Supplementary Material

5-(3-Phosphonated *1H*-1,2,3-triazol-4-yl)isoxazolidines: synthesis, DFT studies and biological properties

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1. Calculation Methods

Computations were performed at the density functional level with employment of the hybrid M062X functional and the 6-31G(d,p) basis set (M062X/6-31G(d,p)). The geometries were optimized by standard gradient techniques and characterized by evaluation of the Hessian matrix and the associated harmonic vibrational frequencies. For the more favored reaction pathway, the intrinsic reaction coordinate (IRC) has been computed. It represents the minimum energy path or the path of steepest decent from the transition state to both reactant and product directions with appropriate mass factor taken into account and provides a representative trajectory for the reaction.[1] The computed electronic energies were corrected for zero-point vibrational and thermal energies and entropies to obtain free energy changes at 298 K (ΔG_{298}). All computation were carried our using the G09 program.[2]

Table S1. Bond lengths and dihedral angles of the forming isoxazolidine ring. Data of the reagents are reported as reference

TS	C1-N2	N2-O3	O3-C5	C4-C5	C1-C4	N2C1C4C5	C1C4C5O3	C4C5CC
(Z) Nitrone	1.302	1.261						
(E) Nitrone	1.314	1.248						
Triazole *s-trans*				1.332				-0.2
Triazole *s-cis*				1.332				179.9
(E) - endo – s-cis	1.338	1.278	2.162	1.387	2.116	31.9	-5.2	-168.3
(E) - endo –s-trans	1.337	1.277	2.123	1.386	2.154	28.8	-2.6	-10.7
(Z) - exo – s-cis	1.336	1.277	2.175	1.382	2.178	-28.9	2.9	149.0
(Z) - exo – s-trans	1.335	1.279	2.175	1.386	2.159	-31.6	5.4	-5.6
(E) - exo – s-cis	1.339	1.277	2.191	1.385	2.104	40.8	-14.0	165.5
(E) - exo – s-trans	1.338	1.276	2.187	1.384	2.125	39.2	-12.2	-123.4
(Z) - endo – s-cis	1.334	1.274	2.187	1.385	2.145	-30.6	4.5	168.3
(Z) - endo –s-trans	1.334	1.274	2.155	1.385	2.179	-29.3	3.4	12.2

Table S2. Bond lengths and dihedral angles of isoxazolidine ring in various conformations.

Kinetic product	C1-N2	N2-O3	O3-C5	C4-C5	C1-C4	N2C1C4C5	C1C4C5O3	C4C5CC
(E) – endo – s-cis	1.466	1.424	1.450	1.538	1.536	32.9	-11.5	-157.4
(E) - endo – s-trans	1.467	1.426	1.443	1.541	1.539	30.3	-7.2	144.7
(Z) - exo – s-cis	1.465	1.416	1.439	1.545	1.545	-22.8	0.5	116.9
(Z) - exo – s-trans	1.467	1.413	1.443	1.548	1.542	-17.8	-5.5	68.6
(E) - exo – s-cis	1.467	1.420	1.450	1.542	1.537	31.2	-8.6	148.1
(E) - exo – s-trans	1.467	1.423	1.444	1.543	1.536	32.5	-11.0	-112.6
(Z) - endo – s-cis	1.462	1.420	1.450	1.537	1.540	-30.6	10.5	154.8
(Z) - endo – s-trans	1.469	1.423	1.440	1.537	1.540	-24.2	4.8	-146.5

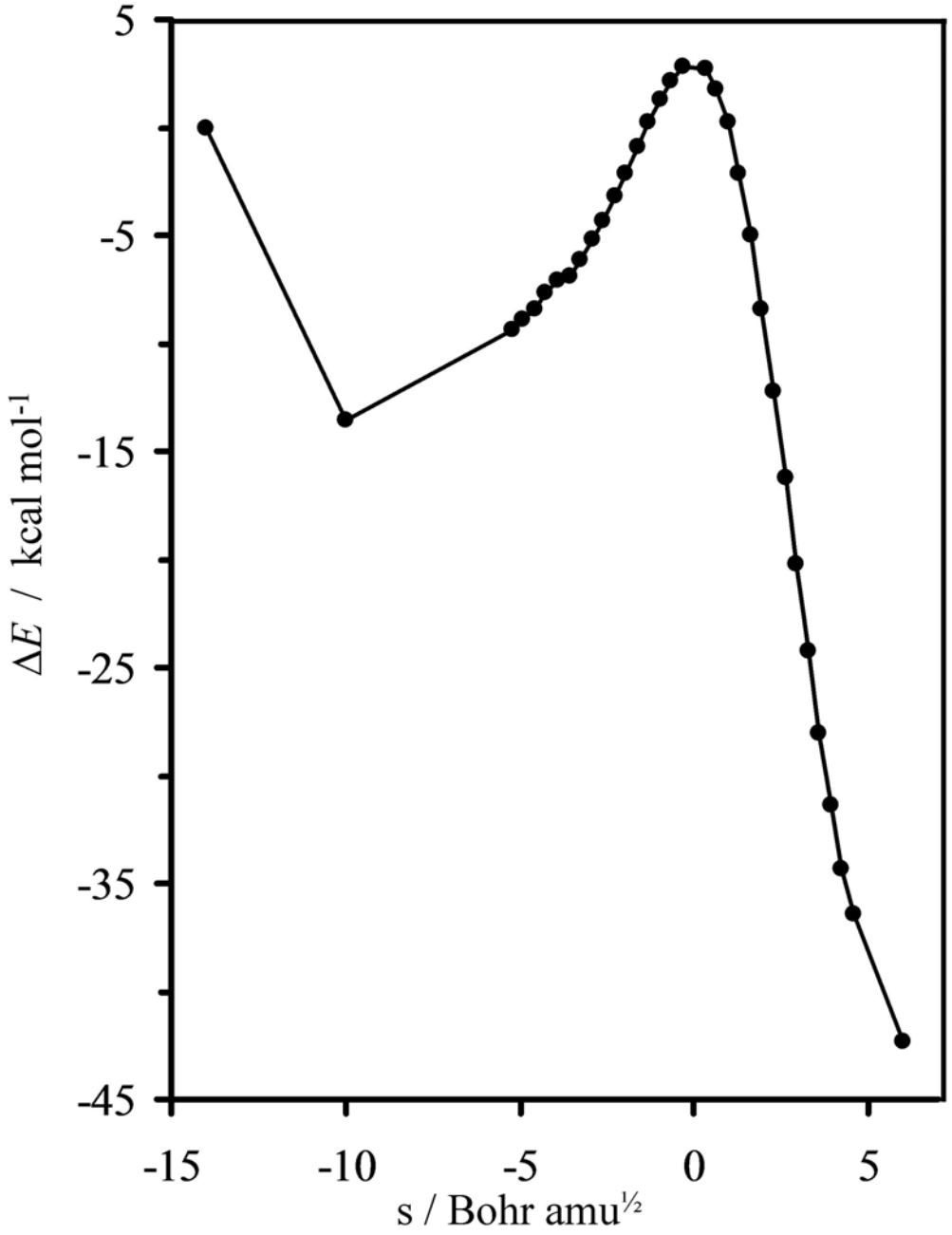


Figure S1. Computed electronic energy profiles along the intrinsic reaction coordinate for the 1,3-dipolar cycloaddition along the (*Z*) – *exo* – *s* – *trans* pathway.

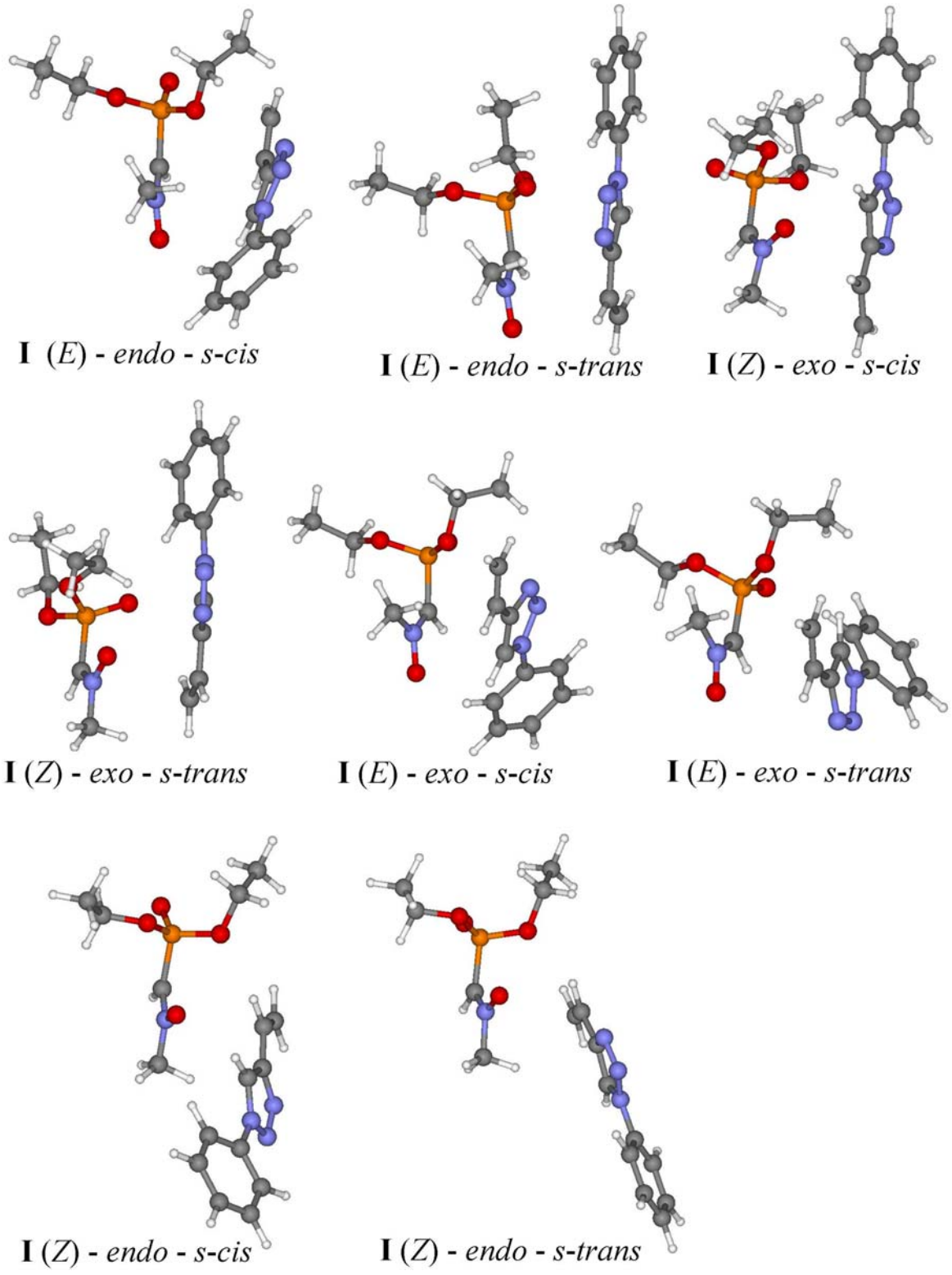


Figure S2. Molecular structures of the eight intermediates for the formation of the *cis* and *trans*-adducts of the 3,5 regioisomer.

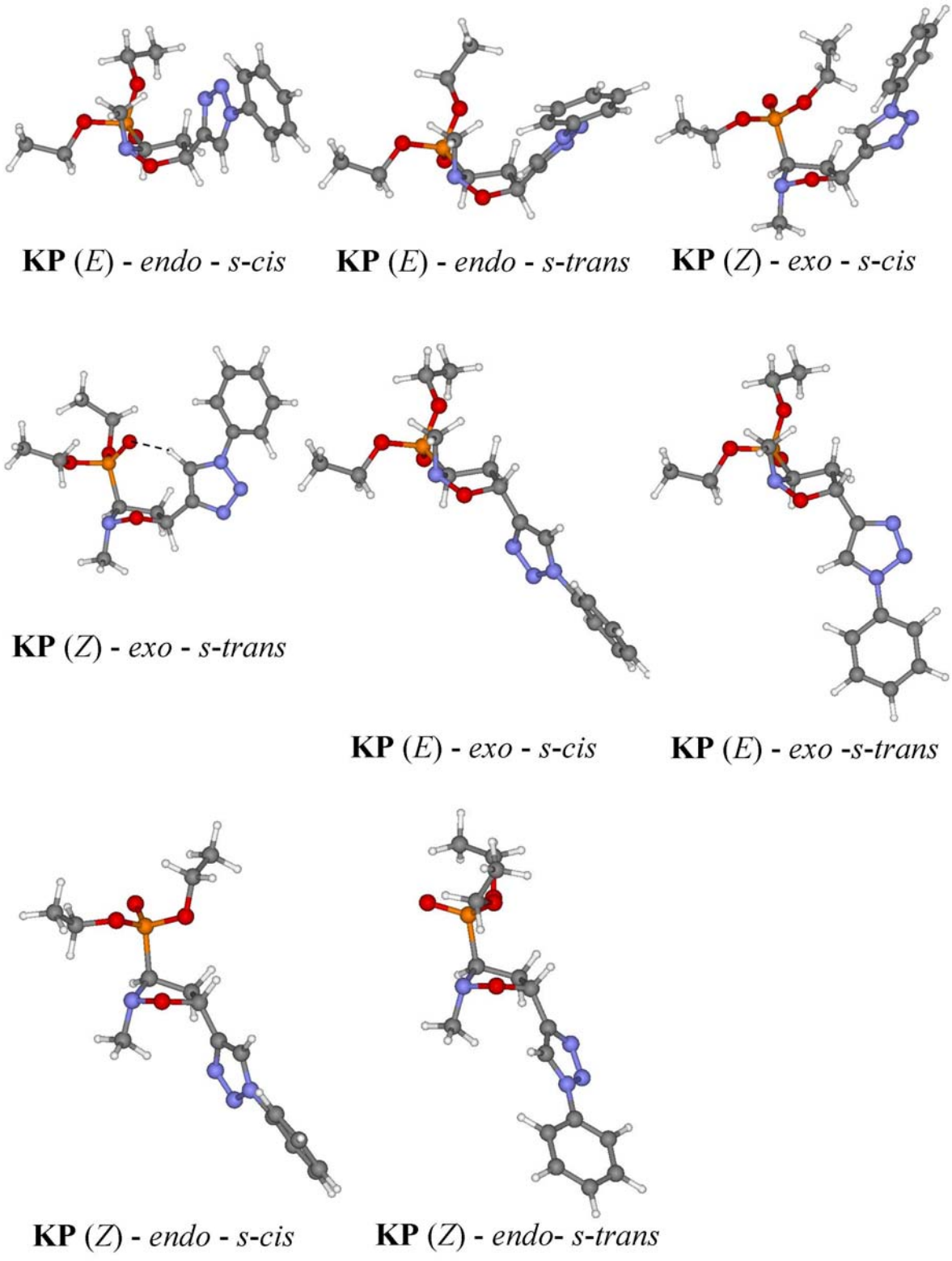


Figure S3. Molecular structures of the eight kinetic products for the formation of the *cis* and *trans*-adducts of the 3,5 regioisomer.

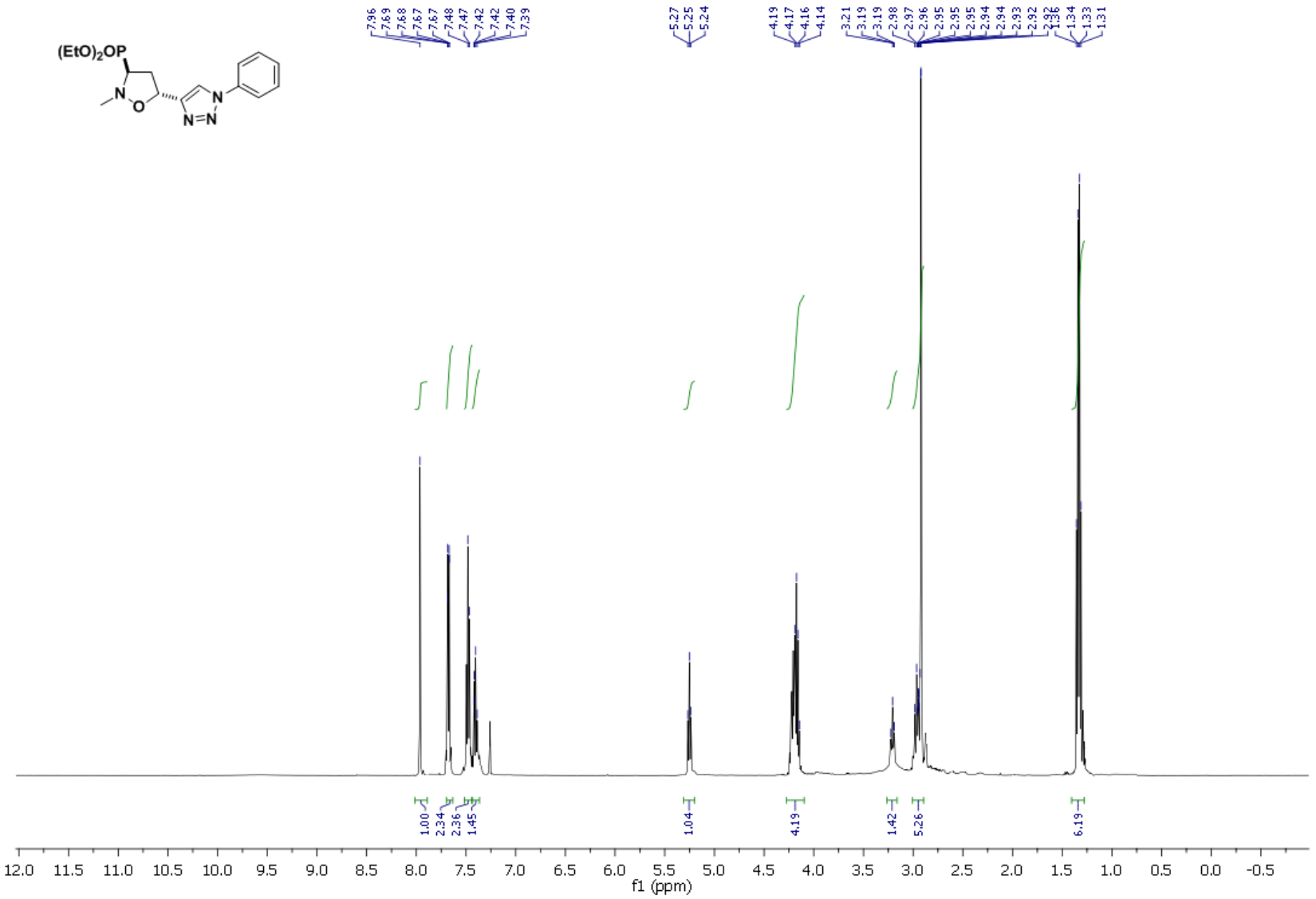
References

1. Fukui, K.; Kato, S.; Fujimoto, H. *J. Am. Chem. Soc.* **1975**, *97*, 1.

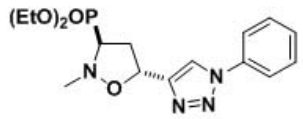
2. Gaussian 09, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford CT, **2010**.

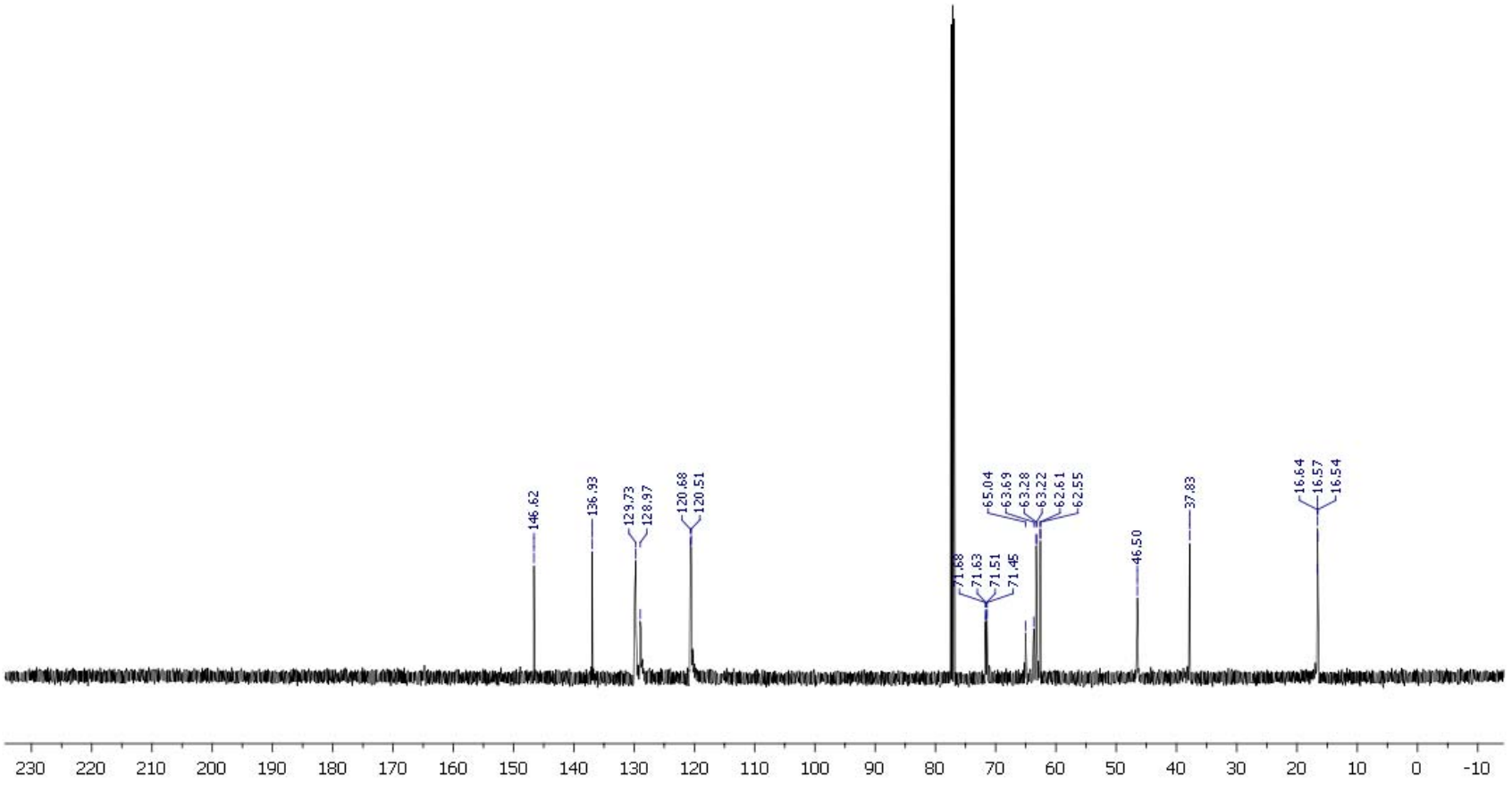
2. ^{1}H and ^{13}C NMR of compounds

^{1}H NMR (500 MHz, $CDCl_3$) of compound **11a**

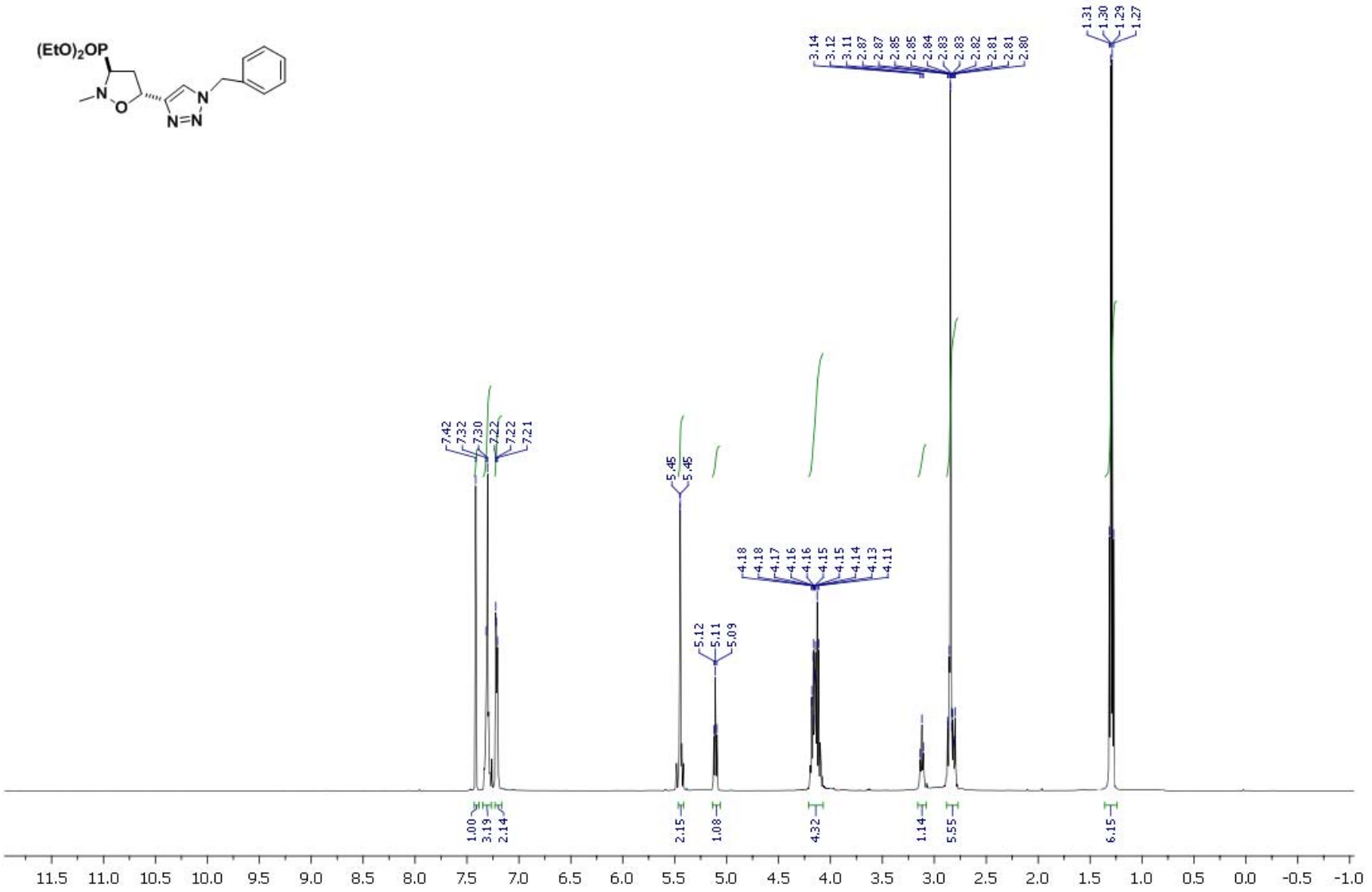


^{13}C NMR (126 MHz, $CDCl_3$) of compound **11a**





^{1}H NMR (500 MHz, $CDCl_3$) of compound **11b**



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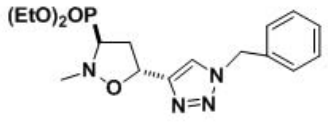
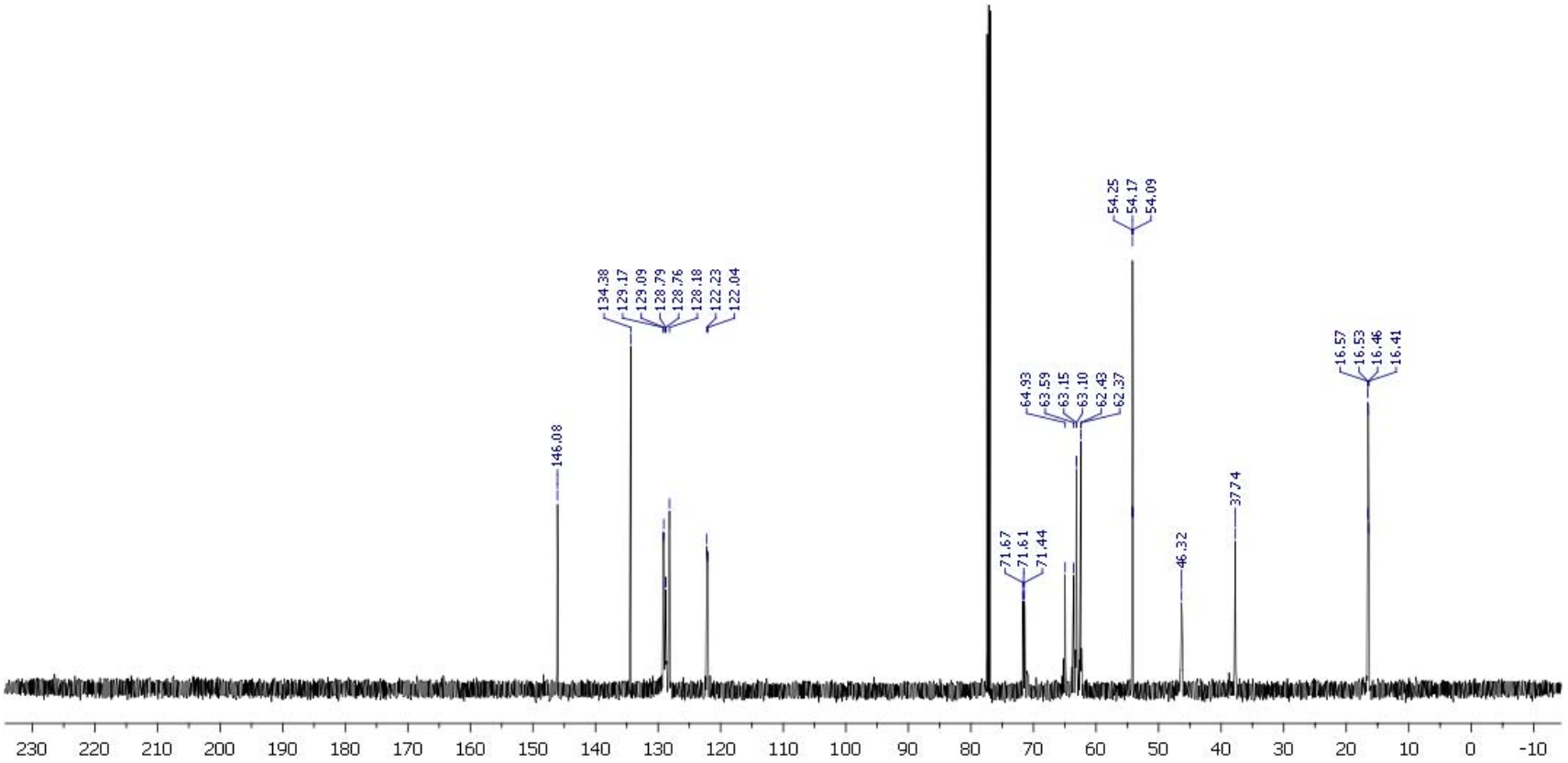
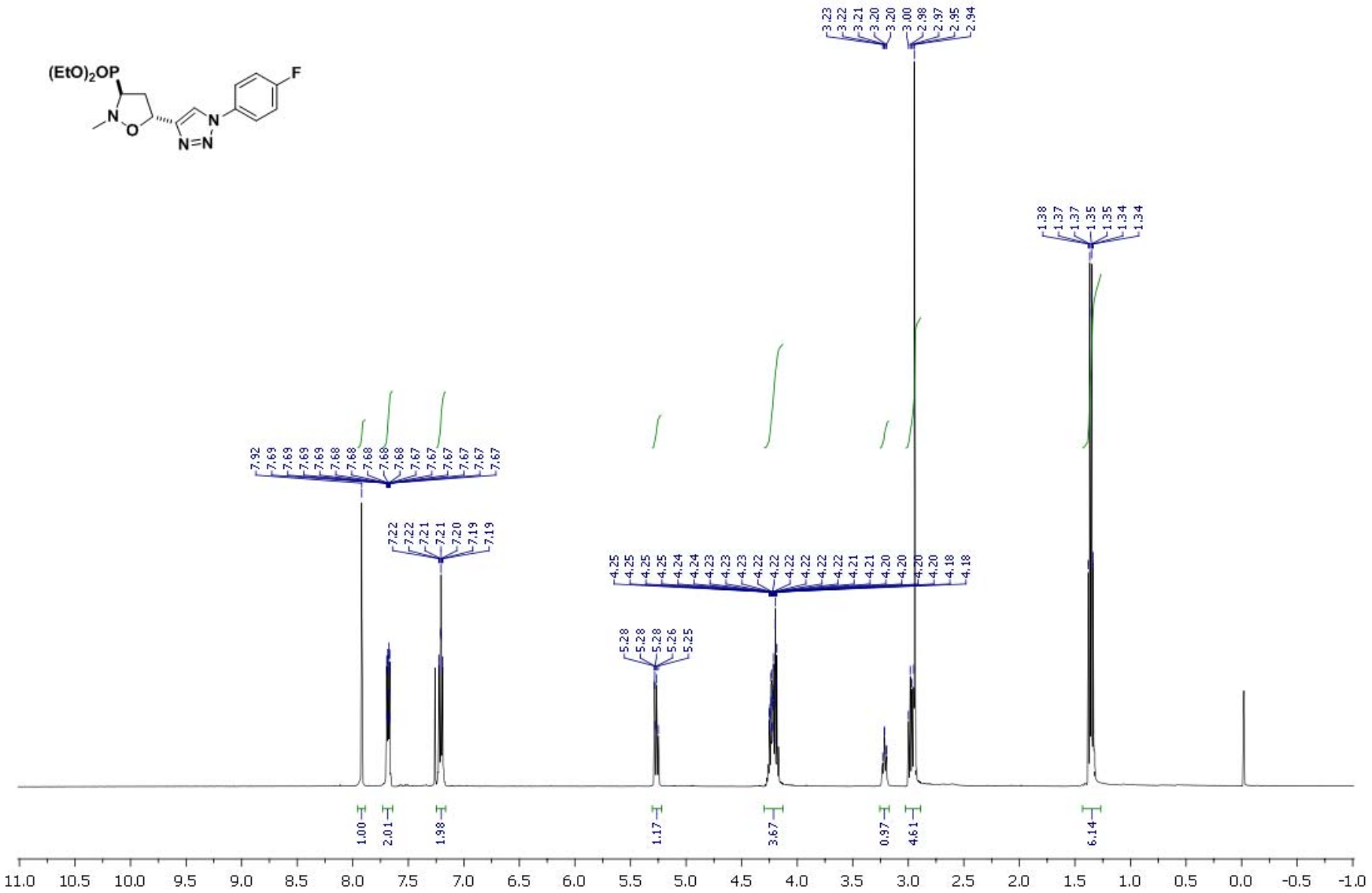
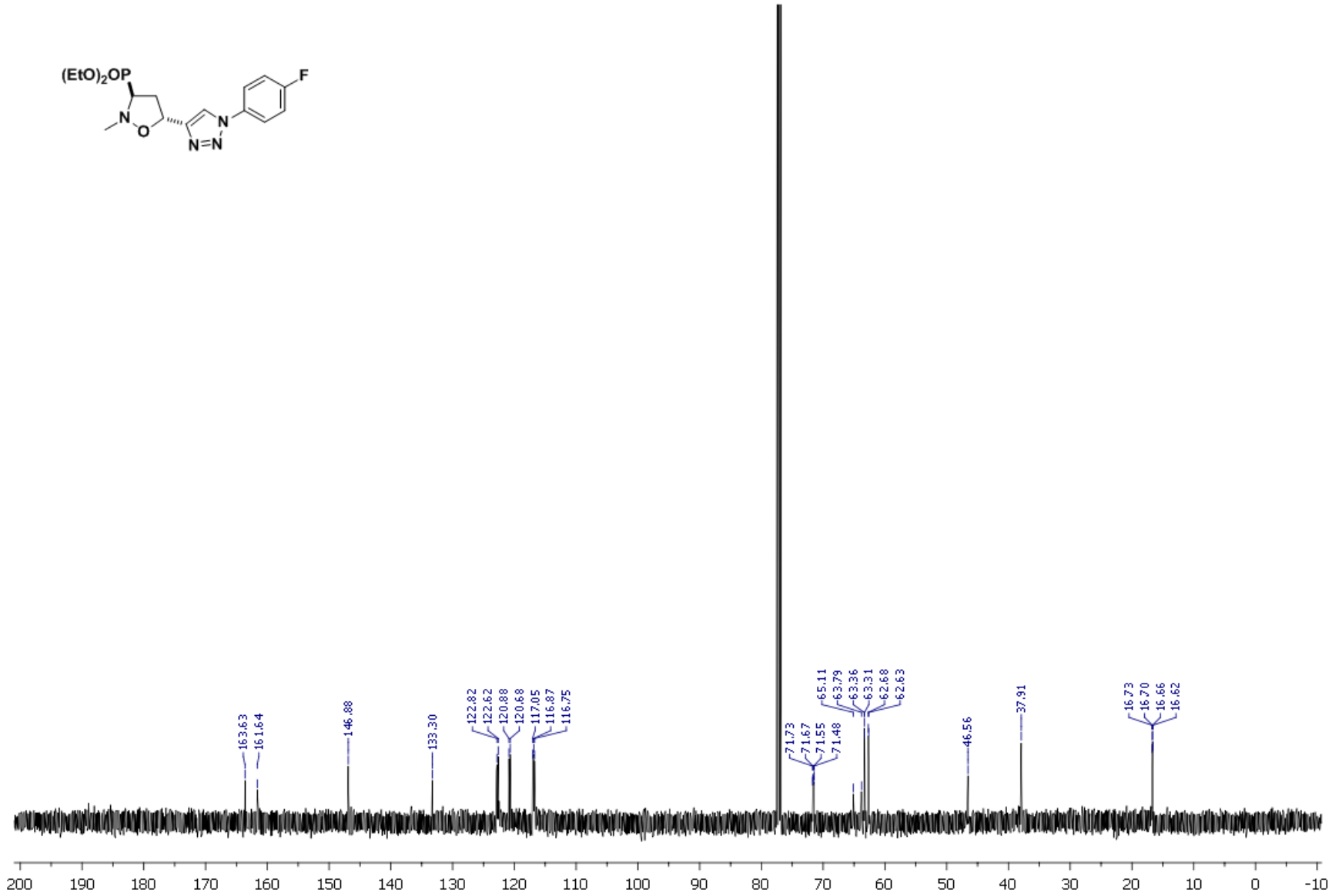




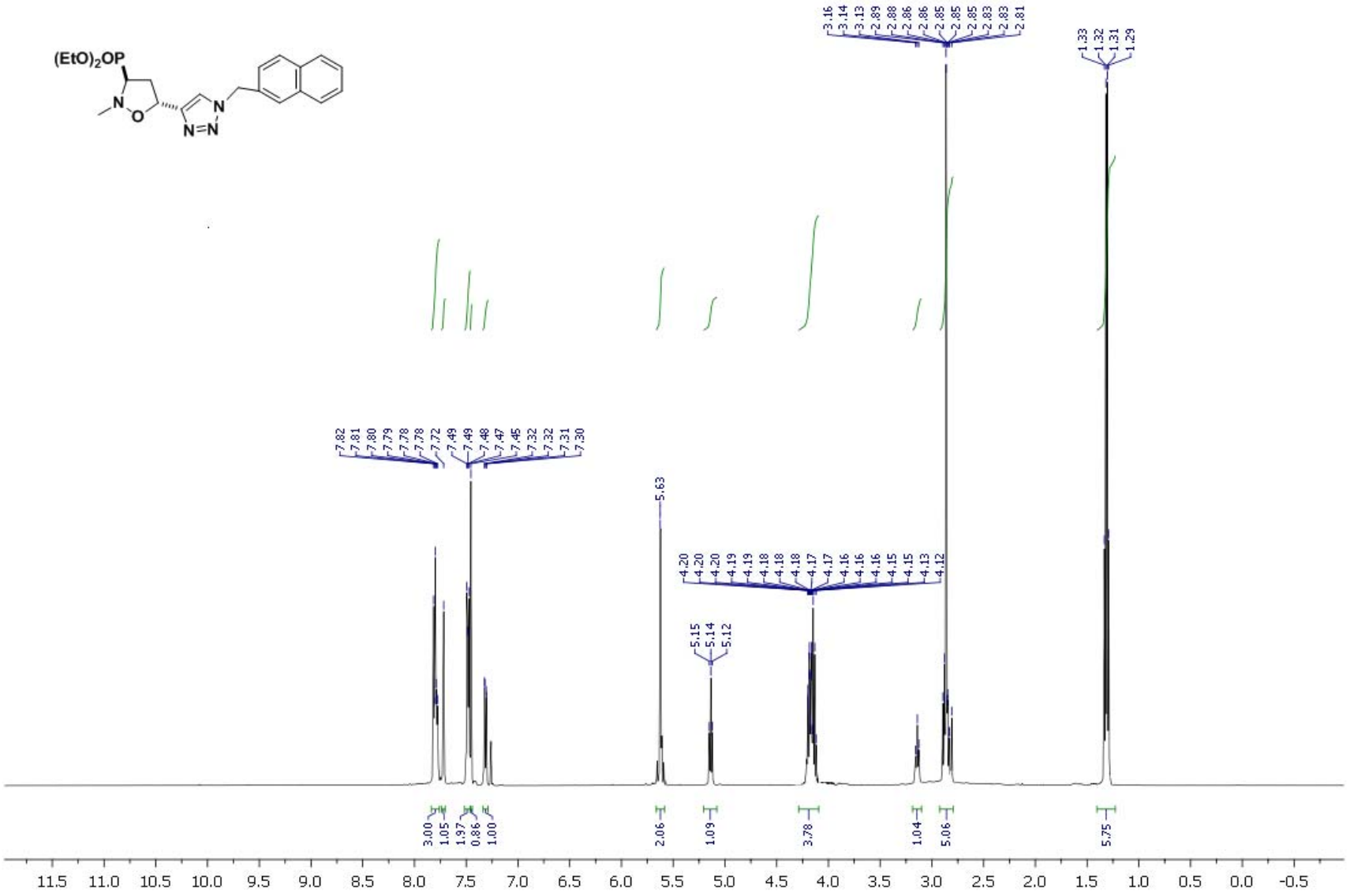
^{1}H NMR (500 MHz, $CDCl_3$) of compound **11c**



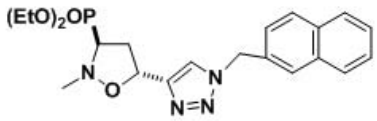
^{13}C NMR (126 MHz, $CDCl_3$) of compound **11c**

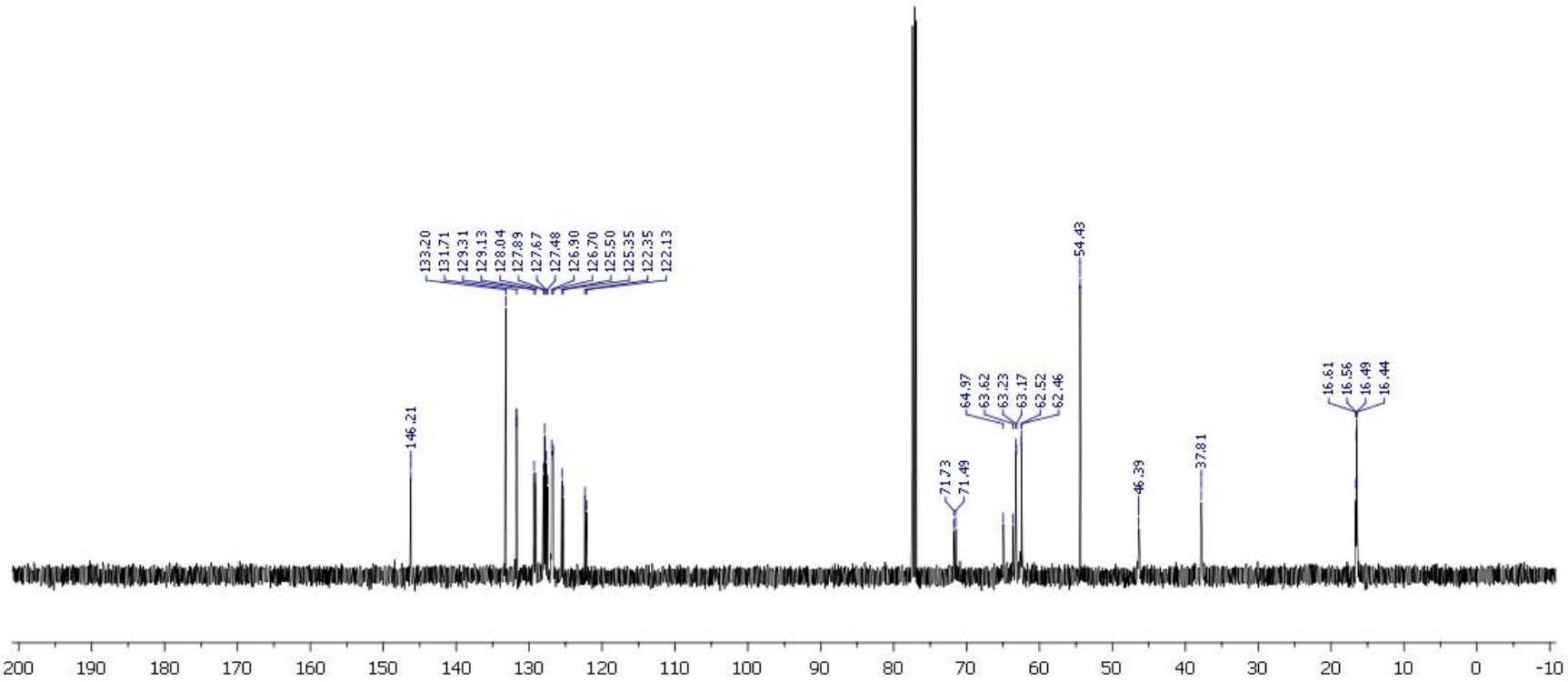


^{1}H NMR (500 MHz, $CDCl_3$) of compound **11d**

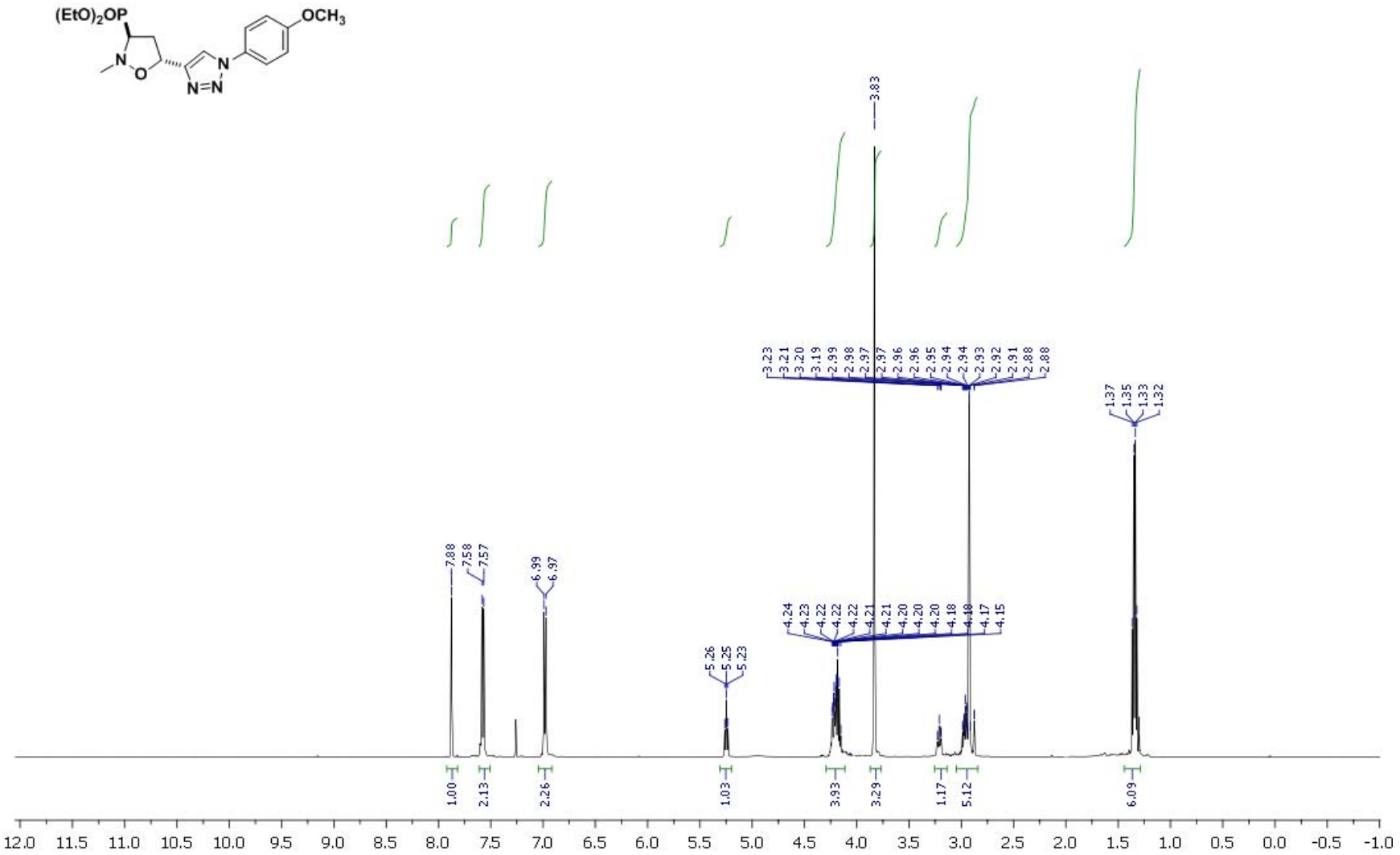


^{13}C NMR (126 MHz, $CDCl_3$) of compound **11d**

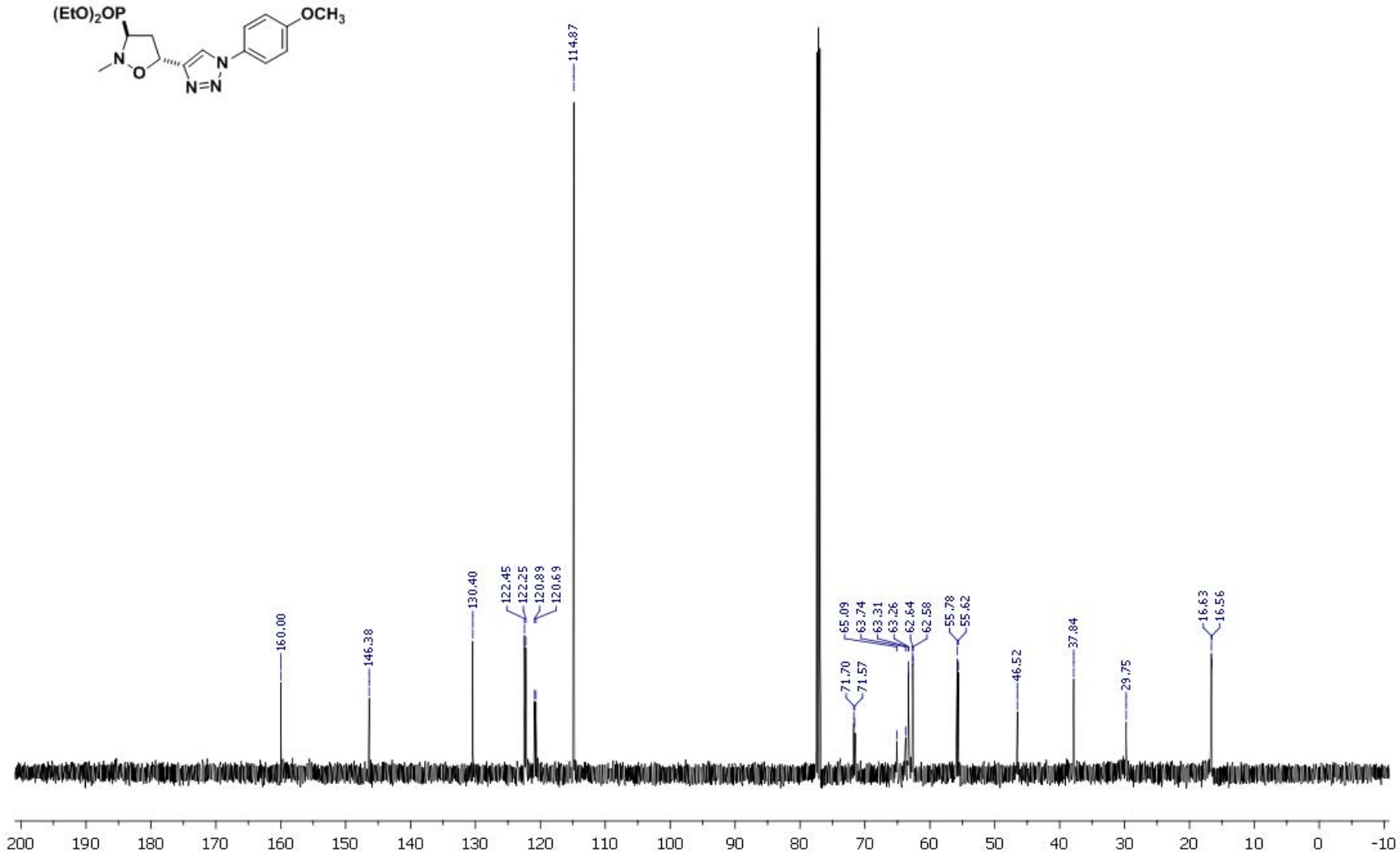




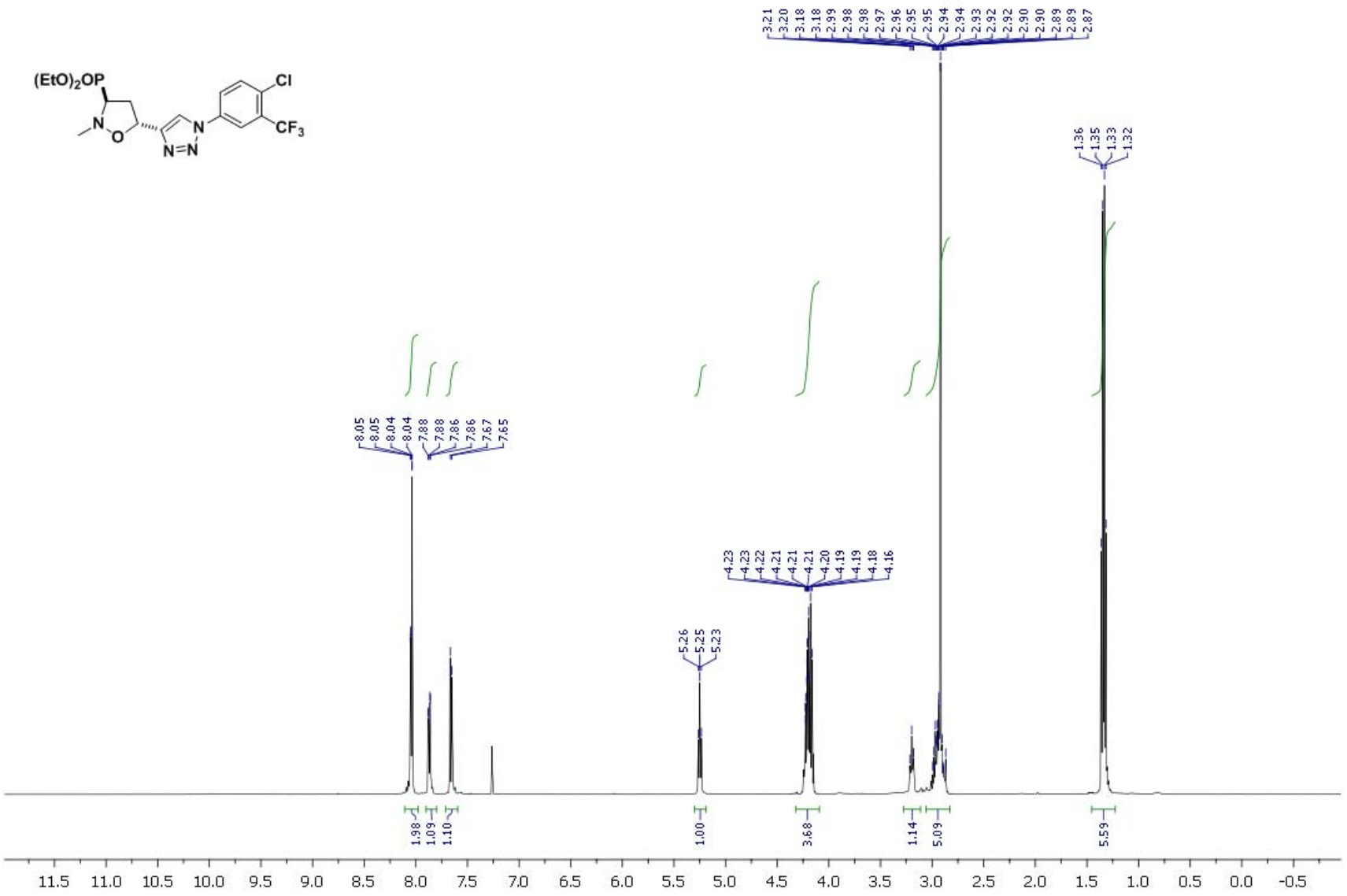
^{1}H NMR (500 MHz, $CDCl_3$) of compound **11e**



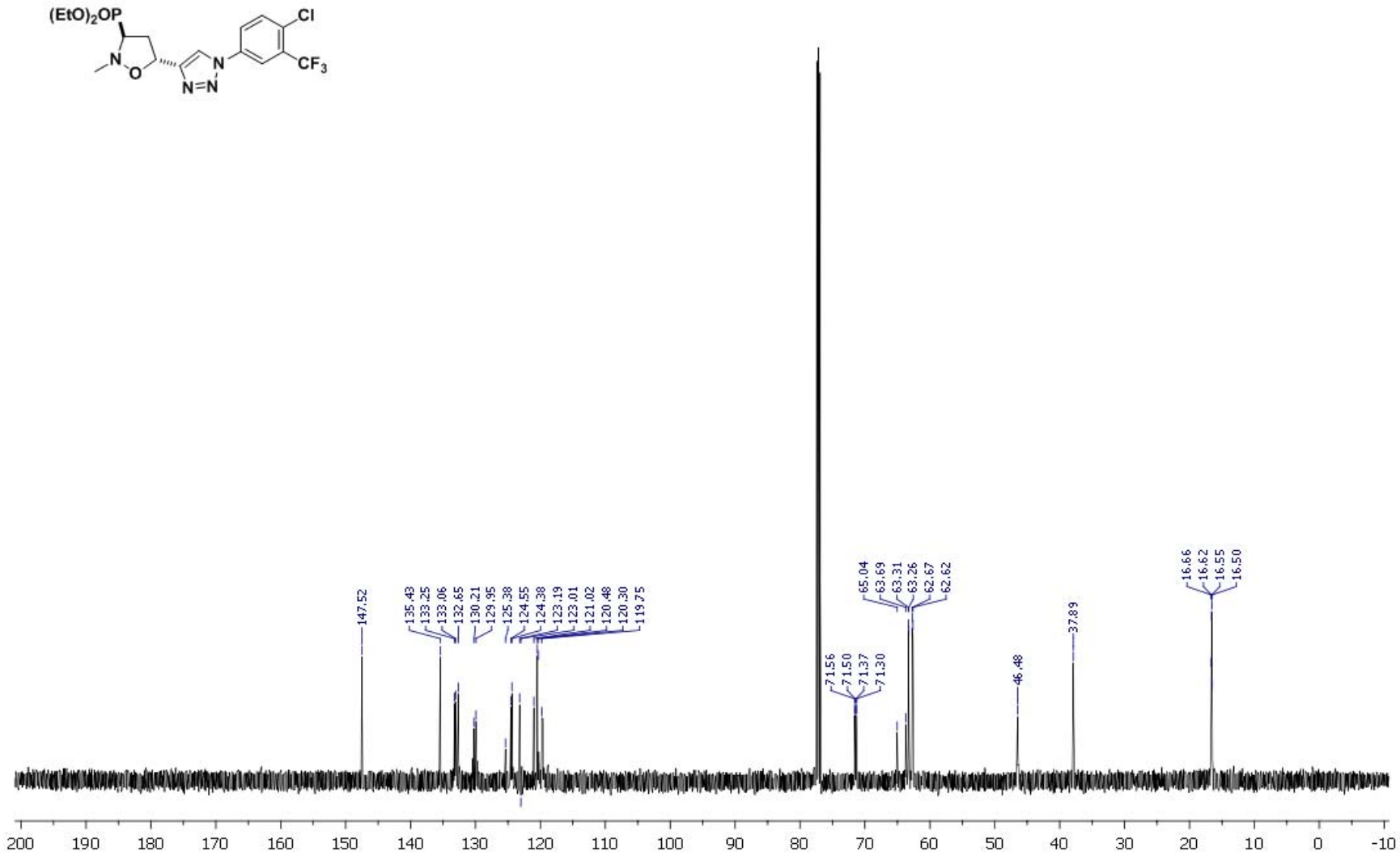
^{13}C NMR (126 MHz, $CDCl_3$) of compound **11e**



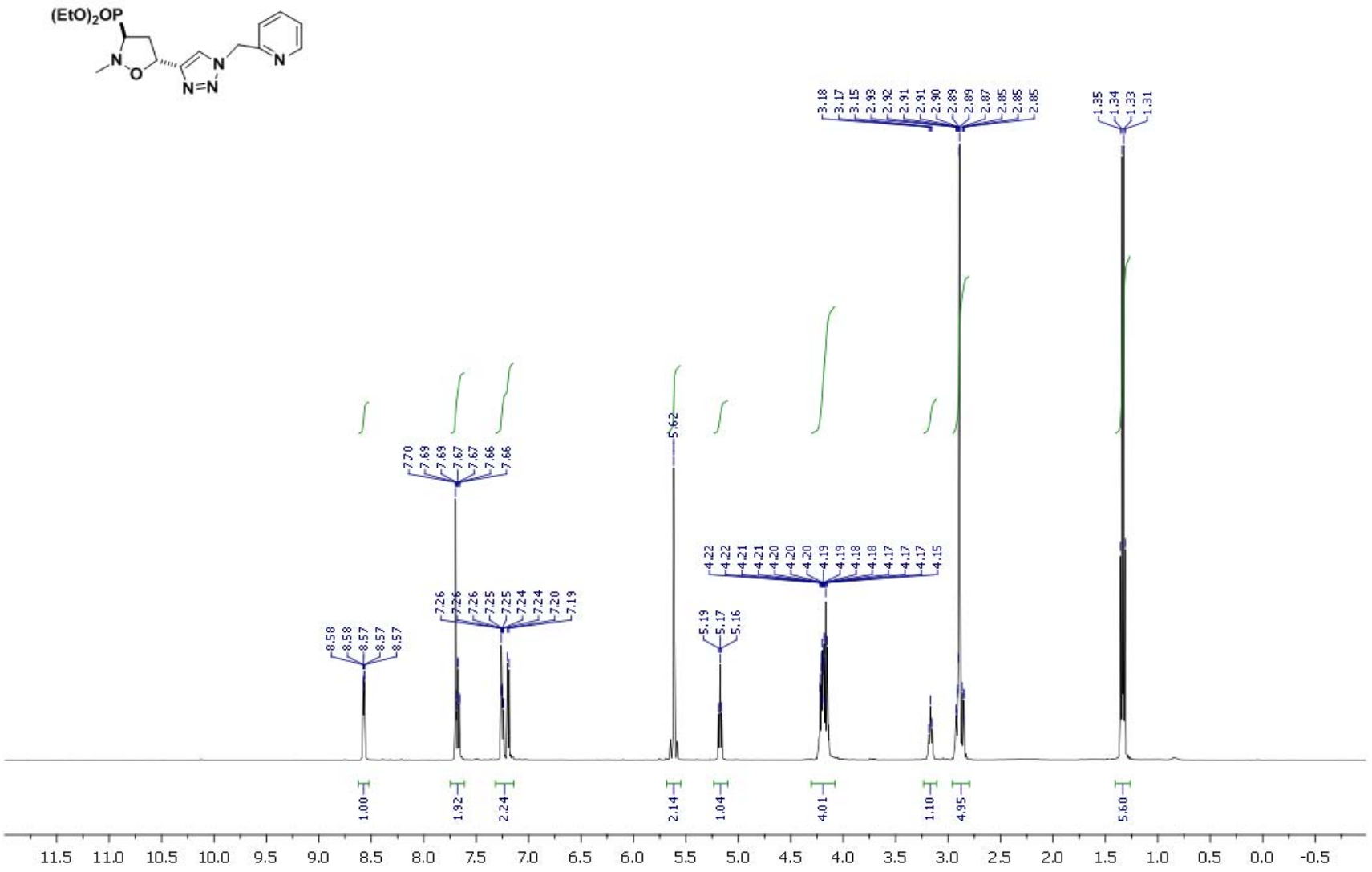
^{1}H NMR (500 MHz, $CDCl_3$) of compound **11f**



^{13}C NMR (126 MHz, $CDCl_3$) of compound **11f**



^{1}H NMR (500 MHz, $CDCl_3$) of compound **11g**



^{13}C NMR (126 MHz, $CDCl_3$) of compound **11g**