Synthesis and fluorescence properties of benzoxazole-1,4-dihydropyridine dyads achieved by multicomponent reaction

Ricardo Ferreira Affeldt,[a] Antônio César de Amorim Borges,[a] Dennis Russowsky*[b] and Fabiano Severo Rodembusch*[a]

[a]Grupo de Pesquisa em Novos Materiais Orgânicos e Fotoquímica. Instituto de Química/UFRGS. Av. Bento Gonçalves, 9500. CEP 91501-970, Porto Alegre, RS, Brazil. Fax: (+) 55 (51) 3308 7304

[b]Laboratório de Síntese Orgânica. Instituto de Química/UFRGS. Av. Bento Gonçalves, 9500. CEP 91501-970, Porto Alegre, RS, Brazil

Electronic Supplementary Information

Summary

1. Attempts to the quinolines synthesis

The initial effort was concentrated on the obtention of quinoline derivatives with aminophenylbenzazoles as starting material for further cyclization reactions. Three derivatives were prepared by an optimized method by condensation of 2-hydroxyaniline with the corresponding *o*-substituted benzoic acid in polyphosphoric acid (**ABO 1-3**).[1] These compounds are highly fluorescent by ESIPT mechanism and its photophysical behavior extensively characterized.[2] Preliminary studies were motivated by literature were several multicomponent reactions were carried out with substituted anilines for obtention of quinoline derivatives.[3] Supported by these syntheses it was believed that the synthesized aminophenylbenzazoles were suited for this kind of transformation, and some tests applying multicomponent strategy were carried out with different aldehydes and carbonyl compounds. In most of the cases the starting materials were fully recovered after the times indicated or condensation of the amino derivatives with aldehydes lead to fluorescent Schiff bases[4] we were not interested at this time (Figure SI1). These results are summarized in Table SI1.

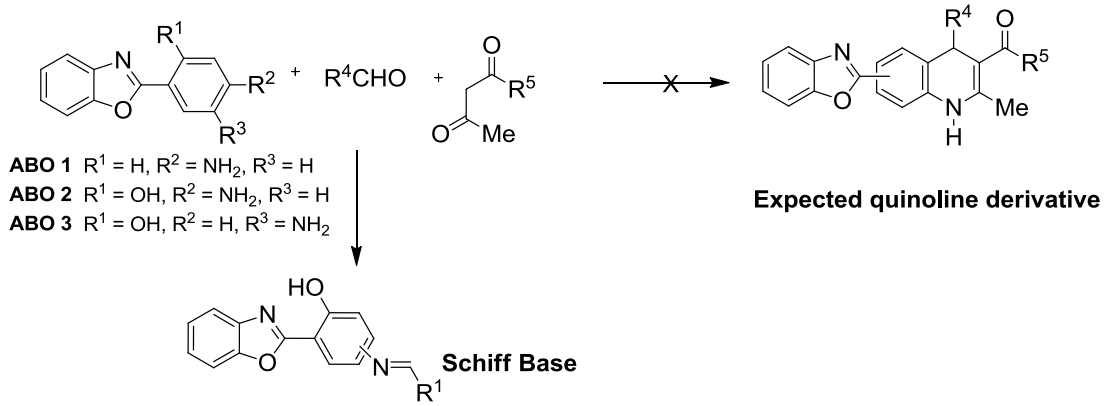

Figure ESI1. Attempts to synthesize the benzoxazolyl-quinoline via multicomponent reaction.

1. (a) D. W. Hein, R. J. Alheim, J. J. Leavitt, *J. Am. Chem. Soc.,* 1957, **79**, 427. (b) E. Barni, P. Savarino, M. Marzona, M. Piva, *J. Heteroc. Chem.,* 1983, **20**, 1517.
2. F. S. Rodembusch, L. F. Campo, F. P. Leusin, V. Stefani, V. *J. Lumin*., 2007, **126**, 728.
3. (a) C. Tratat, S. Giorgi-Renault, H. P. Husson, *Org. Lett*., 2002, **4**, 3187. (b) S. Tu, S. Wu, S. Yan, W. Hao, X. Zhang, X. Cao, Z. Han, B. Jiang, F. Shi, M. Xia, J. Zhou, *J. Comb. Chem.,* 2009**, 11***,* 239.
4. G. Wiethaus, In.: *Síntese e Caracterização de Novas Iminas com Aplicação em Óptica Não-Linear*. M.Sc. Dissertation. 2010. Universidade Federal do Rio Grande do Sul. (In Portuguese).

Table ESI1. Attempts to obtain benzoxazolyl-quinoline via multicomponent reaction using ABO 3 as starting material.

Entry	R^4	R^5	Conditions	Observed	Ref.
1	H	Me	H_2O, 45°C, 5h	N. R.	5
2	H	Me	H_2O, reflux, 5h	N. R.	5
3	Ph	OEt	EtOH, reflux, 5h	Schiff Base	3a
4	2-OH-C_6H_4	OEt	EtOH, reflux, 5h	Schiff Base	3a
5	Ph	OEt	10 mol% In/SiO_2, *i*PrOH, reflux, 16h.	Schiff Base	3a
6	2-OH-C_6H_4	OEt	AcOH, MW, 600W, AcOH, 1h	Schiff Base	3b
7	Ph	OEt	AcOH, 600W, KSF Clay,1h	Schiff Base	3b
8	Ph	OEt	100°C, *i*PrOH, HCl (cat.), 6h	N.R.	6
9	Ph	OEt	10 mol% In/SiO_2, *i*PrOH, reflux, 11h.	N.R.	6
10	C_6H_{13}	OEt	I_2, benzene, reflux, 2h	Complex mixture	7

A quinazolinone heterocycle was also not achieved by multicomponent reaction of ABO 3 with anthranilic acid and triethylortoformiate[8] leading to a complex/insoluble mixture with or without $SnCl_2$ catalyst (Figure SI2).

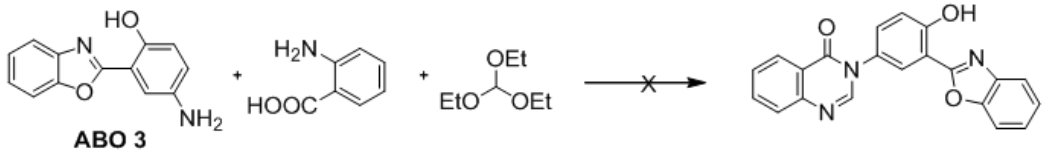

Figure ESI2. Multicomponent synthesis of benzoxazolyl-quinazolinone derivative.

5. Y. Gu, R. De Sousa, G. Frapper, C. Bachmann, J. Barrault, F. Jérôme, *Green Chem.,* 2009, **11**, 1968.
6. V. B. Bojinov, I. K. Grabche, *Org. Lett*., 2003, **5**, 2185.
7. X. F. Ling, S. L. Cui, Y. G. Wang, *Tetrahedron Lett*., 2006, **47**, 3127. (b) X. Geng, S. Li, X. Bian, Z. Xie, C. Wang, C. *Arkivoc* 2008, **xiv**, 50.
8. (a) B. P. Bangdar, P. E. More, V. T. Kamble, *Chin. J. Chem*., 2009, **27**, 1123. (b) J. N. Sangshetti, D. K. Nagnnath, D. B. Shinde, *Monatsh. Chem.,* 2007, **138**, 1289.

Some classical quinoline cyclizations were not able to be reproduced with the ABO compounds as starting material. Skaup glycerol acidic reactions led to complex/insoluble mixture mixtures while Combes, Doebner-Miller and Conrad-Limpach approaches did not yield any product (Figure SI3 and Table SI2).[9]

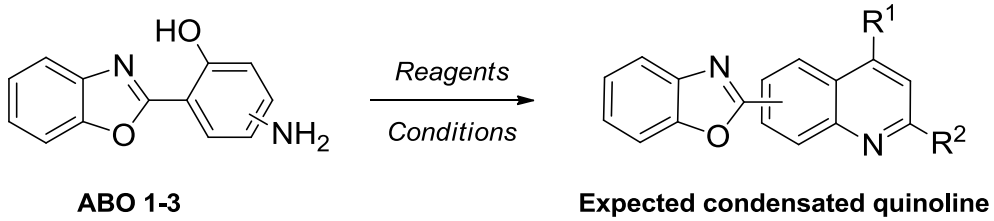

Figure SI3. Synthesis of benzoxazolyl-quinoline via classical condensations.

Table ESI2. Synthesis of benzoxazolyl-quinoline via classical condensations.

Ent.	Synthesis	ABO	Reagents/Conditions	R^1	R^2	Obs.	Ref.
1	Skraup	**1-3**	(i) Glycerol **24**, $FeSO_4$, H_2SO_4, $PhNO_2$, HOAc, 145°C, 4h (ii) H_2O	H	H	Complex mixture	10a
2	Skraup	**1-3**	(i) Glicerol **24**, I_2,, banho de gelo (ii) H_2SO_4, 110°C, 1h. (iii) H_2O, NaOH	H	H	Complex mixture	10b
3	Doebner-Miller	**2**	MVK **86**. In/SiO_2, MW 600W, 30 min.	Me	H	N. R.	11
4	Doebner-Miller	**2**	MVK **86**. In/SiO_2, 100°C, 2h.	Me	H	N. R.	11
5	Conrad-Limpach	**1**	Ethyl acetoacetate **17**. HCl (cat), 4h.	OH	Me	N. R.	12
6	Conrad-Limpach	**1**	Ethyl acetoacetate **17**. In/SiO_2 (cat.), 4h.	OH	Me	N. R.	12
7	Conrad-Limpach	**1**	Ethyl acetoacetate **17**. Diphenyl ether, 260°C, 4h.	OH	Me	N. R.	13

9. V. V. Koutznetsov, L. Y. V. Mendez, C. M. M. Gomez, *Curr. Org. Chem.,* 2005, **9**, 141.
10. (a) Q. Liu, H. Gao, K. Shi, Q. Shujian, H. Wang, *Molecules* 2007, **12**, 988. (b) P. J. Seaton, R. T. Williamson, A. Mitra, A. Assrpour, *J. Chem. Educ*. 2002, **79**, 106.
11. (b) B. C. Ranu, A. Hajra, U. Jana, *Tetrahedron Lett*., 2000, **41**, 531.
12. F. W. Bergstrom, *Chem. Rev.,* 1944, **35**, 156.
13. F. Misani, M. T. Bogert, *J. Org. Chem*., 1945, **10**, 347.

2. Different attempts for formylation of salicylic acid

Table ESI3. Salicylic acid formylation conditions.[14]

Ent.	Solvent.	Time (h)	Temperature (°C)	Product
1	H_2O	16	100	N.R.
2	AcOH	7	100	40%[a]
3	AcOH	7	115	40%[a]
4	AcOH	8	118	16%[b]
5	AcOH	10	130	14%[b]

[a]3 and 5-formyl derivatives mixture; [b] Isolated yields.

3. Additional data for the fluorophore 9

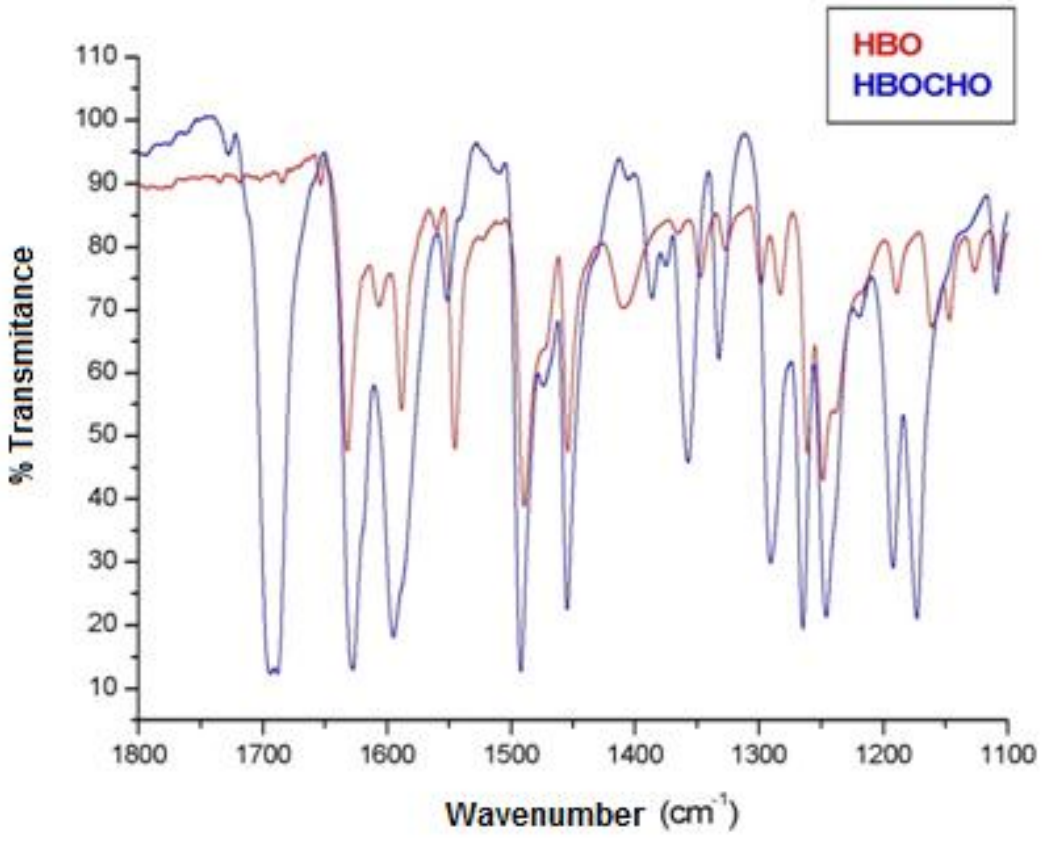

Figure ESI4. FTIR Spectra of HBO **8** and **9** (KBr pellet, 1100-1800 cm^{-1}).

14. (a) J. C. Duff, E. J. Bills, *J. Chem. Soc.,* 1932, 1987. (b) J. C. Duff, E. J. Bills, *J. Chem. Soc.,* 1934, 1305. (c) Y. Suzuki, H. Takahashi, *Chem. Pharm. Bull*., 1983, **31**, 1751. (d) T. V. Shokol, O. A. Lozinskii, A. V. Turov, V. P. Khilya, *Chem. Heteroc. Comp*., 2009, **45**, 1089. (e) W. E. Smith, *J. Org. Chem.*, 1972, **37**, 3972.

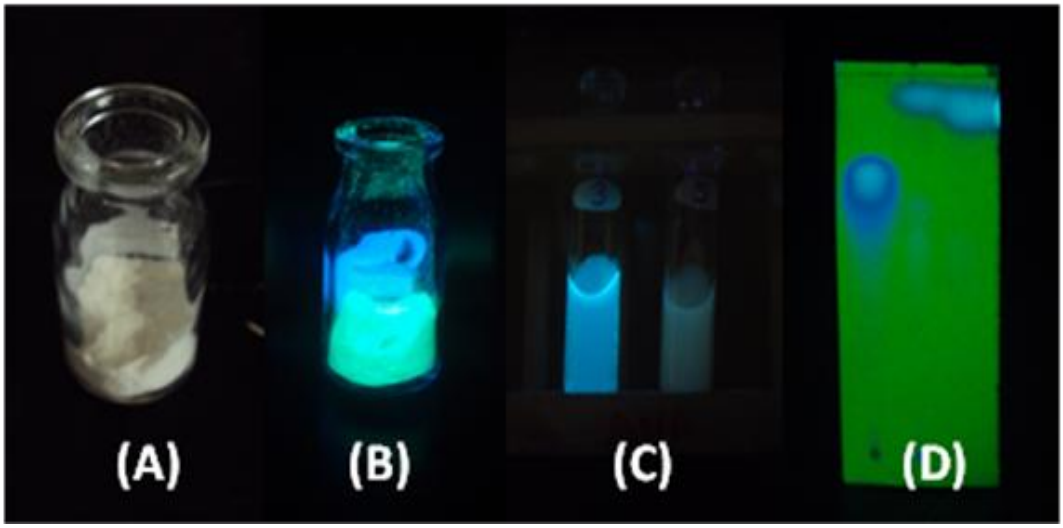

Figure ESI5. Compound **9** (A) solid state under normal light, (B) solid state under UV 365 nm, (C) chloroform solution under UV 365 and (D) TLC under UV 254 nm (left).

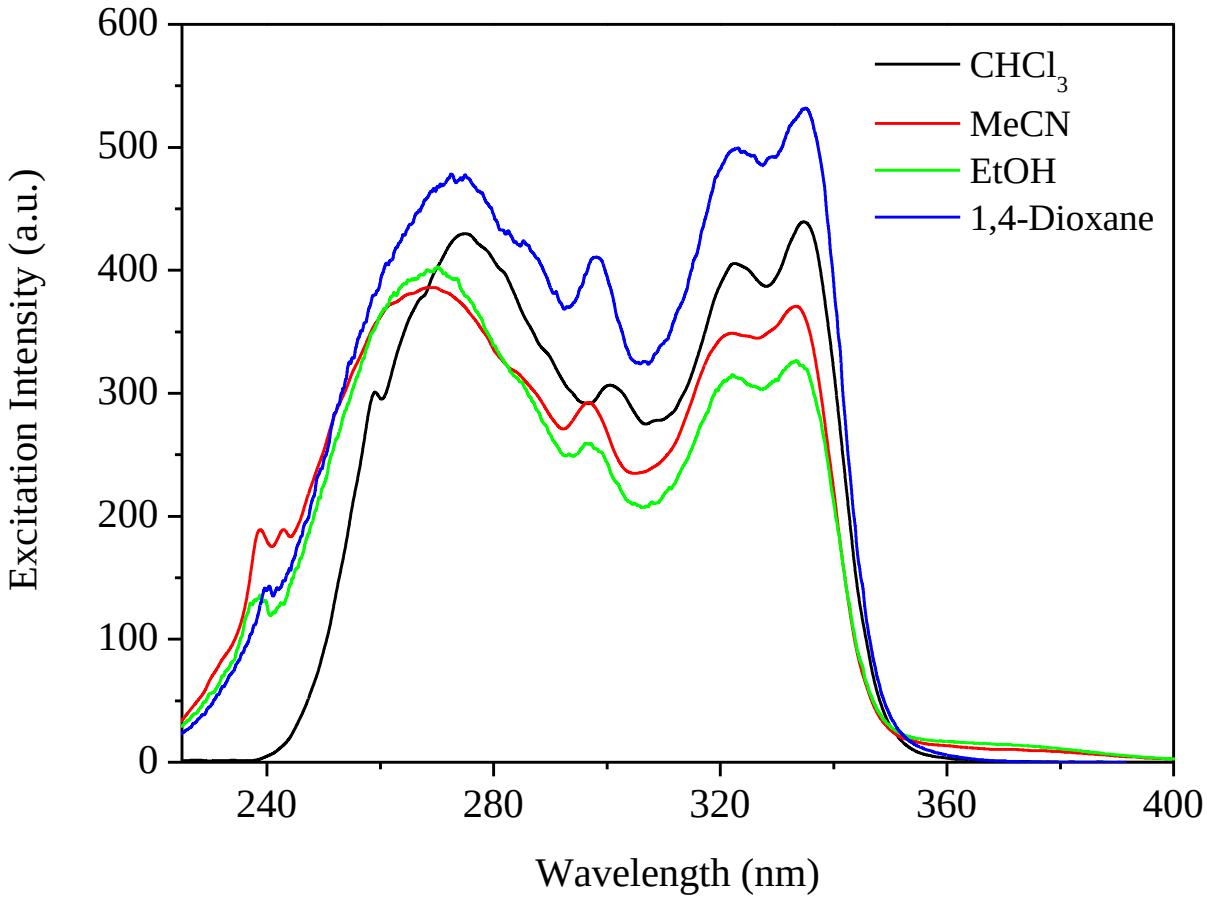

Figure ESI6. Excitation spectra of **9** in solution.

4. 1,4-Dihydropyridines

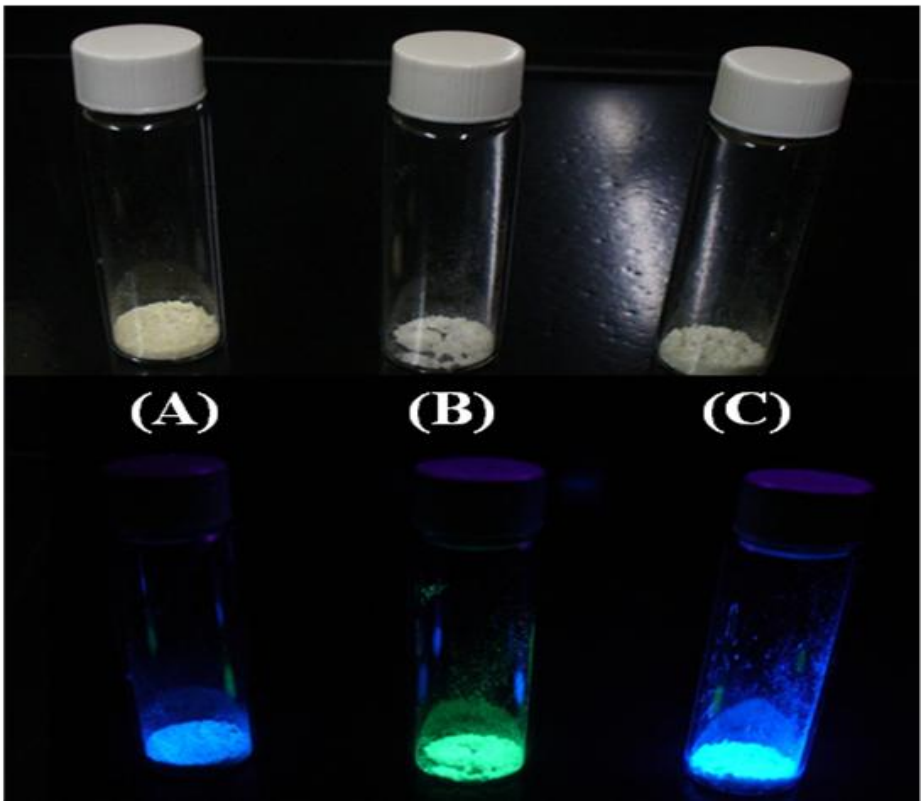

Figure ESI7. (A) **15**, (B) **17** and (C) **16** under irradiation of normal light (above) and UV 365nm (below).

5. Spectral Data

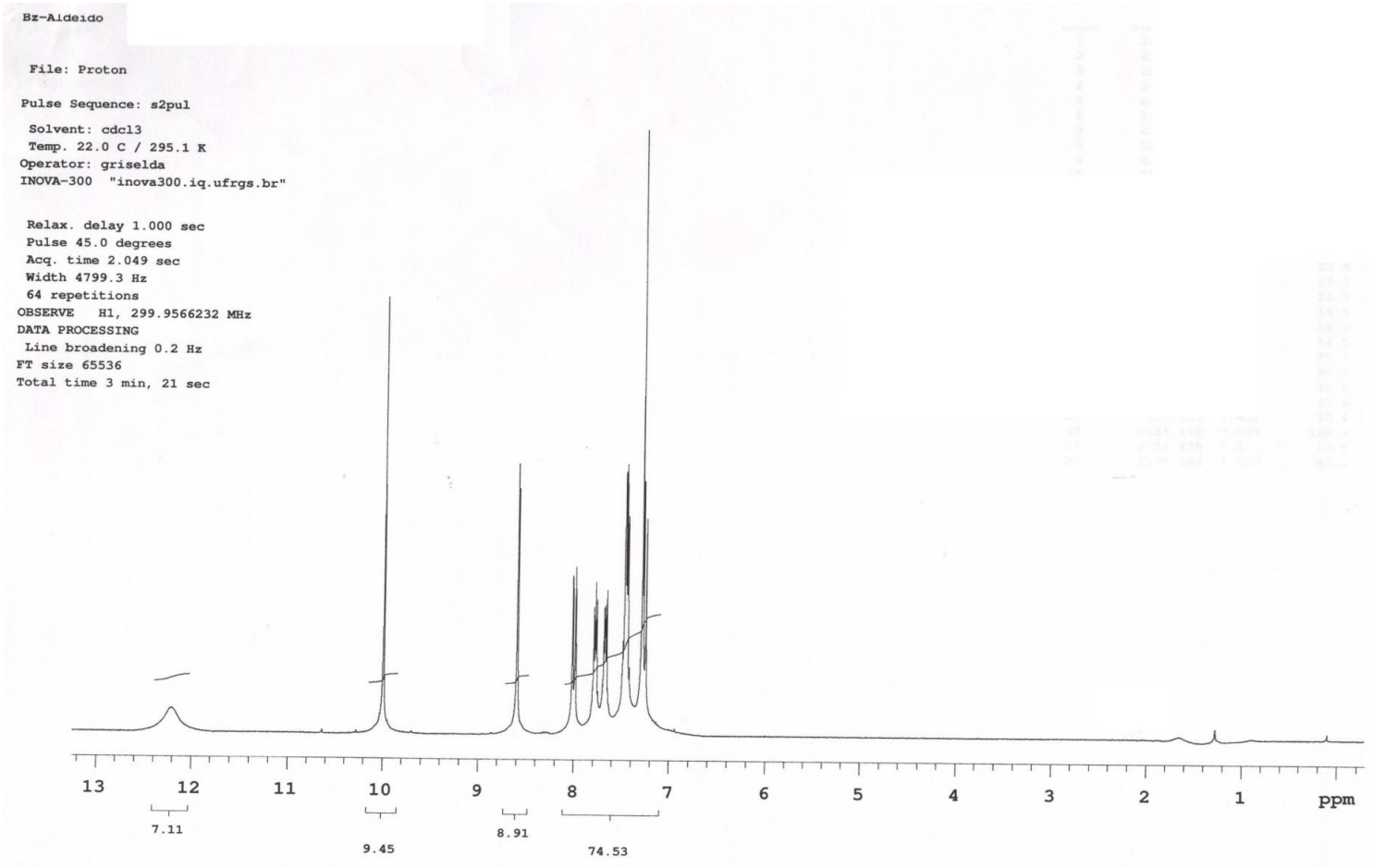

Figure ESI8 ^{1}H-NMR ($CDCl_3$, 300 MHz) of 2-(5'-formyl-2'-hydroxyphenyl)benzoxazol **9**.

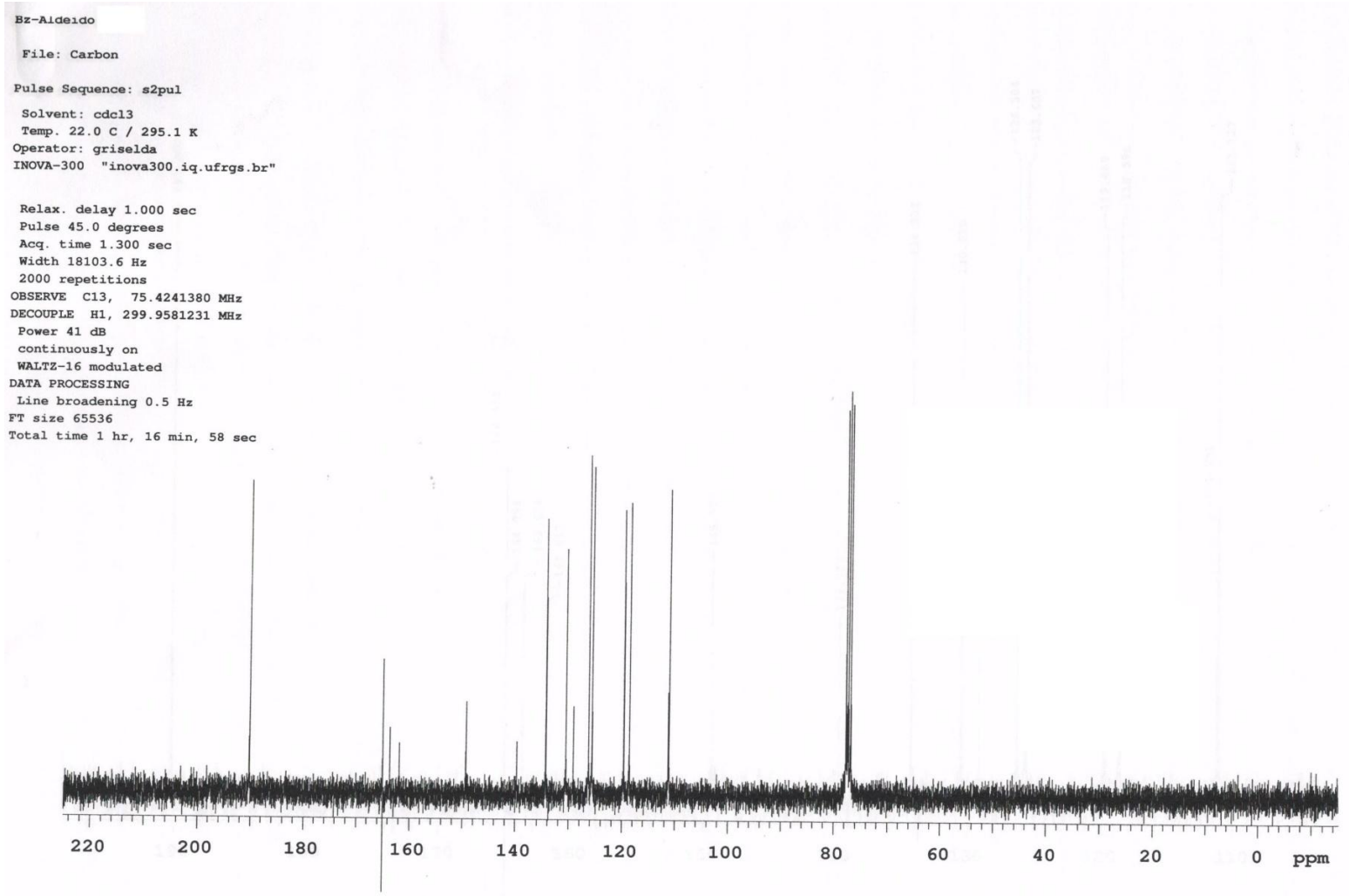

Figure ESI9. ^{13}C-NMR ($CDCl_3$, 75 MHz) of 2-(5'-formyl-2'-hydroxyphenyl)benzoxazol **9**.

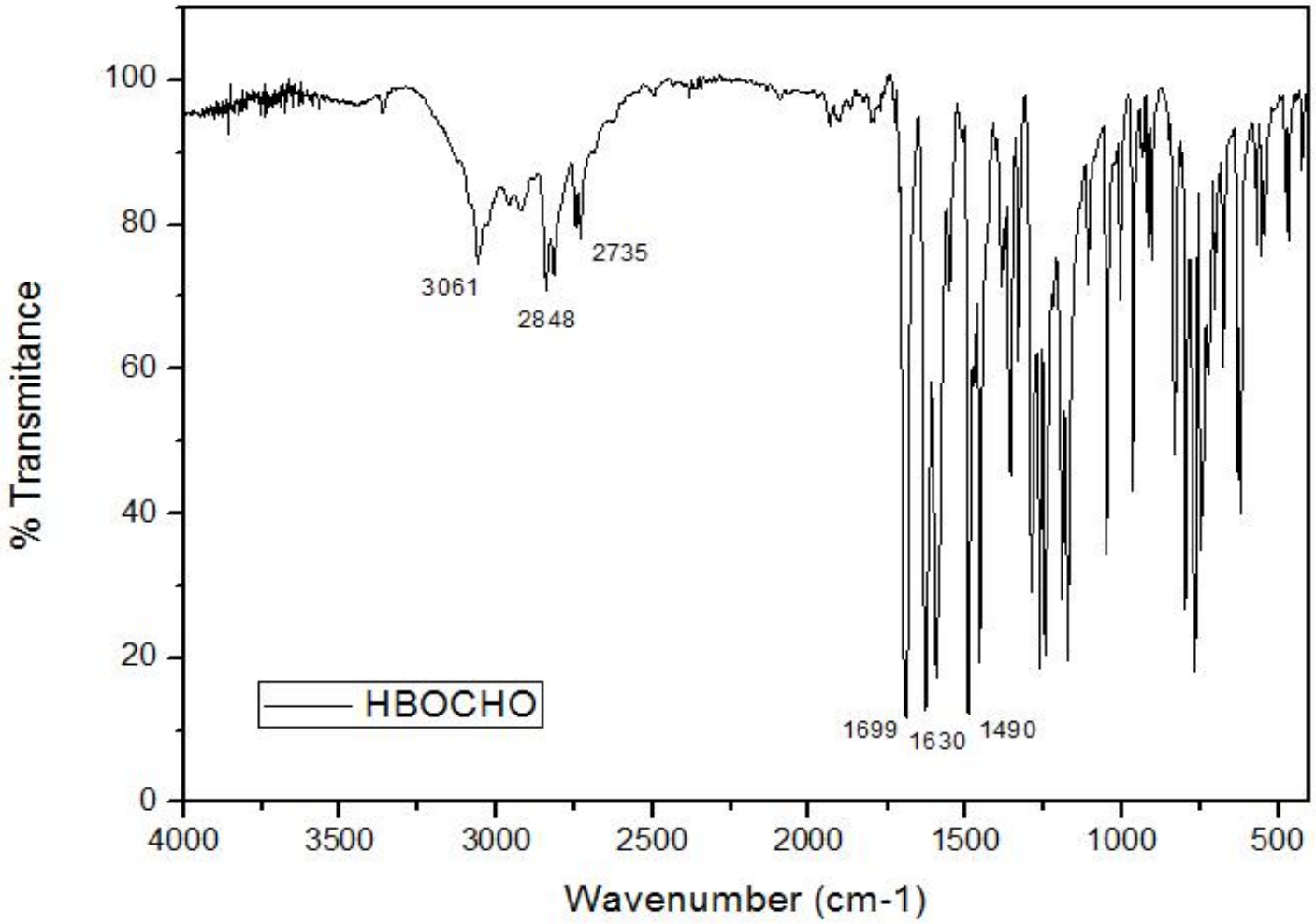

Figure ESI10. FTIR spectrum of 2-(5'-formyl-2'-hydroxyphenyl)benzoxazol **9**.

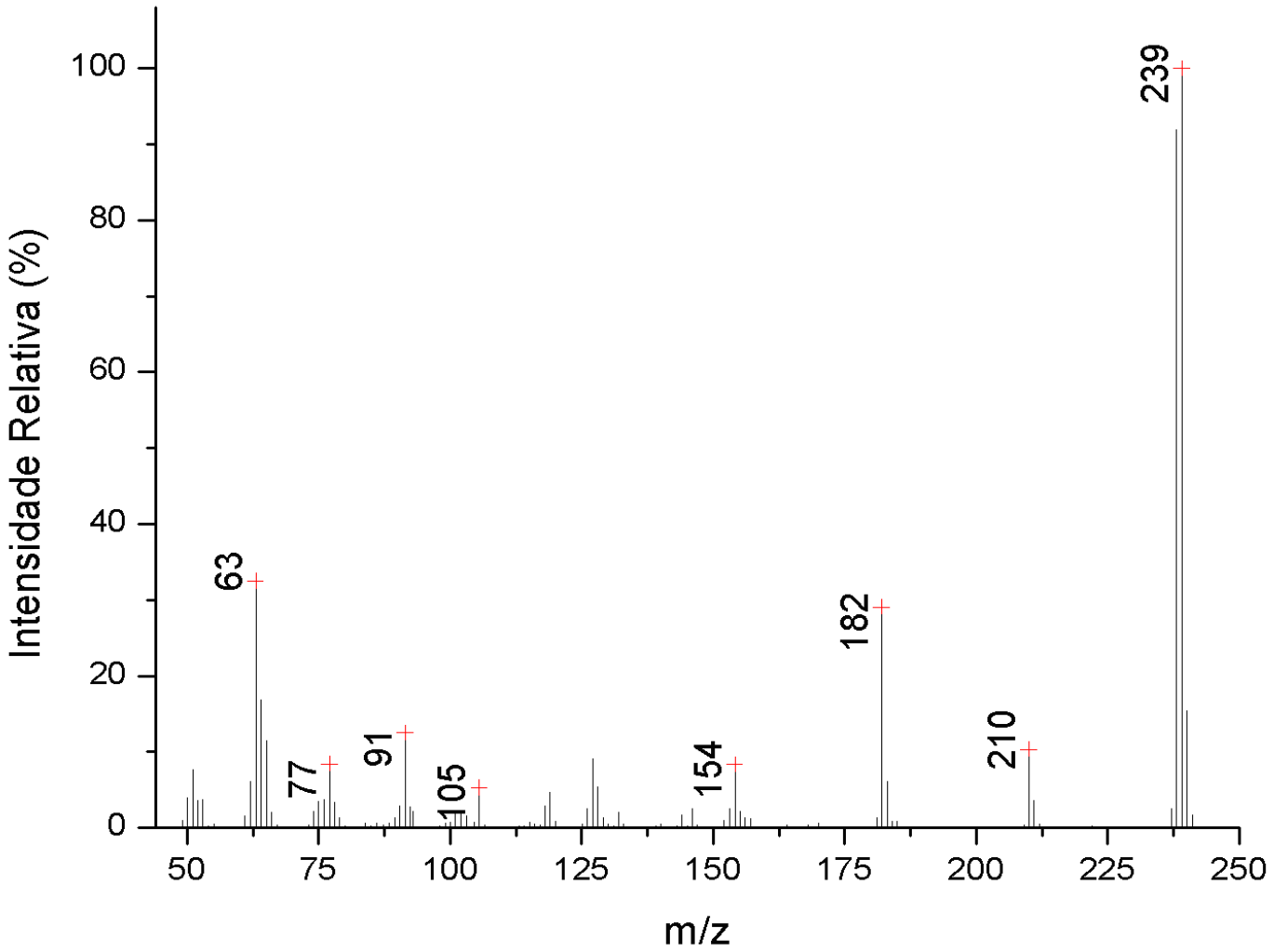

Figure ESI11. MS spectrum (70eV) of 2-(5'-formyl-2'-hydroxyphenyl)benzoxazol **9**.

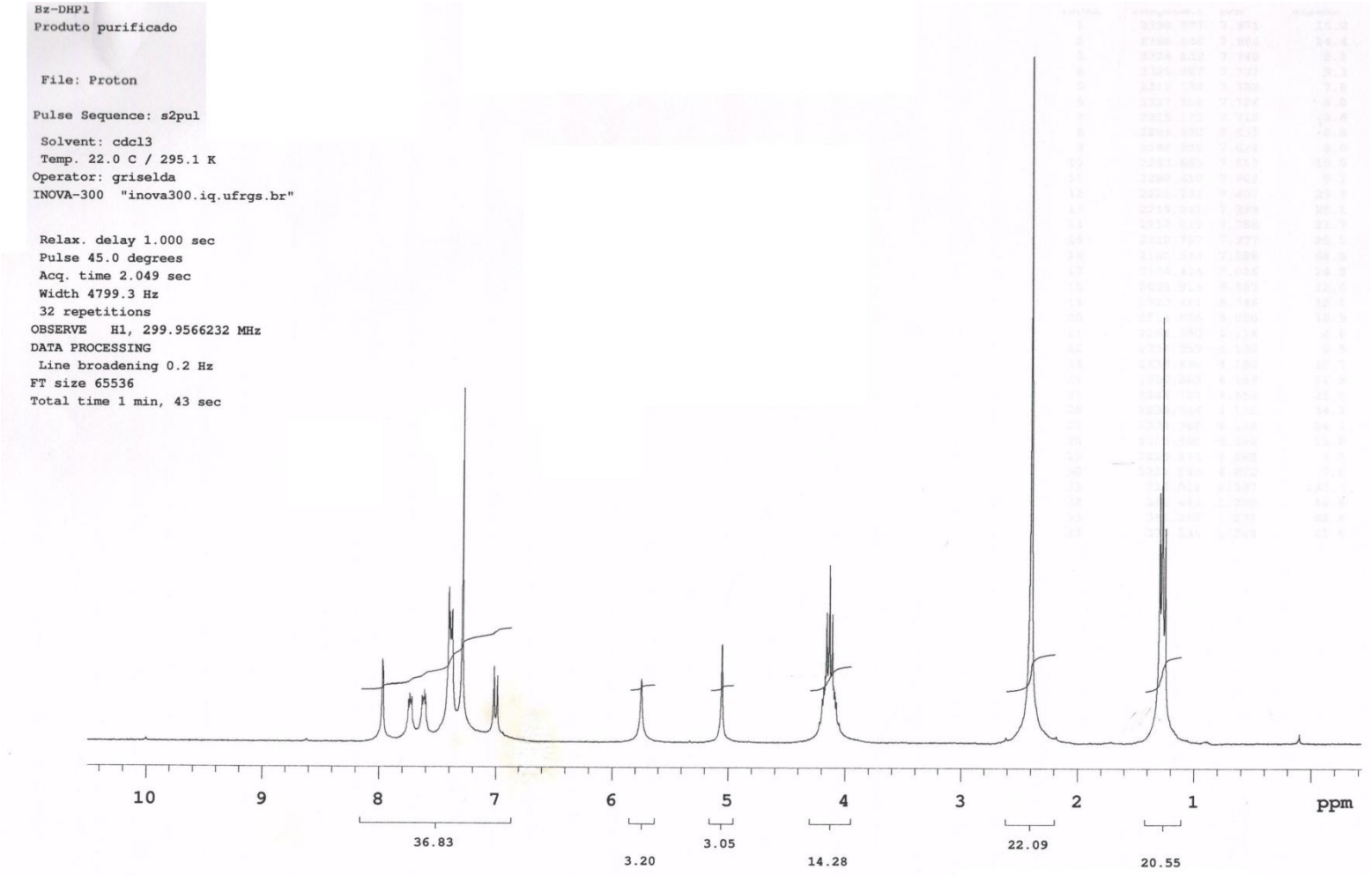

Figure ESI12. ^{1}H-NMR ($CDCl_3$, 300 MHz) of **15**.

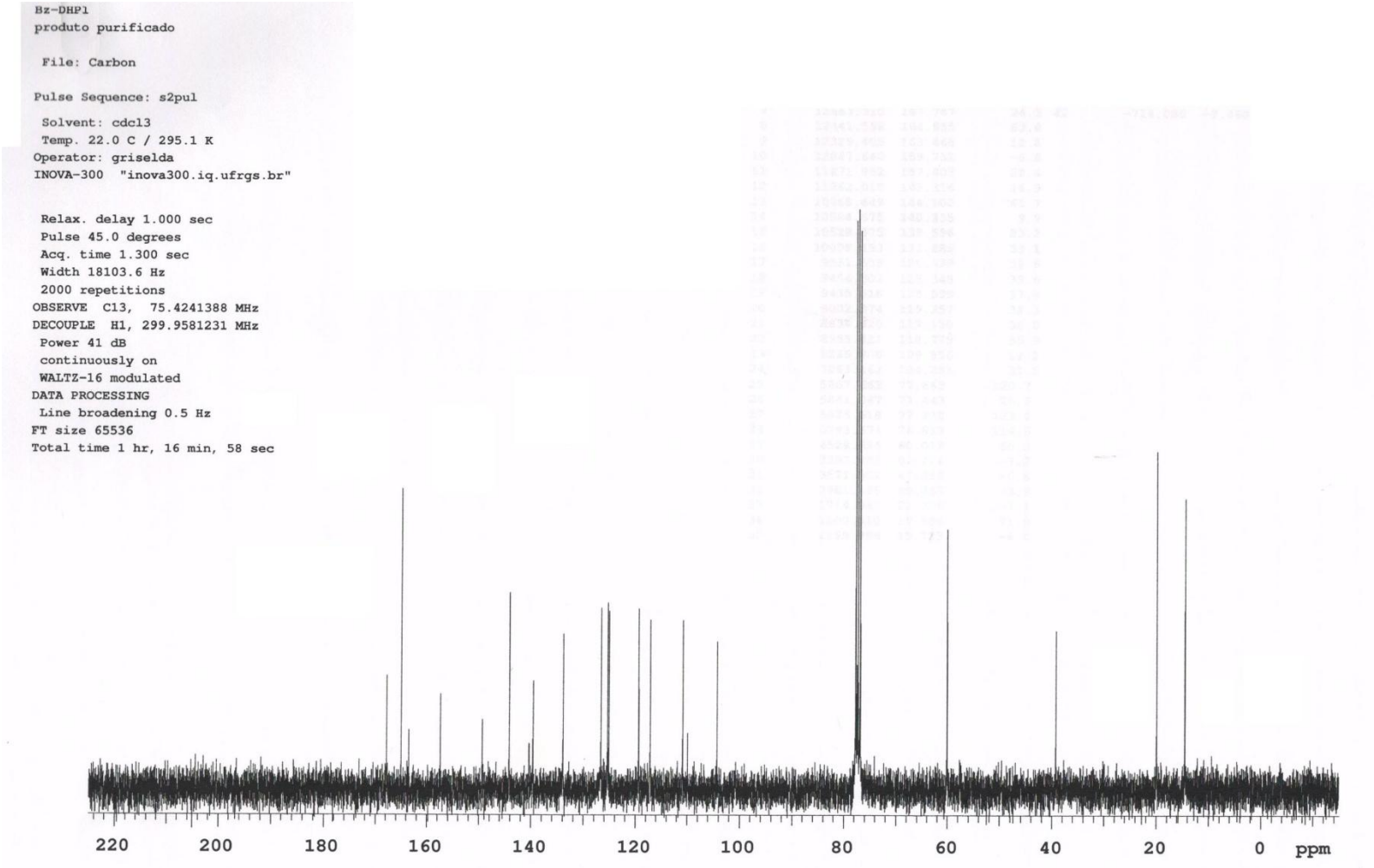

Figure ESI13. ^{13}C-NMR ($CDCl_3$, 75 MHz) of **15**.

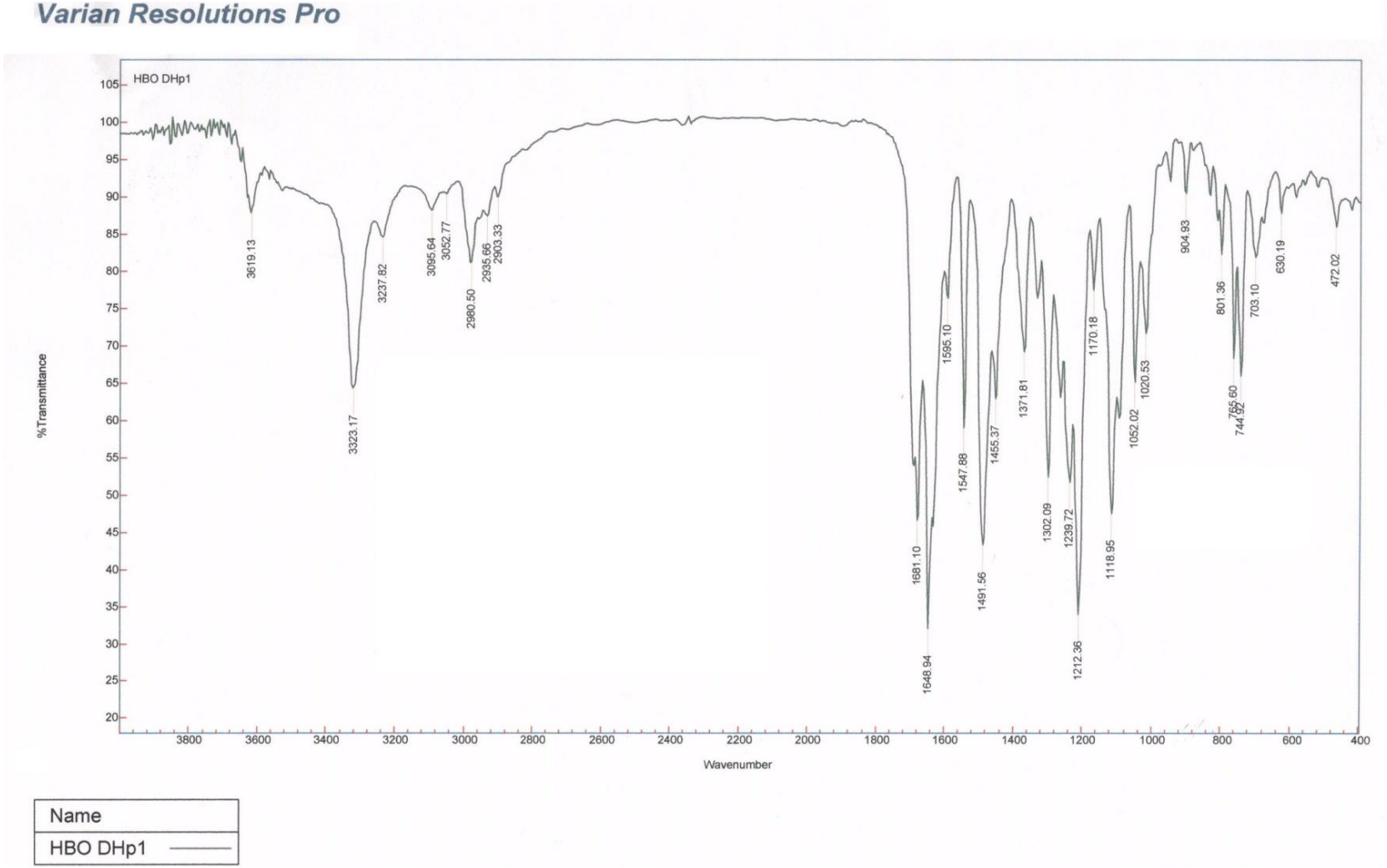

Figure ESI14. FTIR spectrum of **15**.

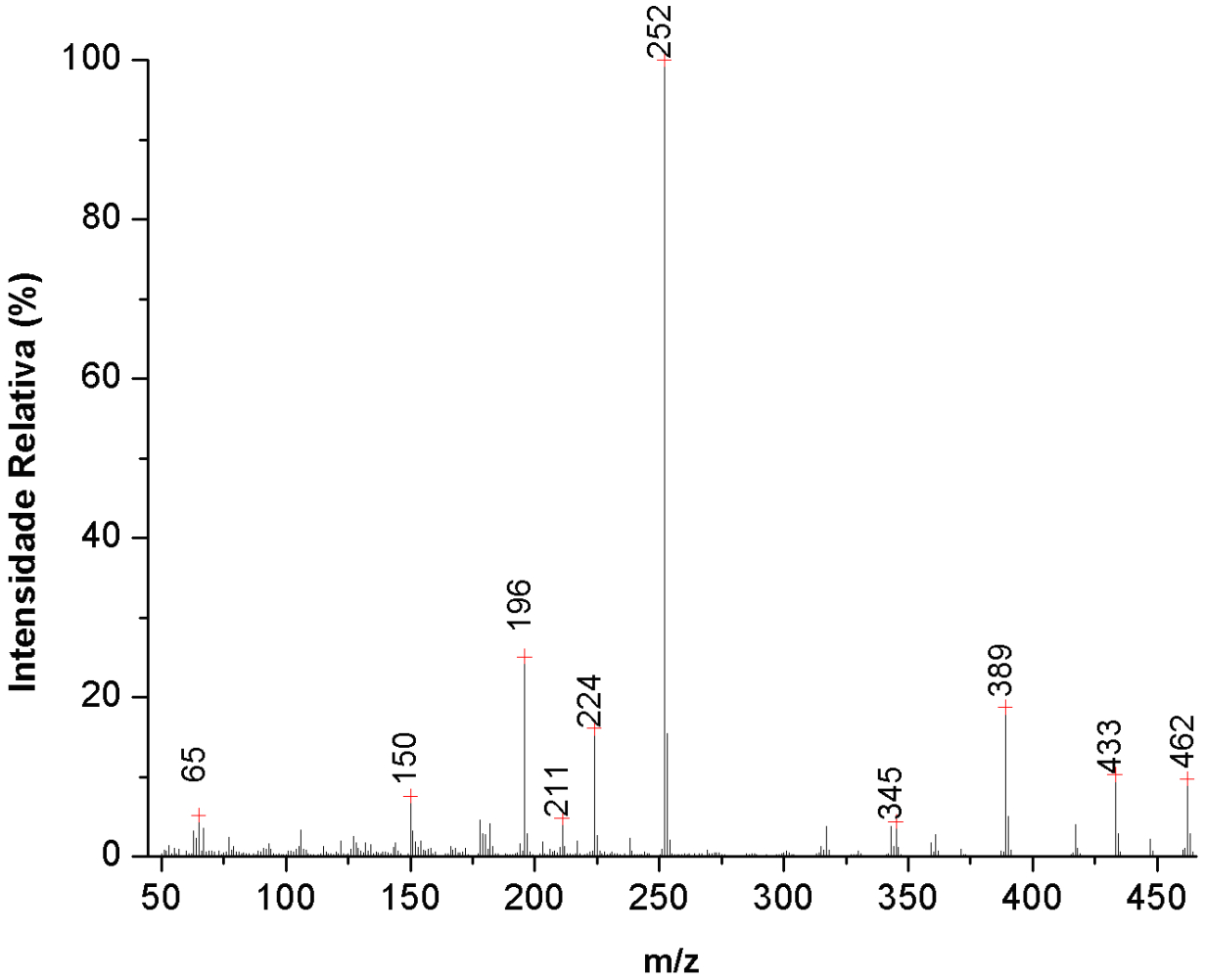

Figure ESI15. MS spectrum (70eV) of **15**.

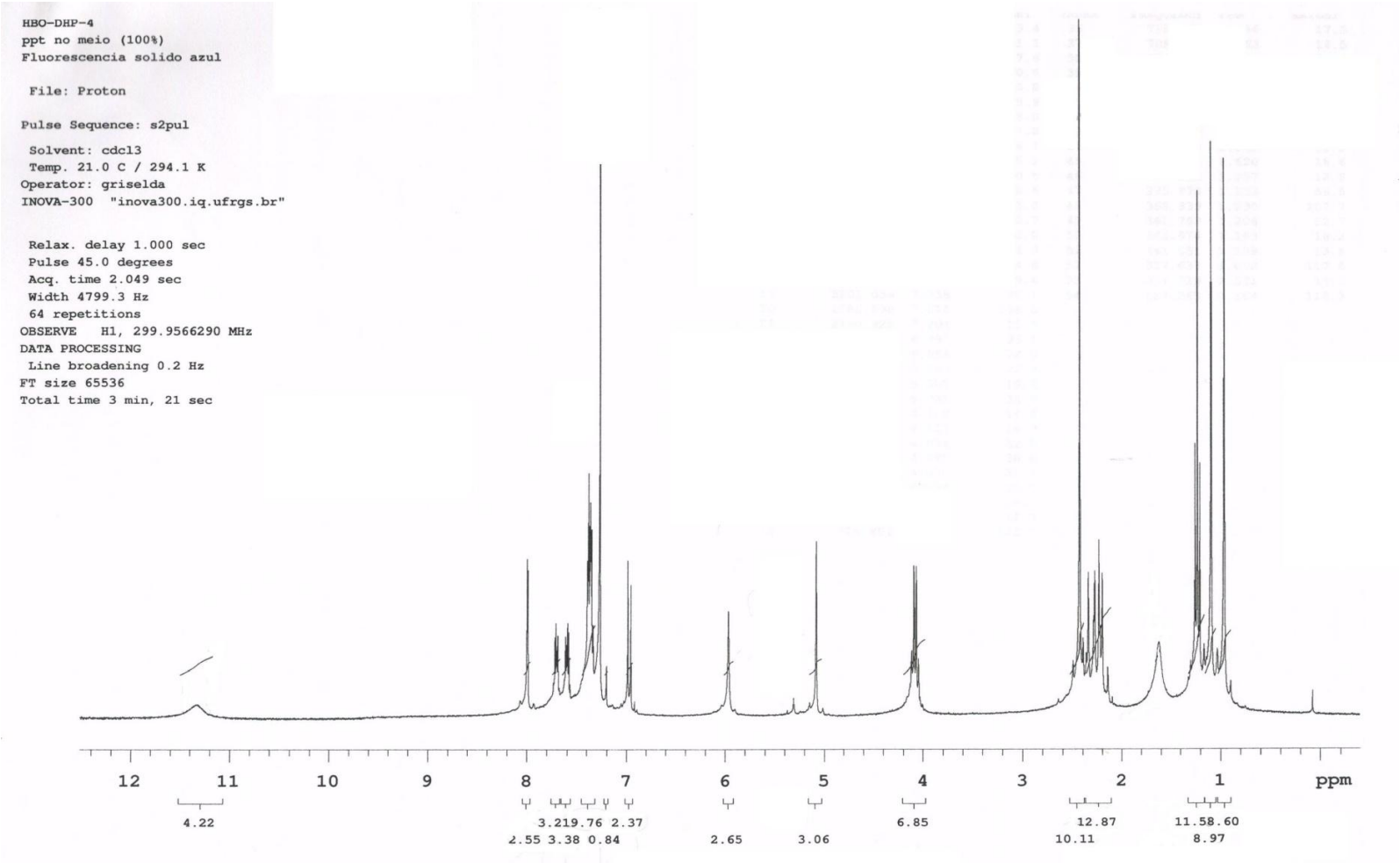

Figure ESI16. ^{1}H-NMR ($CDCl_3$, 300 MHz) of **16**.

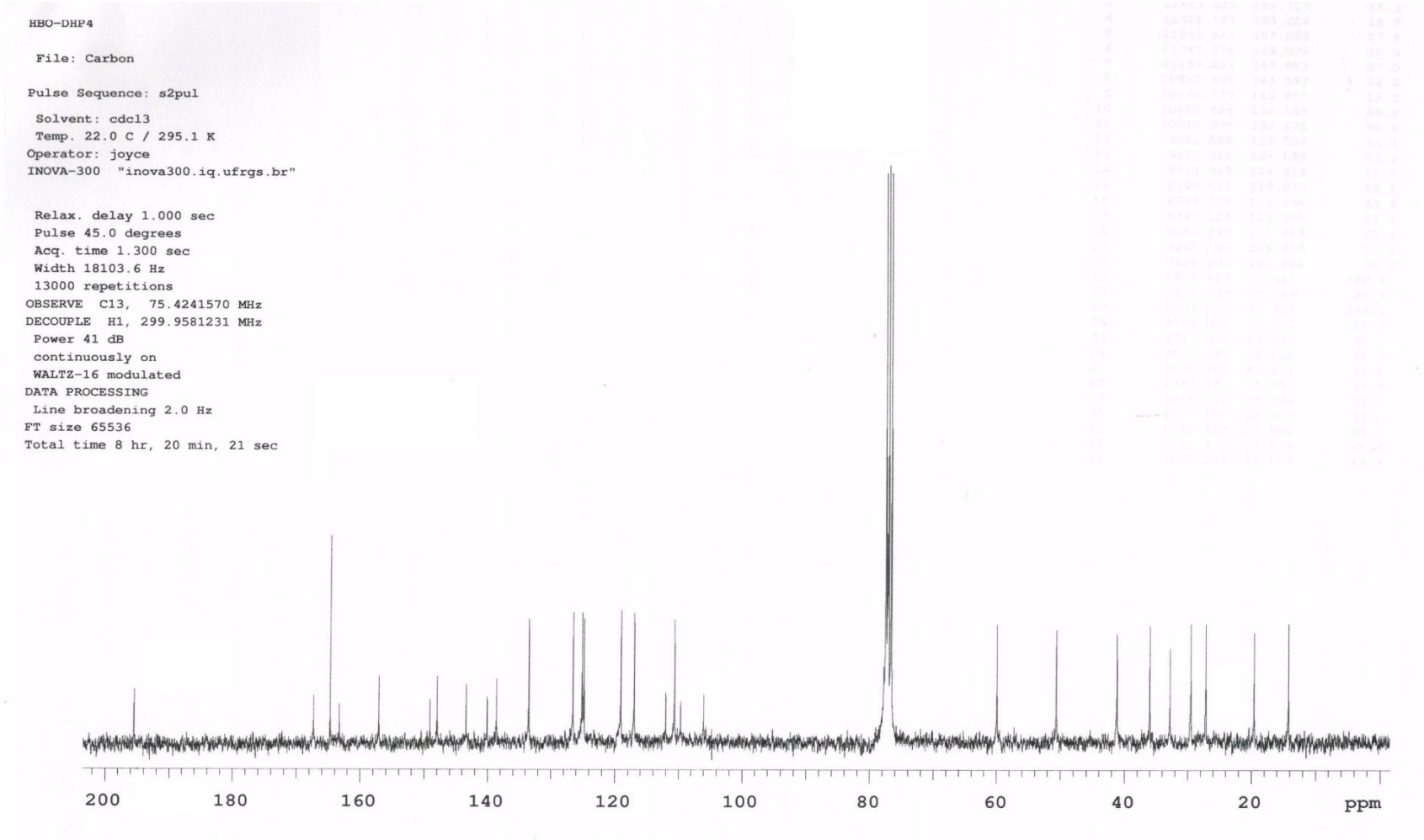

Figure ESI17. ^{13}C-RMN (CDCl3, 75 MHz) of **16**.

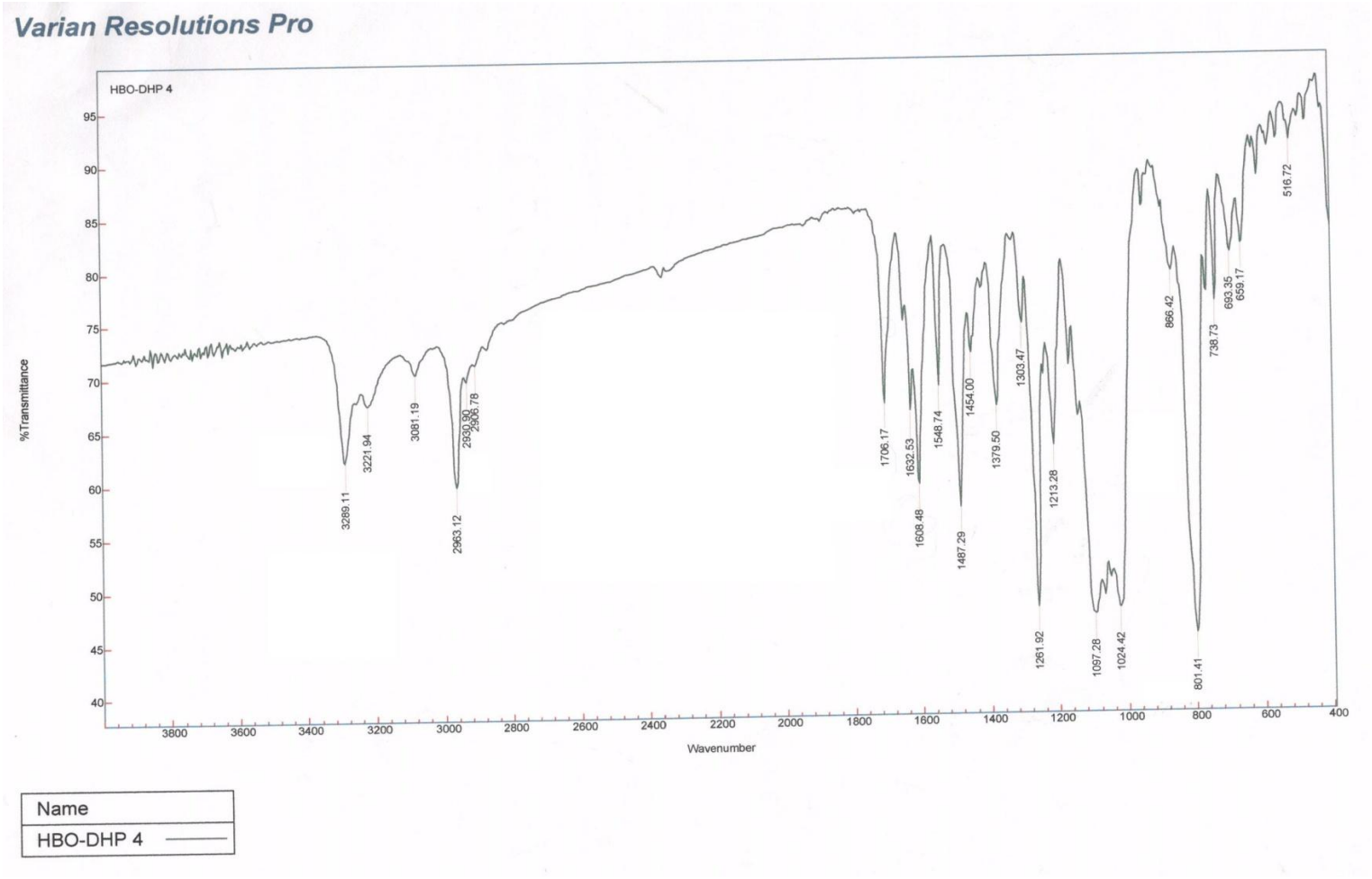

Figure ESI18. FTIR spectrum of **16**.

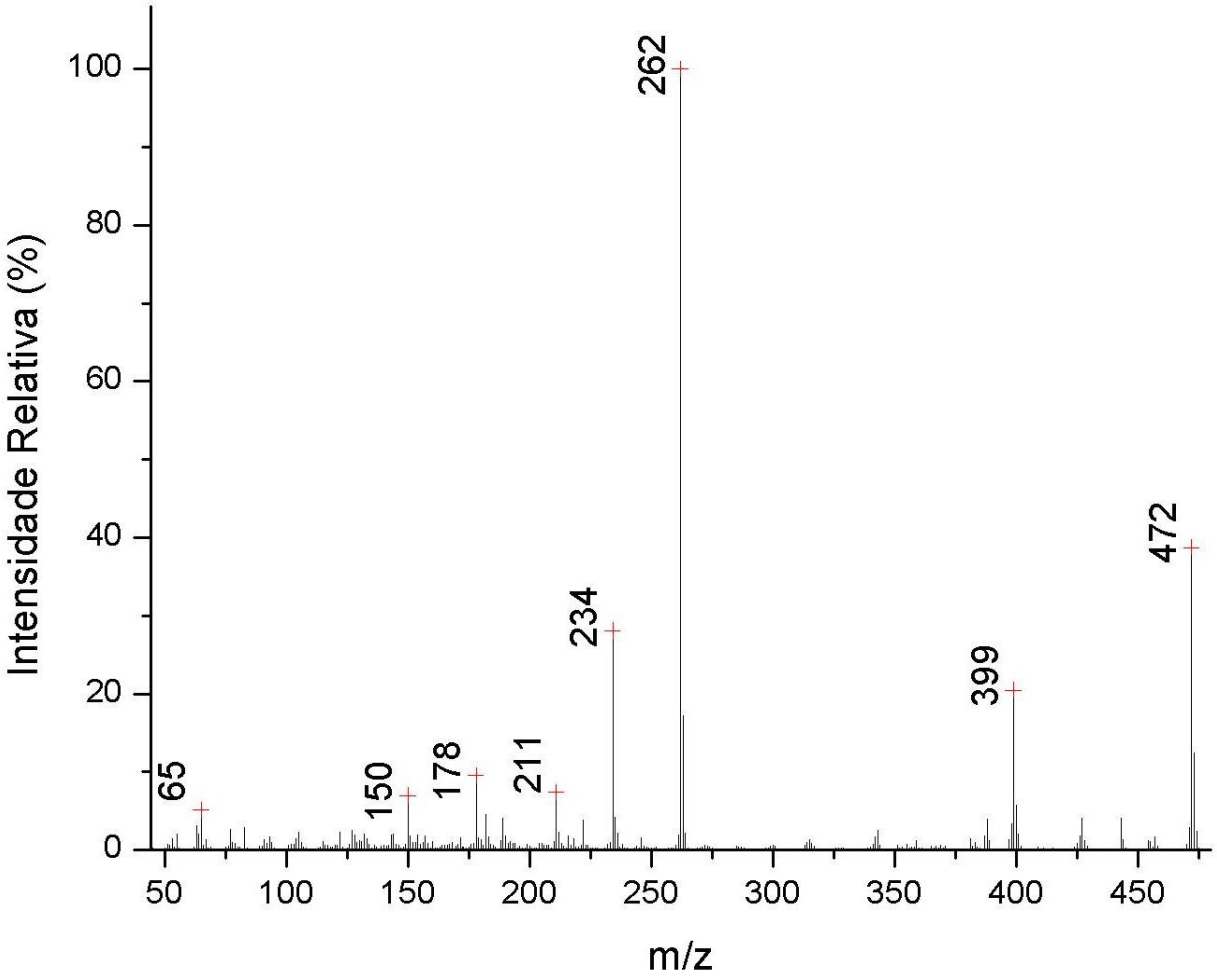

Figure ESI19. MS spectrum of **16**.

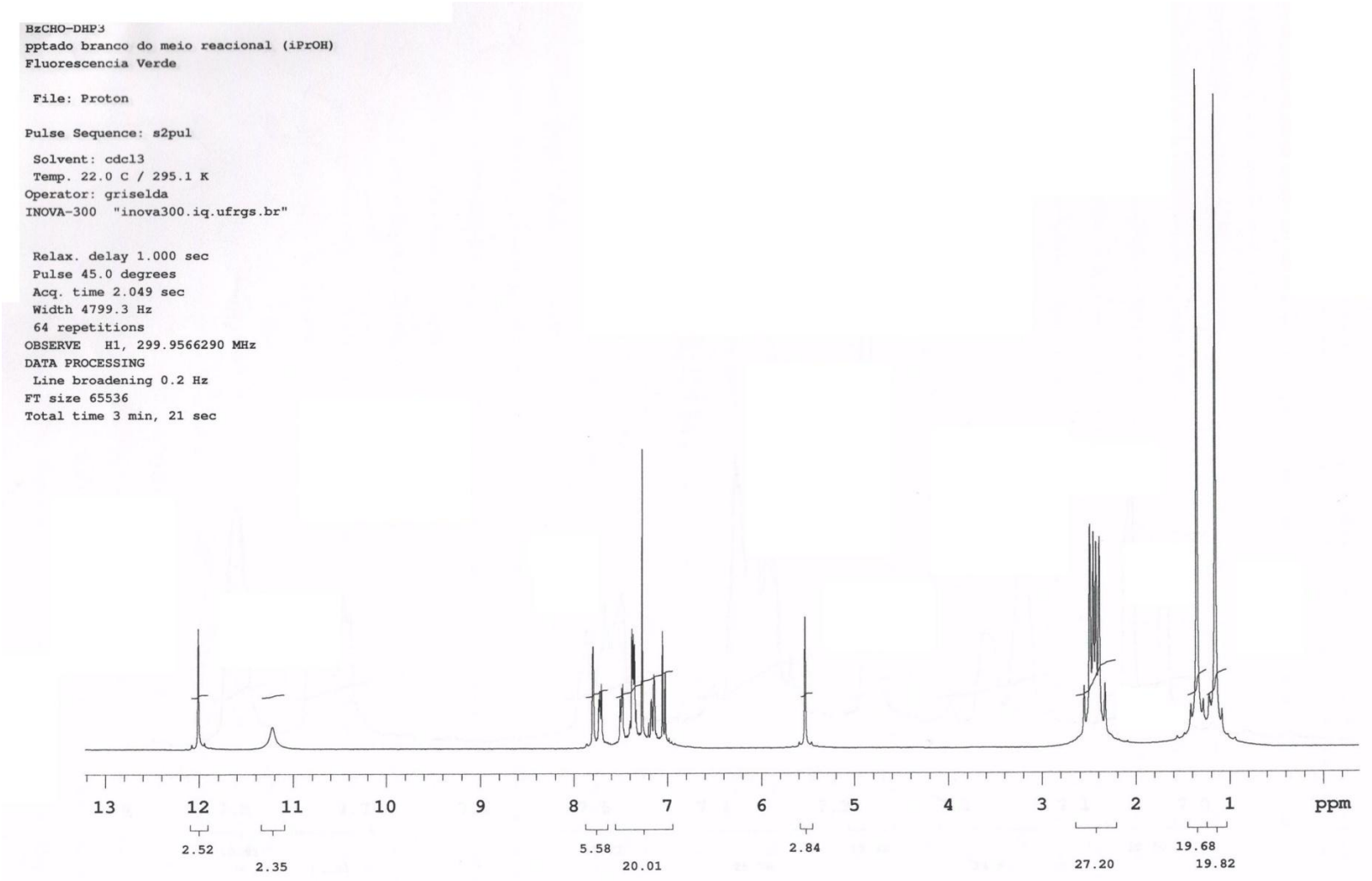

Figure ESI20. ^{1}H-NMR ($CDCl_3$, 300 MHz) of **17**.

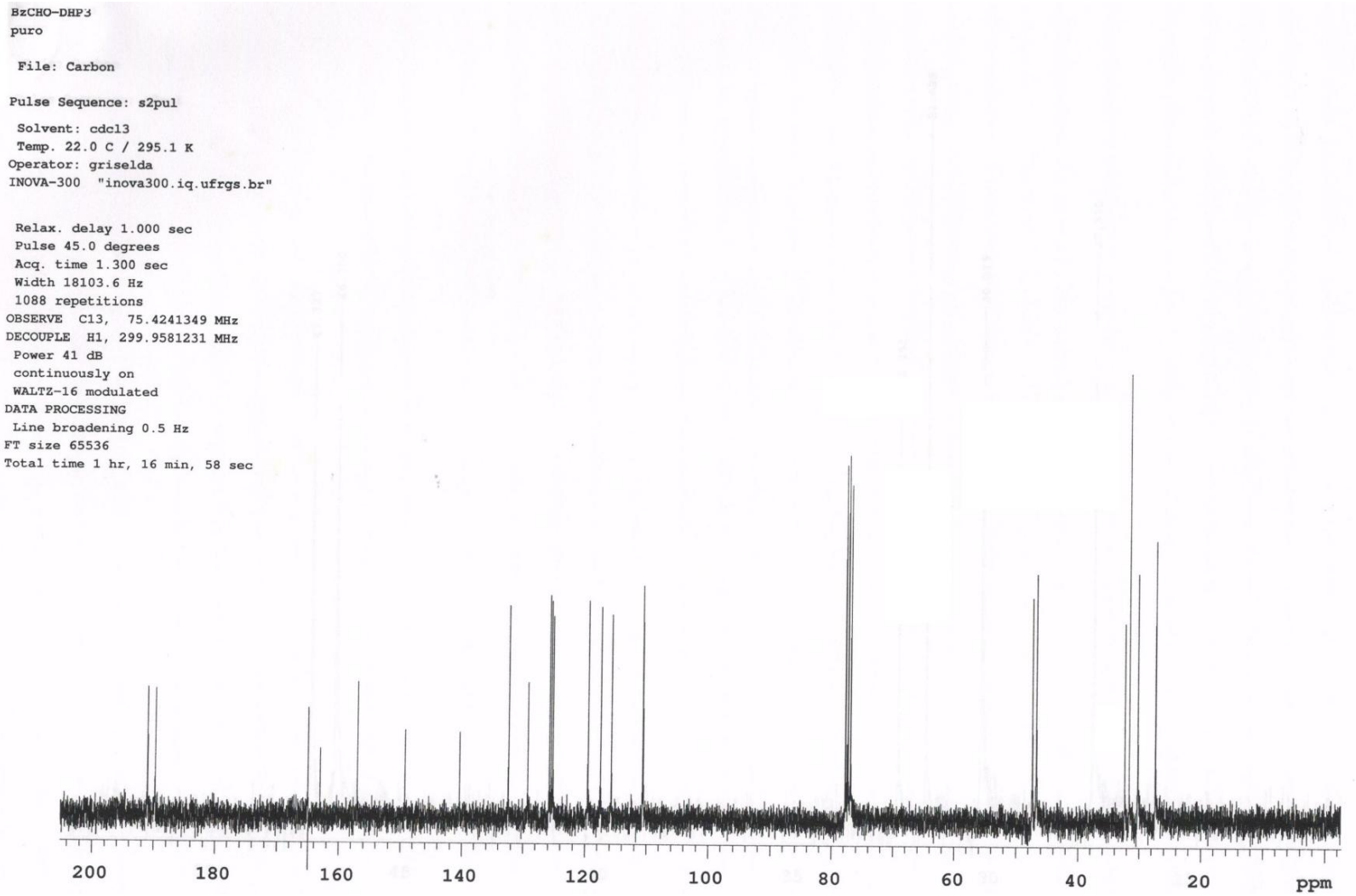

Figure ESI21. ^{13}C-NMR ($CDCl_3$, 75 MHz) of **17**.

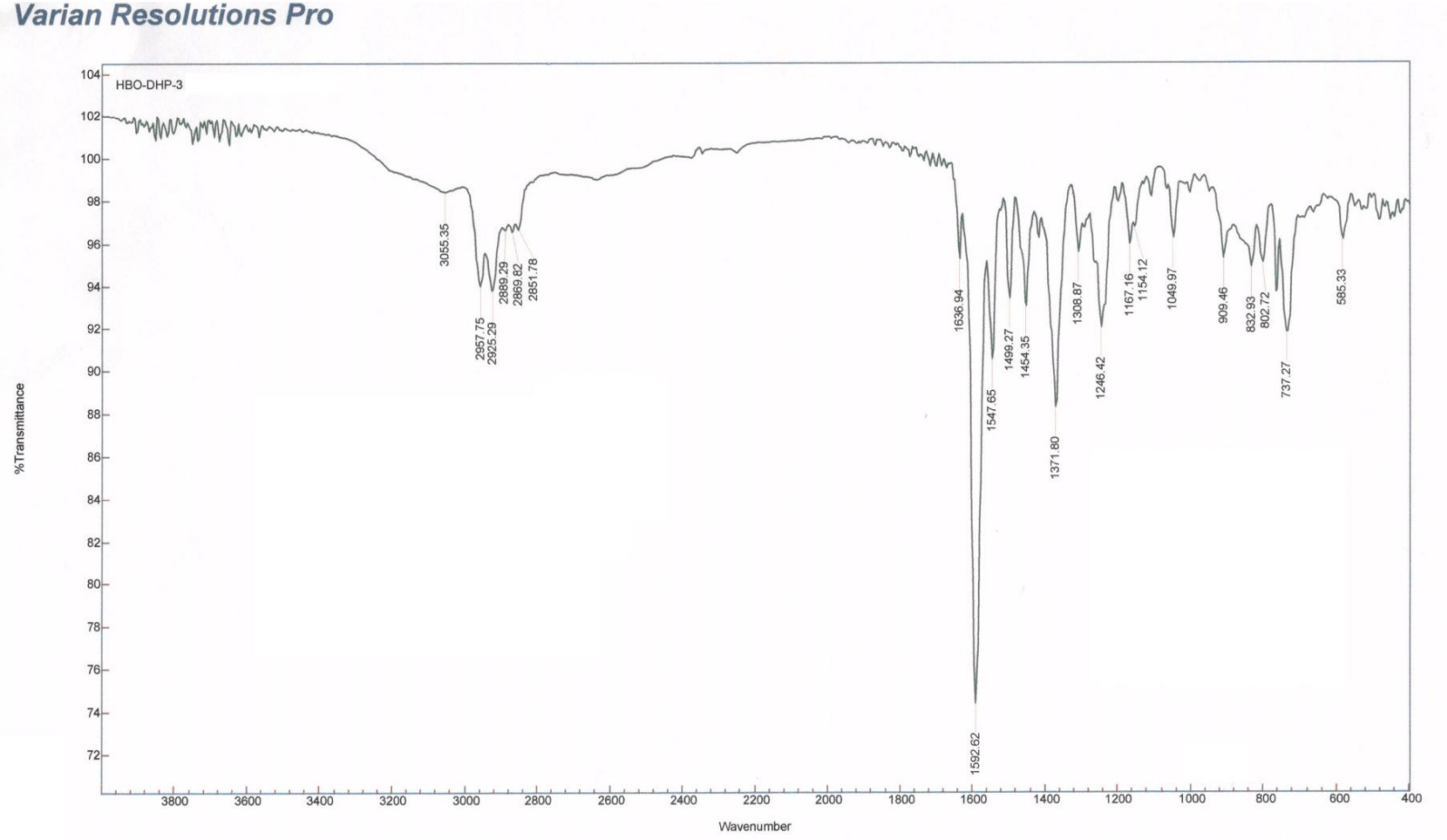

Figura ESI22. FTIR spectrum of **17**.

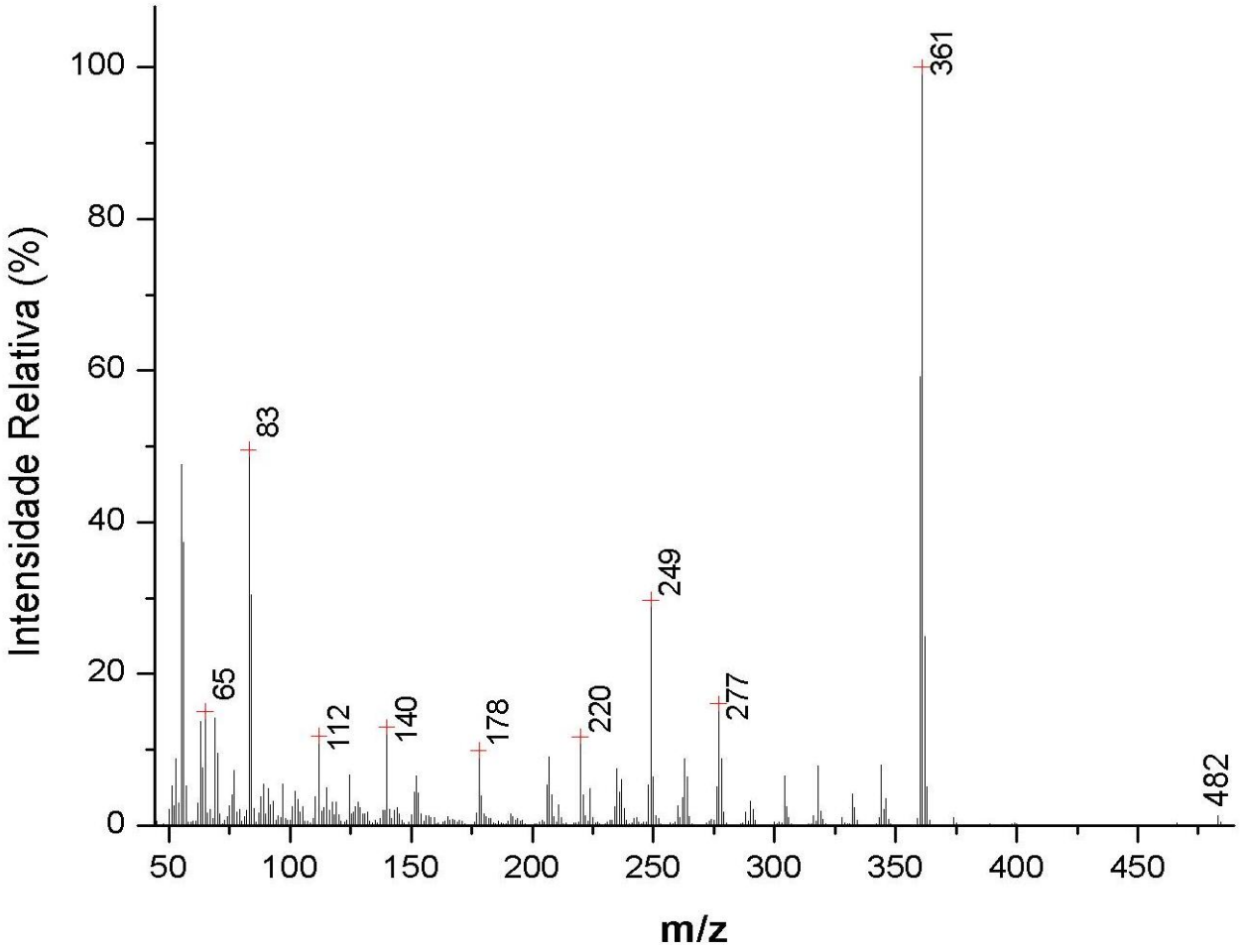

Figure ESI23. MS spectrum of **17**.

7. HRMS Data (Theoretical mass from *Pure Applied Chemistry* 63(7) 975-990 1991)

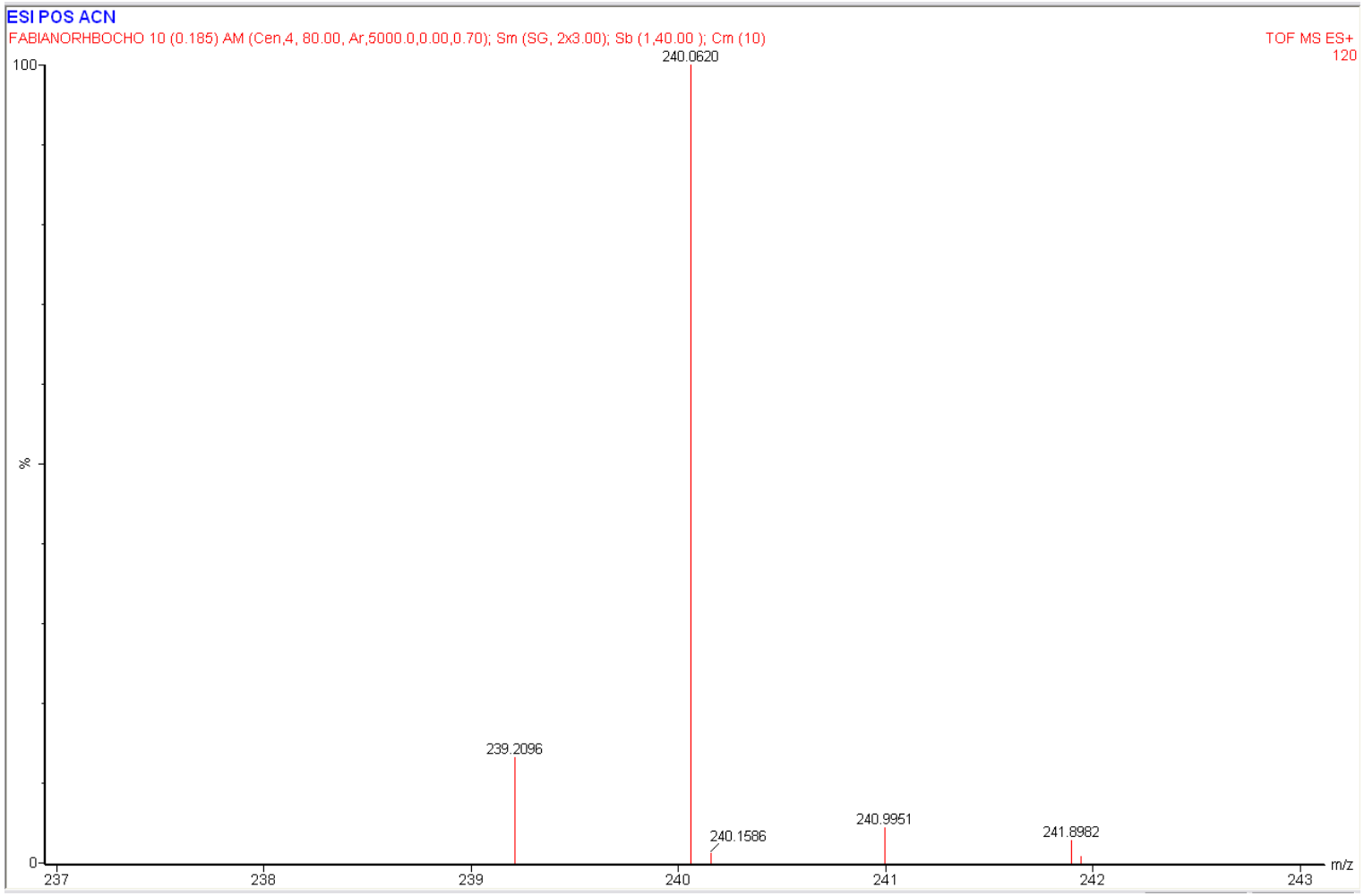

Figure ESI24. HRMS spectrum of HBOCHO **14**.

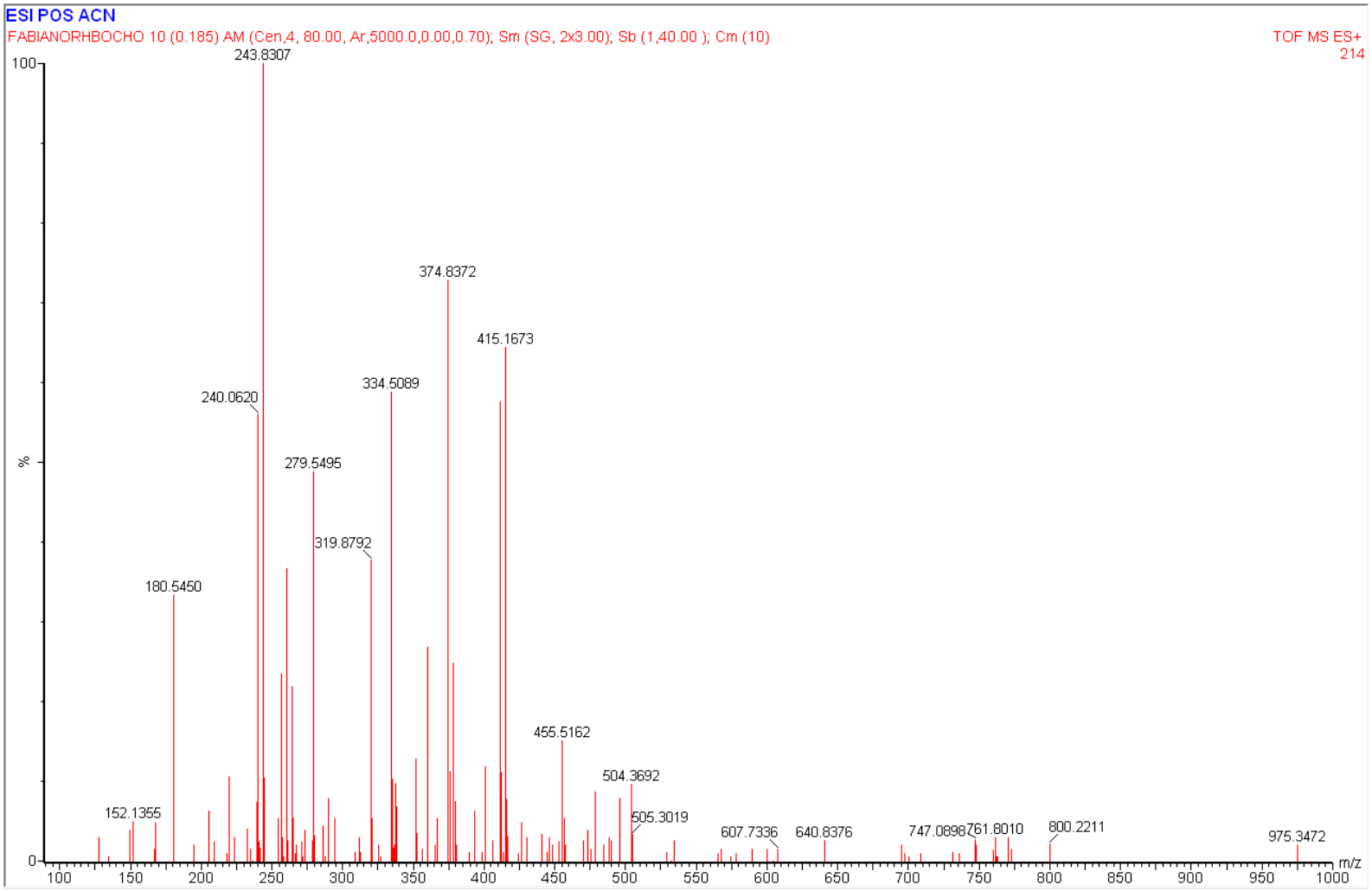

Figure ESI25. HRMS spectrum of **9**.

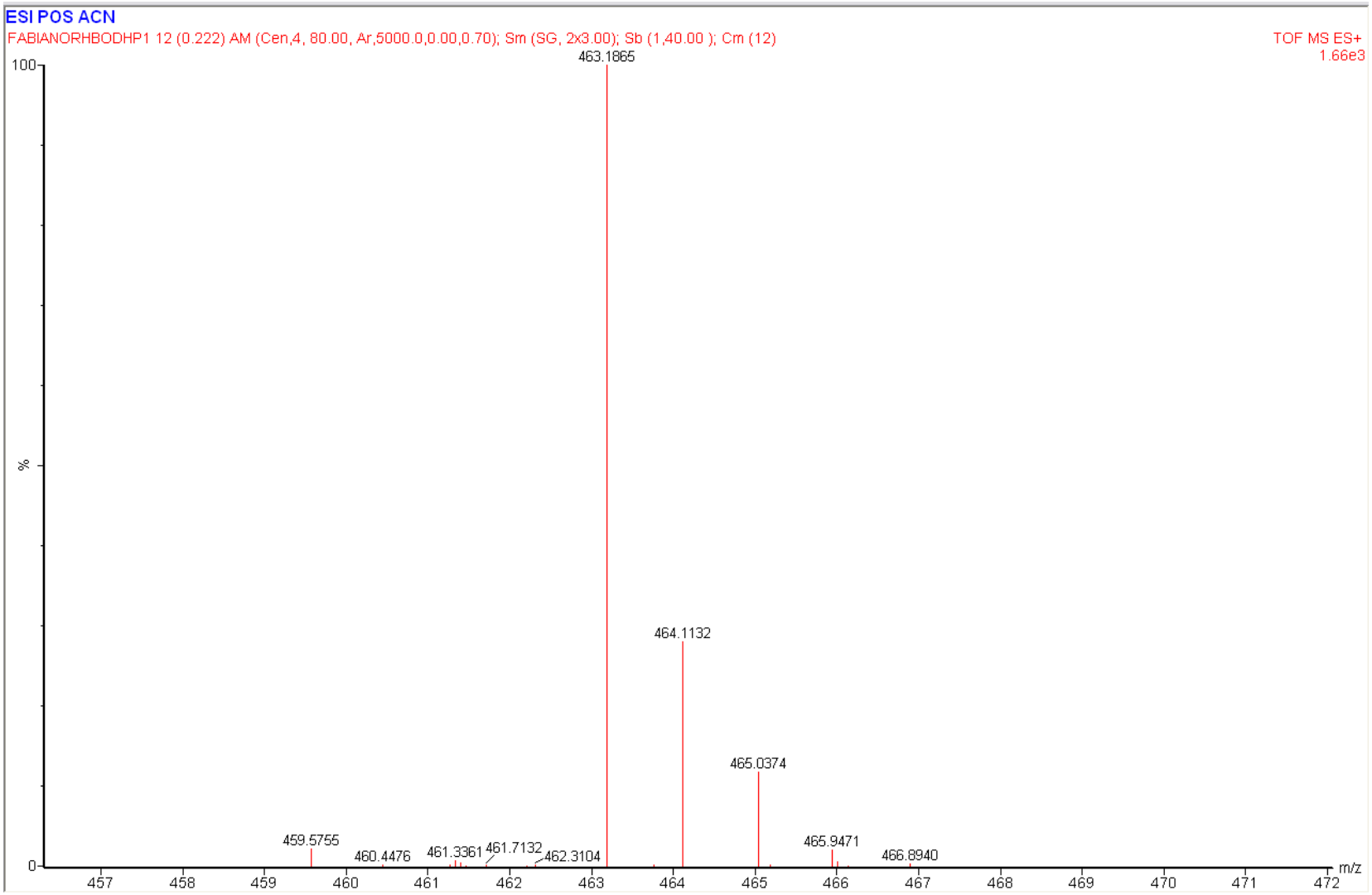

Figure ESI26. HRMS spectrum of **15**.

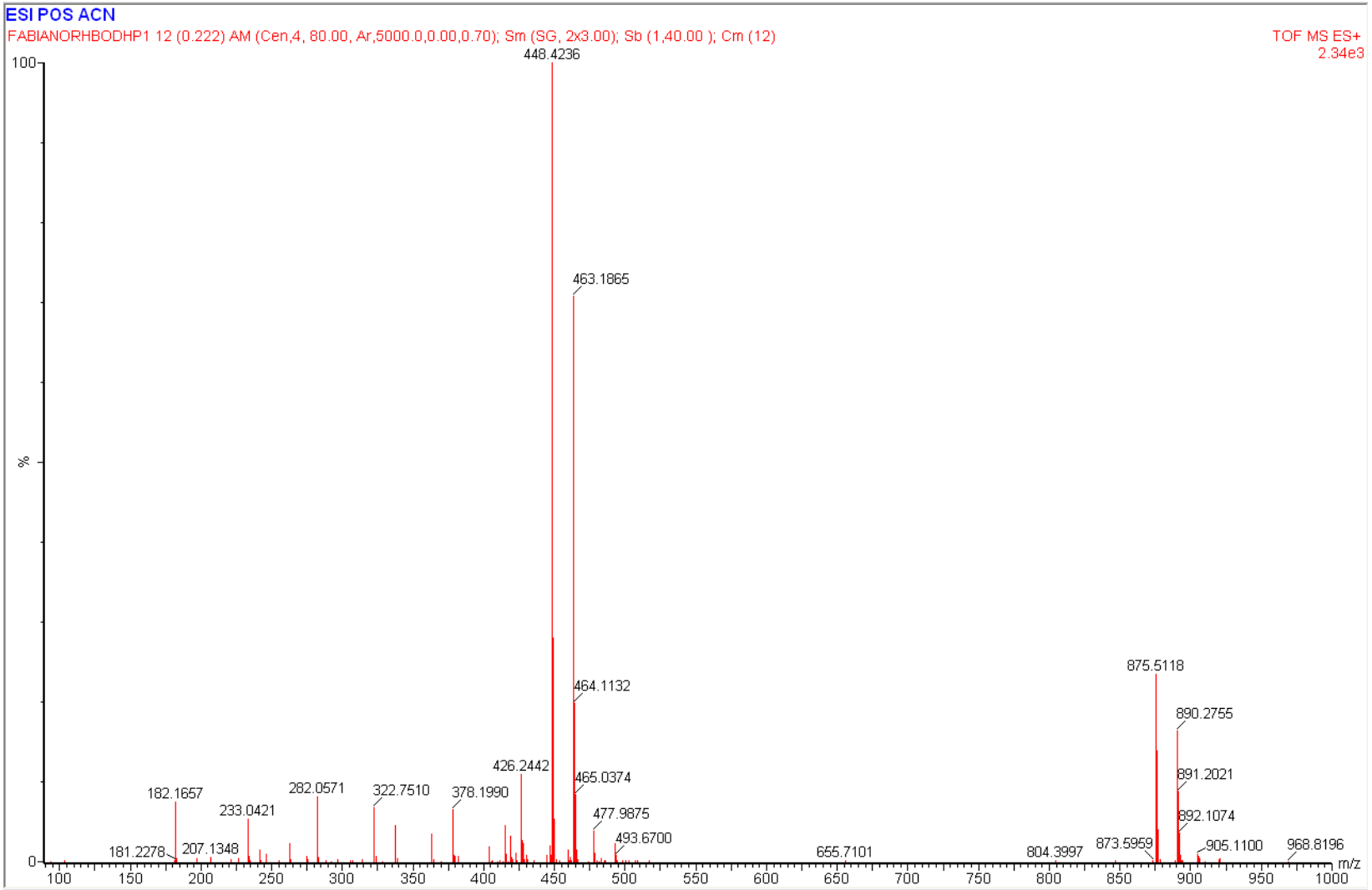

Figure ESI27. HRMS spectrum of **15**.

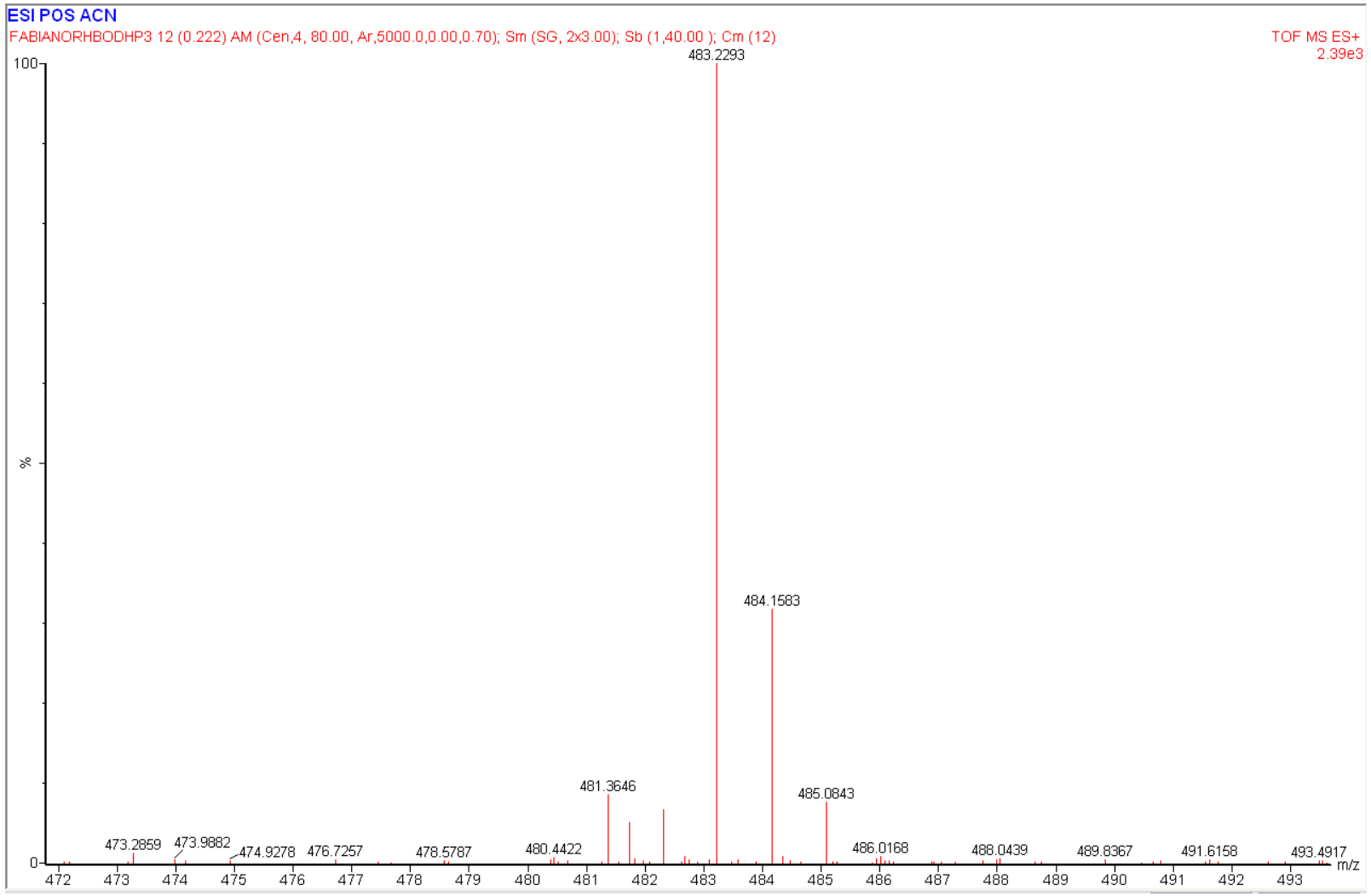

Figure ESI28. HRMS spectrum of **16**.

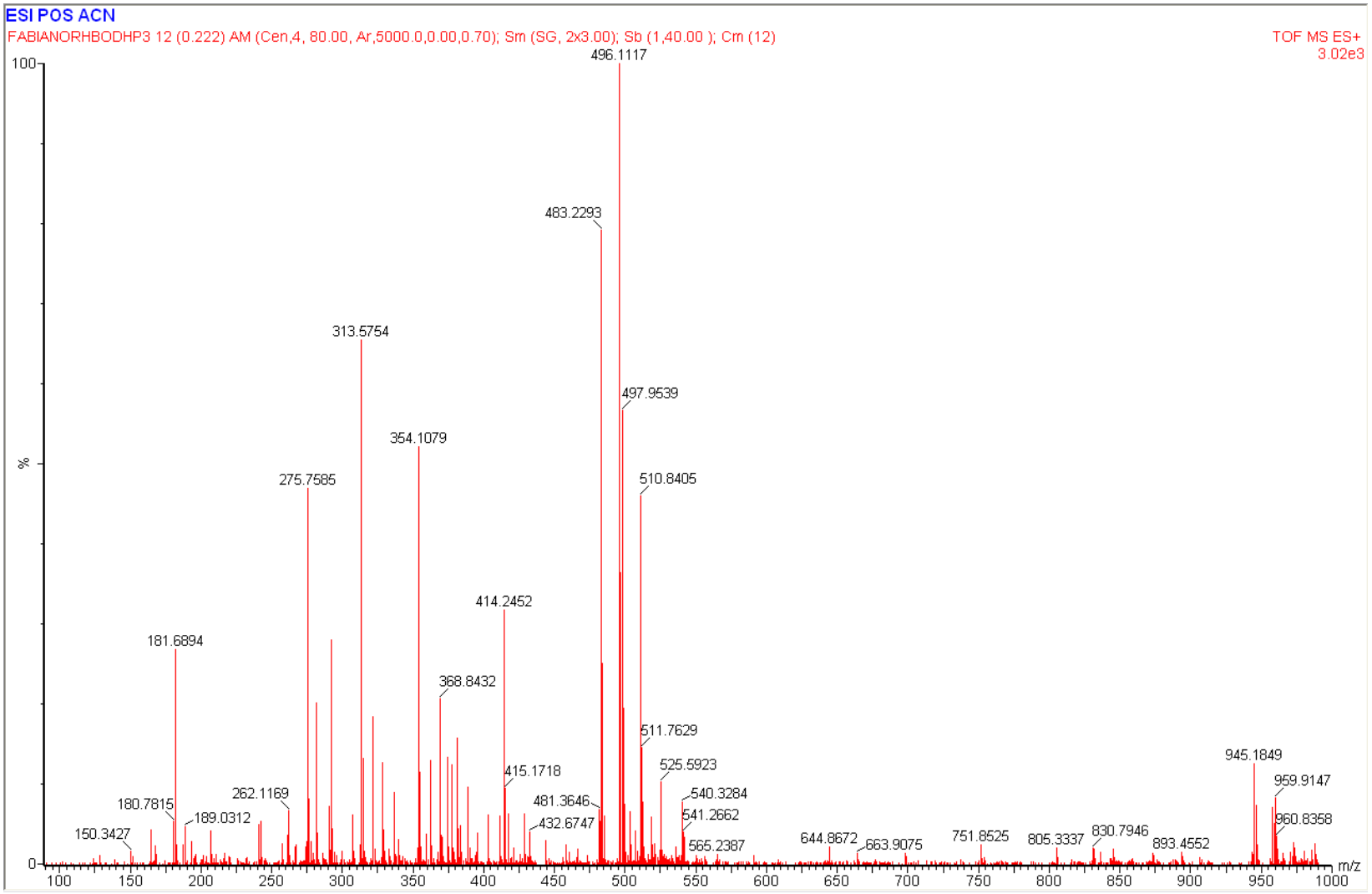

Figure ESI29. HRMS spectrum of **16**.

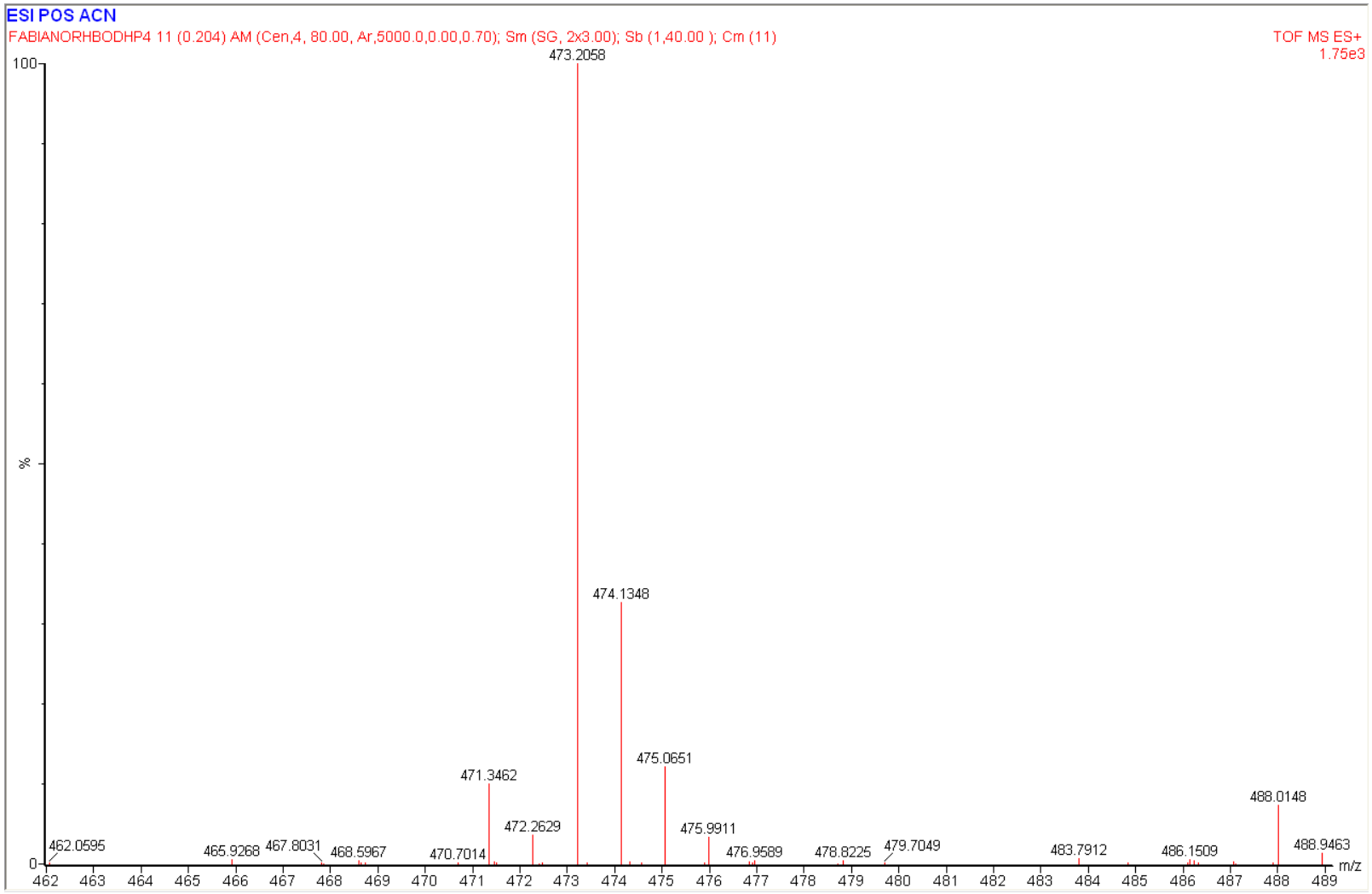

Figure ESI30. HRMS spectrum of **17**.

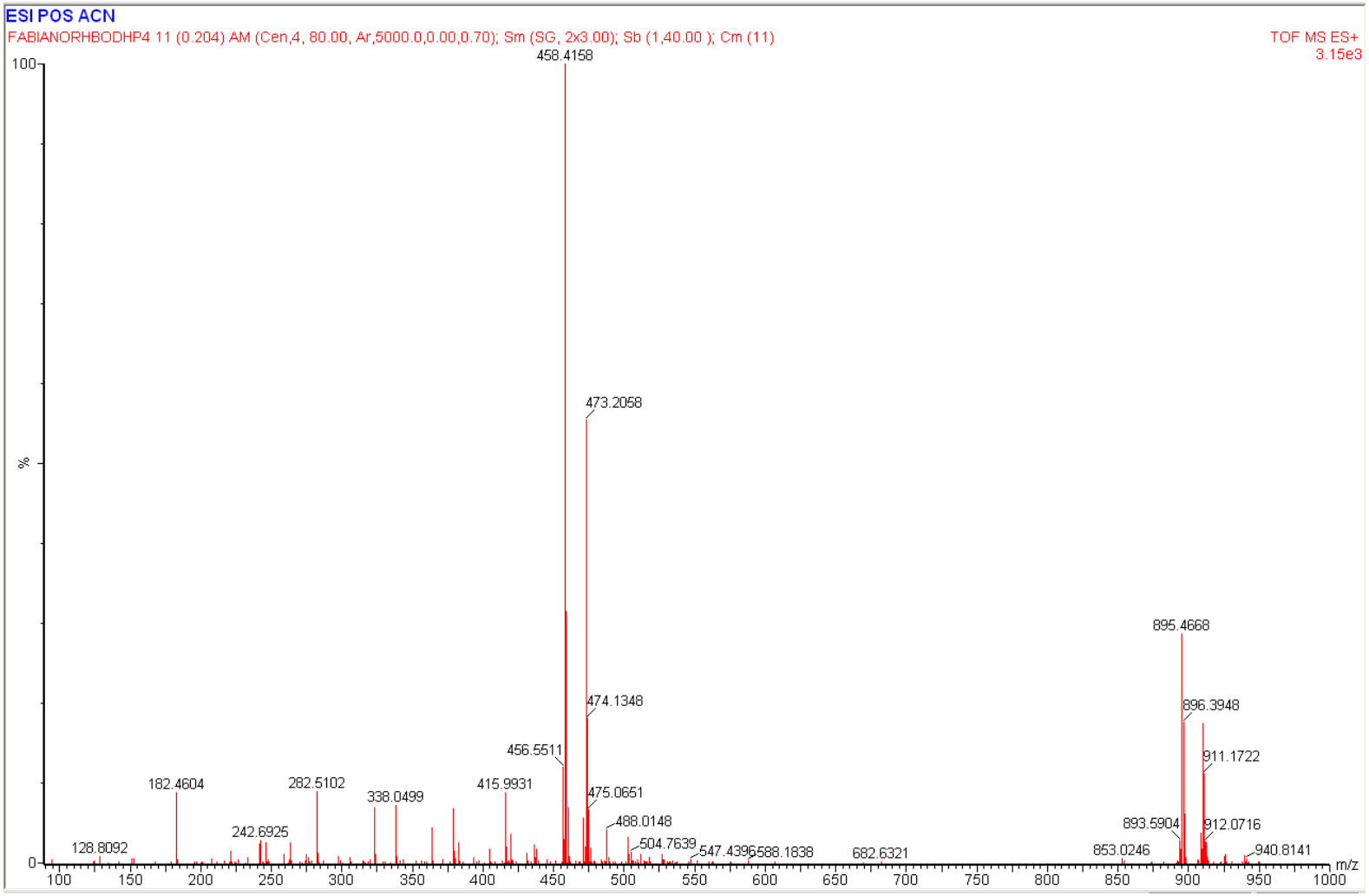

Figure ESI31. HRMS spectrum of **17**.