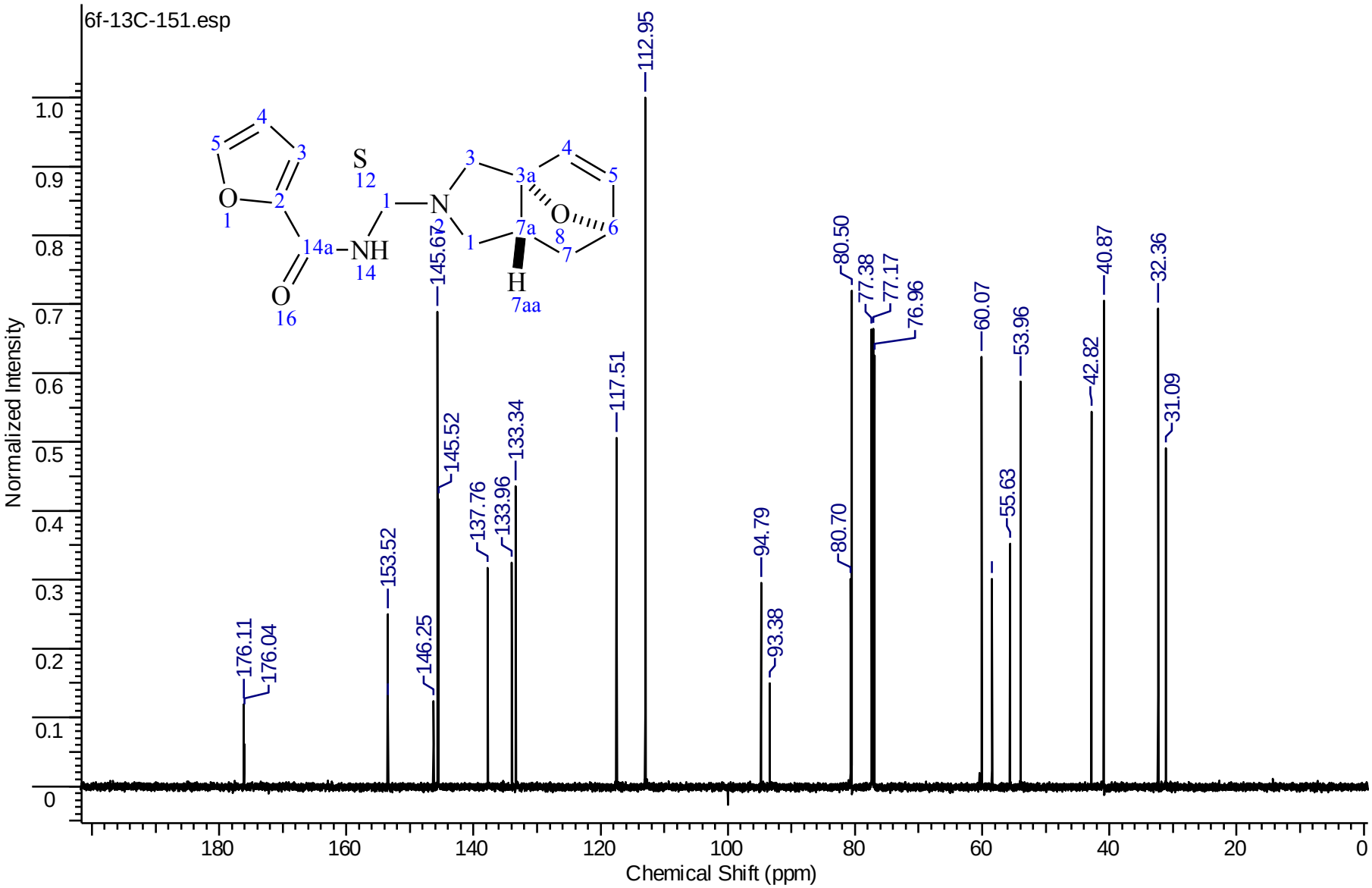


***N*-[(3a*RS*,6*RS*,7a*RS*)-1,6,7,7a-Tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]-2-furamide (6f).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

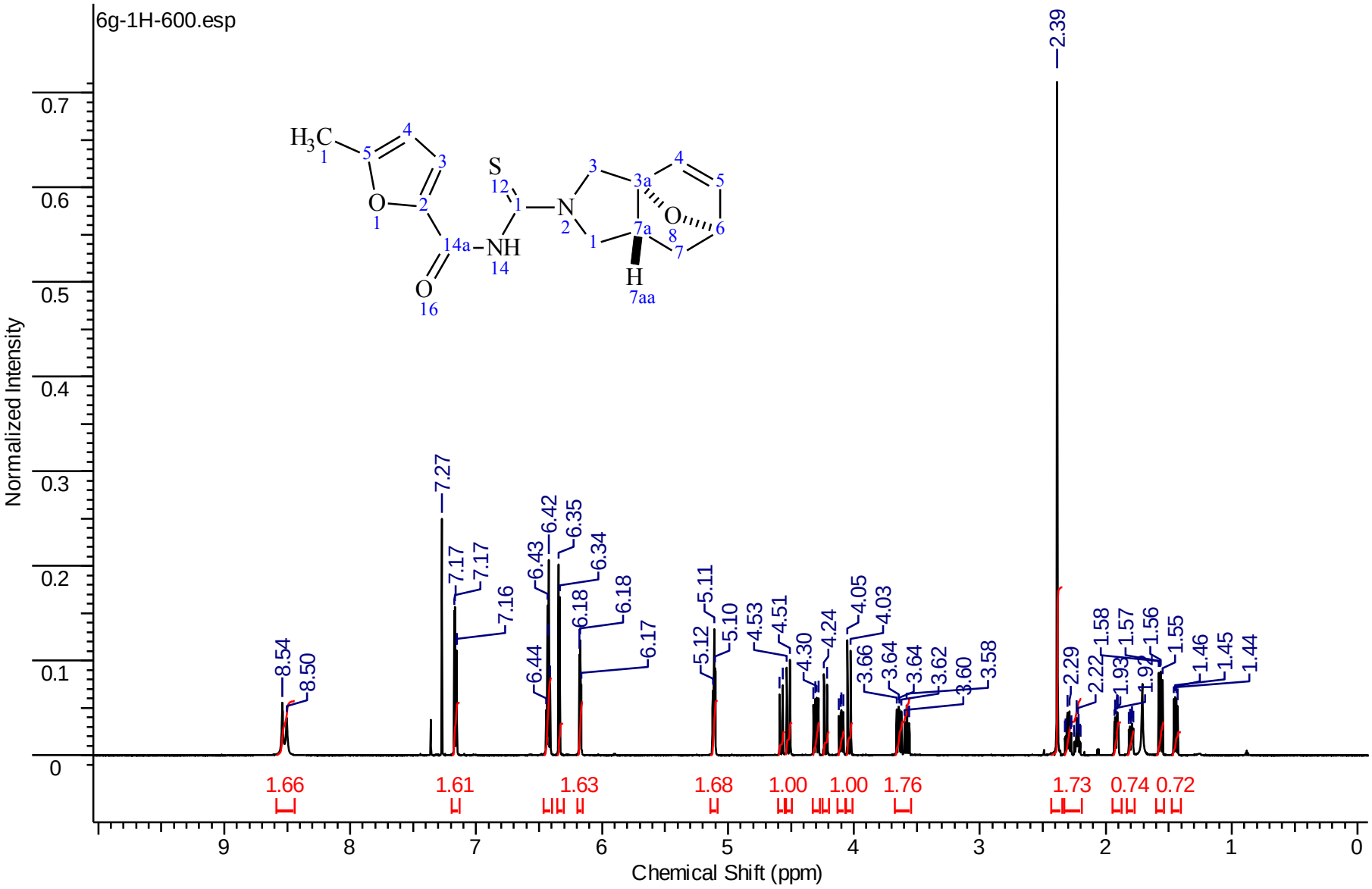


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

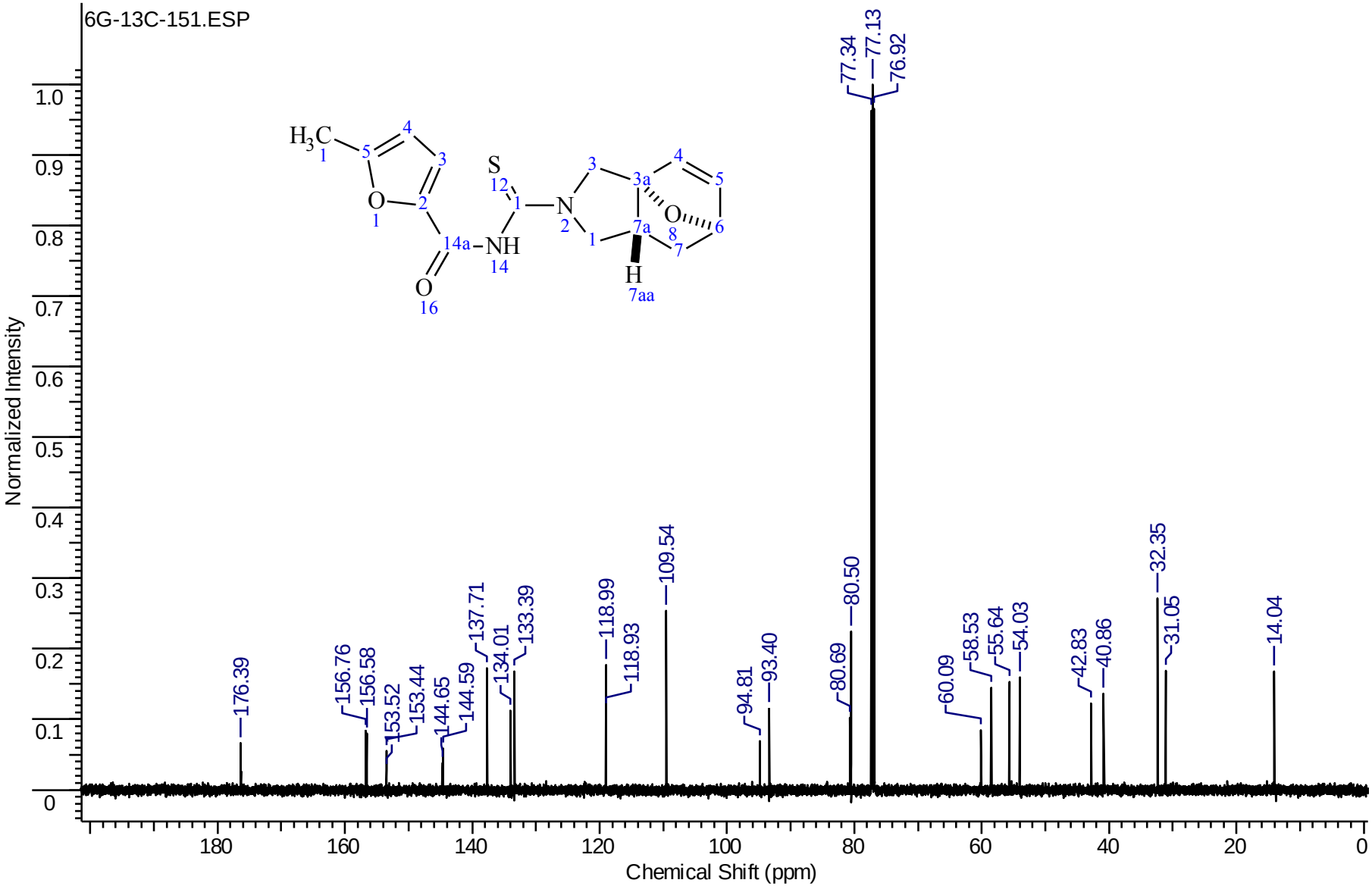


**5-Methyl-*N*-[(3a*RS*,6*RS*,7a*RS*)-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]-2-furamide (6g).**

**$^1$H NMR (600.2 MHz, $CDCl_3$)**

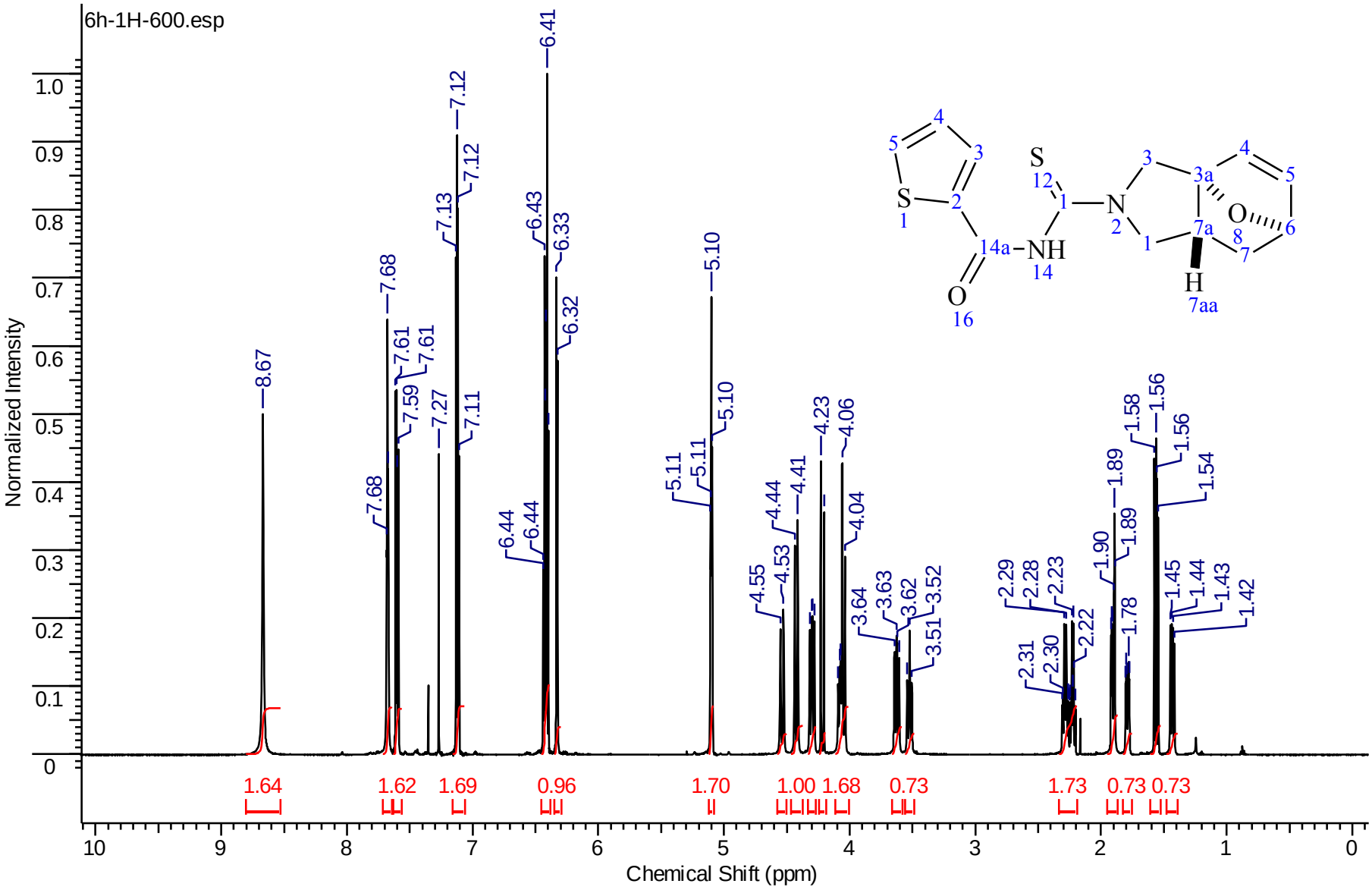


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

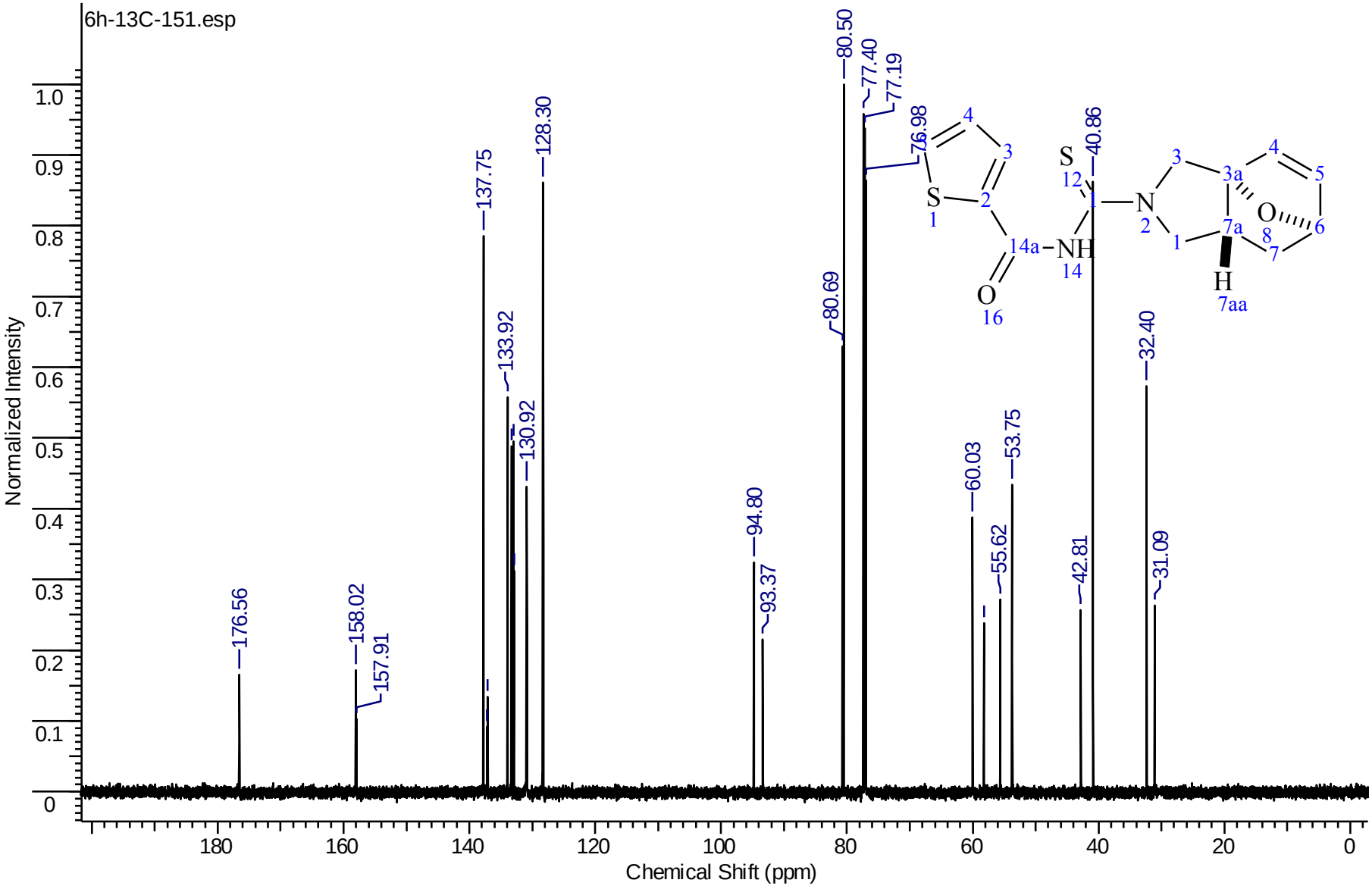


***N*-[(3a*RS*,6*RS*,7a*RS*)-1,6,7,7a-Tetrahydro-3a,6-epoxyisoindol-2-ylcarbonothioyl]thiophene-2-carboxamide (6h).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

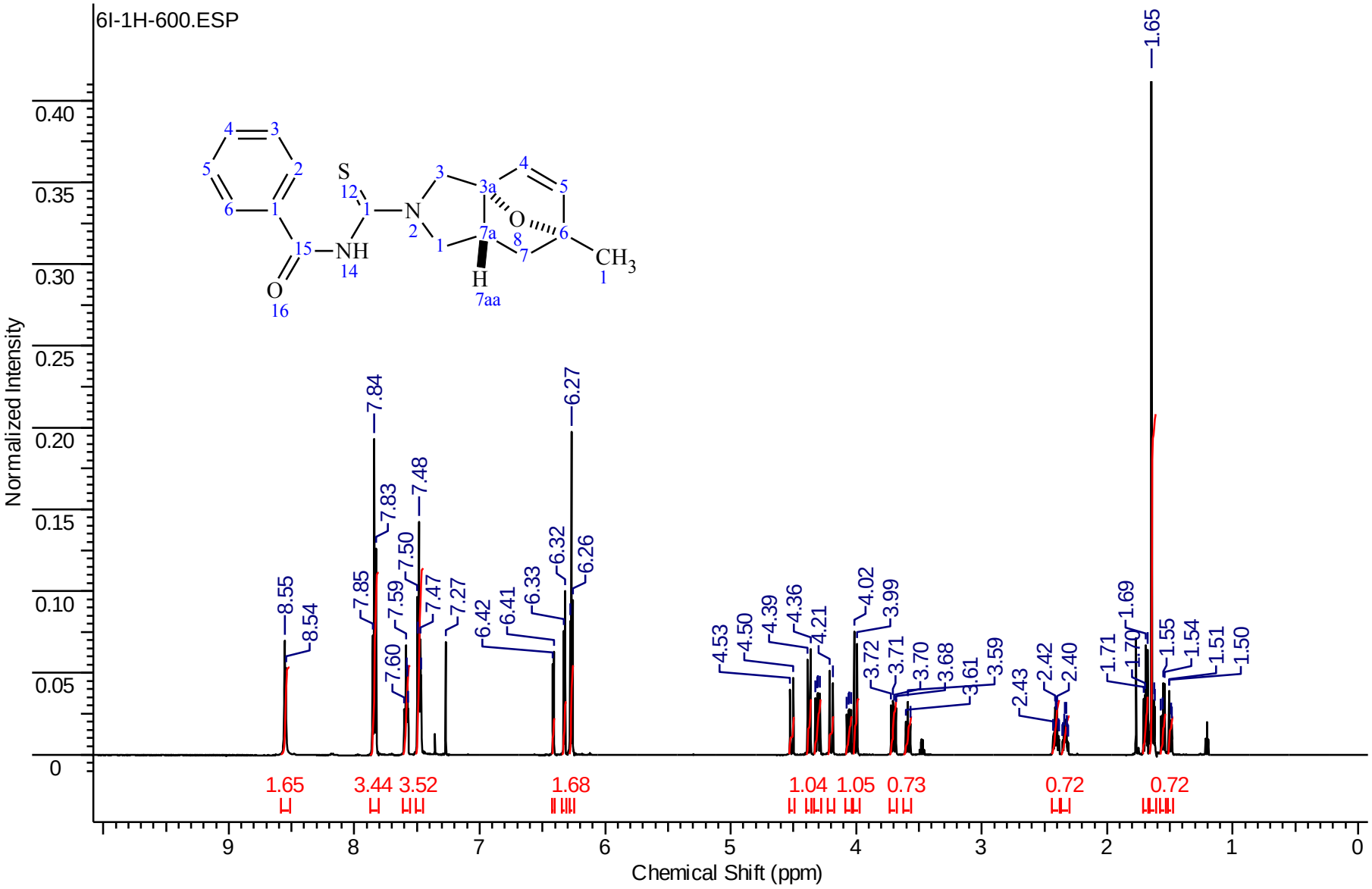


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

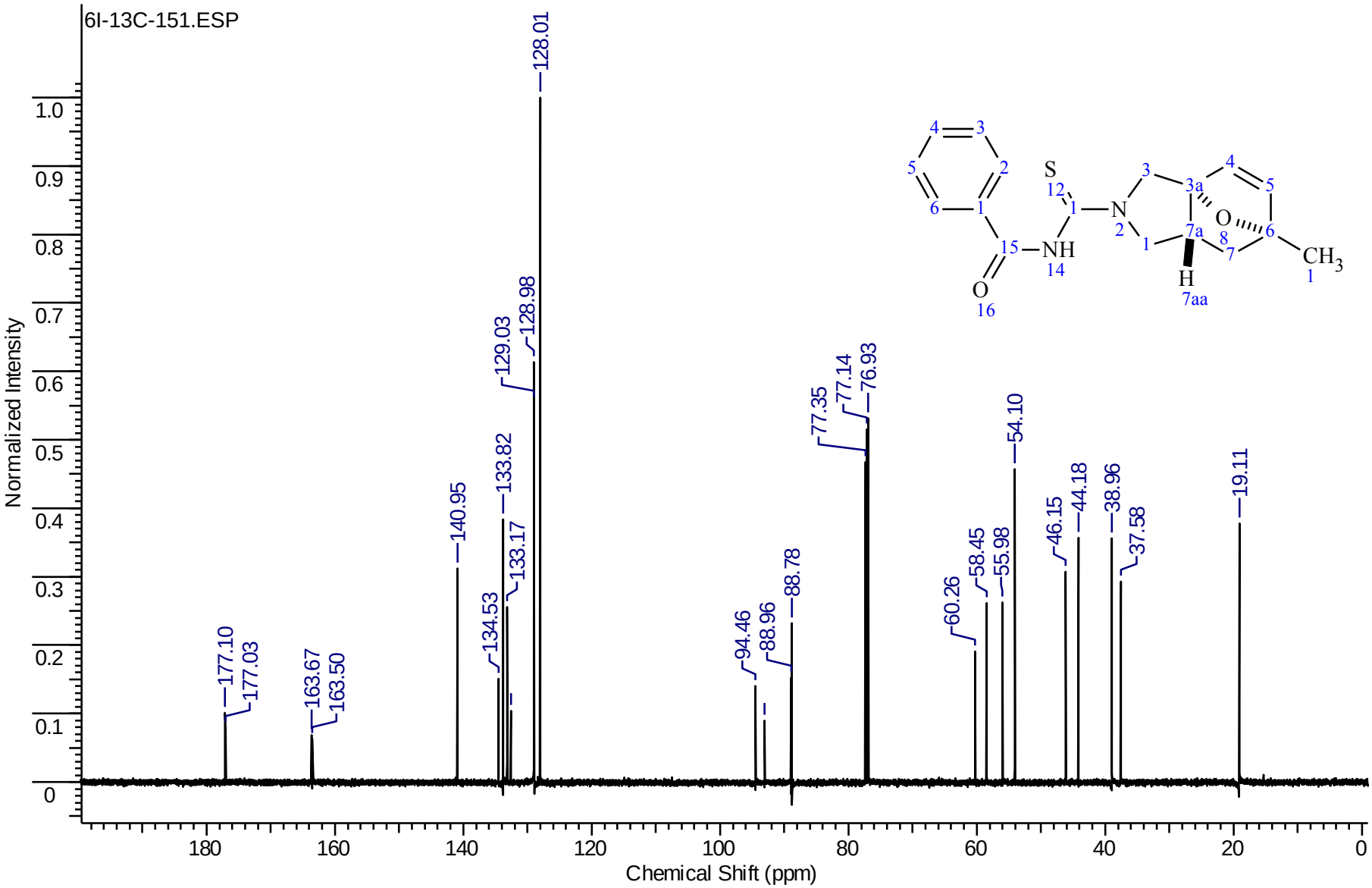


***N*-{[(3a*R*,6*R*,7a*R*)-6-methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6i).**

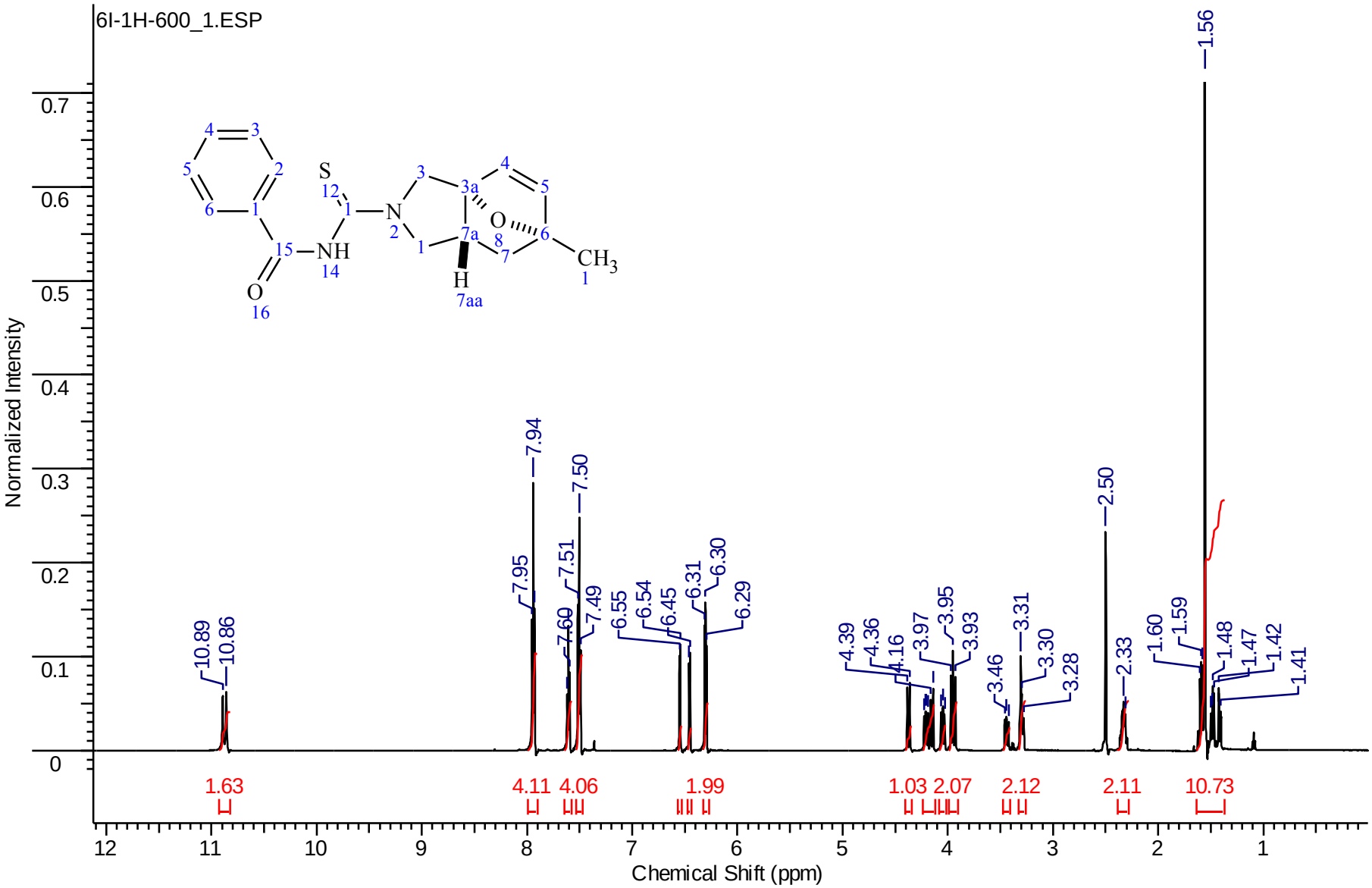
**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**



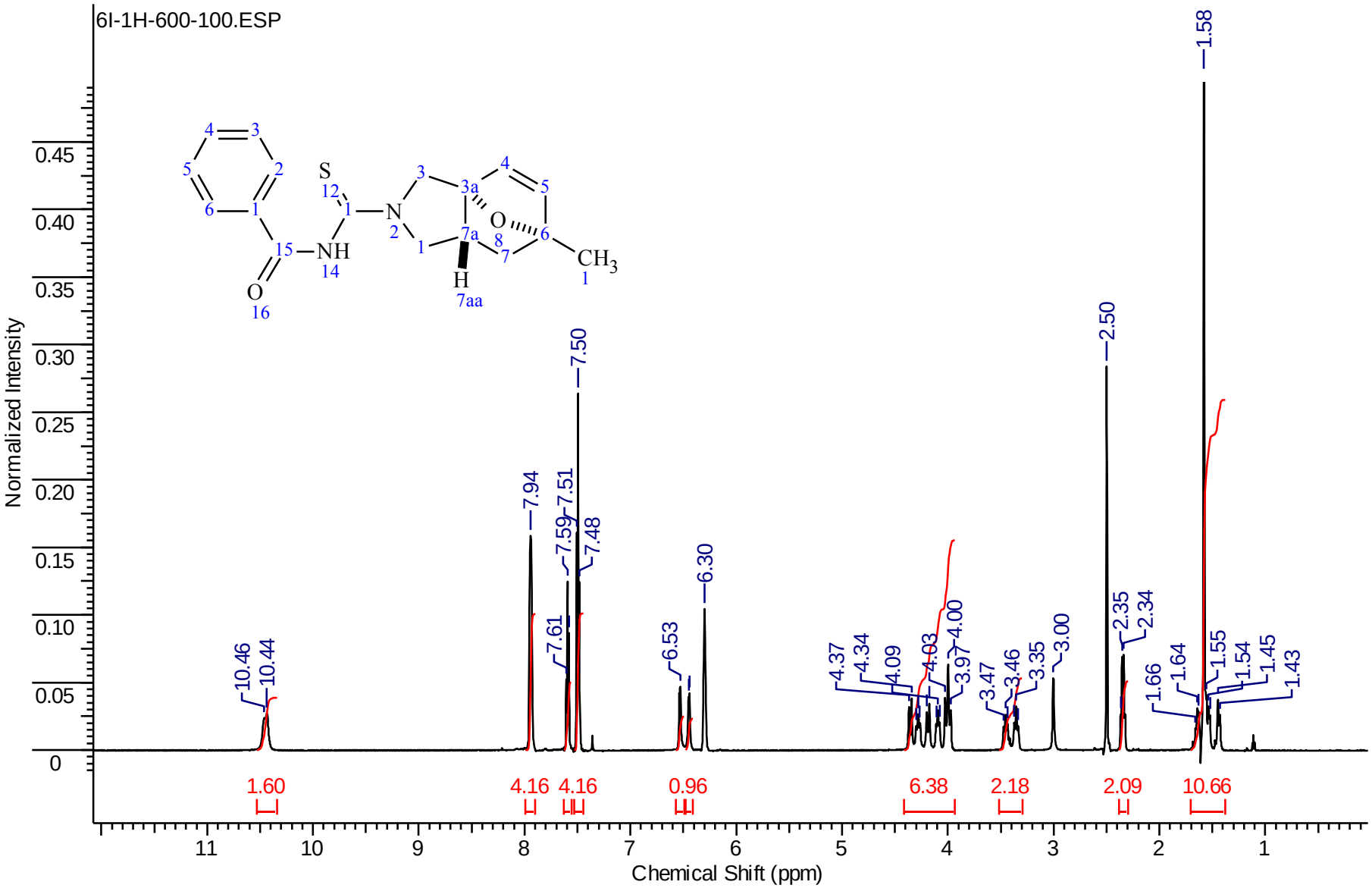
**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**



**$^{1}$H NMR (600.2 MHz, DMSO-$d_6$)**

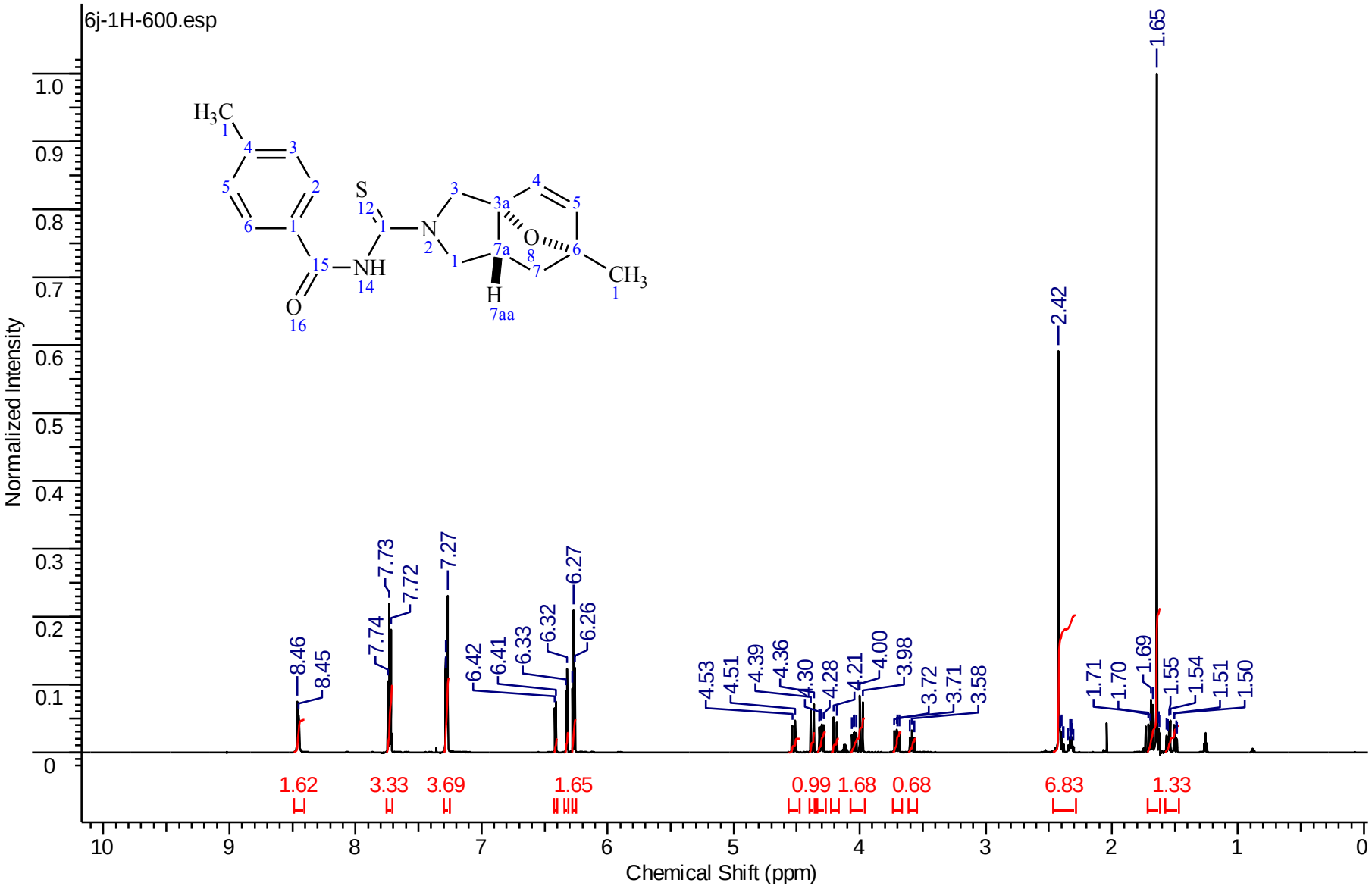


**$^{1}$H NMR (600.2 MHz, DMSO-$d_6$, 100 °C)**

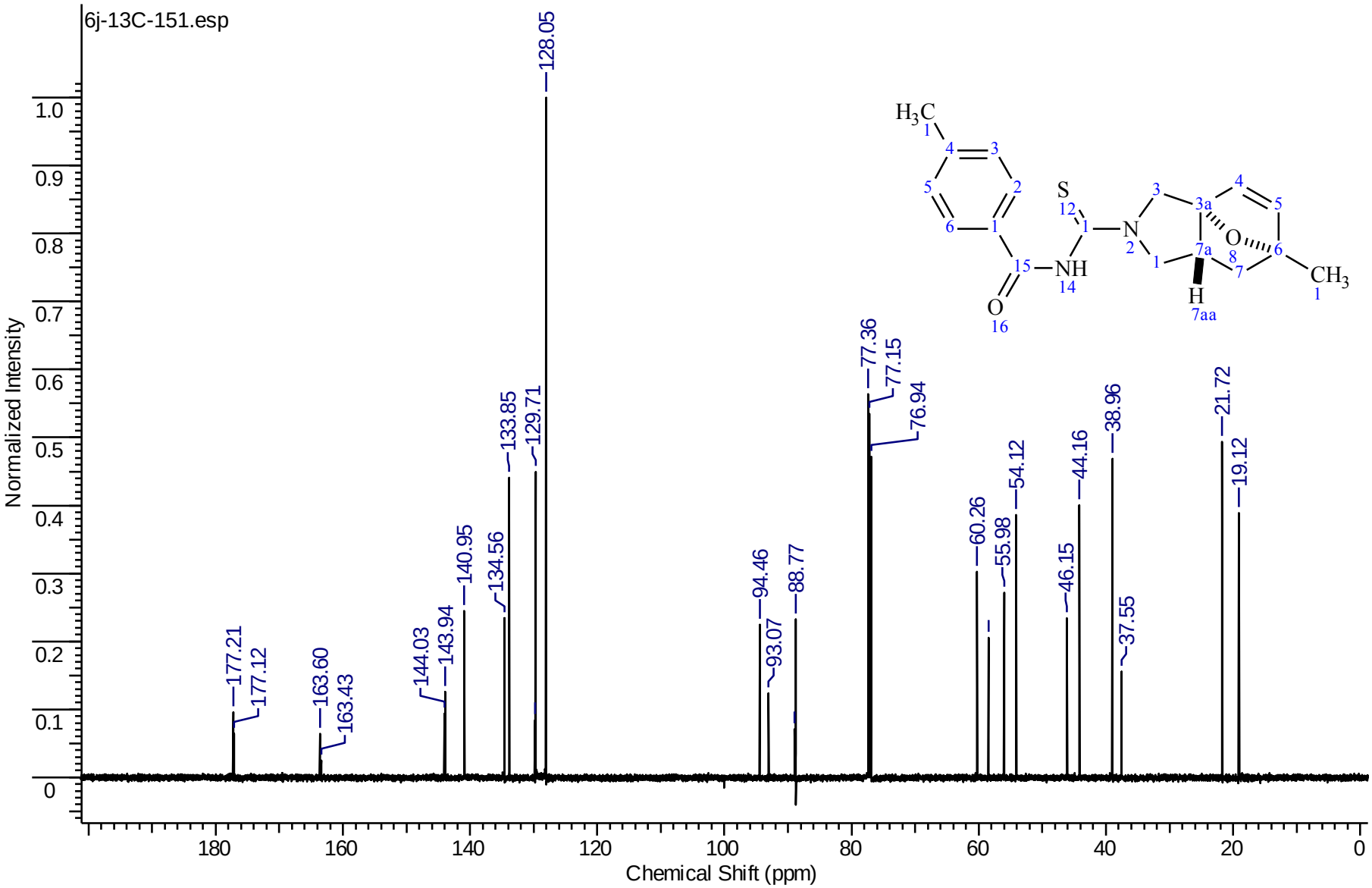


**4-Methyl-*N*-{[(3a*R*,6*R*,7a*R*)-6-methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6j).**

**$^1$H NMR (600.2 MHz, $CDCl_3$)**

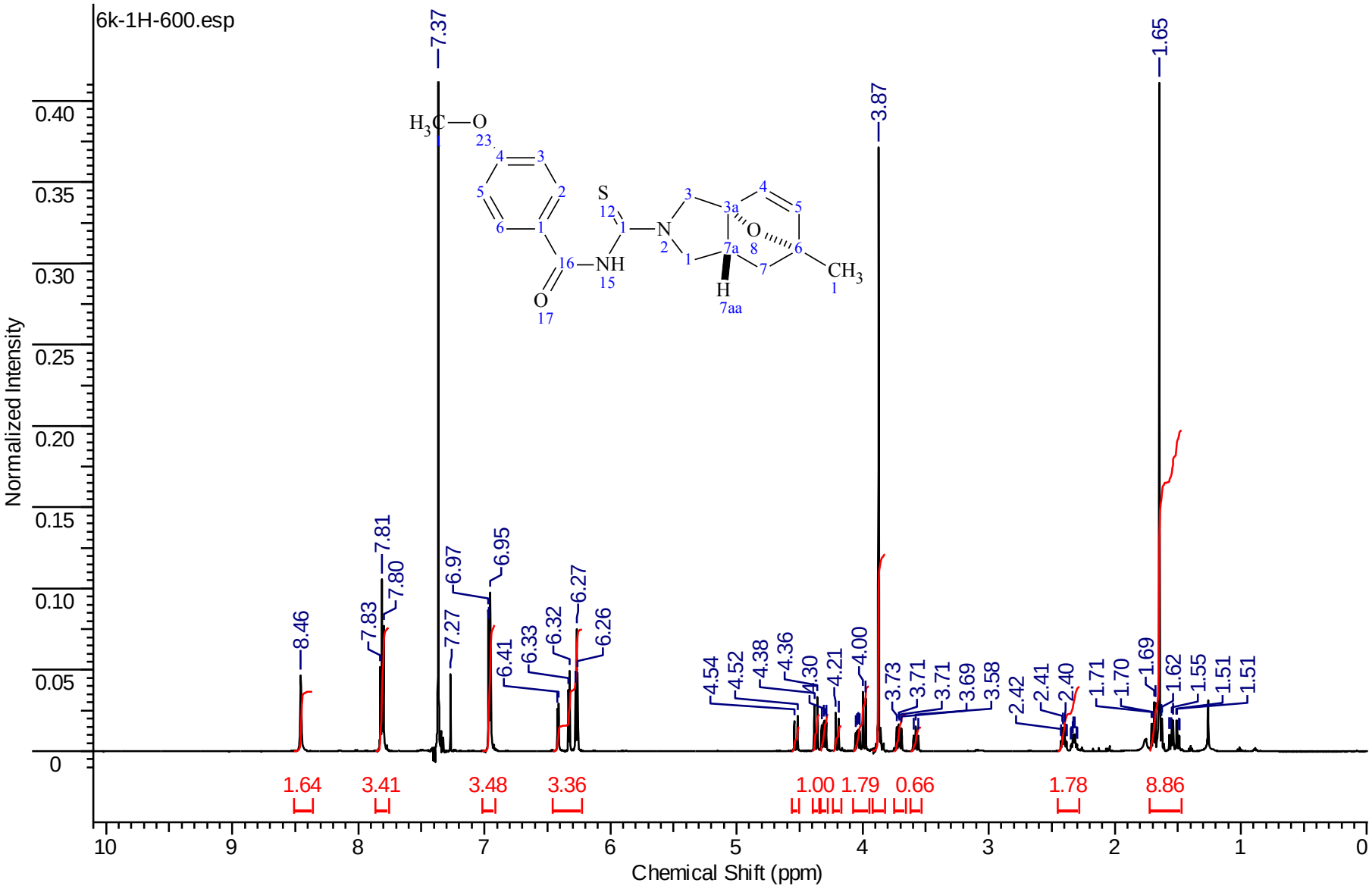


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

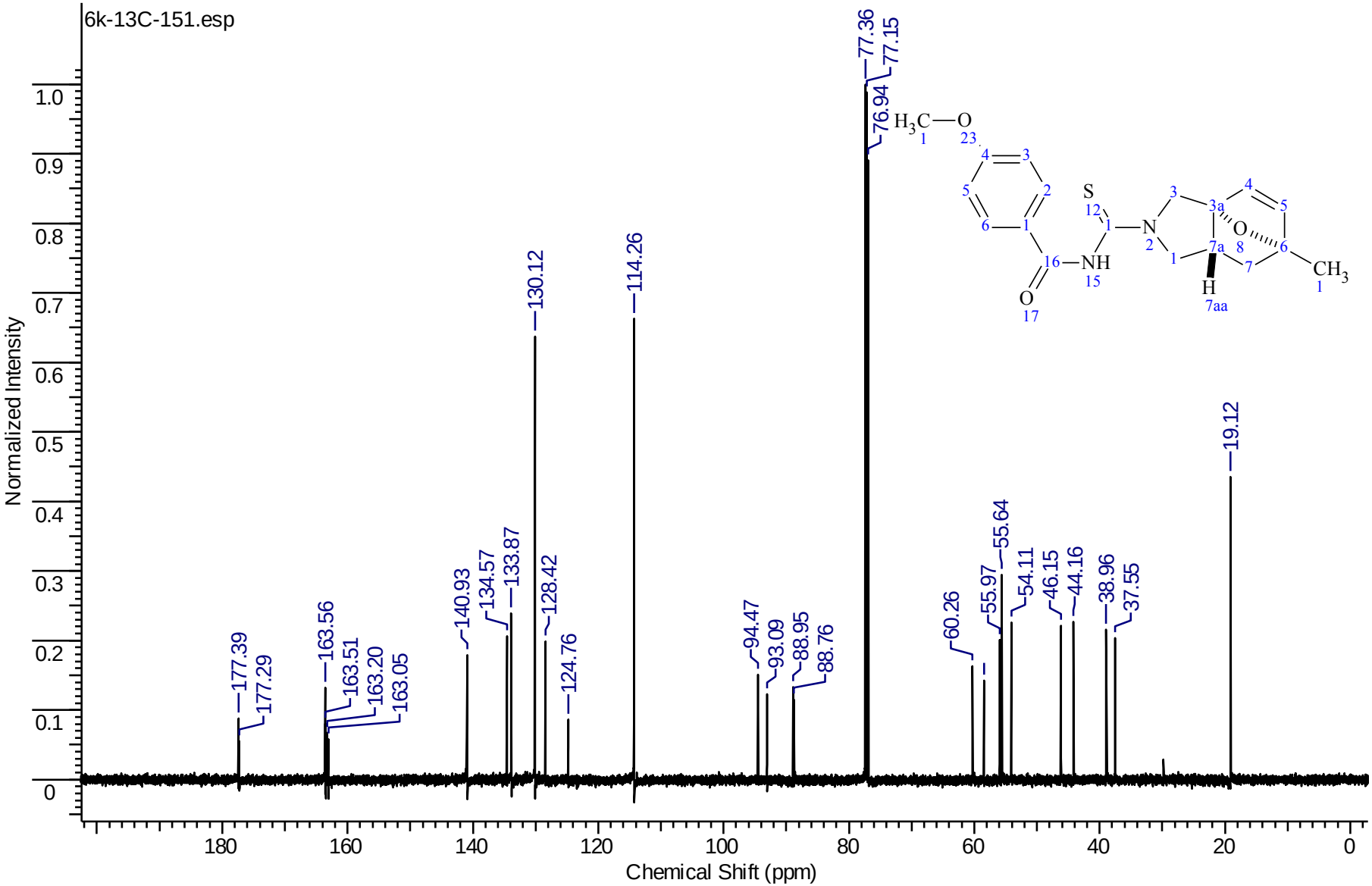


**4-Methoxy-*N*-{[(3a*RS*,6*RS*,7a*RS*)-6-methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6k).**

**$^1$H NMR (600.2 MHz, $CDCl_3$)**

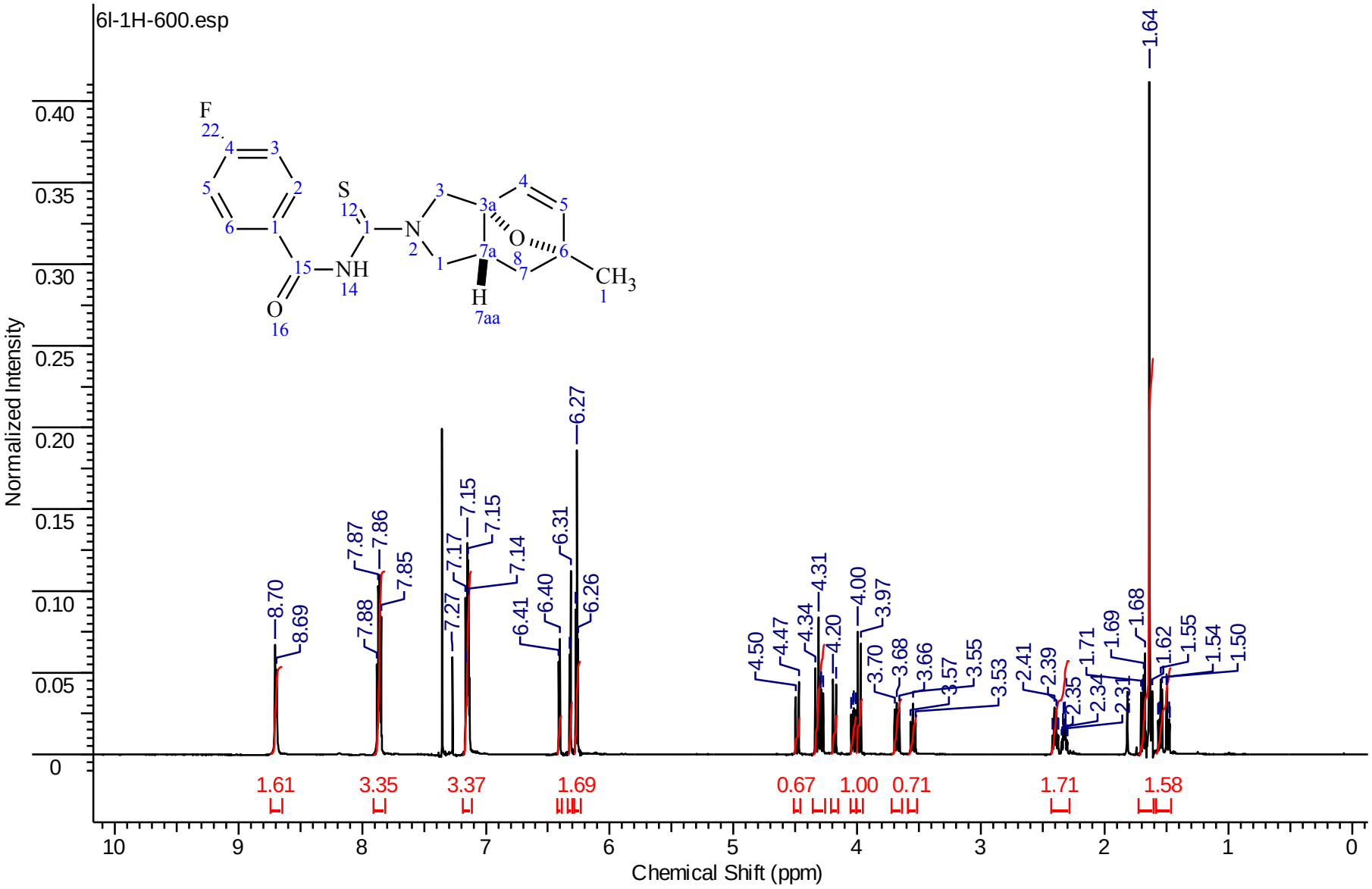


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

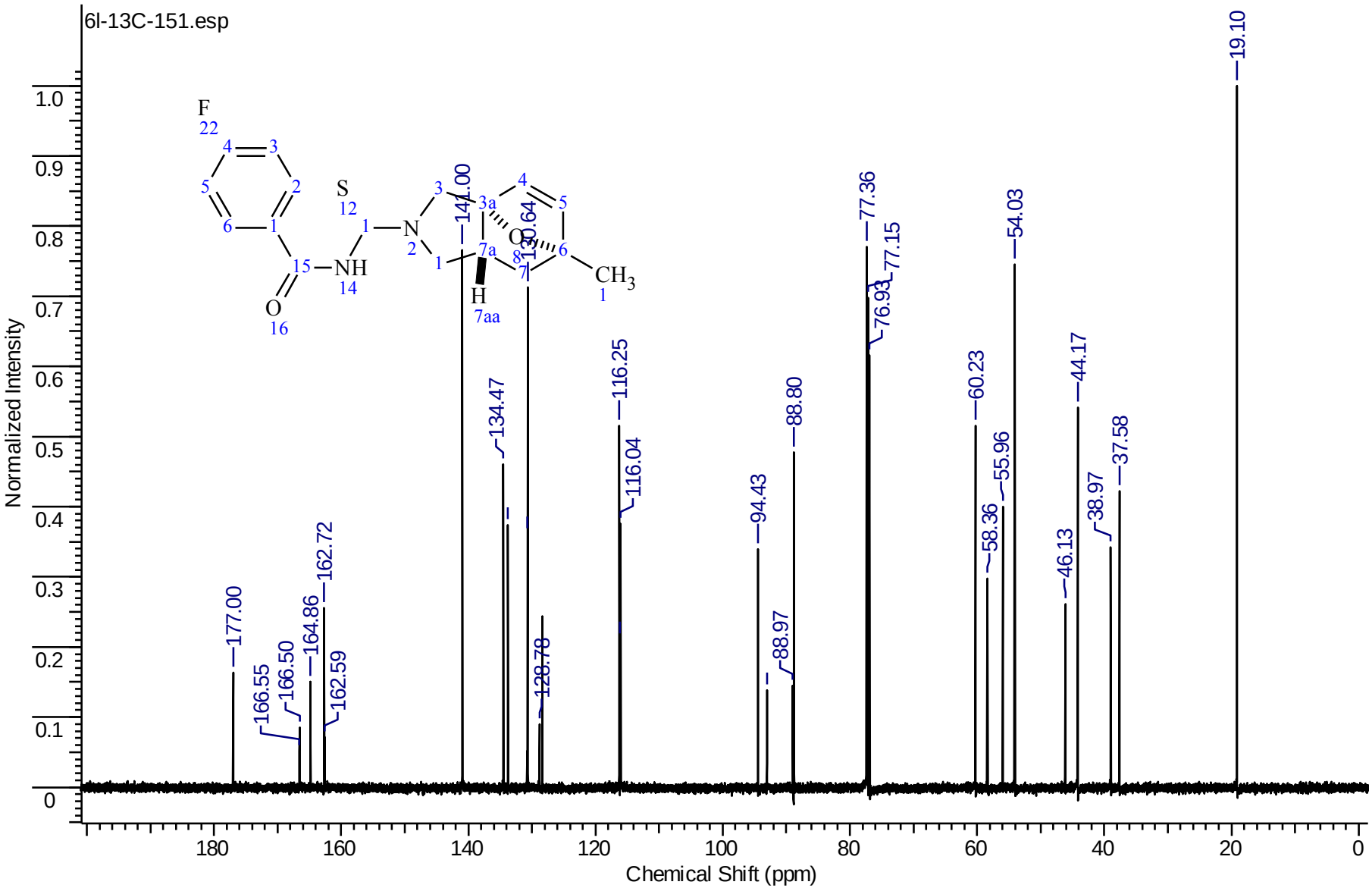


**4-Fluoro-*N*-{[(3a*R*,6*R*,7a*R*)-6-methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6l).**

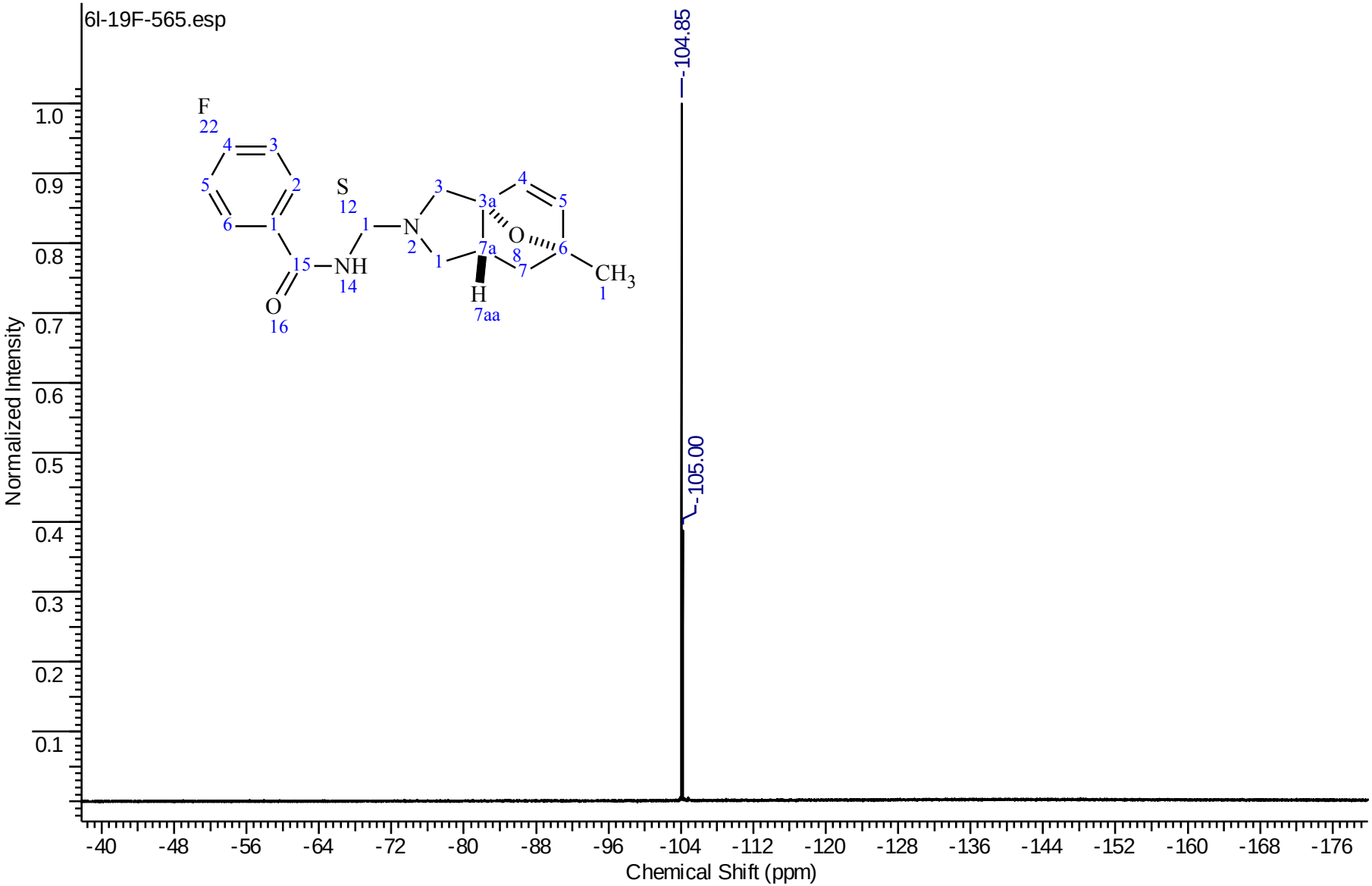
**$^1$H NMR (600.2 MHz, $CDCl_3$)**



**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

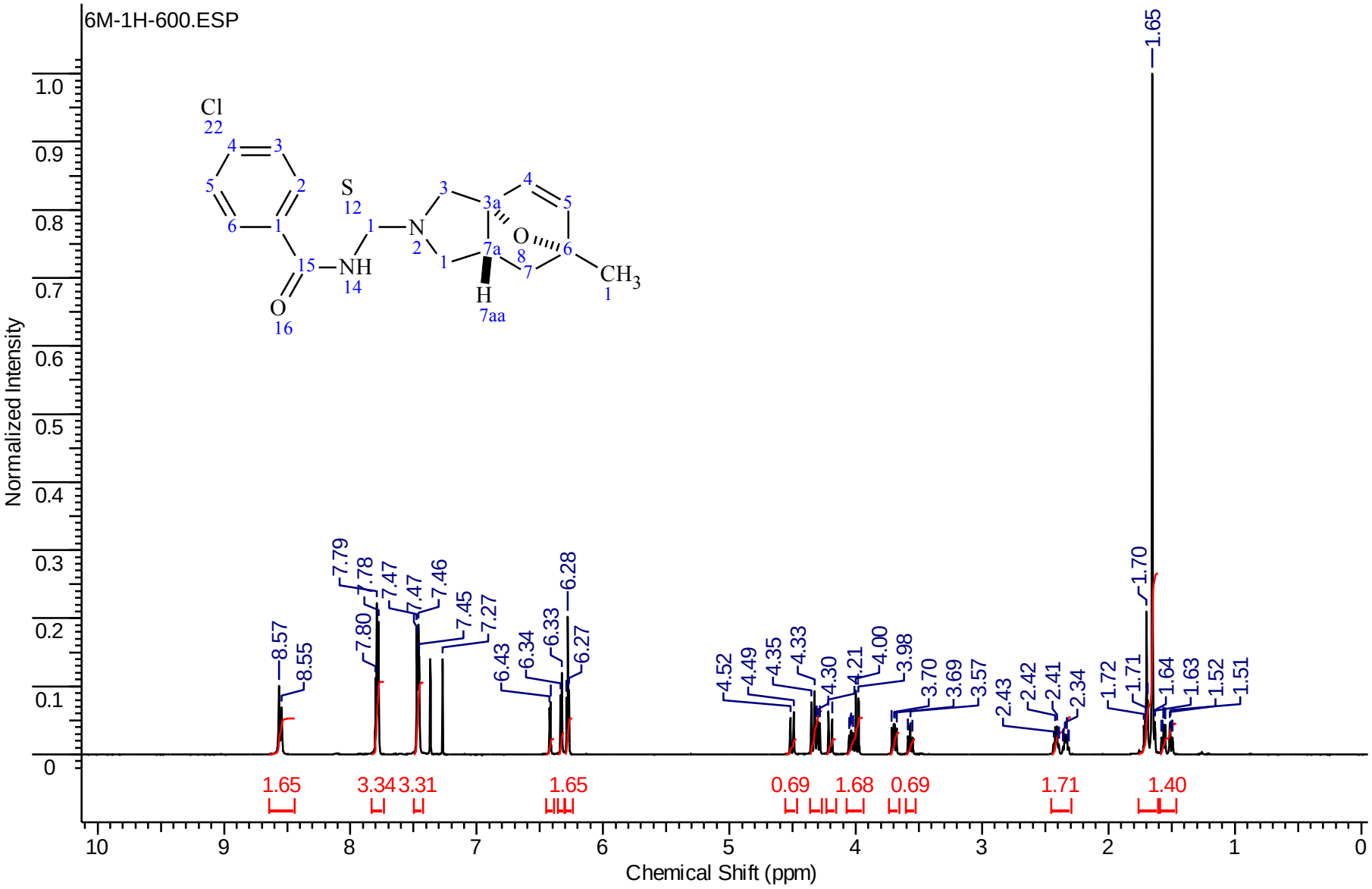


**$^{19}$F NMR (564.7 MHz, $CDCl_3$)**

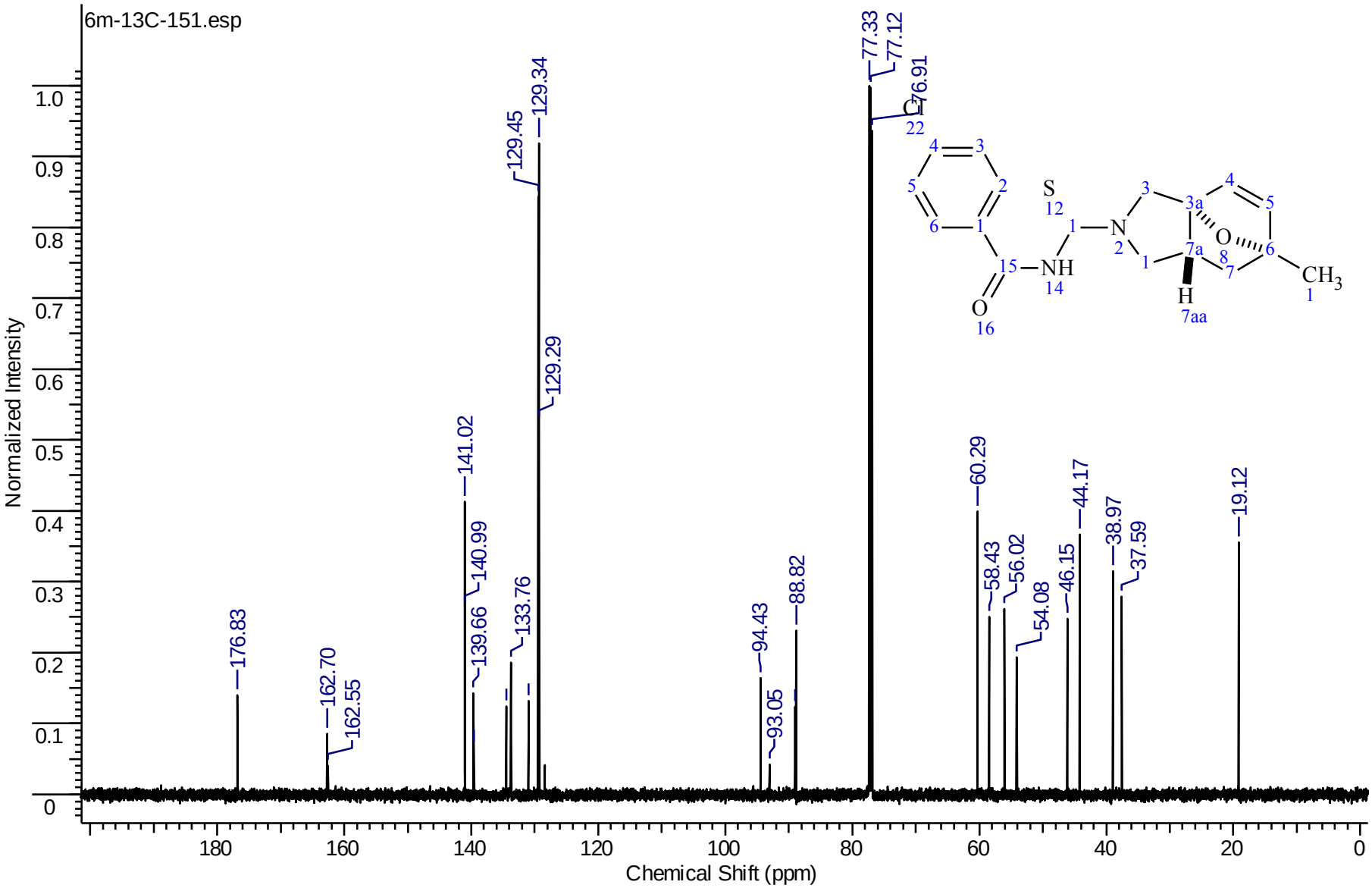


**4-Chloro-*N*-{[(3a*RS*,6*RS*,7a*RS*)-6-methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6m).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

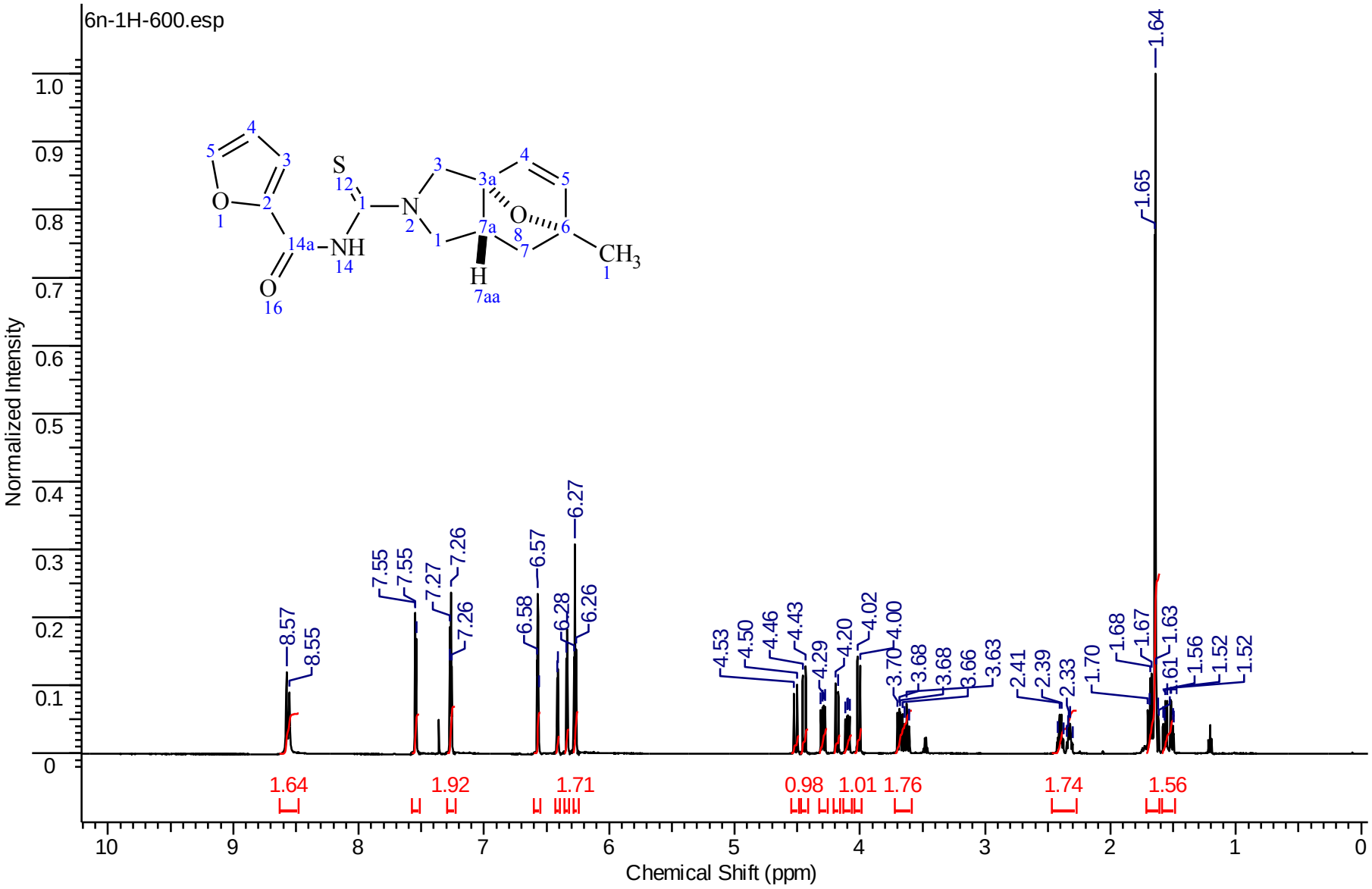


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

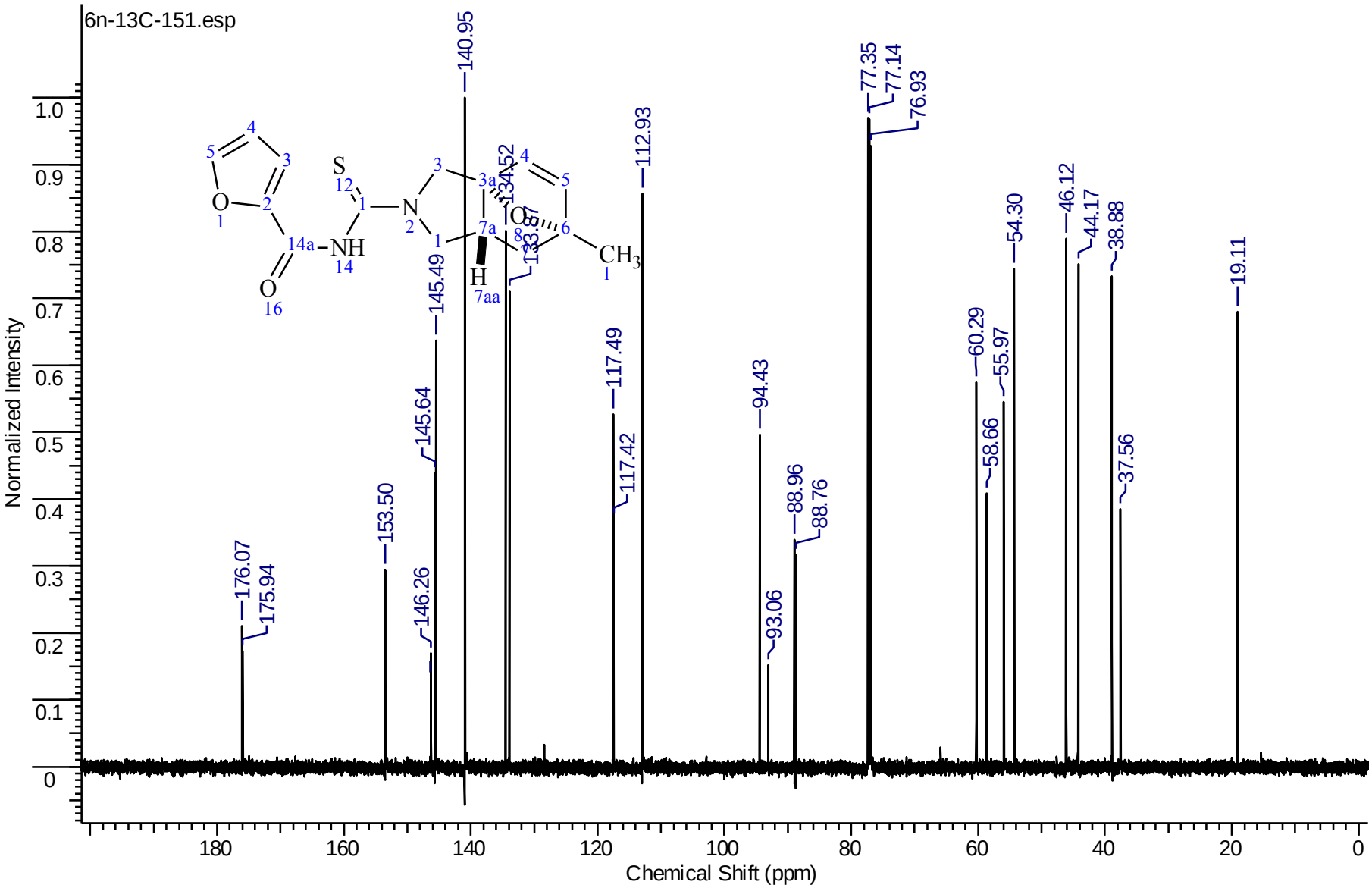


***N*-{[(3a*RS*,6*RS*,7a*RS*)-6-Methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}-2-furamide (6n).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

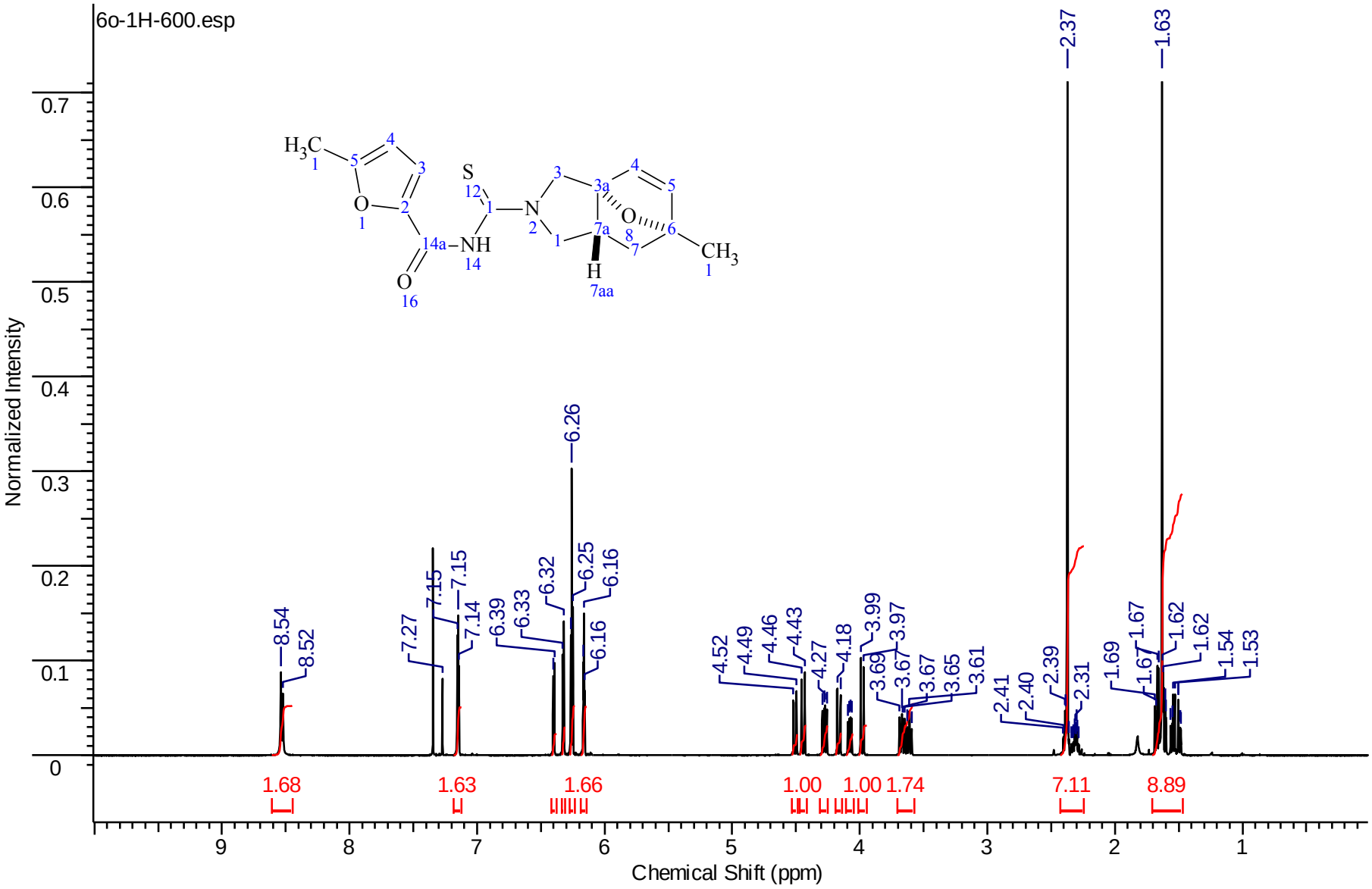


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

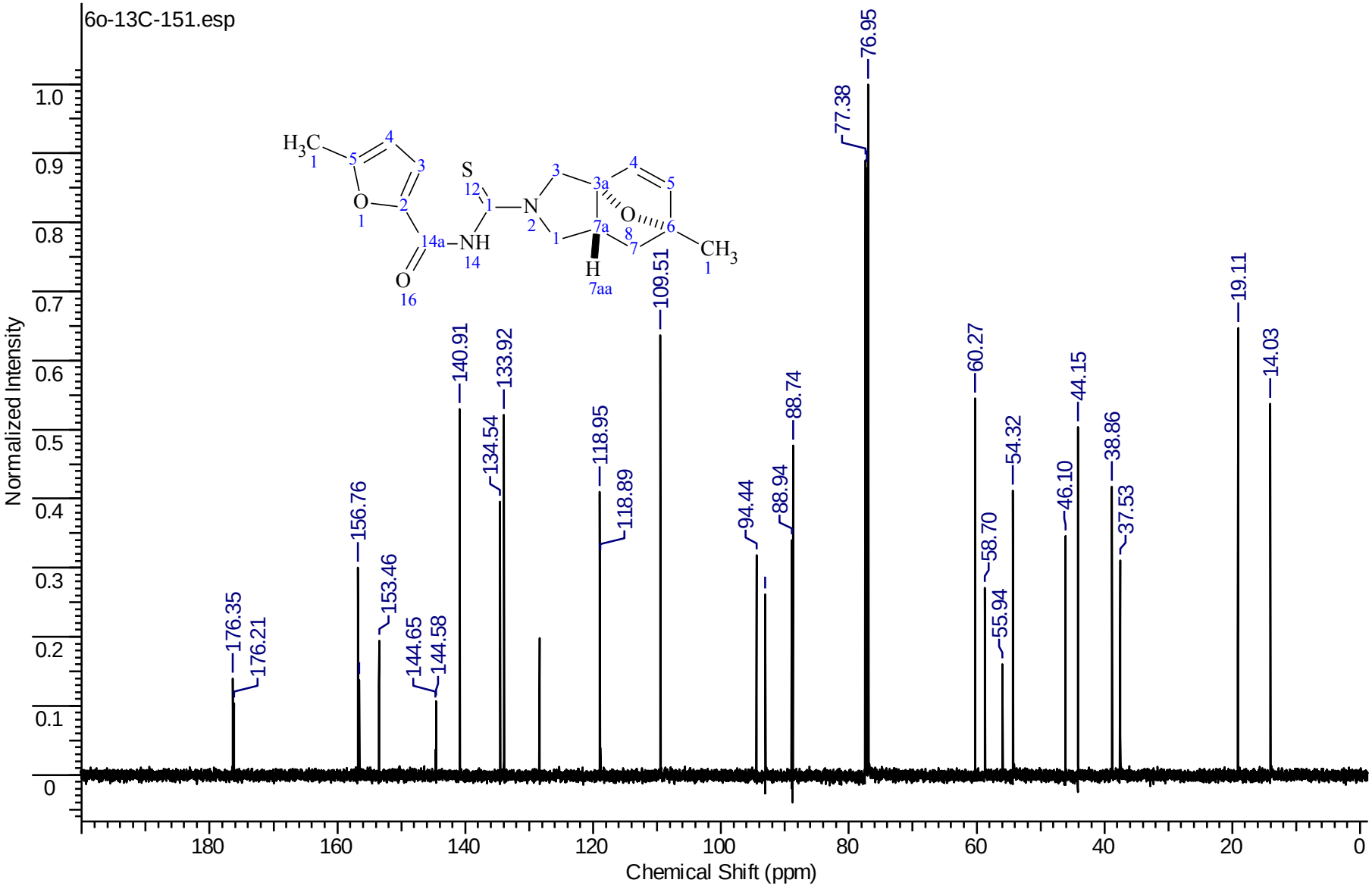


**5-Methyl-*N*-{[(3a*RS*,6*RS*,7a*RS*)-6-methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}-2-furamide (6o).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

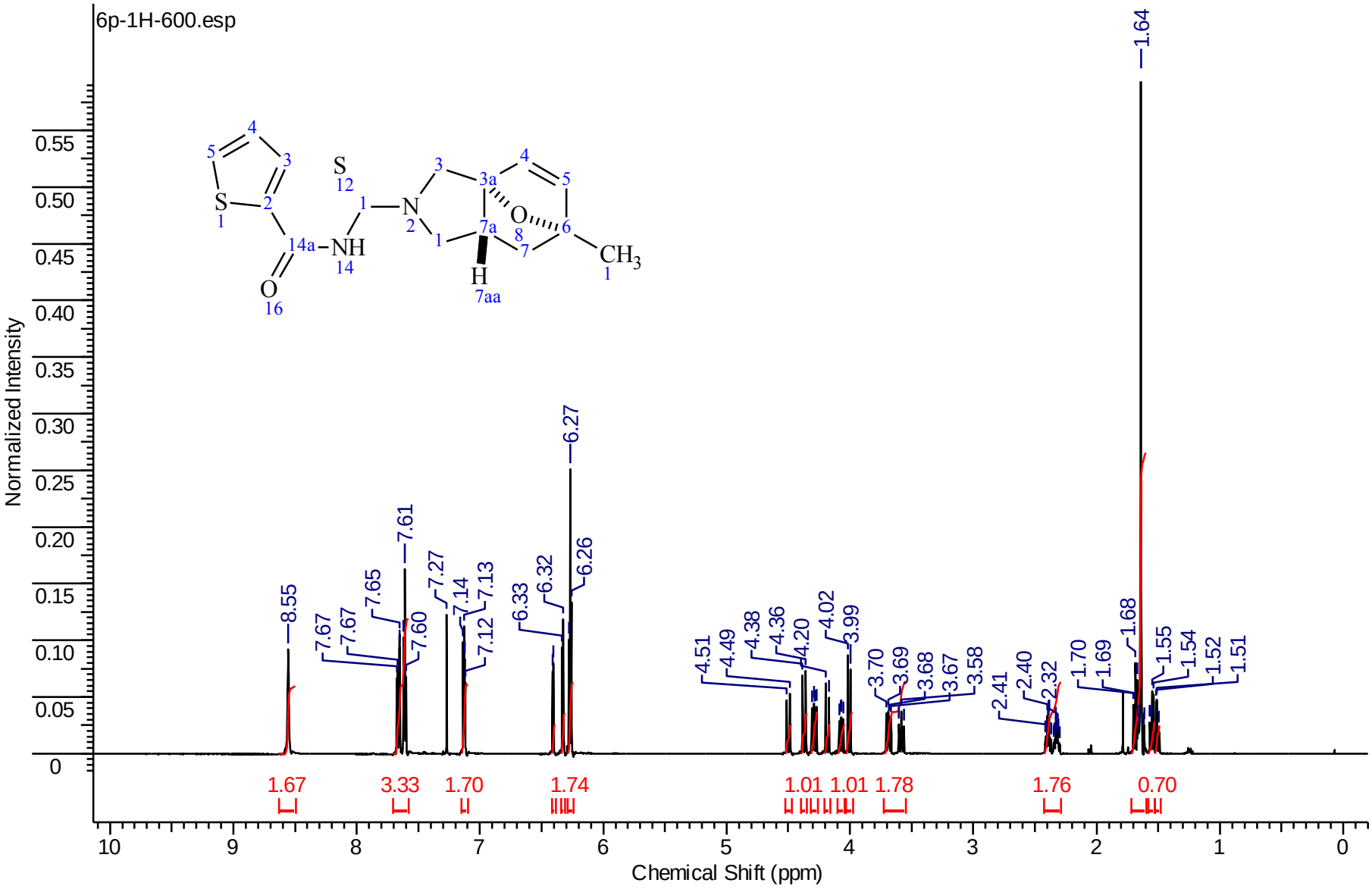


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

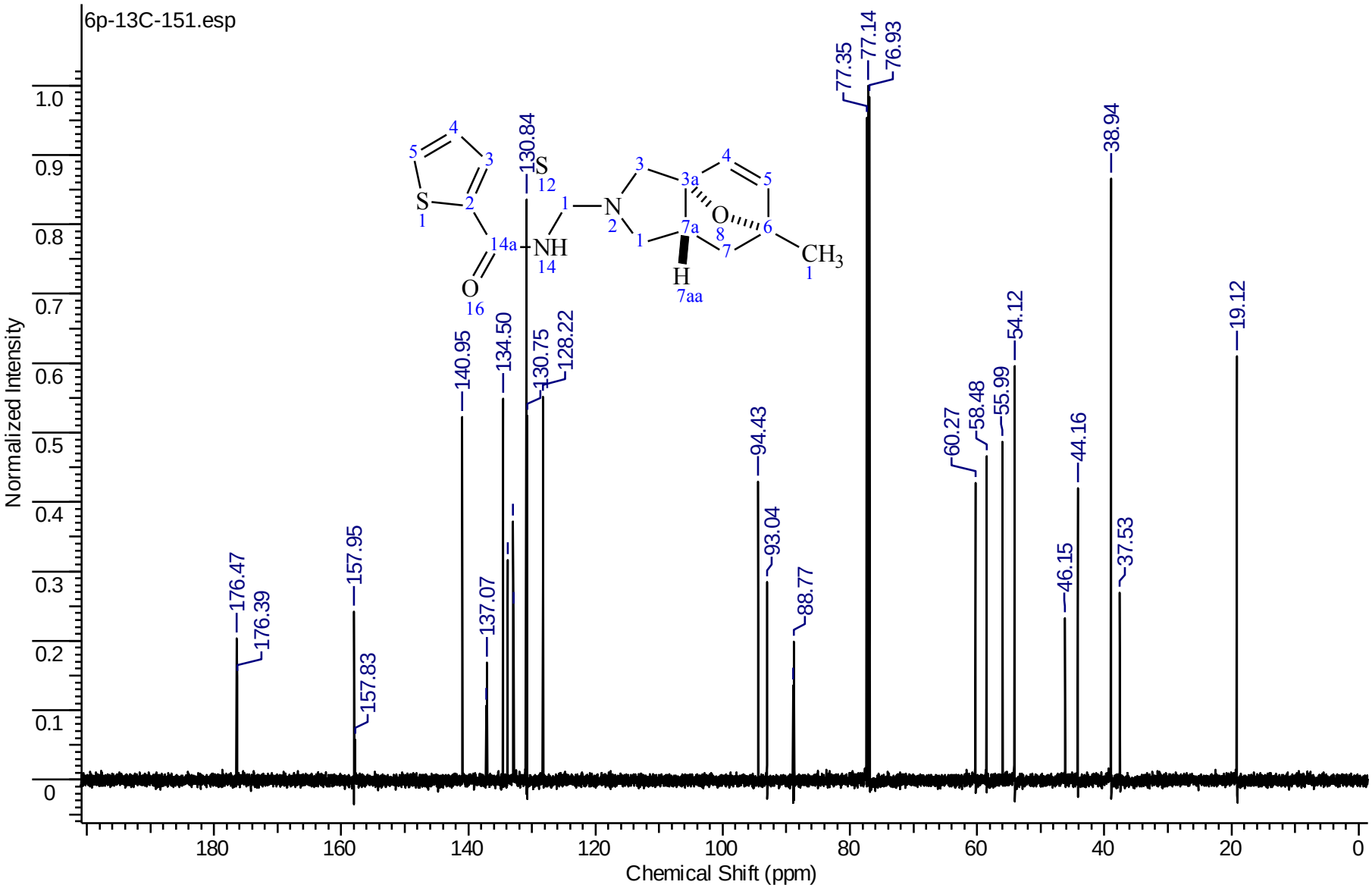


***N*-{[(3a*RS*,6*RS*,7a*RS*)-6-Methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}thiophene-2-carboxamide (6p).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

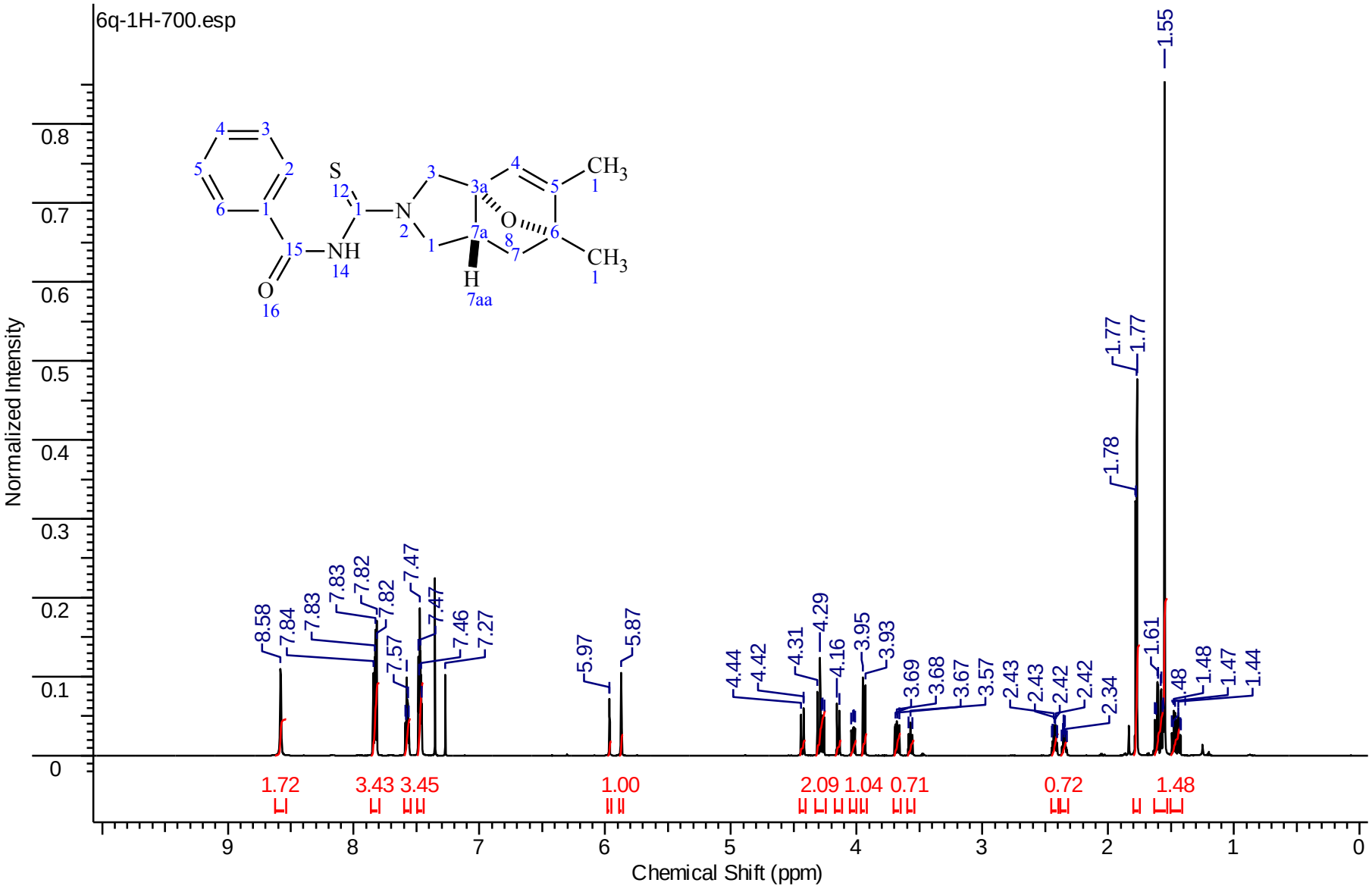


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

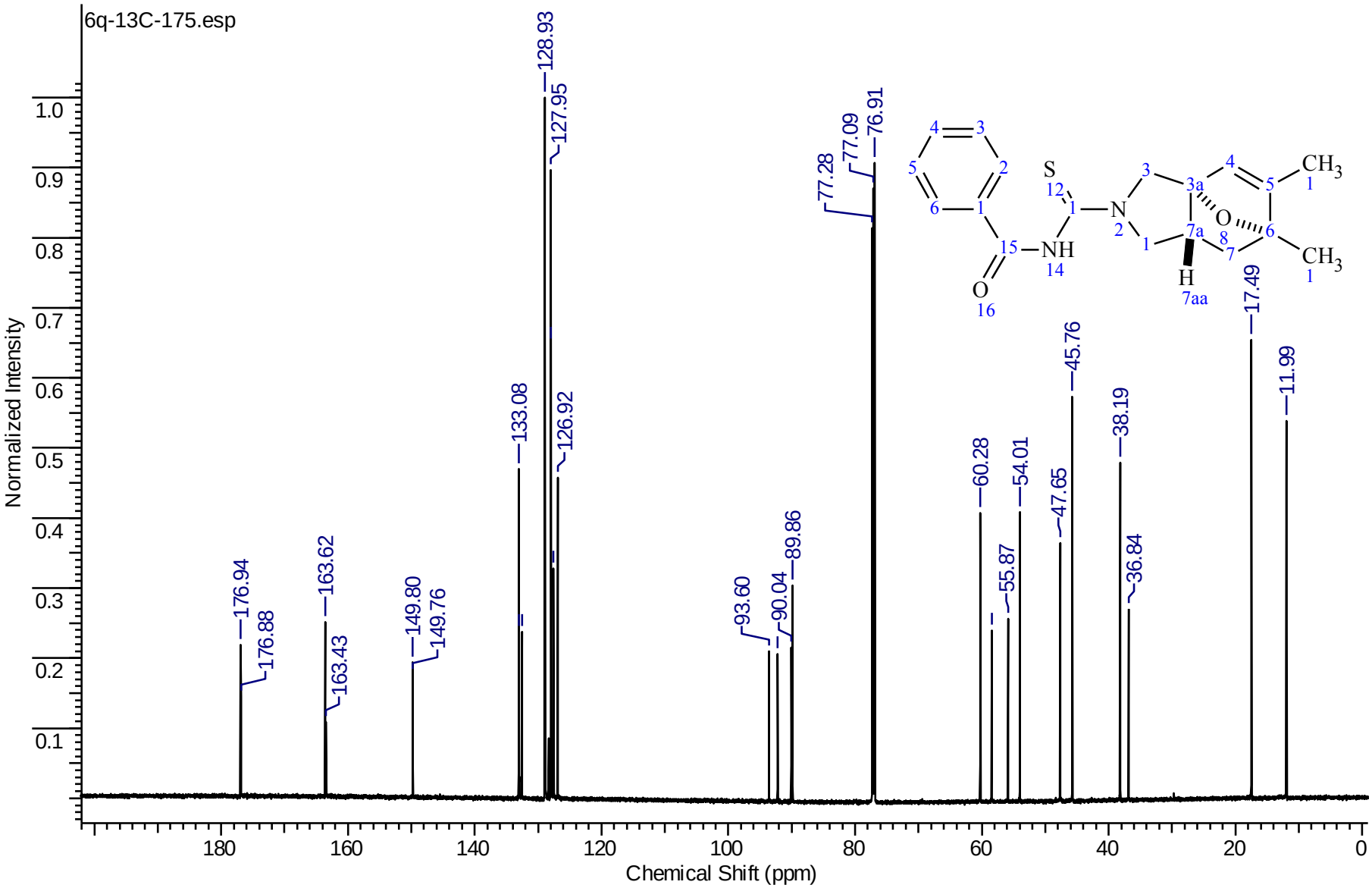


***N*-{[(3a*RS*,6*RS*,7a*RS*)-5,6-Dimethyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6q).**

**$^{1}$H NMR (700.2 MHz, $CDCl_3$)**

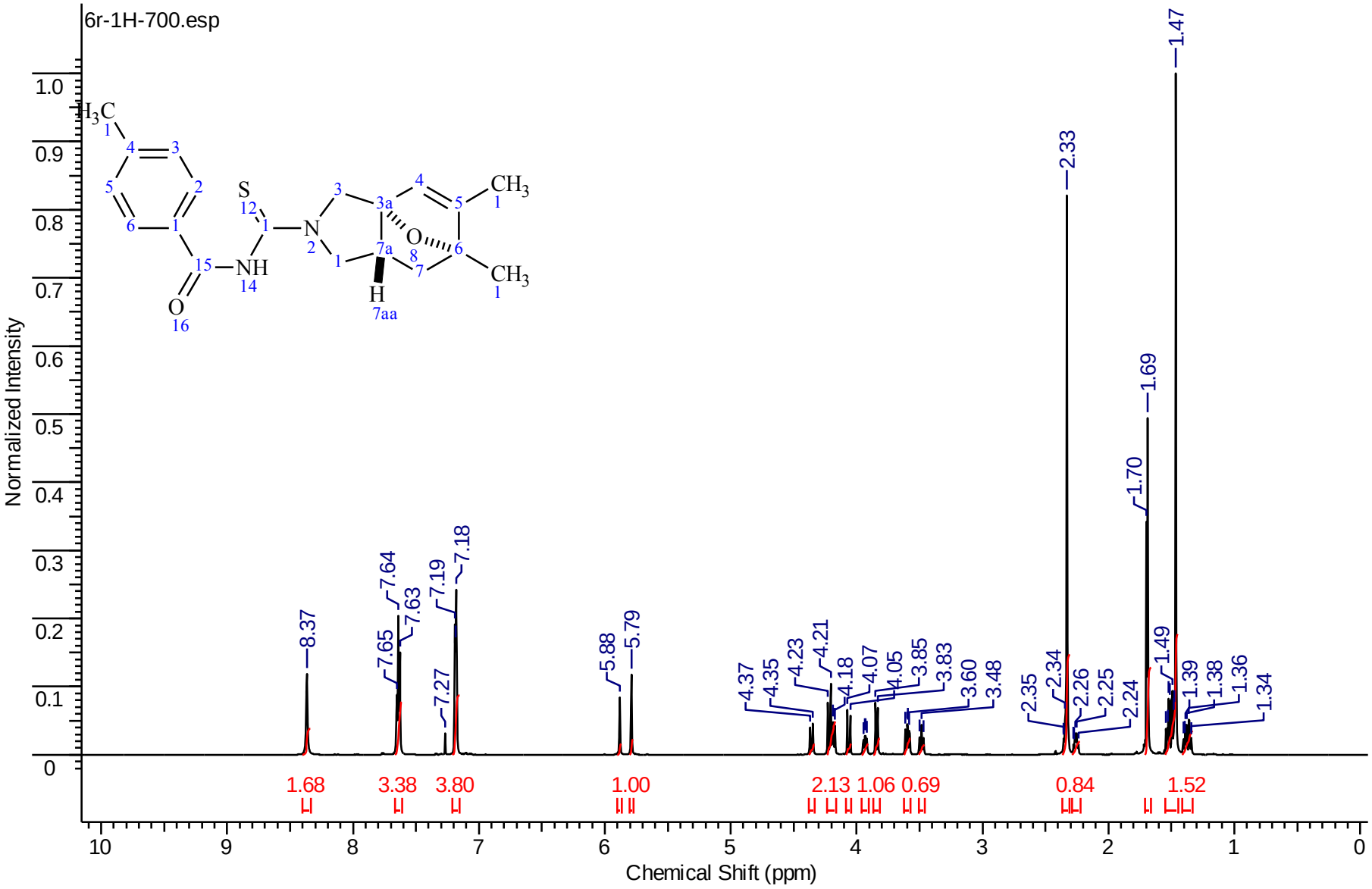


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**

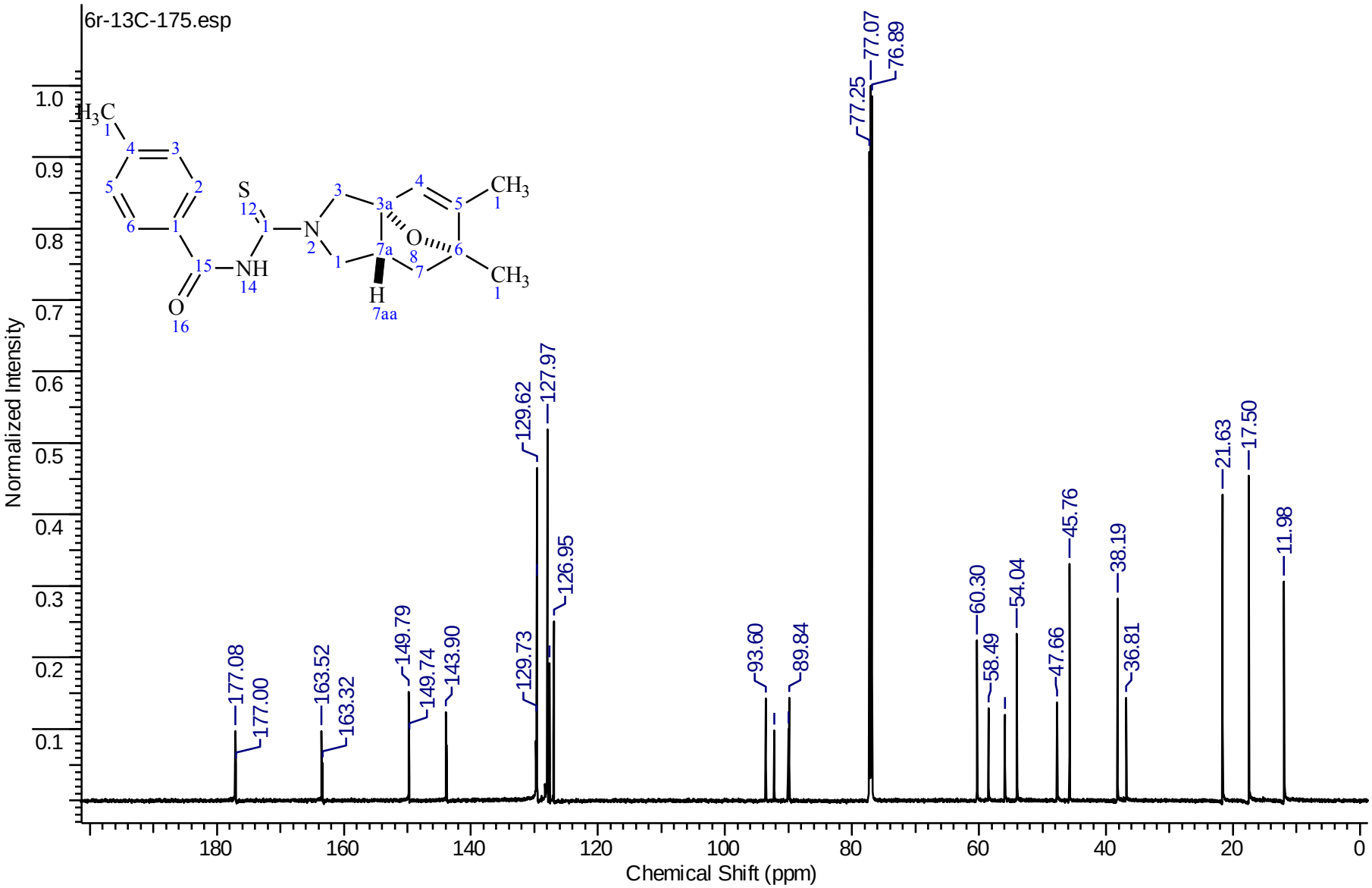


***N*-{[(3a*RS*,6*RS*,7a*RS*)-5,6-dimethyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}-4-methylbenzamide (6r).**

**$^{1}$H NMR (700.2 MHz, $CDCl_3$)**

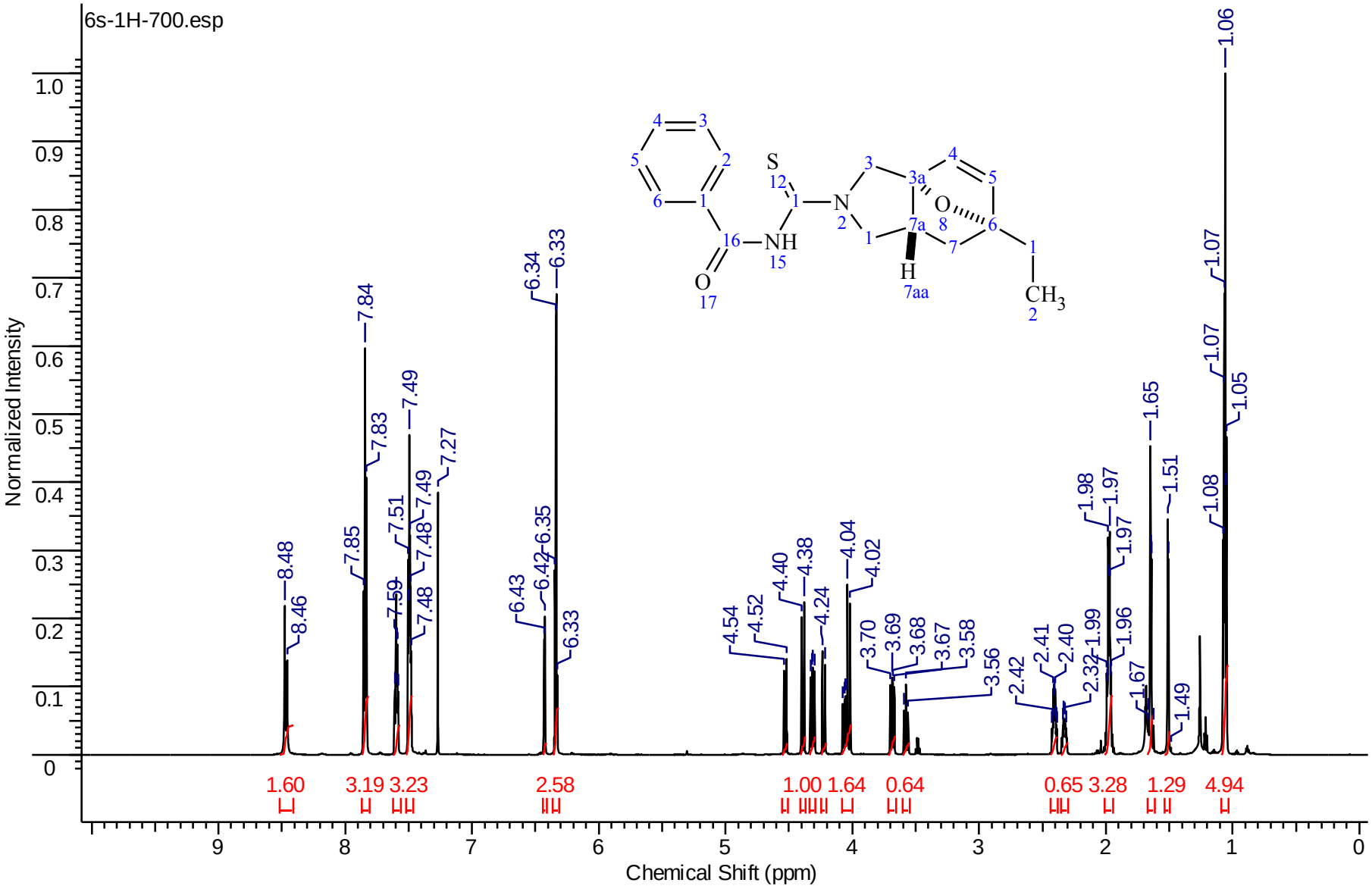


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**

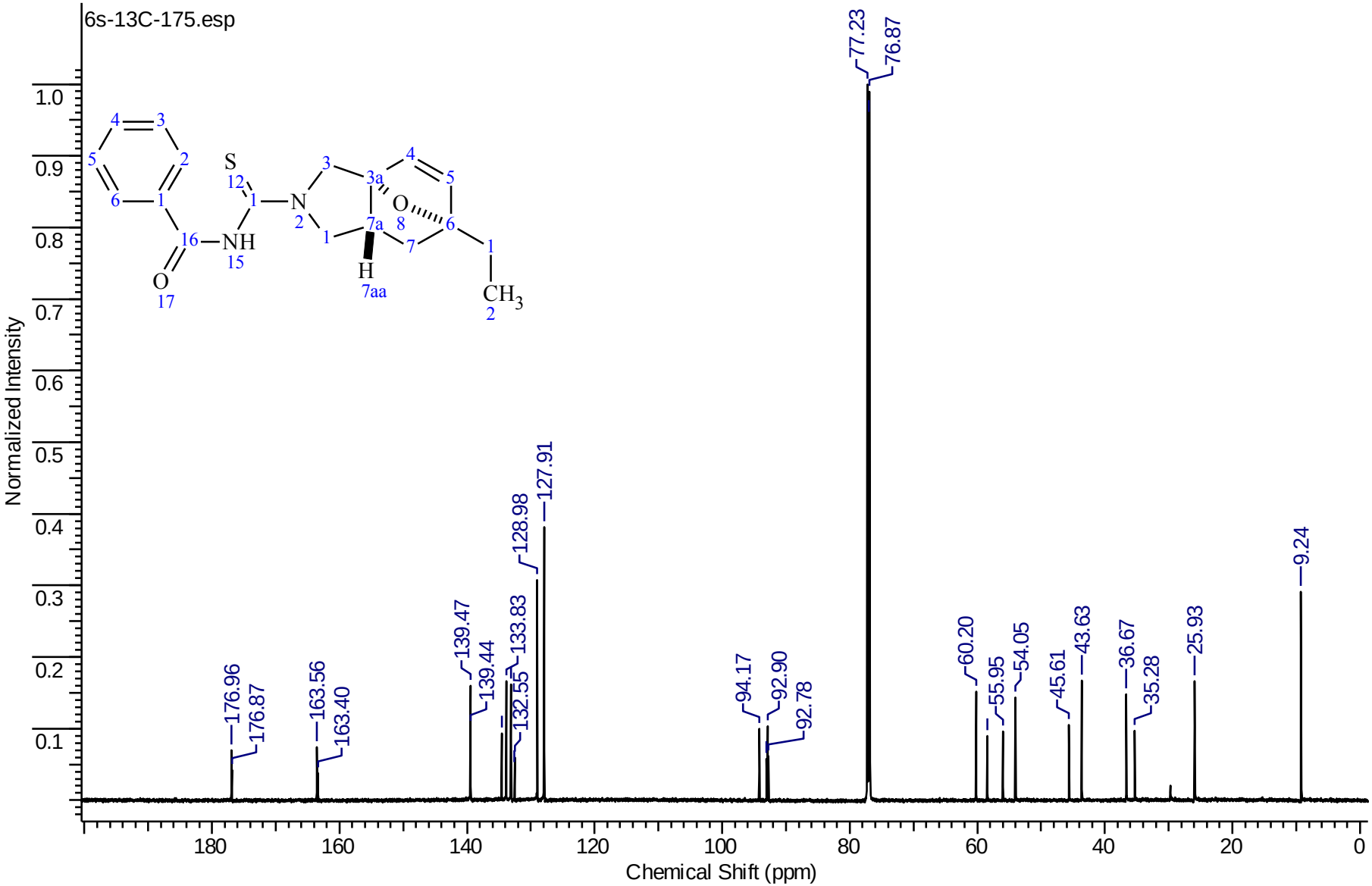


***N*-{[(3a*RS*,6*RS*,7a*RS*)-6-Ethyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6s).**

**$^{1}$H NMR (700.2 MHz, $CDCl_3$)**

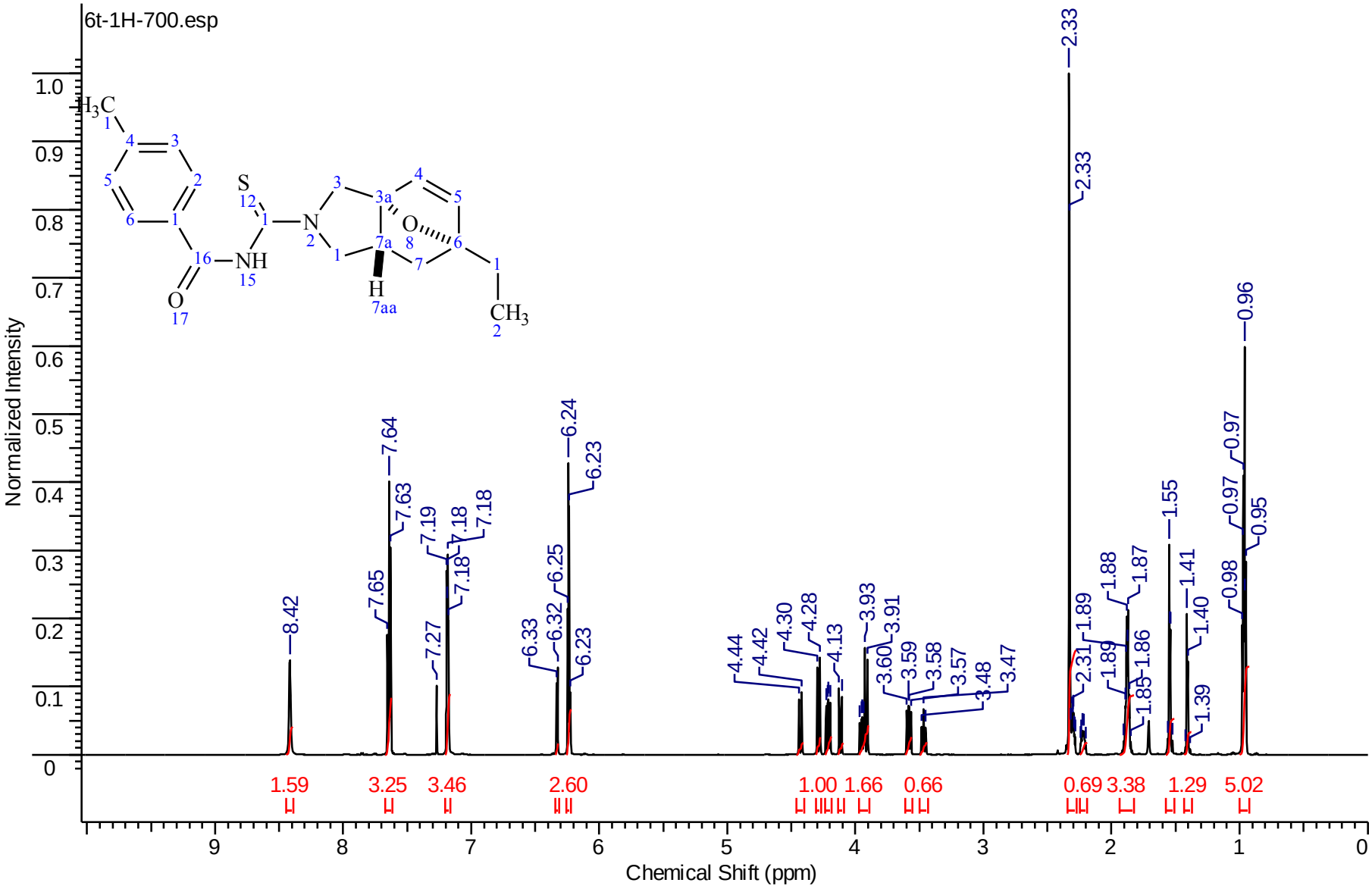


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**

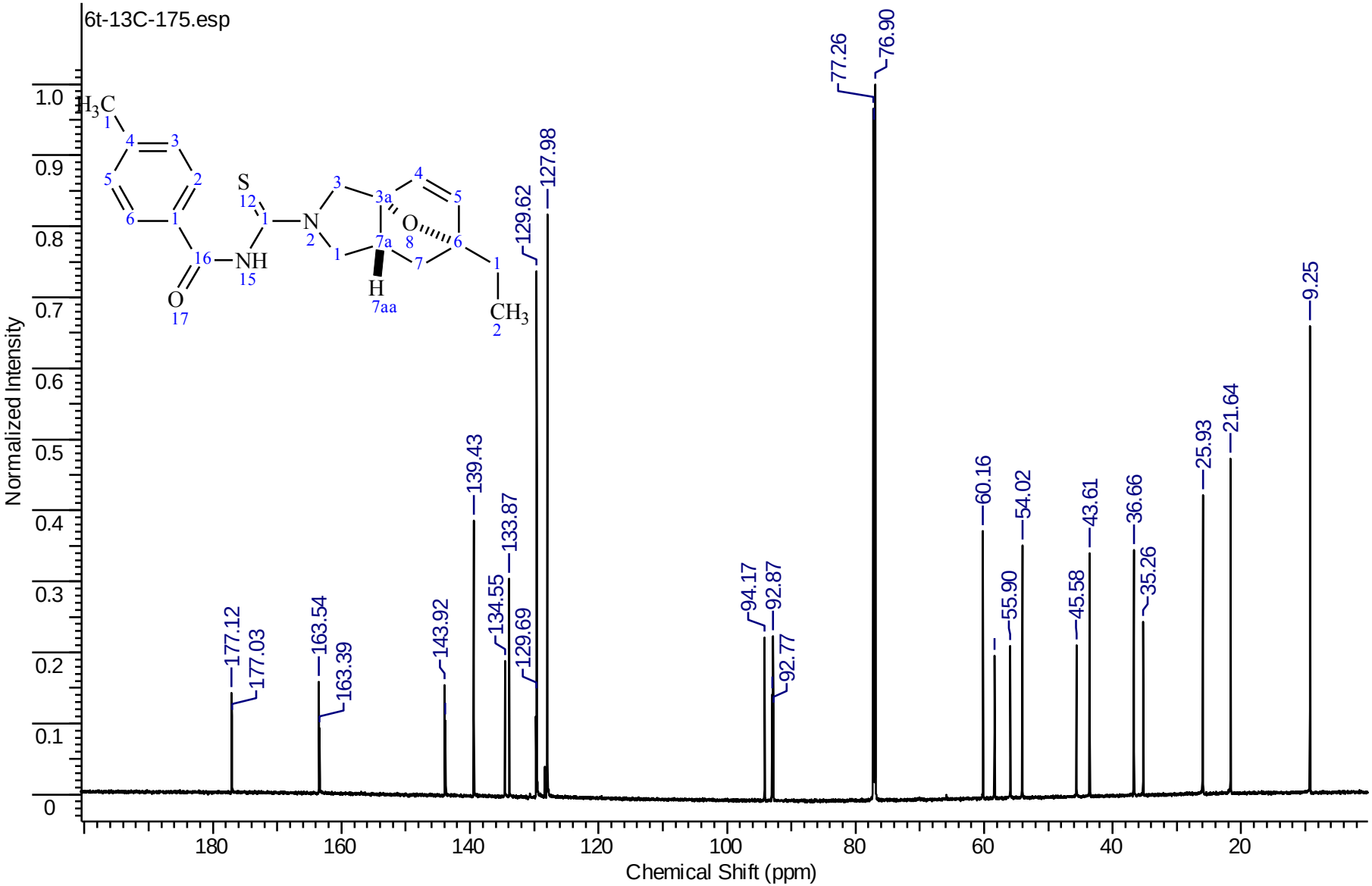


***N*-{[(3a*RS*,6*RS*,7a*RS*)-6-Ethyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}-4-methylbenzamide (6t).**

**$^1$H NMR (700.2 MHz, $CDCl_3$)**

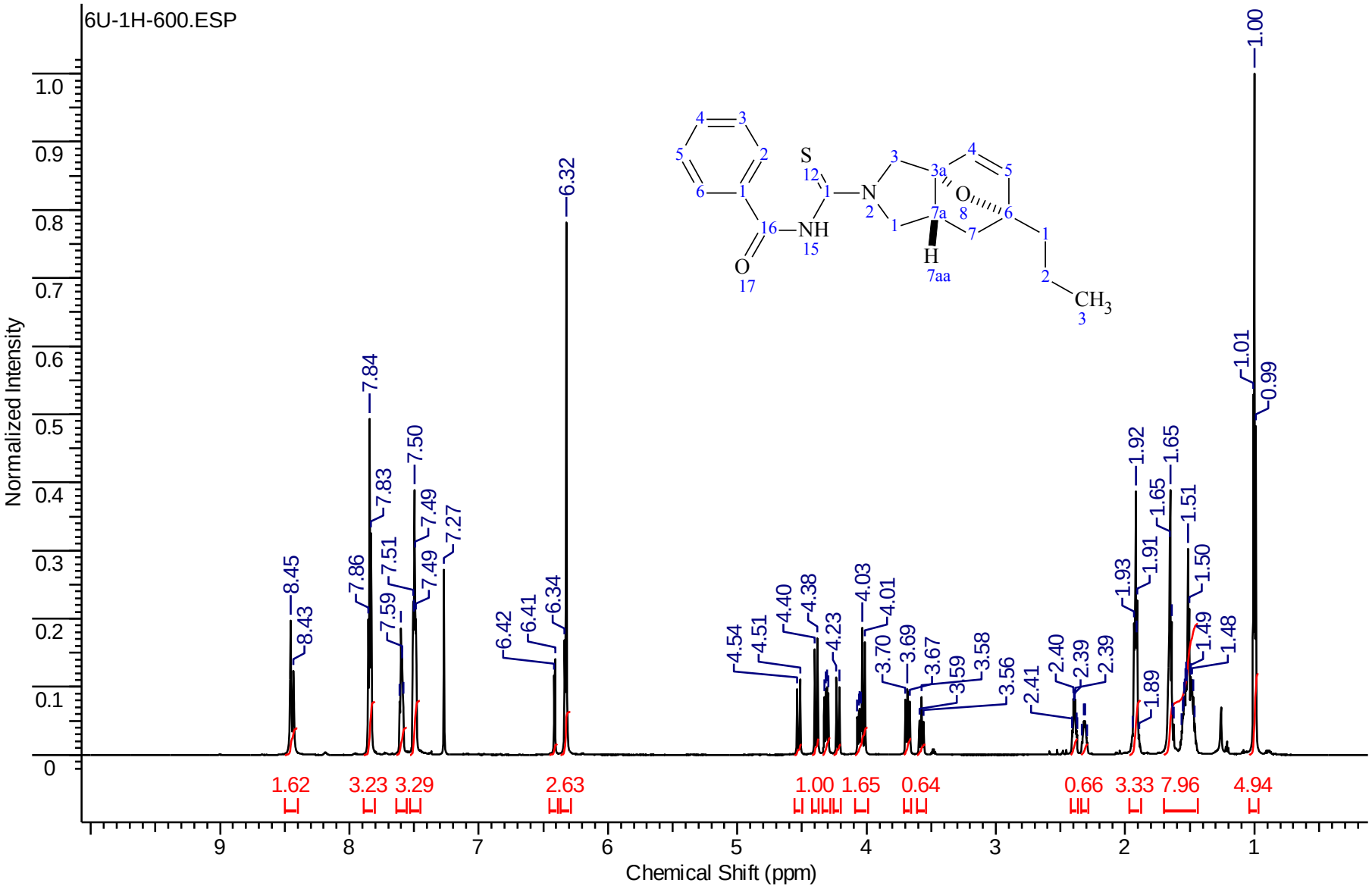


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**

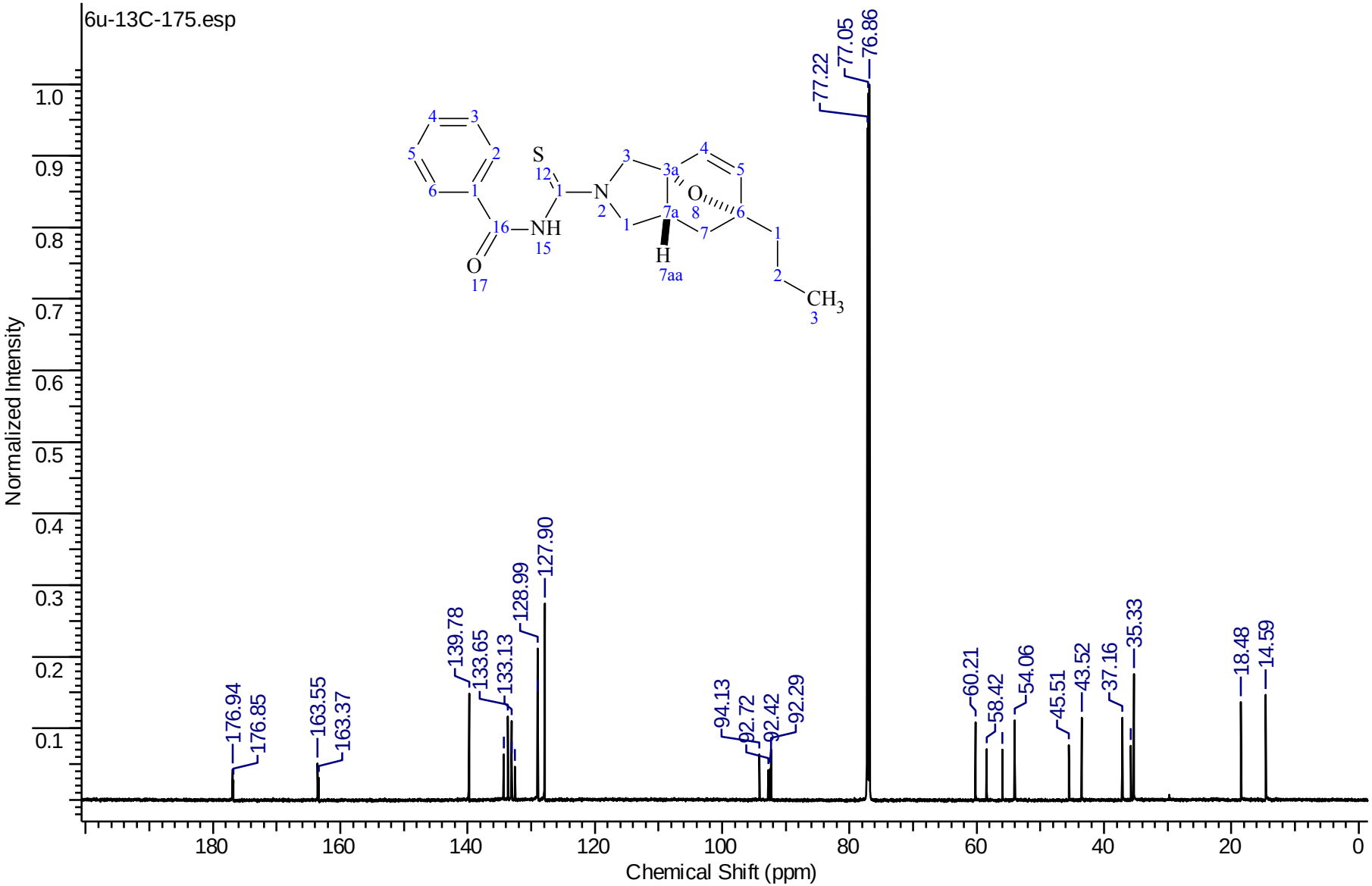


***N*-{[(3a*RS*,6*RS*,7a*RS*)-6-Propyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6u).**

**$^{1}$H NMR (700.2 MHz, $CDCl_3$)**

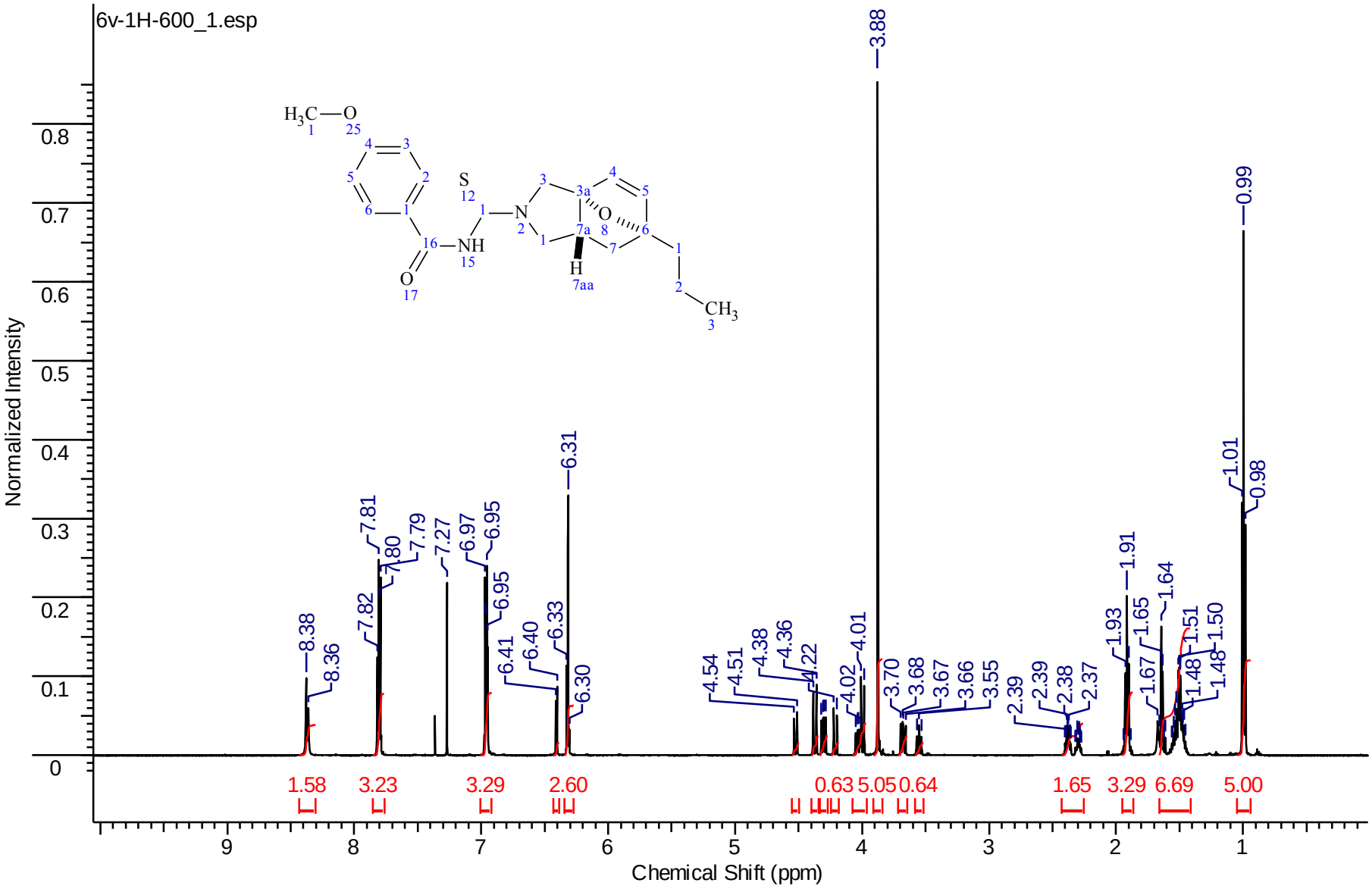


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**

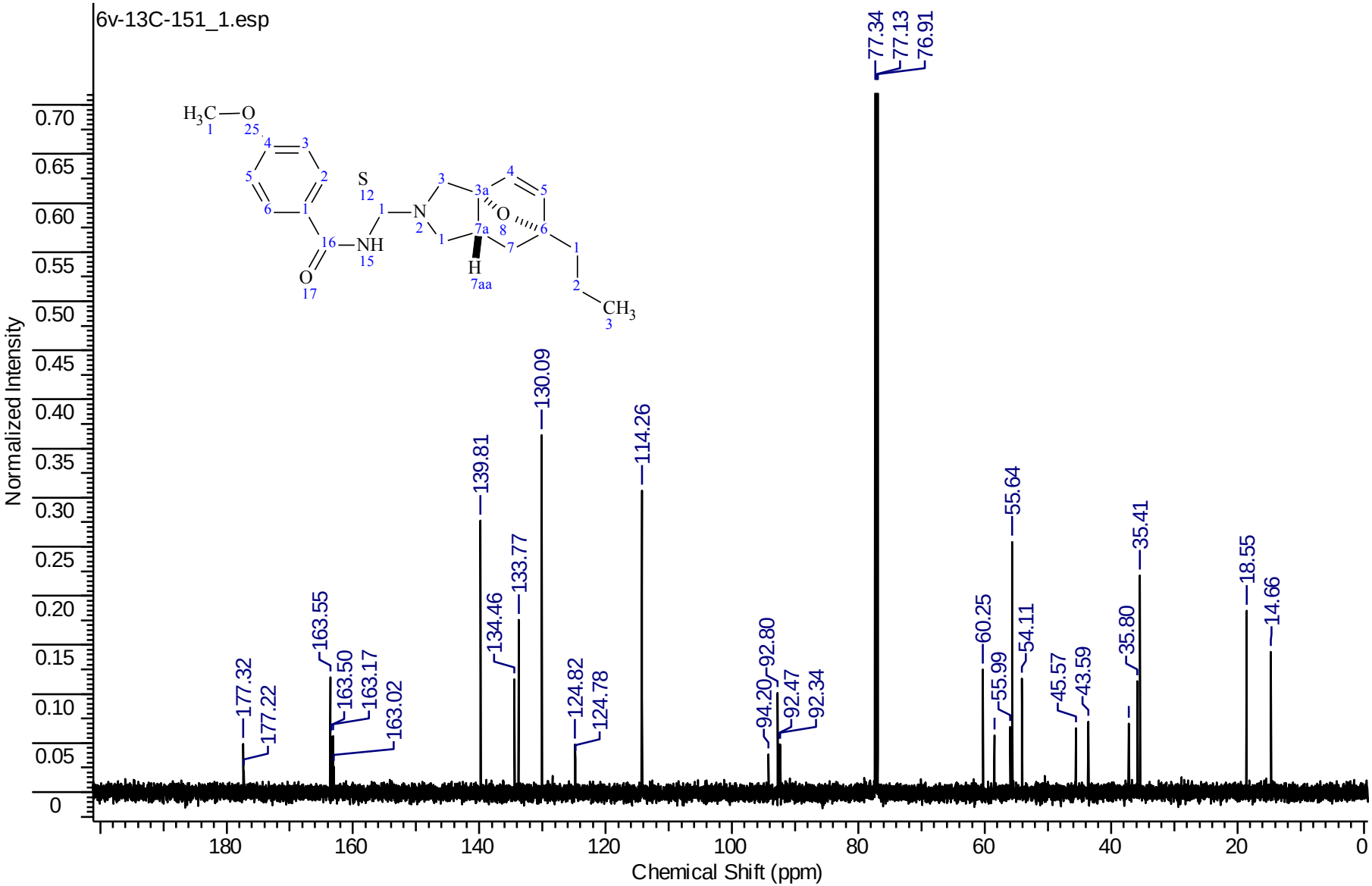


**4-Methoxy-*N*-{[(3a*RS*,6*RS*,7a*RS*)-6-propyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6v).**

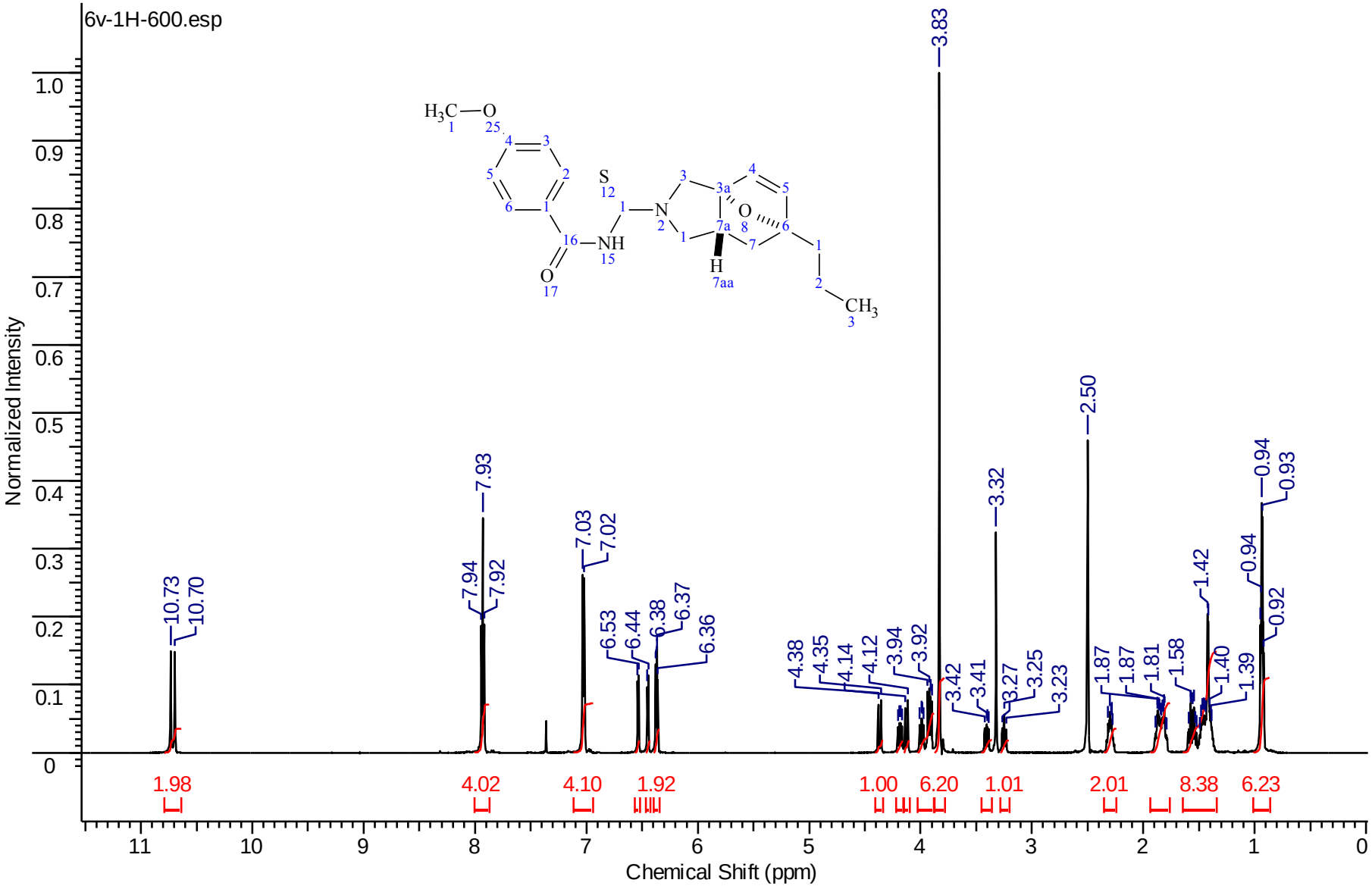
**$^1$H NMR (600.2 MHz, $CDCl_3$)**



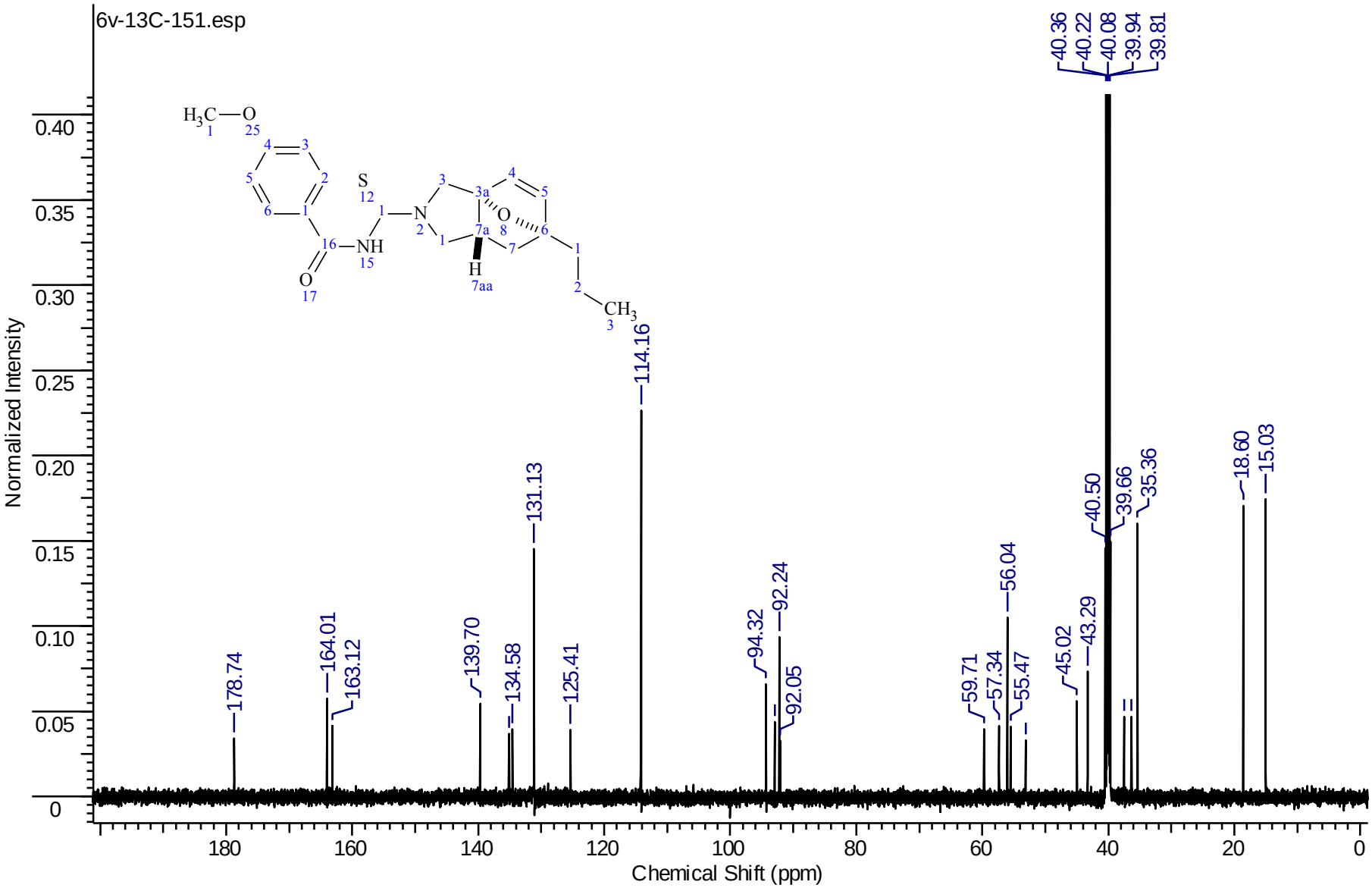
**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**



**$^{1}$H NMR (600.2 MHz, DMSO-$d_6$)**

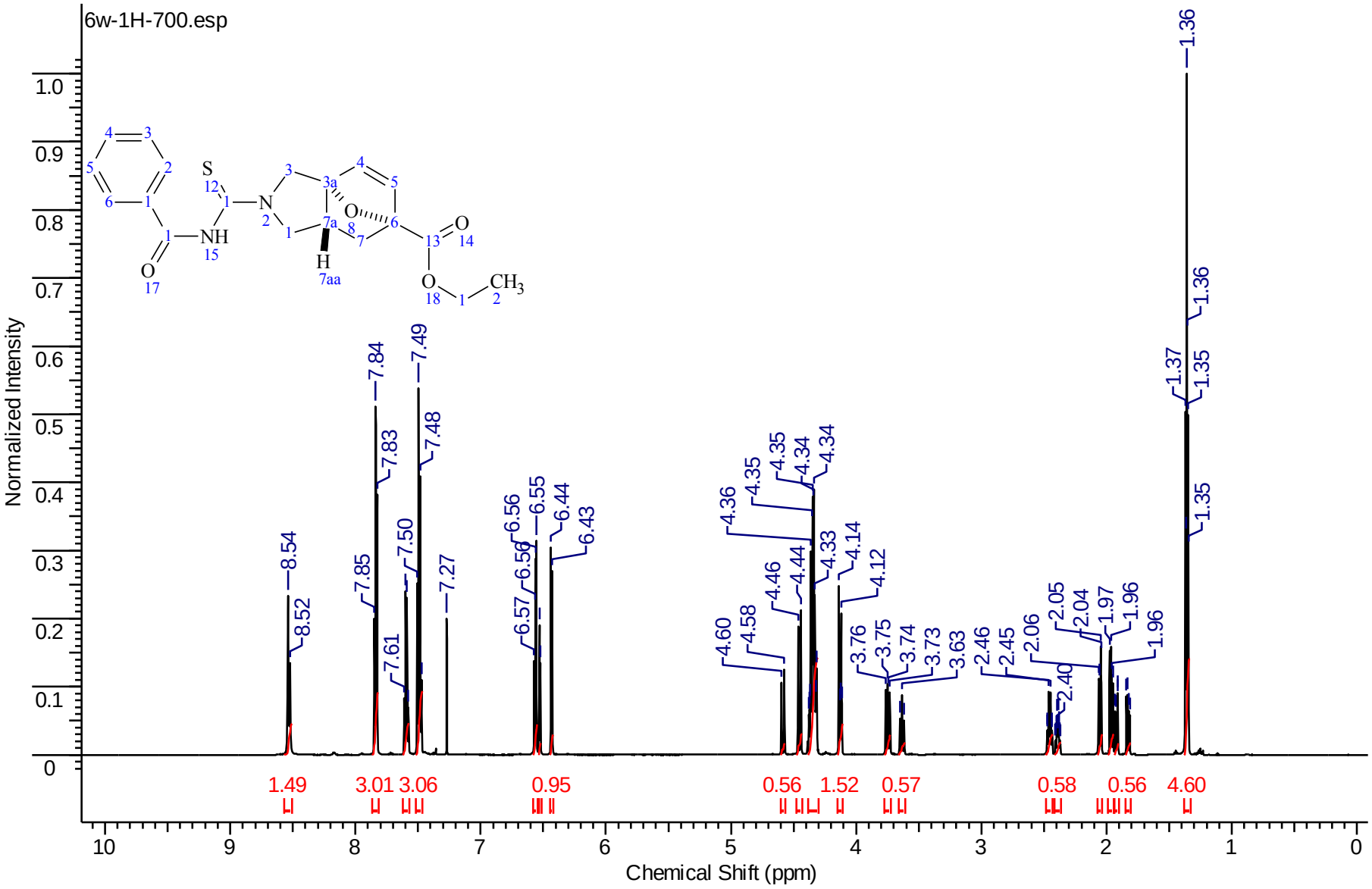


**$^{13}$C NMR (150.9 MHz, DMSO-$d_6$)**

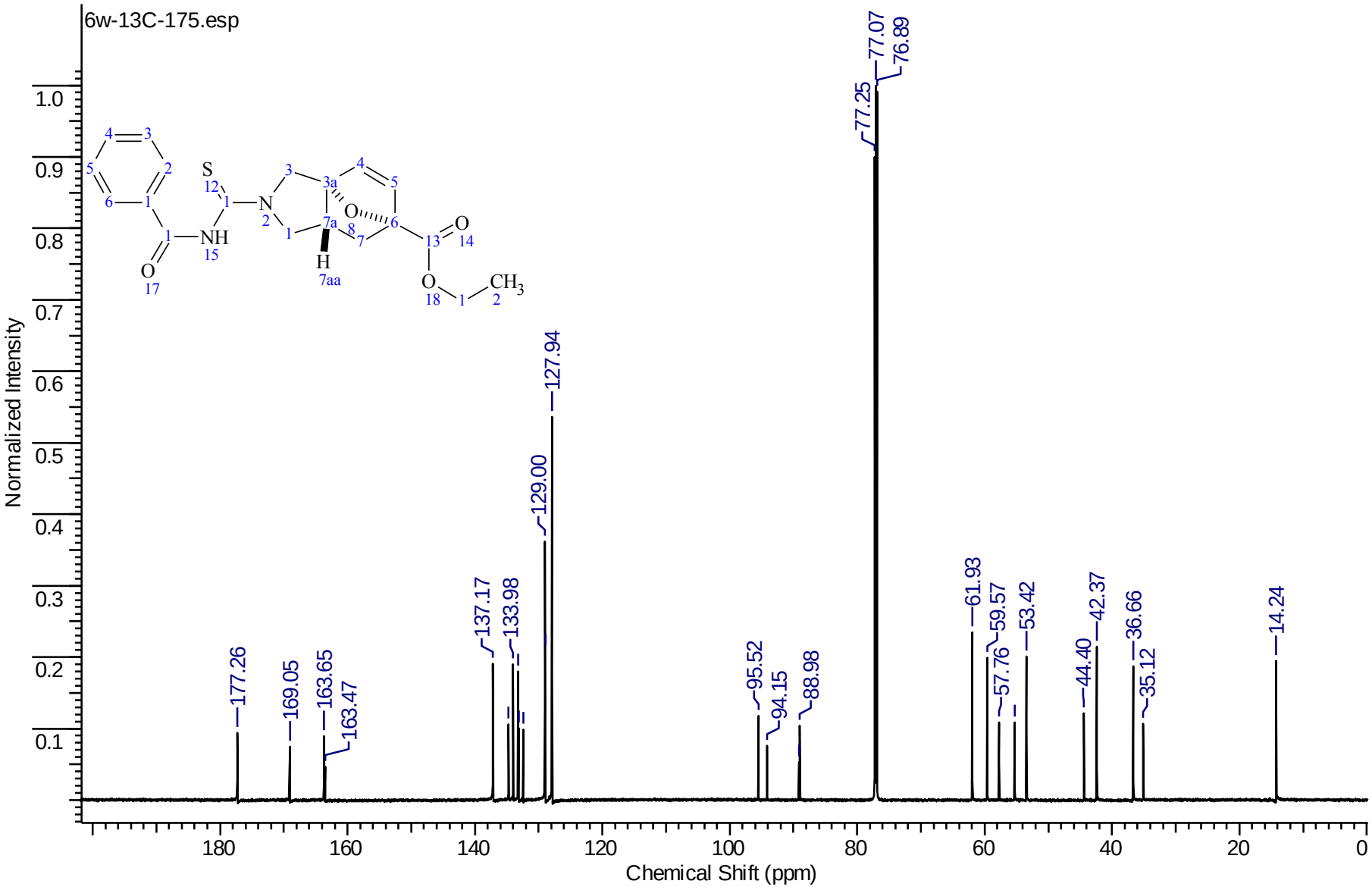


**Ethyl (3a*RS*,6*RS*,7a*RS*)-2-[(benzoylamino)carbonothioyl]-2,3,7,7a-tetrahydro-3a,6-epoxyisoindole-6(1*H*)-carboxylate (6w).**

**$^{1}$H NMR (700.2 MHz, $CDCl_3$)**

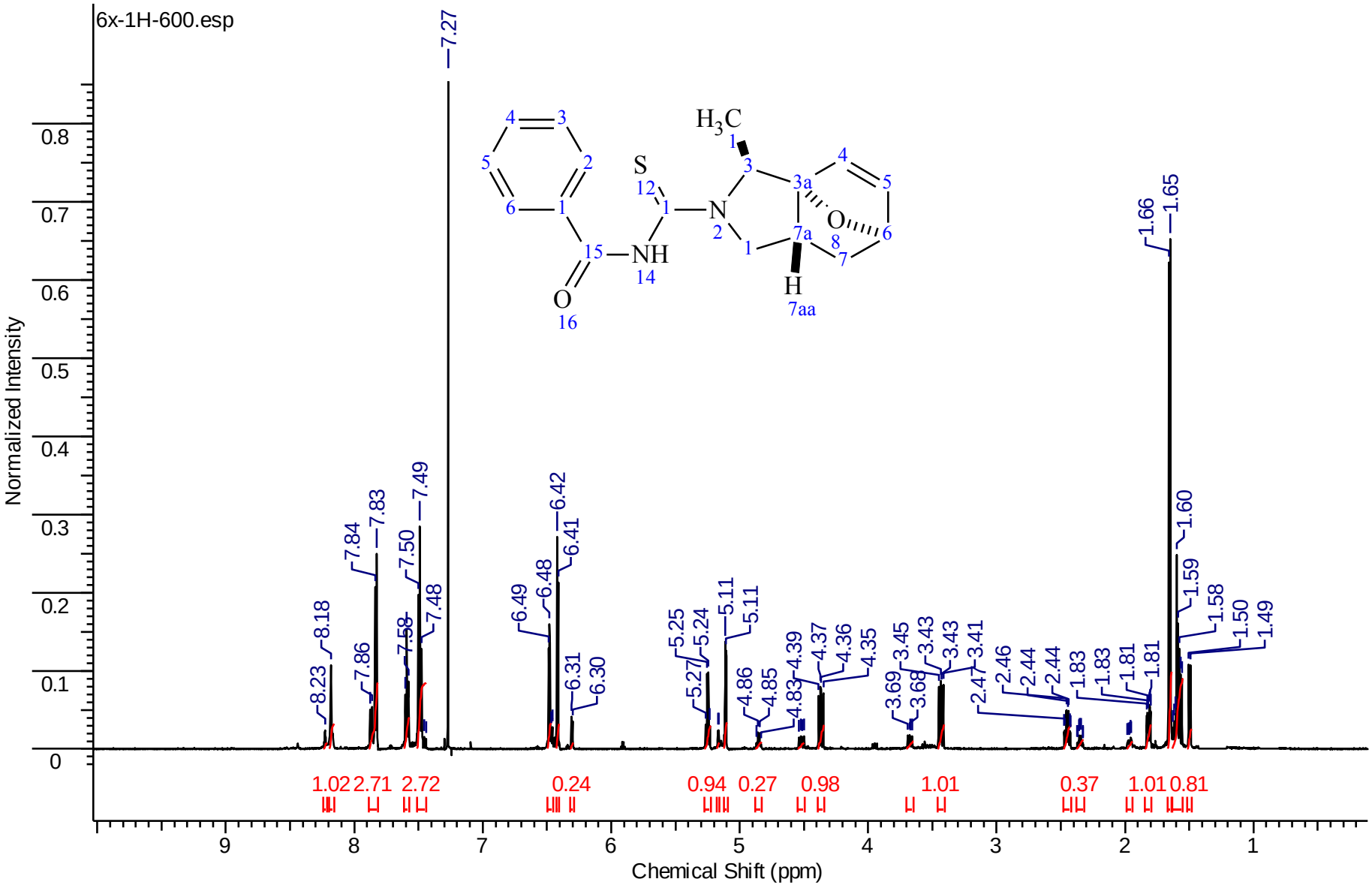


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**

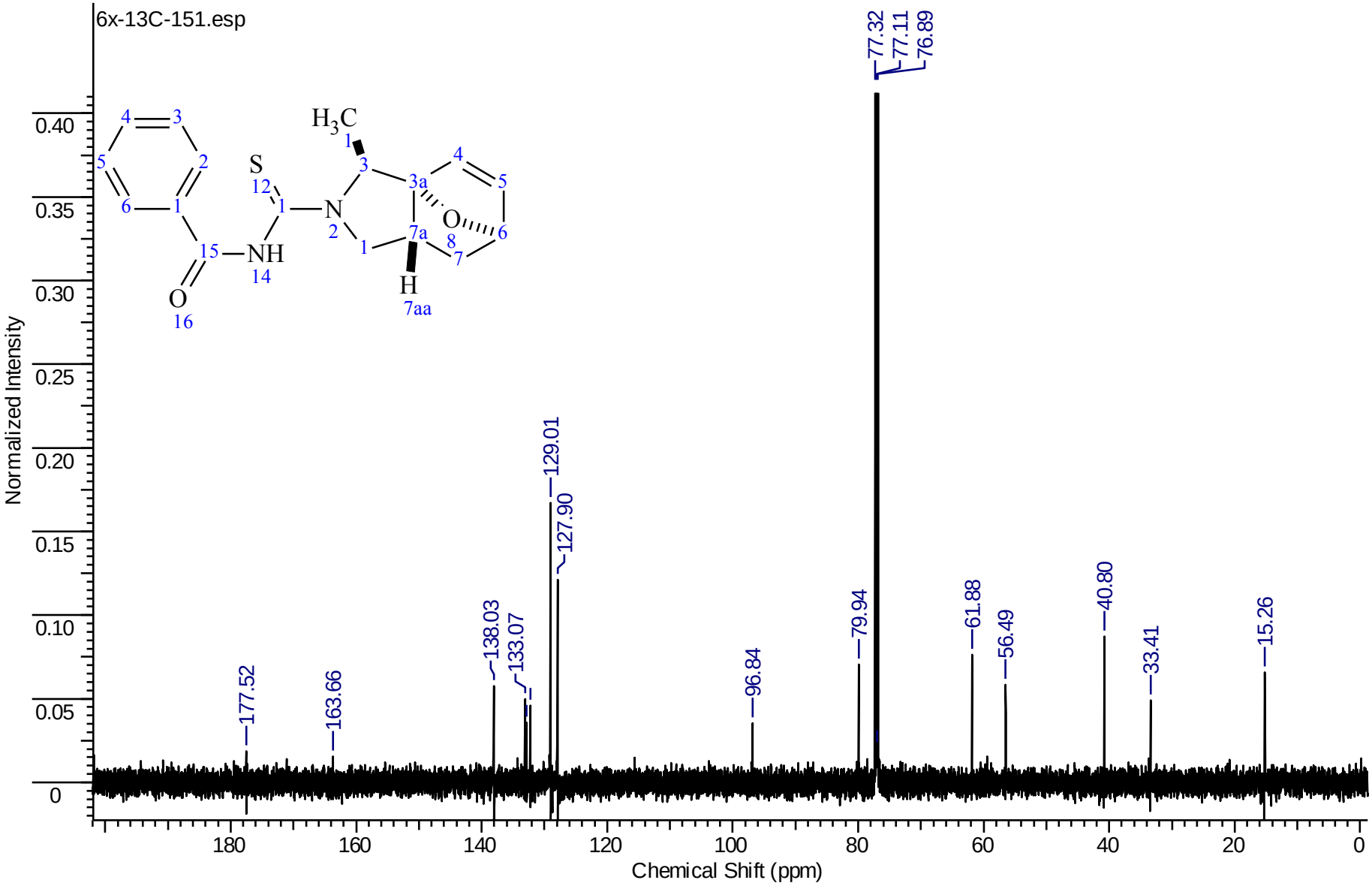


***N*-{[(3*SR*,3a*RS*,6*RS*,7a*RS*)-3-Methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6x).**

**$^{1}$H NMR (600.2 MHz, $CDCl_3$)**

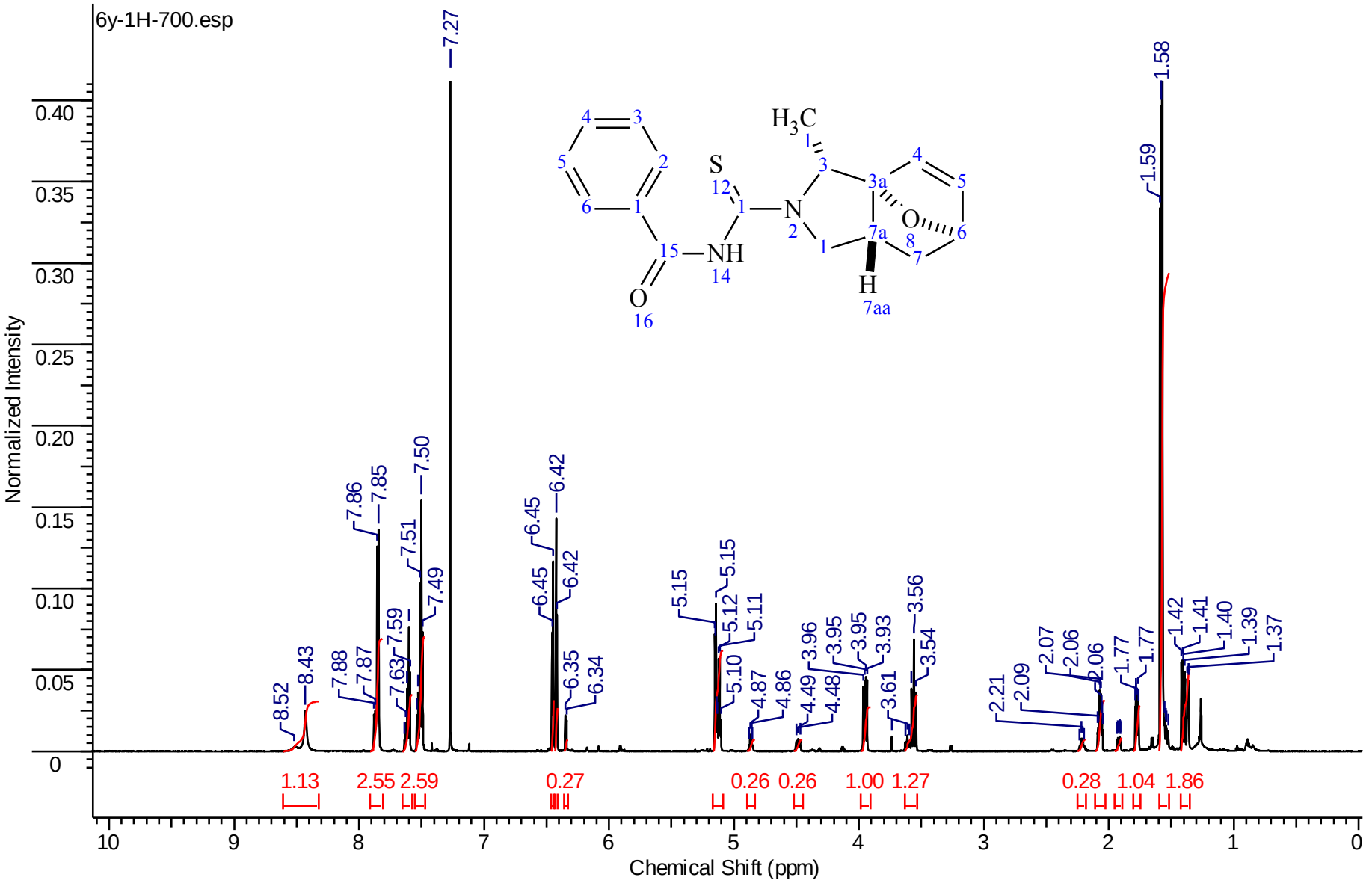


**$^{13}$C NMR (150.9 MHz, $CDCl_3$)**

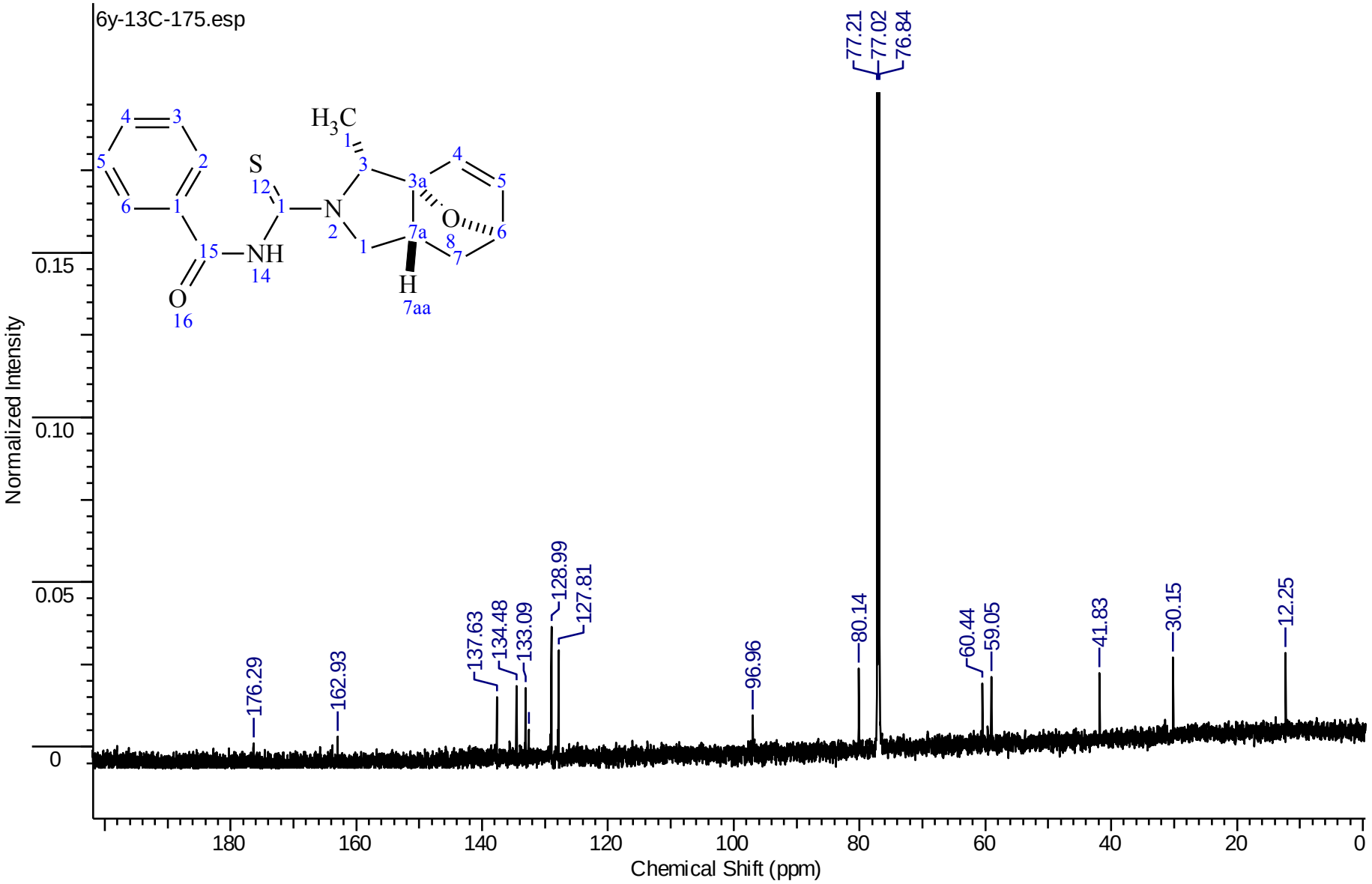


***N*-{[(3*RS*,3a*RS*,6*RS*,7a*RS*)-3-Methyl-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6y).**

**$^1$H NMR (700.2 MHz, $CDCl_3$)**

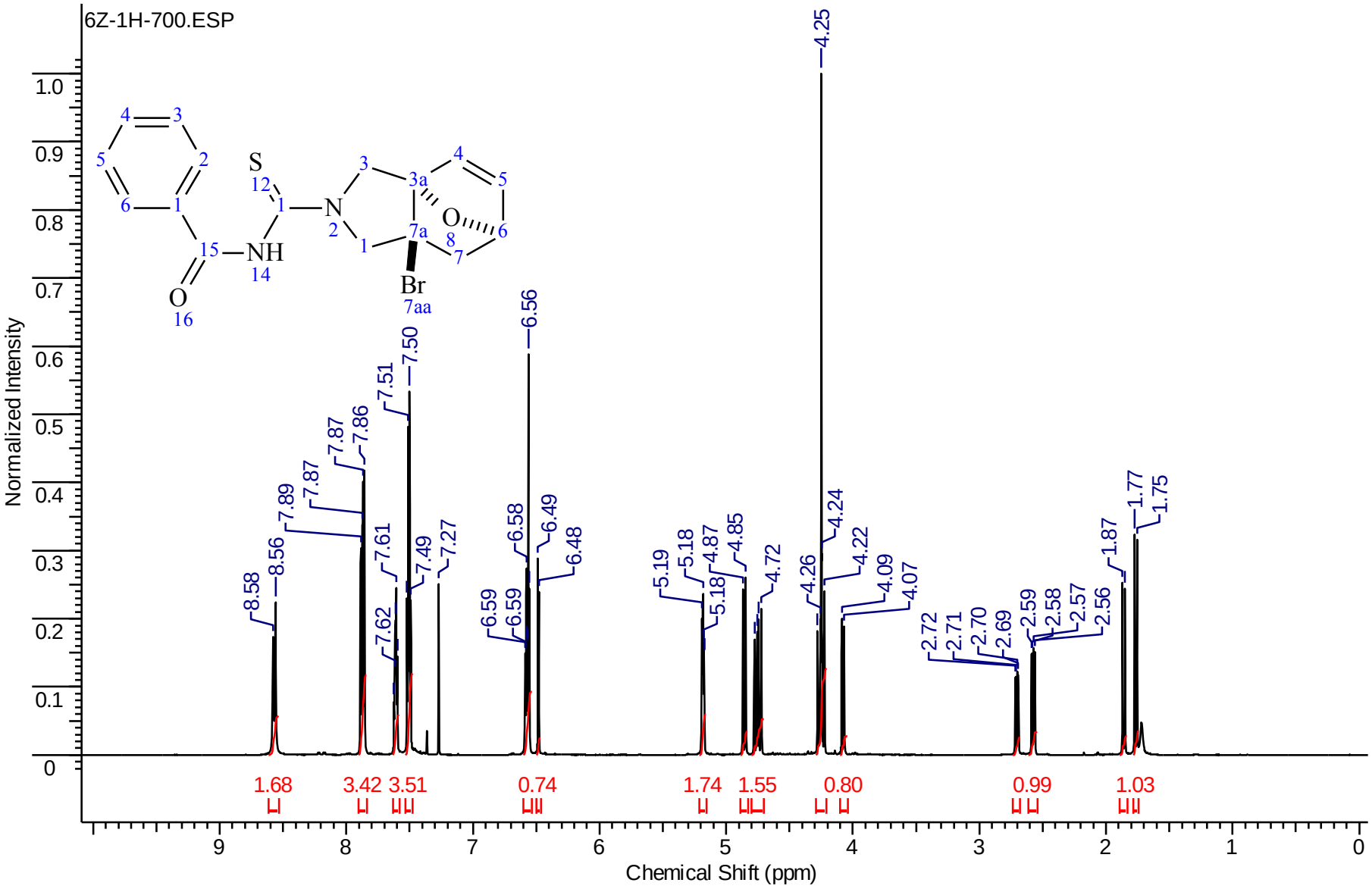


**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**



***N*-{[(3a*SR*,6*RS*,7a*SR*)-7a-Bromo-1,6,7,7a-tetrahydro-3a,6-epoxyisoindol-2-yl]carbonothioyl}benzamide (6z).**

**$^{1}$H NMR (700.2 MHz, $CDCl_3$)**



**$^{13}$C NMR (175.1 MHz, $CDCl_3$)**