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PII: S0040-4020(13)01478-6

DOI: 10.1016/j.tet.2013.09.056

Reference: TET 24831

To appear in: *Tetrahedron*

Received Date: 21 August 2013

Revised Date: 15 September 2013

Accepted Date: 18 September 2013

Please cite this article as: Basavaiah D, Reddy BS, Lingam H, Synthesis of fused nine membered rings: A simple protocol for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine frameworks from the Baylis-Hillman acetates, *Tetrahedron* (2013), doi: 10.1016/j.tet.2013.09.056.

Graphical Abstract

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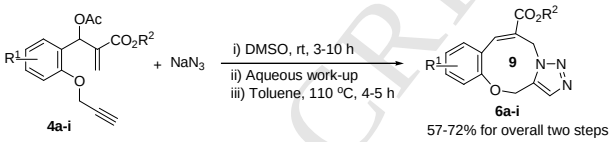

57-72% for overall two steps

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Baylis-Hillman reaction
Azido-alkyne
Click reaction
[1,2,3]-Triazolo-[1,4]-benzoxazonines

ABSTRACT

A simple and facile protocol for synthesis of tricyclic [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives has been developed from the Baylis-Hillman acetates by treatment with sodium azide followed by heating the resulting azido-alkyne in toluene under reflux [Huisgen reaction (click reaction)] in the absence of any copper salts.

1. Introduction

Development of efficient and simple protocols for obtaining medium sized rings (particularly eight and nine membered rings) still continues to be one of the fascinating endeavors in organic chemistry because of challenges involved in their synthesis.[1] 1,4-Oxazonine framework is one such skeleton which has attracted the attention of synthetic chemists in recent years.[2] [1,2,3]-Triazole framework is medicinally important structural organization present in many bioactive molecules showing various activities like anti-HIV (**1a**),[3a] anti-allergic (**1b**),[3b] anti-bacterial (**1c**[3c]&**1d**[3d]) and antimicrobial (**1e**)[3e] (Figure **1**). Therefore there has been increasing interest in the synthesis of diverse classes of [1,2,3]-triazole frameworks.[4] Also there has been growing interest in [1,2,3]-triazole frameworks fused with various other moieties, particularly [1,4]-oxaza cyclic units containing 6/7/8-membered rings (**A**, **B**, **C**) (Figure 2) because of their biological properties.[5] In most of these protocols the key step is the formation of [1,2,3]-triazole unit via the well known click reaction (Huisgen cycloaddition reaction).[4] In continuation of our interest in the development of different aspects of the Baylis-Hillman reaction and its applications in synthesis of various carbocyclic and heterocyclic compounds,[6] we became interested in triazolo-[1,4]-oxazonine system **D** (Figure 2) because of two main reasons: 1) there is not much literature available on this framework 2) due to the challenges in the construction of 9-membered rings *i.e.* [1,4]-oxazonine ring. Accordingly we herein report a one-pot facile protocol for synthesis of tricyclic triazolo-[1,4]-benzoxazonine frameworks from the Baylis-Hillman acetates.

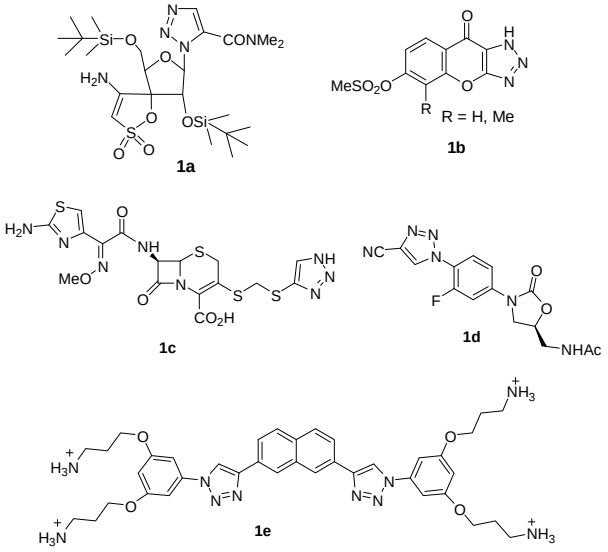

Figure 1 Bioactive molecules containing [1,2,3]-triazole framework.

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2. Results and discussion

Functional group transformation is one of the most important operations in organic synthesis and therefore preparation of molecules containing several functional groups is considered to be a challenging and attractive endeavor in organic chemistry. The Baylis-Hillman reaction is one such synthetic tool which provides densely functionalized molecules via the reaction of activated alkenes with electrophiles in the presence of a suitable catalyst.[7,8] These densely functionalized molecules have been

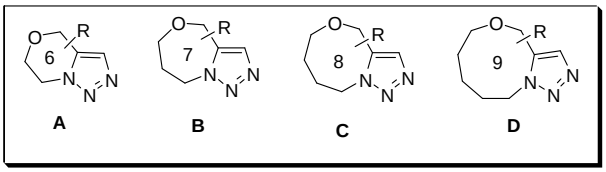
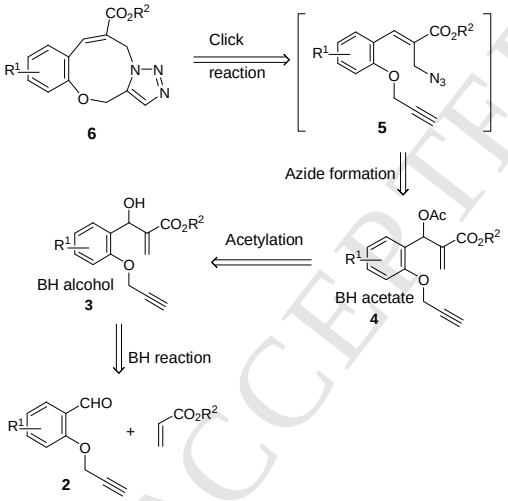


Figure 2

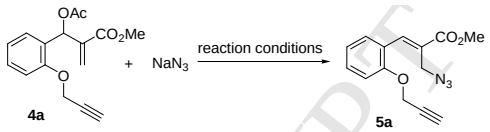
meticulously and systematically employed in various organic transformations including in the synthesis of molecules of medicinal relevance. In the literature there are some reports[9] on the utility of the Baylis-Hillman acetates for preparation of triazole derivatives,[9c,d] triazole-fused bi/ tricyclic systems such as triazolo-1,4-oxazepines[5d] triazolodiazepines[9b] and triazolo-benzazepines[9e,f] via Huisgen (click) reaction of azido-alkyne units as the key step. However there are no reports available in the literature on synthesis of triazolo-[1,4]-benzo-xazonine framework from the BH adducts / acetates. Attracted by the challenges involved in obtaining oxazonine (nine membered ring) skeleton we have directed our studies towards transformation of BH acetates into [1,2,3]-triazolo-[1,4]-benzoxazonine derivatives according to the retro-synthetic sequence shown in Scheme 1.



Scheme 1. Retro-Synthetic strategy

Accordingly we have first selected methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**4a**), the Baylis-Hillman acetate, which was obtained *via* the acetylation of B-H alcohol, methyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**3a**), [which was in turn derived *via* the coupling of 2-(prop-2-ynyloxy)benzaldehyde (**2a**) with methyl acrylate in the presence of DABCO][10] as a substrate for reaction with sodium azide. We have carried out this reaction under different conditions and the best results were obtained when the reaction was performed in DMSO as a solvent at room temperature (entry 6, Table 1). Thus the treatment of B-H acetate (**4a**) (1.0 mmol) with sodium azide (1.5 mmol), in DMSO at room temperature for 3 h provided methyl (*E*)-2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]prop-2-enoate (**5a**), in 85% isolated yield.

Table 1
Optimization: Synthesis of azido alkyne **5a**[a,b]



Entry	Conditions	Yield(%)[c]
1	Toluene, rt, 1 day	-
2	Toluene-H_2O, rt, 1 day	11
3	THF-H_2O (1:1), rt, 1 day	-
4	DMSO-H_2O, rt, 12 h	23
5	DMSO, rt, 2 h	65
6	DMSO, rt, 3 h	85
7	DMSO, rt, 12 h	73

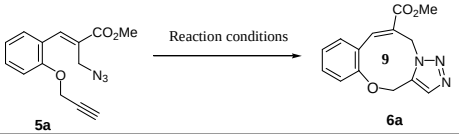
[a]All reactions were carried out on a 1.0 mmol scale of B-H acetate (**4a**) with sodium azide (1.5 eq.) at room temperature.

[b]Fully characterized.

[c]Yields were based on B-H acetate **4a**.

After having azido-alkyne (**5a**) in hand, we tried for intramolecular [3+2] Huisgen cyclization under usual conditions using Cu(0)/$CuSO_4$ as a catalytic system (entry 1, Table 2). The desired triazole was obtained in low yield. In order to increase the yield of the desired triazolo-[1,4]-benzoxazonine, we have examined this reaction under different conditions and observed that just refluxing in toluene provided better yields (Entry 4, Table 2). Thus heating methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (**5a**) (1 mmol) in refluxing toluene for 4 h provided 10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo-[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6a**) in 80% isolated yield. We have also obtained single crystal for this compound and further confirmed the structure of molecule **6a** by single crystal X-ray data analysis (Figure 3).[11]

Table 2
Optimization: Synthesis of triazolo-[1,4]-benzoxazonine **6a**[a,b]



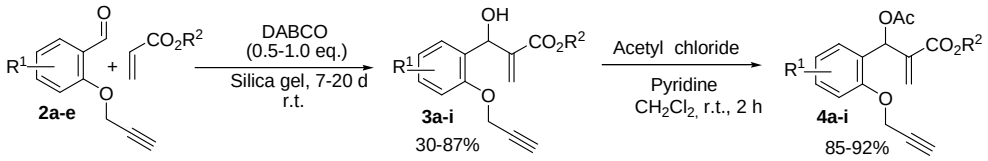
Entry	Conditions	Yield(%)[c]
1	Cu/$CuSO_4$, EtOH, reflux, 4 h	30
2	DMSO, reflux, 4 h	67
3	Toluene, reflux, 2 h	59
4	Toluene, reflux, 4 h	80

[a]All reactions were carried out on a 1 mmol scale of azido-alkyne (**5a**)

[b]Fully characterized

[c]Yields were based on azido-alkyne **5a**.

Table 3
Synthesis of BH alcohols (**3a-i**)[a] and BH acetates (**4a-i**)[b]



Entry	R^1	R^2	Aldehyde	BH alcohol[c]	Yield(%)[d]	BH acetate[c]	Yield(%)[e]
1	H	Me	**2a**	**3a**	70	**4a**	85
2	3-OMe	Me	**2b**	**3b**	57	**4b**	90
3	4-OMe	Me	**2c**	**3c**[f]	30	**4c**	85
4	5-Br	Me	**2d**	**3d**	83	**4d**	90
5	5-Cl	Me	**2e**	**3e**	65	**4e**	91
6	H	Et	**2a**	**3f**	81	**4f**	88
7	3-OMe	Et	**2b**	**3g**	71	**4g**	86
8	4-OMe	Et	**2c**	**3h**[f]	41	**4h**	87
9	5-Br	Et	**2d**	**3i**	87	**4i**	92

[a] All reactions were carried out on a 20 mmol scale of aldehydes (**2a-e**) with 30 mmol of alkyl acrylates, under the influence of DABCO (50 mol%) in the silica gel-solid phase medium (mesh >200-400) at room temperature for 7-14 days (see experimental).

[b]All reactions were carried out on a 10 mmol scale of Baylis-Hillman alcohols (**3a-i**) with acetyl chloride, in the presence of pyridine at room temperature for 2 h (see experimental).

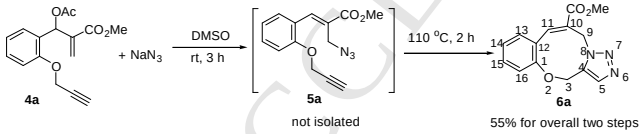
[c]The molecules **3a-i** and **4a-i** are fully characterized (see experimental).

[d]Yields are based on aldehydes (**2a-e**).

[e]Yields are based on B-H alcohols (**3a-i**).

[f]These reactions were carried out under influence of 1 eq. of DABCO for 20 days.

Encouraged by the success in obtaining [1,2,3]-triazolo-[1,4]-benzoxazonine **6a** in reasonably high yields we turned our attention to achieve [1,2,3]-triazolo-[1,4]-benzoxazonine without purifying the intermediate azido-alkyne **5a** in a one-pot reaction. In this direction we have treated the Baylis-Hillman acetate **4a** with sodium azide in DMSO for 3 h at room temperature and then heated the resulting mixture for 2 h at 110 ^{o}C in the same solvent to provide 10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6a**) in overall 55% isolated yield (Scheme 2).



Scheme 2. One-pot synthesis of 6a

Since in the two pot operation process, second step using toluene as a solvent (under reflux) gave high yields (entry 4, Table 2) we have treated methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**4a**) with sodium azide in DMSO for 3 h at room temperature. Then the resulting crude compound methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]propenoate (**5a**), obtained after aqueous work-up (after removing DMSO), without further purification was heated in toluene under reflux for 4 h at 110 ^{o}C to provide 10-methoxycarbonyl-2-oxa-6,7,8-triazatricyclo[10.4.0.0^{4,8}]hexadeca-1(12)-4,6,10,13,15-hexaene (**6a**), in 72% overall isolated yield for two steps (Scheme 3). We were indeed pleased to see the better yield of **6a** in this two-step process.

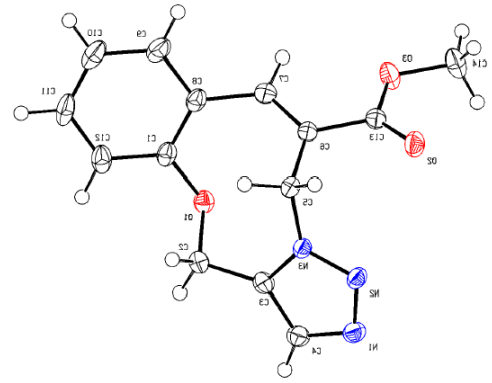
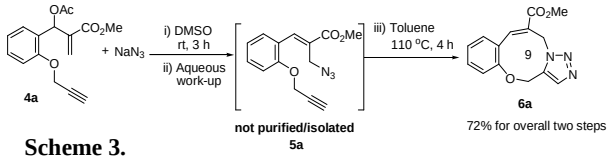


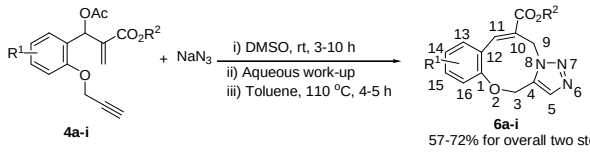
Figure 3. ORTEP diagram of compound **6a**



Scheme 3.
Synthesis of 6a without isolating 5a

With a view to understand the generality of this reaction sequence and to obtain different triazolo-[1,4]-benzoxazonine derivatives we have prepared various Baylis-Hillman acetates (**4b-i**) from the BH adducts [which were in turn obtained from 2-(prop-2-ynyloxy)arylaldehydes (**2b-e**) and alkyl acrylates] by acetylation (Table 3). BH acetates **4b-i** were successfully converted into the desired triazolo-[1,4]-benzoxazonine derivatives (**6b-i)** in 57-71% isolated yields (for two steps) *via* the treatment with sodium azide in DMSO and then heating the resulting crude azides (after aqueous work-up) in toluene under reflux (Table 4).

Table 4
Synthesis of triazolo-[1,4]-benzoxazonine derivatives (**6a-i**)[a]



Entry	BH acetate	R^1	R^2	Product[b,c]	Yield(%)[d]
1	**4a**	H	Me	**6a**[e]	72
2	**4b**	3-OMe	Me	**6b**	68
3	**4c**	4-OMe	Me	**6c**	63
4	**4d**	5-Br	Me	**6d**	57
5	**4e**	5-Cl	Me	**6e**	62
6	**4f**	H	Et	**6f**	58
7	**4g**	3-OMe	Et	**6g**	65
8	**4h**	4-OMe	Et	**6h**	68
9	**4i**	5-Br	Et	**6i**	71

[a]All reactions were carried out on 1.0 mmol scale of B-H acetate (**4a-i**) with sodium azide (1.5 mmol) in DMSO (2 mL) for 3-10 h at room temperature followed by aqueous work-up and heating the resulting crude in toluene (2 mL) for 4-5 h under reflux (see experimental).

[b]These compounds are fully characterized (see experimental).

[c] (*E*)-Stereochemistry of the double bond for the compounds **6a-i** at C-10 is confirmed by ^{1}H NMR spectral analysis.[12]

[d]Yields are based on B-H acetates (**4a-i**).

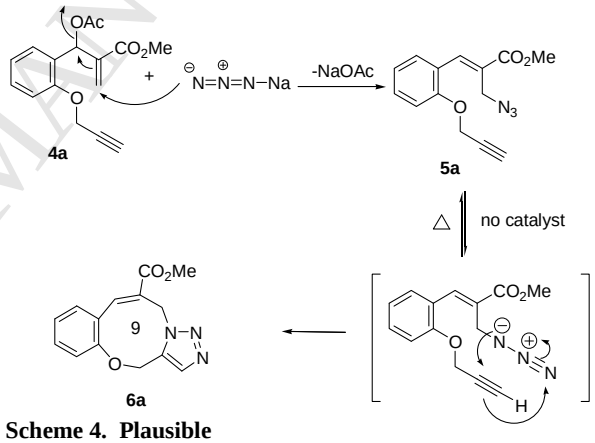
[e] Structure and double bond stereochemistry were further confirmed by single crystal X-ray data analysis[11] of **6a**.

It is interesting to note the easy formation of even nine membered rings in the click reaction without using any copper catalyst in all our reactions. From these results it may be possible to understand that intramolecular version of click reaction provides an easy access to the formation of nine-membered rings (otherwise difficult to prepare)[1] even in the absence of any copper catalyst. It is appropriate to mention here that Lee and coworkers reported copper free Huisgen intramolecular cyclization of azido-alkyne systems, obtained from Baylis-Hillman acetates, to provide triazolo-benzazepines[9e,f] in refluxing THF[9e] and also in refluxing toluene.[9f] Lamaty[9b] and Batra[5d] reported respectively synthesis of triazolo-diazepines[9b] and triazolo-1,4-oxazepines[5d] via copper free intra-molecular click reaction of azido-alkyne systems obtained from the Baylis-Hillman adducts/ acetates, in toluene. In recent years, copper free click reactions has attracted the attention of synthetic chemists. There has been in fact, some interesting reports on the copper free click reactions for intramolecular azide-alkyne cyclization,[4e, 5d,9b,e,f] for substrates containing electron-deficient alkynes[13a] and strained units like octynes[13b-f] & benzynes.[13g]

Mechanism for the formation of triazolo-[1,4]-benzoxazonine derivatives from the Baylis-Hillman acetates is presented in Scheme 4 by taking reaction between methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**4a**) and NaN_3 as a model case. Treatment of **4a** with NaN_3 provided alkynyl-azide **5a** intermediate, which would then undergo intramolecular [3+2] cycloaddition reaction leading to the formation of the triazole derivative **6a**.

3. Conclusion

In conclusion we have developed a facile strategy for synthesis of tricyclic [1,2,3]-triazolo-[1,4]-benzoxazonine frameworks from the Baylis-Hillman acetates by treatment with sodium azide and subsequent [3+2] cyclization of the resulting crude azido-alkyne in refluxing toluene. It needs to be mentioned here that [1,2,3]-triazolo-[1,4]-oxazonine framework is an interesting structural moiety that is not well studied in the literature and is believed to be very useful in the medicinal chemistry point of view. This methodology demonstrates the applicability of Baylis-Hillman adducts for synthesis of nine membered rings containing [1,4]-benzoxazonine framework fused with [1,2,3]-triazole skeleton.



Scheme 4. Plausible mechanism

4. Experimental section

4.1. General remarks

Melting points were recorded on a Superfit (India) capillary melting point apparatus and were uncorrected. IR spectra were recorded on a JASCO FT / IR-5300 spectrophotometer, solid samples were recorded as KBr wafers and liquid samples as thin film between NaCl plates. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker-AVANCE-400 spectrometer in deuterochloroform ($CDCl_3$) with tetramethyl-silane (TMS, δ = 0) as an internal standard for ^{1}H NMR and chloroform-*d* middle peak of the triplet (δ = 77.10 ppm) as an internal standard for ^{13}C NMR spectra. HRMS spectra were recorded on Bruker maXis ESI-TOF spectrometer. The X-ray diffraction measurements were carried out at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite-monochromated Mo-*Kα* radiation with the wavelength of 0.71073 Å.

4.2. Representative procedure

4.2.1 All the aldehydes **2a-e** were prepared by treating propargyl bromide with corresponding 2-hydroxyarylaldehyde in the presence of K_2CO_3 following the literature procedure.[14]

*4.2.2. Methyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)-phenyl]propanoate **(3a)**:* To a solution of 2-(prop-2-ynyloxy)benzaldehyde (**2a**) (20 mmol, 3.20 g) in methyl acrylate (30 mmol, 2.58 g, 2.7 mL) was added DABCO (10 mmol, 1.12 g) at room temperature. Then silica gel (mesh >200-400) was added and thoroughly mixed. After keeping the resulting solid at room temperature for 7 days, the reaction mixture was washed with ethyl acetate (3 X 20 mL). Combined organic layer was washed successively, with 2N HCl (15 mL), saturated $NaHCO_3$ solution (15 mL), water (15 mL) and then dried over anhydrous Na_2SO_4. Solvent was evaporated and the crude thus obtained was purified by column chromatography to provide the title compound in 70% (3.44 g) isolated yield.

R_f (20% EtOAc in hexanes) 0.46; pale yellow viscous liquid; IR (neat): ν 3466, 3287, 2953, 2121, 1712, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 2.50 (t, 1H, *J* = 2.4 Hz), 3.36 (d, 1H, *J* = 6.0 Hz), 3.74, (s, 3H), 4.72 (d, 2H, *J* = 2.4 Hz), 5.75 (s, 1H), 5.89 (d, 1H, *J* = 6.4 Hz), 6.32 (s, 1H), 6.95-7.06 (m, 2H), 7.27-7.31 (m, 1H), 7.41 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz): δ 51.67, 55.87, 67.33, 75.62, 78.36, 112.04, 121.45, 125.78, 127.59, 128.55, 129.94, 141.24, 154.42, 166.81; HRMS (ESI) exact mass calc'd for $C_{14}H_{14}O_4$+Na $(M+Na)^+$: 269.0790, found: 269.0794.

Similar procedure was followed for preparation of compounds **3b-e**, *via* the reaction between the corresponding aldehyde (**2a-e**) with methyl acrylate in the presence of DABCO. The compounds **3f-i** were synthesized by treatment of arylaldehyde (**2a-d**)with ethyl acrylate in presence of DABCO. For synthesis of compounds **3c** and **3h**, 1 equivalent of DABCO was used.

*4.2.3. Methyl 3-hydroxy-3-[3-methoxy-2-(prop-2-ynyloxy)-phenyl]-2-methylenepropanoate **(3b)**.* Reaction time: 14 days; yield 57%; R_f (20% EtOAc in hexanes) 0.38; colorless viscous liquid; IR (neat): ν 3489, 3287, 2951, 2123, 1716, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 2.51 (t, 1H, *J* = 2.4 Hz), 3.23 (d, 1H, *J* = 5.2 Hz), 3.72 (s, 3H), 3.86 (s, 3H), 4.74 & 4.82 (dABq, 2H, *J* = 2.4 & 15.2 Hz), 5.85-5.89 (m, 1H), 6.01 (d, 1H, *J* = 5.6 Hz), 6.36 (s, 1H), 6.87 (dd, 1H, *J* = 1.6 & 8.0 Hz), 6.97 (dd, 1H, *J* = 1.6 & 8.0 Hz), 7.05-7.12 (m, 1H); ^{13}C NMR (100 MHz): δ 51.84, 55.75, 59.91, 67.64, 75.46, 79.56, 111.94, 119.33, 124.64, 126.01, 135.58, 141.41, 144.01, 152.25, 166.81; HRMS (ESI) exact mass calc'd for $C_{15}H_{16}O_5$+Na $(M+Na)^+$: 299.0895, found: 299.0891.

*4.2.4. Methyl 3-hydroxy-3-[4-methoxy-2-(prop-2-ynyloxy)-phenyl]-2-methylenepropanoate **(3c)**.* Reaction time: 20 days; yield: 30%; R_f (20% EtOAc in hexanes) 0.30; colorless viscous liquid; IR (neat): ν 3493, 3287, 2953, 2121, 1722, 1612 cm^{-1}; ^1H NMR (400 MHz): δ 2.52 (t, 1H, *J* = 2.4 Hz), 3.25 (d, 1H, *J* = 6.0 Hz), 3.73 (s, 3H), 3.80 (s, 3H), 4.69 (d, 2H, *J* = 2.0 Hz), 5.78 (s, 1H), 5.82 (d, 1H, *J* = 6.0 Hz), 6.31 (s, 1H), 6.53 (dd, 1H, *J* = 2.4 & 8.8 Hz), 6.57 (d, 1H, *J* = 2.4 Hz), 7.27 (d, 1H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz): δ 51.77, 55.26, 56.06, 67.32, 75.81, 78.28, 99.96, 105.39, 122.43, 125.57, 128.42, 141.44, 155.59, 160.16, 166.95; HRMS (ESI) exact mass calc'd for $C_{15}H_{16}O_5$+Na $(M+Na)^+$: 299.0895, found: 299.0893.

*4.2.5. Methyl 3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate **(3d)**.* Reaction time: 14 days; yield: 83%; R_f (20% EtOAc in hexanes) 0.53; pale yellow viscous liquid; IR (neat): ν 3466, 3292, 2953, 2121, 1716, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 2.51 (t, 1H, *J* = 2.4 Hz), 3.33 (d, 1H, *J* = 5.6 Hz), 3.77 (s, 3H), 4.69 (d, 2H, *J* = 2.0 Hz), 5.71 (s, 1H), 5.85 (d, 1H, *J* = 6.0 Hz), 6.33 (s, 1H), 6.87 (d, 1H, *J* = 8.8 Hz), 7.38 (dd, 1H, *J* = 2.4 & 8.8 Hz), 7.55 (d, 1H, *J* = 2.4 Hz); ^{13}C NMR (100 MHz): δ 52.05, 56.25, 67.23, 76.10, 77.95, 113.94, 114.25, 126.63, 130.68, 131.42, 132.26, 140.59, 153.51, 166.89; HRMS (ESI) exact mass calc'd for $C_{14}H_{13}BrO_4$+Na $(M+Na)^+$: 346.9895, found: 346.9891.

*4.2.6. Methyl 3-[5-chloro-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate **(3e)**.* Reaction time: 14 days; yield: 65%; R_f (20% EtOAc in hexanes) 0.51; pale yellow viscous liquid; IR (neat): ν 3470, 3294, 2953, 2121, 1718, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 2.51 (t, 1H, *J* = 2.4 Hz), 3.34 (d, 1H, *J* = 5.6 Hz), 3.77 (s, 3H), 4.69 (d, 2H, *J* = 2.4 Hz), 5.71 (s, 1H), 5.85 (d, 1H, *J* = 5.6 Hz), 6.33 (s, 1H), 6.92 (d, 1H, *J* = 8.8 Hz), 7.24 (dd, 1H, *J* = 2.8 & 8.8 Hz), 7.42 (d, 1H, *J* = 2.8 Hz); ^{13}C NMR (100 MHz): δ 52.01, 56.32, 67.20, 76.05, 78.00, 113.50, 126.56, 126.80, 127.78, 128.40, 131.92, 140.63, 152.99, 166.87; HRMS (ESI) exact mass calc'd for $C_{14}H_{13}ClO_4$+Na $(M+Na)^+$: 303.0400, found: 303.0397.

*4.2.7. Ethyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)-phenyl]propanoate **(3f)**.* Reaction time: 7 days; yield: 81%; R_f (20% EtOAc in hexanes) 0.50; pale yellow viscous liquid; IR (neat): ν 3468, 3288, 2984, 2121, 1712, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 1.26 (t, 3H, *J* = 7.2 Hz), 2.50 (t, 1H, *J* = 2.4 Hz), 3.40 (d, 1H, *J* = 6.4 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 4.71 (d, 2H, *J* = 2.4 Hz), 5.74 (s, 1H), 5.89 (d, 1H, *J* = 6.0 Hz), 6.32 (s, 1H), 6.96-7.05 (m, 2H), 7.24-7.31 (m, 1H), 7.41 (dd, 1H, *J* = 1.2 & 7.6 Hz); ^{13}C NMR (100 MHz): δ 13.96, 56.00, 60.72, 67.66, 75.64, 78.42, 112.11, 121.56, 125.61, 127.77, 128.64, 130.06, 141.48, 154.56, 166.51; HRMS (ESI) exact mass calc'd for $C_{15}H_{16}O_4$+Na $(M+Na)^+$: 283.0946, found: 283.0946.

*4.2.8. Ethyl 3-hydroxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate **(3g)**.* Reaction time: 14 days; yield: 71%; R_f (20% EtOAc in hexanes) 0.45; pale yellow viscous liquid; IR (neat): ν 3489, 3287, 2939, 2119, 1714, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.51 (t, 1H, *J* = 2.4 Hz), 3.27 (d, 1H, *J* = 5.6 Hz), 3.86 (s, 3H), 4.13-4.22 (m, 2H), 4.75 & 4.81 **(**dABq, 2H, *J* = 2.4 & 17.6 Hz**),** 5.85 (s, 1H), 6.01 (d, 1H, *J* = 5.6 Hz), 6.35 (s, 1H), 6.87 (d, 1H, *J* = 8.0 Hz), 6.98 (d, 1H, *J* = 7.6 Hz), 7.05-7.13 (m, 1H); ^{13}C NMR (100 MHz): δ 14.01, 55.73, 59.89, 60.71, 67.66, 75.42, 79.57, 111.88, 119.36, 124.59, 125.67, 135.68, 141.67, 144.02, 152.22, 166.35; HRMS (ESI) exact mass calc'd for $C_{16}H_{18}O_5$+Na $(M+Na)^+$: 313.1052, found: 313.1057.

*4.2.9. Ethyl 3-hydroxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate **(3h)**.* Reaction time: 20 days; yield: 41%; R_f (20% EtOAc in hexanes) 0.37; pale yellow viscous liquid; IR (neat): ν 3477, 3287, 2982, 2121, 1711, 1612 cm^{-1}; ^1H NMR (400 MHz): δ 1.26 (t, 3H, *J* = 7.2 Hz), 2.52 (t, 1H, *J* = 2.4 Hz), 3.25 (b s, 1H), 3.80 (s, 3H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.69 (d, 2H, *J* = 2.4 Hz), 5.77 (s, 1H), 5.83 (s, 1H), 6.31 (s, 1H), 6.53 (dd, 1H, *J* = 2.0 & 8.4 Hz), 6.57 (d, 1H, *J* = 2.4 Hz), 7.28 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz): δ 13.97, 55.25, 56.05, 60.65, 67.29, 75.78, 78.29, 99.91, 105.35, 122.53, 125.21, 128.44, 141.72, 155.60, 160.12, 166.51; HRMS (ESI) exact mass calc'd for $C_{16}H_{18}O_5$+Na $(M+Na)^+$: 313.1052, found: 313.1049.

*4.2.10. Ethyl 3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-3-hydroxy-2-methylenepropanoate **(3i)**.* Reaction time: 14 days; yield: 87%; R_f (20% EtOAc in hexanes) 0.54; pale yellow viscous liquid; IR (neat): ν 3460, 3294, 2982, 2121, 1709, 1630 cm^{-1}; ^1H NMR (400 MHz): δ 1.29 (t, 3H, *J* = 7.2 Hz), 2.51 (t, 1H, *J* = 2.4 Hz), 3.37 (d, 1H, *J* = 5.6 Hz), 4.22 (q, 2H, *J* = 7.2 Hz), 4.69 (d, 2H, *J* = 2.4 Hz), 5.70 (s, 1H), 5.84 (d, 1H, *J* = 5.6 Hz), 6.33 (s, 1H), 6.87 (d, 1H, *J* = 8.8 Hz), 7.38 (dd, 1H, *J* = 2.4 & 8.8 Hz), 7.56 (d, 1H, *J* = 2.4 Hz); ^{13}C NMR (100 MHz): δ 14.09, 56.27, 61.03, 67.36, 76.09, 77.96, 113.92, 114.22, 126.34, 130.76, 131.38, 132.33,

140.82, 153.55, 166.46; HRMS (ESI) exact mass calc'd for $C_{15}H_{15}BrO_4$+Na $(M+Na)^+$: 361.0051, found: 361.0056.

*4.2.11. Methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)-phenyl]propanoate (**4a**).* To a stirring solution of methyl 3-hydroxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**3a**) (10 mmol, 2.46 g) in dichloromethane (10 mL) was added pyridine (20 mmol, 1.58 g, 1.62 mL) followed by acetyl chloride (20 mmol, 1.57 g, 1.42 mL) at 0 ^oC. After stirring at room temperature for 2 h, reaction mixture was diluted with diethyl ether (20 mL) and 2N HCl (15 mL). Organic layer was separated and was washed successively with saturated aq. $NaHCO_3$ solution, water and dried over anhydrous Na_2SO_4. Crude product thus obtained after solvent evaporation, was purified by column chromatography (5% EtOAc in hexanes) to provide the desired product as a colorless viscous liquid in 85% (2.46 g) isolated yield.

R_f (20% EtOAc in hexanes) 0.49; colorless viscous liquid; IR (neat): ν 3287, 2955, 2121, 1739, 1728, 1635 cm^{-1}; ^1H NMR (400 MHz): δ 2.11 (s, 3H), 2.48 (t, 1H, *J* = 2.4 Hz), 3.73 (s, 3H), 4.72 (d, 2H, *J* = 2.4 Hz), 5.67 (s, 1H), 6.41 (s, 1H), 6.97-7.06 (m, 3H), 7.27-7.34 (m, 2H); ^{13}C NMR (100 MHz): δ 20.86, 51.84, 56.00, 67.90, 75.52, 78.38, 112.41, 121.30, 126.63, 127.11, 127.78, 129.34, 138.80, 154.81, 165.53, 169.26; HRMS (ESI) exact mass calc'd for $C_{16}H_{16}O_5$+Na $(M+Na)^+$: 311.0895, found: 311.0898.

Similar procedure was followed for synthesis of Baylis-Hilman acetates **4b-i**.

*4.2.12. Methyl 3-acetoxy-3-[3-methoxy-2-(prop-2-ynyloxy)-phenyl]-2-methylenepropanoate (**4b**).* Reaction time: 2 h; yield: 90%; R_f (20% EtOAc in hexanes) 0.40; pale yellow viscous liquid; IR (neat): ν 3288, 2951, 2125, 1736, 1720, 1635 cm^{-1}; ^1H NMR (400 MHz): δ 2.10 (s, 3H), 2.49 (t, 1H, *J* = 2.4 Hz), 3.73 (s, 3H), 3.86 (s, 3H), 4.75 & 4.81 (dABq, 2H, *J* = 2.4 & 14.8 Hz), 5.70 (d, 1H, *J* = 0.8 Hz), 6.42 (s, 1H), 6.87-6.92 (m, 2H), 7.03-7.10 (m, 2H); ^{13}C NMR (100 MHz): δ 20.91, 51.82, 55.69, 59.88, 68.44, 75.13, 79.15, 112.46, 119.50, 124.33, 127.08, 131.82, 138.90, 144.54, 152.45, 165.42, 169.17; HRMS (ESI) exact mass calc'd for $C_{17}H_{18}O_6$+Na $(M+Na)^+$: 341.1001, found: 341.0998.

*4.2.13. Methyl 3-acetoxy-3-[4-methoxy-2-(prop-2-ynyloxy)-phenyl]-2-methylenepropanoate (**4c**).* Reaction time: 2 h; yield: 85%; R_f (20% EtOAc in hexanes) 0.38; pale yellow viscous liquid; IR (neat): ν 3285, 2955, 2121, 1739, 1728, 1614 cm^{-1}; ^1H NMR (400 MHz): δ 2.09 (s, 3H), 2.50 (t, 1H, *J* = 2.0 Hz.), 3.72 (s, 3H), 3.80 (s, 3H), 4.70 (d, 2H, *J* = 2.0 Hz), 5.71 (d, 1H, *J* = 0.8 Hz), 6.40 (s, 1H), 6.51 (dd, 1H, *J* = 2.0 & 8.4 Hz), 6.60 (d, 1H, *J* = 2.0 Hz), 6.96 (s, 1H), 7.17 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz): δ 20.88, 51.81, 55.24, 56.11, 67.81, 75.65, 78.28, 100.11, 105.42, 118.92, 126.40, 128.80, 138.99, 156.04, 160.76, 165.56, 169.32; HRMS (ESI) exact mass calc'd for $C_{17}H_{18}O_6$+Na $(M+Na)^+$: 341.1001, found: 341.1006.

*4.2.14. Methyl 3-acetoxy-3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**4d**).* Reaction time: 2 h; yield: 90%; R_f (20% EtOAc in hexanes) 0.45; pale yellow viscous liquid; IR (neat): ν 3292, 2953, 2123, 1743, 1732, 1635 cm^{-1}; ^1H NMR (400 MHz): δ 2.12 (s, 3H), 2.49 (s, 1H)*, 3.75 (s, 3H), 4.71 (s, 2H), 5.69 (s, 1H), 6.43 (s, 1H), 6.92 (d, 1H, *J* = 8.4 Hz), 6.97 (s, 1H), 7.36-7.44 (m, 2H); * unresolved triplet. ^{13}C NMR (100 MHz): δ 20.93, 52.02, 56.34, 67.34, 76.01, 77.92, 113.83, 114.34, 127.63, 129.12, 130.70, 132.08, 138.34, 153.88, 165.33, 169.20; HRMS (ESI) exact mass calc'd for $C_{16}H_{15}BrO_5$+Na $(M+Na)^+$: 389.0001, found: 388.9999.

*4.2.15. Methyl 3-acetoxy-3-[5-chloro-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**4e**).* Reaction time: 2 h; yield: 91%; R_f (20% EtOAc in hexanes) 0.48; colorless viscous liquid; IR (neat): ν 3292, 2953, 2123, 1743, 1728, 1635 cm^{-1}; ^1H NMR (400 MHz): δ 2.12 (s, 3H), 2.49 (s, 1H), 3.75 (s, 3H), 4.71 (s, 2H), 5.69 (s, 1H), 6.43 (s, 1H), 6.94-7.00 (m, 2H), 7.23-7.29 (m, 2H); ^{13}C NMR (100 MHz): δ 20.95, 52.04, 56.43, 67.45, 75.98, 78.00, 113.91, 126.54, 127.66, 127.86, 128.74, 129.12, 138.37, 153.39, 165.38, 169.25. HRMS (ESI) exact mass calc'd for $C_{16}H_{15}ClO_5$+Na $(M+Na)^+$: 345.0506, found: 345.0510.

*4.2.16. Ethyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)-phenyl]propanoate (**4f**).* Reaction time: 2 h; yield: 88%; R_f (20% EtOAc in hexanes) 0.50; pale yellow viscous liquid; IR (neat): ν 3287, 2984, 2121, 1743, 1720, 1637 cm^{-1}; ^1H NMR (400 MHz): δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.11 (s, 3H), 2.48 (s, 1H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.73 (s, 2H), 5.64 (s, 1H), 6.40 (s, 1H), 6.93-7.07 (m, 3H), 7.22-7.34 (m, 2H); ^{13}C NMR (100 MHz): δ 13.98, 20.93, 56.08, 60.77, 67.98, 75.52, 78.44, 112.44, 121.34, 126.77, 126.82, 127.91, 129.34, 139.13, 154.89 165.14, 169.30. HRMS (ESI) exact mass calc'd for $C_{17}H_{18}O_5$+Na $(M+Na)^+$: 325.1052, found: 325.1050.

*4.2.17. Ethyl 3-acetoxy-3-[3-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**4g**).* Reaction time: 2 h; yield: 86%; R_f (20% EtOAc in hexanes) 0.45; pale yellow viscous liquid; IR (neat): ν 3285, 2982, 2945, 2125, 1743, 1722, 1637 cm^{-1}; ^1H NMR (400 MHz): δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.10 (s, 3H), 2.49 (t, 1H, *J* = 2.4 Hz), 3.86 (s, 3H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.74 & 4.81 (dABq, 2H, *J* = 2.4 & 15.2 Hz), 5.66 (s, 1H), 6.41 (s, 1H), 6.89 (s, 1H) 6.91 (s, 1H), 7.03-7.10 (m, 2H); ^{13}C NMR (100 MHz): δ 14.09, 21.10, 55.84, 60.06, 60.87, 68.67, 75.17, 79.32, 112.51, 119.72, 124.45, 127.04, 132.09, 139.28, 144.71, 152.57, 165.15, 169.34. HRMS (ESI) exact mass calc'd for $C_{18}H_{20}O_6$+Na $(M+Na)^+$: 355.1158, found: 355.1164.

*4.2.18. Ethyl 3-acetoxy-3-[4-methoxy-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**4h**).* Reaction time: 2 h; yield: 87%; R_f (20% EtOAc in hexanes) 0.41; pale yellow viscous liquid; IR (neat): ν 3283, 2982, 2123, 1743, 1724, 1612 cm^{-1}; ^1H NMR (400 MHz): δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.09 (s, 3H), 2.50 (t, 1H, *J* = 2.0 Hz), 3.80 (s, 3H), 4.16 (q, 2H, *J* = 7.2 Hz), 4.71 (d, 2H, *J* = 1.6 Hz), 5.68 (s, 1H), 6.40 (s, 1H), 6.51 (dd, 1H, *J* = 2.4 & 8.4 Hz), 6.61 (d, 1H, *J* = 2.0 Hz), 6.97 (s, 1H), 7.17 (d, 1H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz): δ 13.90, 20.84, 55.19, 56.07, 60.64, 67.78, 75.64, 78.26, 100.02, 105.36, 118.95, 126.00, 128.81, 139.26, 156.01, 160.70, 165.06, 169.25; HRMS (ESI) exact mass calc'd for $C_{18}H_{20}O_6$+Na $(M+Na)^+$: 355.1158, found: 355.1160.

*4.2.19. Ethyl 3-acetoxy-3-[5-bromo-2-(prop-2-ynyloxy)phenyl]-2-methylenepropanoate (**4i**).* Reaction time: 2 h; yield: 92%; R_f (20% EtOAc in hexanes) 0.50; pale yellow viscous liquid; IR (neat): ν 3292, 2984, 2123, 1745, 1722, 1635 cm^{-1}; ^1H NMR (400 MHz): δ 1.25 (t, 3H, *J* = 7.2 Hz), 2.12 (s, 3H), 2.49 (t, 1H, *J* = 2.0 Hz), 4.19 (q, 2H, *J* = 7.2 Hz), 4.71 (d, 2H, *J* = 1.6 Hz), 5.66 (s, 1H), 6.43 (s, 1H), 6.91 (d, 1H, *J* = 8.0 Hz), 6.97 (s, 1H), 7.37-7.44 (m, 2H); ^{13}C NMR (100 MHz): δ 14.04, 20.96, 56.36, 60.95, 67.44, 76.02, 77.94, 113.83, 114.31, 127.37, 129.19, 130.81, 132.04, 138.59, 153.92, 164.90, 169.20; HRMS (ESI) exact mass calc'd for $C_{17}H_{17}BrO_5$+Na $(M+Na)^+$: 403.0157, found: 403.0158.

*4.2.20. Methyl (E)-2-(azidomethyl)-3-[2-(prop-2-ynyloxy)-phenyl]prop-2-enoate (**5a**).* To a stirring solution of methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**4a**) (5 mmol, 1.44 g) in DMSO (10 mL) was added sodium azide (7.5 mmol, 0.48 g) and stirred for 3 h at room temperature. Then the reaction mixture was diluted with ethyl acetate (50 mL) and washed with water (3 X 10 mL) (to remove DMSO). Organic layer was dried over anhydrous Na_2SO_4. The solvent was removed in vacuo. Residue thus obtained was purified by column

chromatography (10% ethyl acetate in hexanes) on silica gel to afford 85% (1.160 g) of the title compound as a colorless viscous liquid. (optimization for obtaining **5a** from **4a** was performed on 1.0 mmol scale of **4a**).

R_f (20% EtOAc in hexanes) 0.52; colorless viscous liquid; IR (neat): ν 3292, 2951, 2094, 1714, 1633 cm^{-1}; ^1H NMR (400 MHz): δ 2.53 (t, 1H, *J* = 2.4 Hz), 3.89 (s, 3H), 4.15 (s, 2H), 4.76 (d, 2H, *J* = 2.4 Hz), 7.02-7.11 (m, 2H), 7.35-7.43 (m, 2H), 8.11 (s, 1H); ^{13}C NMR (100 MHz): δ 47.48, 52.34, 56.04, 76.09, 78.12, 112.26, 121.51, 123.81, 126.84, 130.36, 131.03, 140.27, 155.67, 167.45; HRMS (ESI) exact mass calc'd for $C_{14}H_{13}N_3O_3$+Na $(M+Na)^+$: 294.0855, found: 294.0858.

*4.2.21. 10-Methoxycarbonyl-2-oxa-6,7,8-triazatricyclo-[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6a**).*

Method A: To a stirring solution of methyl 2-(azidomethyl)-3-[2-(prop-2-ynyloxy)phenyl]prop-2-enoate (**5a**) (1 mmol, 0.271 g) in toluene (2 ml) was heated under reflux for 4 h (reaction monitered by TLC) and reaction mixture was cooled to room temperature. Solvent was removed in vacuo and purification of the residue by column chromatography (60% ethyl acetate in hexanes) on silica gel afforded 0.217 g (80%) of the title compound as a colorless solid.

R_f (50% EtOAc in hexanes) 0.30; colorless solid; mp: 148-150 °C; IR (KBr): ν 1714, 1628 cm^{-1}; ^1H NMR (400 MHz): δ 3.86 (s, 3H), 5.29 (s, 2H), 5.38 (s, 2H), 7.16-7.22 (m, 2H), 7.29-7.34 (m, 1H), 7.37-7.45 (m, 1H), 7.58 (s, 1H), 7.87 (s, 1H); ^{13}C NMR (100 MHz): δ 46.46, 52.65, 64.87, 121.44, 124.29, 124.87, 125.93, 131.60, 132.09, 132.68, 133.65, 140.96, 157.16, 166.38; HRMS (ESI) exact mass calc'd for $C_{14}H_{13}N_3O_3$+H $(M+H)^+$: 272.1035, found: 272.1035.

Crystal data for **6a**: Empirical formula, $C_{14}H_{13}N_3O_3$; Formula weight, 271.27; crystal color, colorless; habit, block; crystal dimensions, 0.52 x 0.48 x 0.40 mm^3; crystal system, monoclinic; lattice type, C centered; lattice parameters, a = 19.4754(15) Å, b = 10.3699(8) Å, c = 15.3638(12) Å, α = 90.00, β = 125.1930(10), γ = 90.00; V = 2535.7(3) $Å^3$; space group, C2/c; Z = 8; D_{cald} = 1.421 g / cm^3; F_{000} = 1136; λ (Mo-Kα) = 0.71073 Å; R(I≥2σ$_1$) = 0.0384, wR^2 = 0.0958. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **6a** CCDC # 956293).

Method B: (From methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**4a**) without isolating azido-alkyne **5a**)

To a stirring solution of methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propanoate (**4a**) (1.0 mmol, 0.288 g) in DMSO (2 mL) was added sodium azide (1.5 mmol, 0.096 g) and stirred for 3 h at room temperature. Then the reaction mixture was diluted with ethyl acetate (15 mL) and washed with water (3 X 2 mL) (to remove the DMSO). Organic layer was dried over anhydrous Na_2SO_4. The solvent was removed in vacuo. The crude azido-alkyne **5a** was dissolved in toluene (2 ml) and refluxed for 4 h and reaction mixture was cooled to room temperature and solvent was removed in vacuo and purification of the residue by column chromatography (60% ethyl acetate in hexanes) on silica gel afforded 0.195 g (72%) of the title compound as a colorless solid for overall two steps from methyl 3-acetoxy-2-methylene-3-[2-(prop-2-ynyloxy)phenyl]propaneate (**4a)**. Mp, spectral data (IR, ^{1}HNMR, ^{13}CNMR, HRMS) data of this compound are in complete agreement with the data of the compound prepared *via* method A.

Compounds **6b-i** were prepared following the procedure as in Method B.

*4.2.22. 16-Methoxy-10-methoxycarbonyl-2-oxa-6,7,8-triazatri-cyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6b**).* Reaction time: 3 h + 4 h; yield: 68%; R_f (50% EtOAc in hexanes) 0.16; colorless solid; mp: 185-188 °C; IR (KBr): ν 1709, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 3.88 (s, 3H), 3.94 (s, 3H), 5.28 (s, 4H), 6.81-6.86 (m, 1H), 6.98 (dd, 1H, *J* = 1.2 & 8.0 Hz), 7.10-7.17 (m, 1H), 7.57 (s, 1H), 7.77 (s, 1H); ^{13}C NMR (100 MHz): δ 46.04, 52.42, 55.86, 64.38, 113.22, 122.20, 124.64, 126.95, 127.24, 132.09, 134.84, 140.37, 145.29, 152.47, 166.21; HRMS (ESI) exact mass calc'd for $C_{15}H_{15}N_3O_4$+Na $(M+Na)^+$: 324.0960, found: 324.0956.

*4.2.23. 15-Methoxy-10-methoxycarbonyl-2-oxa-6,7,8-triazatri-cyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6c**).* Reaction time: 4 h + 4 h; yield: 63%; R_f (50% EtOAc in hexanes) 0.18; colorless solid; mp: 145-148 °C; IR (KBr): ν 1714, 1632 cm^{-1}; ^1H NMR (400 MHz): δ 3.83 (s, 3H), 3.85 (s, 3H), 5.26 (s, 2H), 5.43 (s, 2H), 6.70 (d, 1H, *J* = 2.4 Hz), 6.74 (dd, 1H, *J* = 2.8 & 8.8 Hz), 7.25 (d, 1H, *J* = 8.8 Hz, [one of the peak of the doublet merges with [$CDCl_3$] $CHCl_3$ peak], 7.58 (s, 1H), 7.86 (s, 1H), ^{13}C NMR (100 MHz): δ 46.36, 52.41, 55.51, 64.65, 107.10, 110.41, 116.91, 123.14, 131.92, 133.01, 134.65, 141.41, 158.69, 162.17, 166.61; HRMS (ESI) exact mass calc'd for $C_{15}H_{15}N_3O_4$+Na $(M+Na)^+$: 324.0960, found: 324.0967**.**

*4.2.24. 14-Bromo-10-methoxycarbonyl-2-oxa-6,7,8-triazatri-cyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6d**).* Reaction time: 3 h + 5 h; yield: 57%; R_f (50% EtOAc in hexanes) 0.30; colorless solid; mp: 212-214 °C; IR (KBr): ν 1711, 1631 cm^{-1}; ^1H NMR (400 MHz): δ 3.86 (s, 3H), 5.27 (s, 2H), 5.36 (s, 2H), 7.06 (d, 1H, *J* = 8.4 Hz), 7.43 (d, 1H, *J* = 2.4 Hz), 7.50 (dd, 1H, *J* = 2.8 & 8.4 Hz), 7.58 (s, 1H), 7.76 (s, 1H); ^{13}C NMR (100 MHz): δ 46.40, 52.82, 65.01, 116.88, 123.20, 126.97, 127.24, 132.28, 133.45, 134.31, 134.84, 139.15, 156.15, 166.01; HRMS (ESI) exact mass calc'd for $C_{14}H_{12}BrN_3O_3$+Na $(M+Na)^+$: 371.9960, found: 371.9959.

*4.2.25. 14-Chloro-10-methoxycarbonyl-2-oxa-6,7,8-triazatri-cyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6e**).* Reaction time: 3 h + 4 h; yield: 62%; R_f (50% EtOAc in hexanes) 0.28; colorless solid; mp: 204-206 °C; IR (KBr): ν 1711, 1633 cm^{-1}; ^1H NMR (400 MHz): δ 3.86 (s, 3H), 5.27 (s, 2H), 5.36 (s, 2H), 7.12 (d, 1H, *J* = 8.4 Hz), 7.28 (d, 1H, *J* = 2.8 Hz), 7.35 (dd, 1H, *J* = 2.8 & 8.4 Hz), 7.58 (s, 1H), 7.76 (s, 1H); ^{13}C NMR (100 MHz): δ 46.33, 52.74, 65.00, 122.80, 126.50, 127.20, 129.38, 131.30, 131.76, 132.19, 133.48, 139.14, 155.53, 165.97; HRMS (ESI) exact mass calc'd for $C_{14}H_{12}ClN_3O_3$+Na $(M+Na)^+$: 328.0465, found: 328.0475.

*4.2.26. 10-Ethoxycarbonyl-2-oxa-6,7,8-triazatricyclo-[10.4.0.-0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6f**).* Reaction time: 4 h + 4 h; yield: 58%; R_f (50% EtOAc in hexanes) 0.26; colorless solid; mp: 88-89 °C; IR (KBr): ν 1709, 1639 cm^{-1}; ^1H NMR (400 MHz): δ 1.35 (t, 3H, *J* = 7.2 Hz), 4.30 (q, 2H, *J* = 7.2 Hz), 5.29 (s, 2H), 5.39 (s, 2H), 7.15-7.22 (m, 2H), 7.31 (d, 1H, *J* = 7.2 Hz), 7.37-7.43 (m, 1H), 7.57 (s, 1H), 7.86 (s, 1H); ^{13}C NMR (100 MHz): δ 14.20, 46.51, 61.80, 64.88, 121.51, 124.32, 124.93, 126.19, 131.55, 132.11, 132.78, 133.60, 140.67, 157.20, 165.93; HRMS (ESI) exact mass calc'd for $C_{15}H_{15}N_3O_3$+Na $(M+Na)^+$: 308.1011, found: 308.1017.

*4.2.27. 10-Ethoxycarbonyl-16-methoxy-2-oxa-6,7,8-triazatri-cyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene (**6g**).* Reaction time: 3 h + 4 h; yield: 65%; R_f (50% EtOAc in hexanes) 0.21; colorless solid; mp: 160-162 °C; IR (KBr): ν 1705, 1633 cm^{-1}; ^1H NMR (400 MHz): δ 1.37 (t, 3H, *J* = 7.2 Hz), 3.94 (s, 3H), 4.33 (q, 2H, *J* = 7.2 Hz), 5.277 (s, 2H), 5.284 (s, 2H), 6.81-6.86 (m, 1H), 6.98 (dd, 1H, *J* = 1.2 & 8.0 Hz), 7.10-7.16 (m, 1H), 7.56 (s, 1H), 7.76 (s, 1H); ^{13}C NMR (100 MHz): δ 14.10, 46.10, 55.90, 61.54, 64.39, 113.20, 122.32, 124.64, 127.08, 127.56, 132.11, 134.78, 139.98, 145.34, 152.52, 165.75; HRMS (ESI) exact mass calc'd for $C_{16}H_{17}N_3O_4$+Na $(M+Na)^+$: 338.1117, found: 338.1114.

4.2.28. 10-Ethoxycarbonyl-15-methoxy-2-oxa-6,7,8-triazatricyclo[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene ***(6h)****.* Reaction time: 10 h + 4 h; yield: 68%; R_f (50% EtOAc in hexanes) 0.27; colorless solid; mp: 140-142 °C; IR (KBr): ν 1703, 1610 cm^{-1}; ^{1}H NMR (400 MHz): δ 1.33 (t, 3H, *J* = 7.2 Hz), 3.85 (s, 3H), 4.27 (q, 2H, *J* = 7.2 Hz), 5.26 (s, 2H), 5.44 (s, 2H), 6.69 (d, 1H, *J* = 2.4 Hz), 6.74 (dd, 1H, *J* = 2.4 & 8.8 Hz), 7.25 (d, 1H, *J* = 8.4 Hz), 7.57 (s, 1H), 7.84 (s, 1H); ^{13}C NMR (100 MHz): δ 14.20, 46.53, 55.63, 61.63, 64.78, 107.27, 110.55, 117.07, 123.57, 132.07, 132.98, 134.86, 141.21, 158.86, 162.23, 166.25; HRMS (ESI) exact mass calc'd for $C_{16}H_{17}N_3O_4$+Na $(M+Na)^+$: 338.1117, found: 338.1119.

4.2.29. 14-Bromo-10-ethoxycarbonyl-2-oxa-6,7,8-triazatricyclo-[10.4.0.0^{4,8}]hexadeca-1(12),4,6,10,13,15-hexaene ***(6i)****.* Reaction time: 3 h + 4 h; yield: 71%; R_f (50% EtOAc in hexanes) 0.23; colorless solid; mp: 166-169 °C; IR (KBr): ν 1712, 1630 cm^{-1}; ^{1}H NMR (400 MHz): δ 1.35 (t, 3H, *J* = 7.2 Hz), 4.30 (q, 2H, *J* = 7.2 Hz), 5.27 (s, 2H), 5.36 (s, 2H), 7.06 (d, 1H, *J* = 8.8 Hz), 7.44 (d, 1H *J* = 2.0 Hz), 7.48 (dd, 1H, *J* = 2.4 & 8.8 Hz), 7.57 (s, 1H), 7.75 (s, 1H); ^{13}C NMR (100 MHz): δ 14.25, 46.48, 62.06, 65.05, 116.96, 123.30, 127.05, 127.53, 132.36, 133.34, 134.29, 135.02, 138.86, 156.22, 165.57; HRMS (ESI) exact mass calc'd for $C_{15}H_{14}N_3O_3Br$+Na $(M+Na)^+$: 386.0116, found: 386.0112.

Acknowledgement: We thank DST (New Delhi) for funding this project. BSR thanks CSIR and DST (New Delhi) for research fellowships. HL thanks CSIR for her research fellowship. We thank UGC (New Delhi) for support and for providing some instrumental facilities. We thank the National Single-Crystal X-ray facility funded by DST. We also thank Professor S. Pal, School of Chemistry, University of Hyderabad, for helpful discussions regarding X-ray data analysis.

References and notes

[@] Preliminary results were presented as a poster in *3rdInternational symposium on organic synthesis and Drug Development (ISOSDD' 2012)* held during May 20-23, 2012 at Changzhou University, China.

1. (a) Shiina, I. *Chem. Rev*. **2007**, *107*, 239-273; (b) Denmark, S. E.; Yang, S. M. *J. Am. Chem. Soc*. **2002**, *124*, 2102-2103; (c) Maier E. *Angew. Chem. Int. Ed*. **2000**, *39*, 2073-2077; (d) Yet, L. *Chem. Rev*. **2000**, *100*, 2963-3007; (e) Petasis, N. A.; Petane, M. A. *Tetrahedron* **1992**, *48*, 5757-5821; (f) Evans, P. A.; Holmes, A. B. *Tetrahedron* **1991**, *47*, 9131-9166.

2. (a) Shintani, R.; Ikehata, K.; Hiyashi, T. *J. Org. Chem*. **2011**, *76*, 4776-4780; (b) Ramesh, N. G.; Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron Lett*. **2001**, *42*, 7707-7709; (c) Bremner, J. B.; Browne, E. J.; Engelhardt, L. M.; Greenwood, C. S.; White, A. K. *Aust. J. Chem*. **1988**, *41*, 1815-1826; (d) Yoshifiji, S.; Tanaka, K-i.; Arata, Y. *Tetrahedron Lett.* **1979,** 809-812; (e) Bose, A. K.; Hoffman, W. A.; Manhas, M. S. *J. Chem. Soc. Perkin Trans. 1* **1976**, 2343-2348.

3. (a) Alvarez, R.; Velazquez, S.; San-Felix, A.; Aquaro, S.; De Clercq, E.; Perno, C-F.; Karlsson, A.; Balzarini, J.; Camarasa, M. J. *J. Med. Chem.* **1994**, *37*, 4185-4194; (b) Buckle, D. R.; Outred, D. J.; Rockell, C. J. M.; Smith, H.; Spicer, B. A. *J. Med. Chem.* **1983**, *26*, 251-254; (c) Kume, M.; Kubota, T.; Kimura, Y.; Nakashimizu, H.; Motokawa, K. *Chem. Pharm. Bull*. **1993**, *41*, 758-762; (d) Genin, M. J.; Allwine, D. A.; Anderson, D. J.; Barbachyn, M. R.; Emmert, D. E.; Garmon, S. A; Graber, D. R.; Grega, K. C.; Hester, J. B.; Hutchinson, D. K.; Morris, J.; Reischer, R. J.; Ford, C. W.; Zurenko, G. E.; Hamel, J. C.; Schaadt, R. D.; Stapert, D.; Yagi, B. H. *J. Med. Chem* . **2000**, *43*, 953-970; (e) Fu, T-h.; Li, Y.; Thaker, H. D.; Scott, R. W.; Tew, G. N. *ACS Med. Chem. Lett*. **2013**, *4*, 841-845.

4. (a) Varizhuk, A. M.; Kaluzhny, D. N.; Novikov, R. A.; Chizhov, A. O.; Smirnov, I. P.; Chuvilin, A. N.; Tatarinova, O. N.; Fisunov, G. Y.; Pozmogova, G. E.; Florentiev, V. L. *J. Org. Chem.* **2013**, *78*, 5964−5969; (b) Zhou, F.; Tan, C.; Tang, J.; Zhang, Y-Y.; Gao, W-M.; Wu, H-H.; Yu, Y-H.; Zhou, J. *J. Am. Chem. Soc*. **2013**, *135*, 10994−10997; (c) Reddy, M. N.; Kumara Swamy, K. C. *Eur. J. Org. Chem.* **2012**, 2013-2022; (d) Hu, Y-Y.; Hu, J.; Wang, X-C.; Guo, L-N.; Shu, X-Z.; Niu, Y-N.; Liang, Y-M. *Tetrahedron* **2010**, *66*, 80–86; (e) Li, R.; Jansen, D. J.; Datta, A. *Org. Biomol. Chem.* **2009**, *7*, 1921–1930; (f) Klemm, C. M.; Berthelmann, A.; Neubacher, S.; Arenz, C. *Eur. J. Org. Chem.* **2009**, 2788–2794; (g) Jin, S.; Choudhary, G.; Cheng, Y.; Dai, C.; Li, M.; Wang, B. *Chem. Commun.* **2009**, 5251–5253; (h) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952–3015; (i) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev*. **2007**, *36*, 1249–1262; (j) Huisgen, R. *Proceedings of the Chemical Society* **1961**, 357- 396.

5. (a) Oliva, A. I.; Christmann, U.; Font, D.; Cuevas, F.; Ballester, P.; Buschmann, H.; Torrens, A.; Yenes, S.; Pericas, M. A. *Org. Lett.* **2008**, *10*, 1617-1619; (b) Chandrasekhar, S.; Seenaiah, M.; Kumar, A.; Reddy, C. R.; Mamidyala, S. K.; Kumar, C. G.; Balasubramanian, S. *Tetrahedron Lett*. **2011**, *52*, 806-808; (c) Hotha, S.; Anegundi, R. I.; Natu, A. A. *Tetrahedron Lett*. **2005**, *46*, 4585-4588;(d) Mishra, A.; Hutait, S.; Bhowmik, S.; Rastogi, N.; Roy, R.; Batra, S. *Synthesis* **2010**, 2731–2748.

6. (a) Basavaiah, D.; Badsara, S. S.; Sahu, B. C. *Chem. Eur. J*. **2013**, *19*, 2961-2965; (b) Basavaiah, D.; Kumar, K. S.; Aravindu, K.; Lingaiah, B. *RSC Adv*, **2013**, *3*, 9629-9632. (c) Basavaiah, D.; Badsara, S. S.; Veeraraghavaiah, G. *Tetrahedron* **2013**, *69*, 7995-8001; (d) Basavaiah, D.; Reddy, D. M. *Org. Biomol. Chem*. **2012**, *10*, 8774-8777. (e) Basavaiah, D.; Roy, S.; Das, U. *Tetrahedron* **2010,** *66*, 5612-5622; (f) Basavaiah, D.; Roy, S. *Org. Lett*. **2008**, *10*, 1819-1822; (g) Basavaiah, D.; Aravindu, K. *Org. Lett.* **2007**, *9*, 2453-2456; (h) Basavaiah, D.; Sharada, D. S.; Veerendhar, A. *Tetrahedron Lett*. **2006**, *47*, 5771-5774; (i) Basavaiah, D.; Satyanarayana, T. *Chem. Comm*. **2004**, 32-33; (j) Basavaiah, D.; Rao, A. J. *Chem. Comm.* **2003**, 604-605.

7. For reviews see (a) Basavaiah, D.; Sahu, B. C. *Chimia* **2013**, *67*, 8-16; (b) Wei, Y.; Shi, M. *Chem. Rev.* **2013**, *113*, 6659-6690; (c) Liu, T. Y.; Xie, M.; Chen, Y. C. *Chem. Soc. Rev*. **2012**, *41*, 4101-4112; (d) Basavaiah, D.; Veeraraghavaiah, G. *Chem. Soc. Rev*. **2012**, *41*, 68-78; (e) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. *Chem. Rev*. **2010**, *110*, 5447-5674; (f) Wei, Y.; Shi, M. *Acc. Chem. Res*. **2010**, *43*, 1005-1018; (g) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev*. **2009**, *109*, 1-48; (h) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64,* 4511-4574; (i) Masson, G.; Housseman, C.; Zhu, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 4614-4628; (j) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev*. **2007**, *36*, 1581-1588; (k) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev*. **2003**, *103*, 811-891; (l) Coelho, F.; Almeida, W. P. *Quimica Nova* **2000**, *23*, 98-101; (m) Ciganek, E. in *Organic Reactions*, Paquette L. A. Ed., New York, Wiley **1997**, *51*, 201-350; (n) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52***,** 8001-8062; (o) Drewes, S. E.; Roos, G. H. P. *Tetrehedron* **1988**, *44*, 4653-4670.

8. For recent references see (a) Correia, J. T. M.; Rodrigues Jr., M. T.; Santos, H.; Tormena, C. F.; Coelho, F. *Tetrahedron* **2013**, *69*, 826-832; (b) Tong, G.; Zhu, B.; Lee, R.; Yang, W.; Tan, D.; Yang, C.; Han, Z.; Yan, L.; Huang, K-W.; Jiang, Z. *J. Org. Chem*. **2013**, *78*, 5067−5072; (c) Lim, J. W.; Kim, K. H.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2013**, *54*, 2595–2599; (d) Hu, F-L.; Wei, Y.; Shi, M.; Pindi, S.; Li, G. *Org. Biomol. Chem.* **2013**, *11*, 1921-1924; (e) Kumar, T.; Mobin, S. M.; Namboothiri, I. N. N. *Tetrahedron* **2013**, *69*, 4964-4972; (f) Basavaiah, D.; Reddy, B. S.; Lingam, H. *Tetrahedron* **2013**, *69*, 1994-2003; (g) Saadi, F.; Arfaoui, A.; Amri, H. *Synth Comm*. **2013**, *43*, 1594–1601; (h) Ramesh, C.; Lei, P-M.; Janreddy, D.; Kavala, V.; Kuo, C-W.; Yao, C-F. *J. Org. Chem*. **2012**, *77*, 8451−8464; (i) Gomes, J. C.; Rodrigues Jr., M. T.; Moyano, A.; Coelho, F. *Eur. J. Org. Chem.* **2012**, 6861–6866; (j) Nair, D. K.; Mobin, S. M.; Namboothiri, I. N. N. *Org. Lett*. **2012**, *14*, 4580-4583; (k) Reddy, Y. S.; Kadigachalam, P.; Basak, R. K.; Pal, A. P. J.; Vankar, Y. D. *Tetrahedron Lett.* **2012**, *53*, 132-136; (l) Lim, J. W.; Kim, K. H.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2012**, *53*, 5449-5454; (m) Krafft, M. E.; Campbell, M. J.; Kerrigan, S.; Cran, J. W. *Tetrahedron Lett.* **2011,** *52*, 1090-1092; (n) Kuan, H-H.; Reddy, R. J.; Chen, K. *Tetrahedron* **2010**, *66*, 9875-9879; (o) Kitulagoda, J. E.; Palmelund, A.; Aggarwal, V. K. *Tetrahedron* **2010**, *66*, 6293-6299; (p) Basavaiah, D.; Lenin, D. V. *Eur. J. Org. Chem.* **2010**, 5650-5658; (q) Basavaiah, D.; Devendar, B.; Lenin, D. V.; Satyanarayana, T. *Synlett* **2009**, 411-416; (r) Kabalka, G. W.;

Dong, G.; Venkataiah, B.; Chen, C. *J. Org. Chem.* **2005**, *70*, 9207-9210.

9. (a) Park, S. P.; Ahn, S-H.; Lee, K-J. *Tetrahedron* **2010**, *66*, 3490–3498; (b) Declerck, V.; Toupet, L.; Martinez, J.; Lamaty, F. *J. Org. Chem.* **2009**, *74*, 2004-2007; (c) Sreedhar, B.; Reddy, P. S.; Kumar, N. S. *Tetrahedron Lett.* **2006**, *47*, 3055-3058; (d) Chandrasekhar, S.; Basu, D.; Rambabu, Ch. *Tetrahedron Lett.* **2006**, *47*, 3059-3063; (e) Song, Y. S.; Lee, K-J. *J. Heterocycl. Chem*. **2006**, *43*, 1721-1724; (f) Ko, S. H.; Lee, K-J. *J. Heterocycl. Chem.* **2004**, *41*, 612-616.

10. Basavaiah, D.; Reddy, R. M. *Indian J. Chem.* **2001**, *40B*, 985-988.

11. Detailed X-ray crystallographic data is available from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK for compound **6a** CCDC # 956293.

12. It is well established that in the ^{1}HNMR spectrum of di/ trisubstituted alkenes the olefinic proton *cis* to the ester group appears downfield in comparison with that of the olefinic protons *trans* to ester group. (*E*)-Stereochemistry of C10-C11- double bond in the compounds **6a-i** is assigned on the basis of chemical shift values (δ 7.75-7.87) of olefinic proton at C-11 carbon. (ref. Jackman, L. M.; Strenhell, S. *Application of nuclear magentic resonance spectroscopy in organic chemistry*, 2nd edition, Pergamon Press, Oxford 1969, *Vol 5*). We have also confirmed the stereochemistry of the double bond in compound **6a** by single crystal X-ray data analysis.[11]

13. (a) Li, Z.; Seo, T. S.; Ju, J. *Tetrahedron Lett.* **2004**, *45*, 3143-3146; (b) Almeida, G. de.; Sletten, E. M.; Nakamura, H.; Palaniappan, K. K.; Bertozzi, C. R. *Angew. Chem. Int. Ed.* **2012**, *51*, 2443-2447; (c) Jewett, J. C.; Bertozzi, C. R. *Chem. Soc. Rev.*, **2010,** *39***,** 1272-1279; (d) Schultz, M. K.; Parameswarappa, S. G.; Pigge, F. C. *Org. Lett.* **2010**, *12*, 2398-2401; (e) Ning, X.; Guo, J.; Wolfert, M. A.; Boons, G-J. *Angew. Chem. Int. Ed.* **2008**, *47*, 2253-2255; (f) Codelli, J. A.; Baskin, J. M.; Agard, N. J.; Bertozzi, C. R. *J. Am. Chem. Soc.* **2008**, *130*, 11486-11493; (g) Shi, F.; Waldo, J. P.; Chen, Y.; Larock, R. C. *Org. Lett.* **2008**, *10*, 2409-2412.

14. Ramachandiran, K.; Karthikeyan, K.; Muralidharan, D.; Perumal, P. T. *Tetrahedron Lett*. **2010**, 51, 3006-3009.

Supporting Information

Synthesis of fused nine membered rings: A simple protocol for synthesis of [1,2,3]-triazolo-[1,4]-benzoxazonine frameworks from the Baylis-Hillman acetates

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CONTENTS

Crystal data for **6a**: Empirical formula, $C_{14}H_{13}N_3O_3$; Formula weight, 271.27; crystal color, colorless; habit, block; crystal dimensions, 0.52 x 0.48 x 0.40 mm^3; crystal system, monoclinic; lattice type, C centered; lattice parameters, a = 19.4754(15) Å, b = 10.3699(8) Å, c = 15.3638(12) Å, α = 90.00, β = 125.1930(10), γ = 90.00; V = 2535.7(3) $Å^3$; space group, C2/c; Z = 8; D_{cald} = 1.421 g / cm^3; F_{000} = 1136; λ (Mo-Kα) = 0.71073 Å; R($I \geq 2\sigma_1$) = 0.0384, wR^2 = 0.0958. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound **6a** CCDC # 956293).

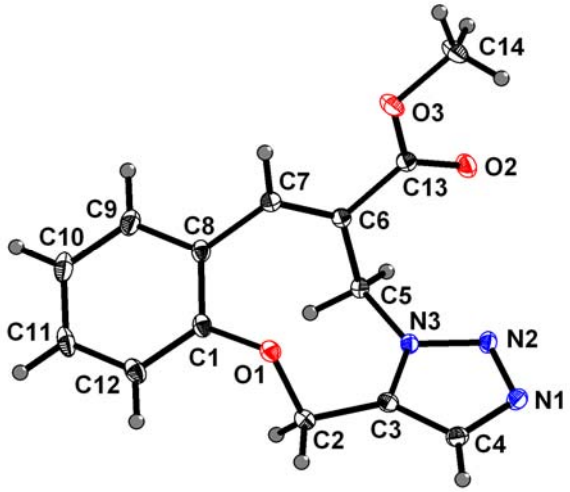
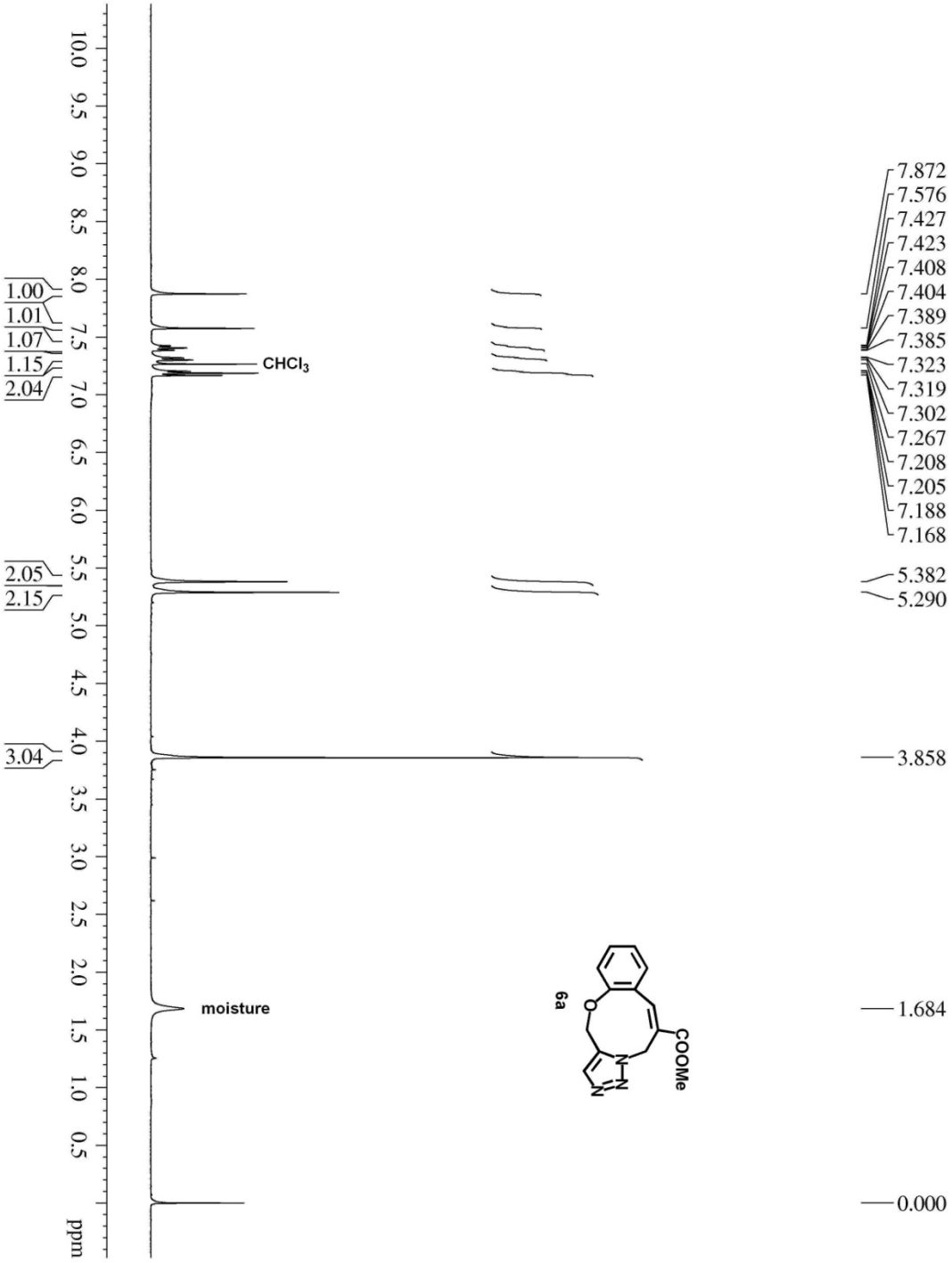


Figure 1. ORTEP diagrams of compound **6a**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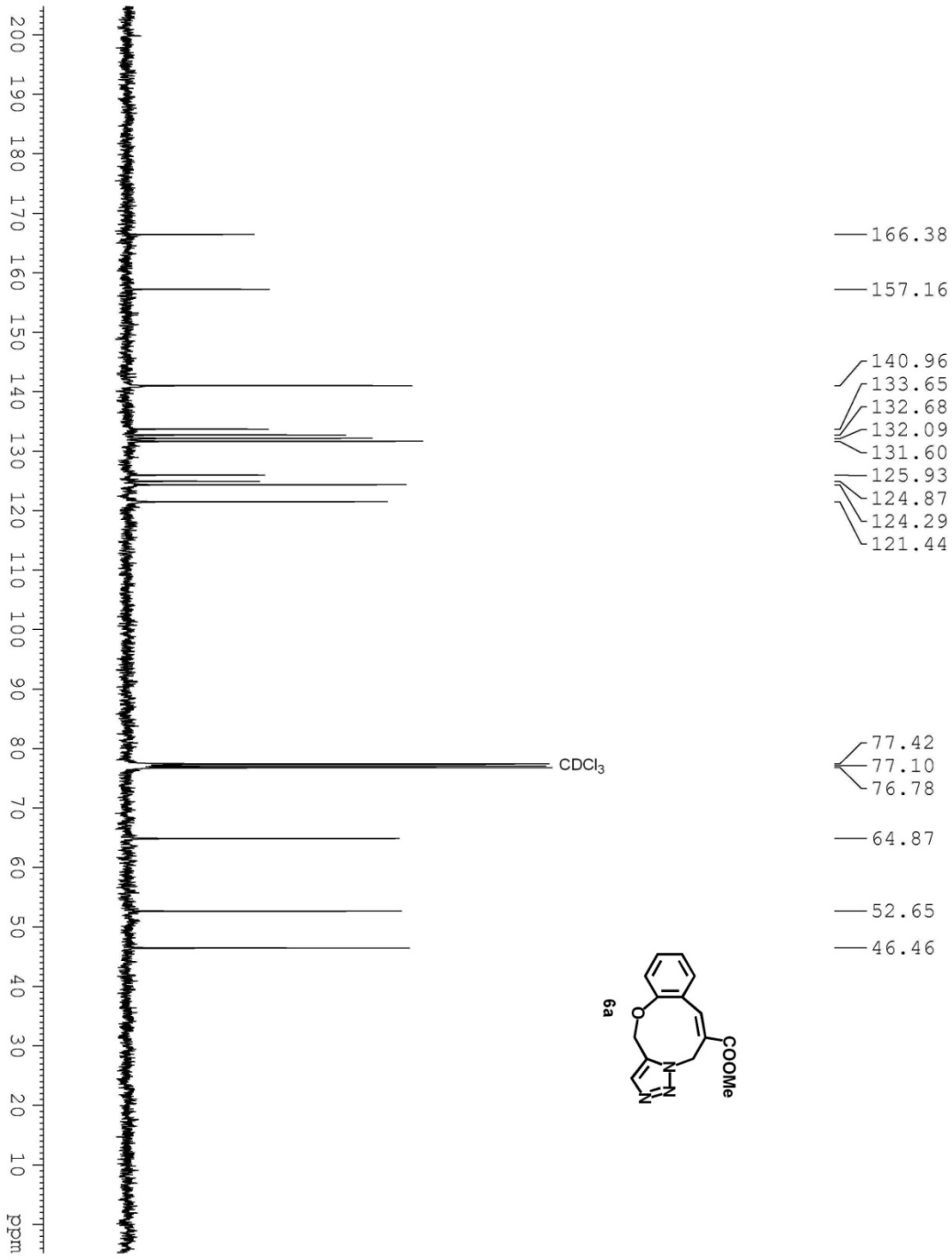
7.208
7.205
7.188
7.168
5.382
5.290
3.858
1.684
0.000
1.00
1.01
1.07
1.15
2.04
2.05
2.15
3.04
CHCl3
moisture
6a
COOMe
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm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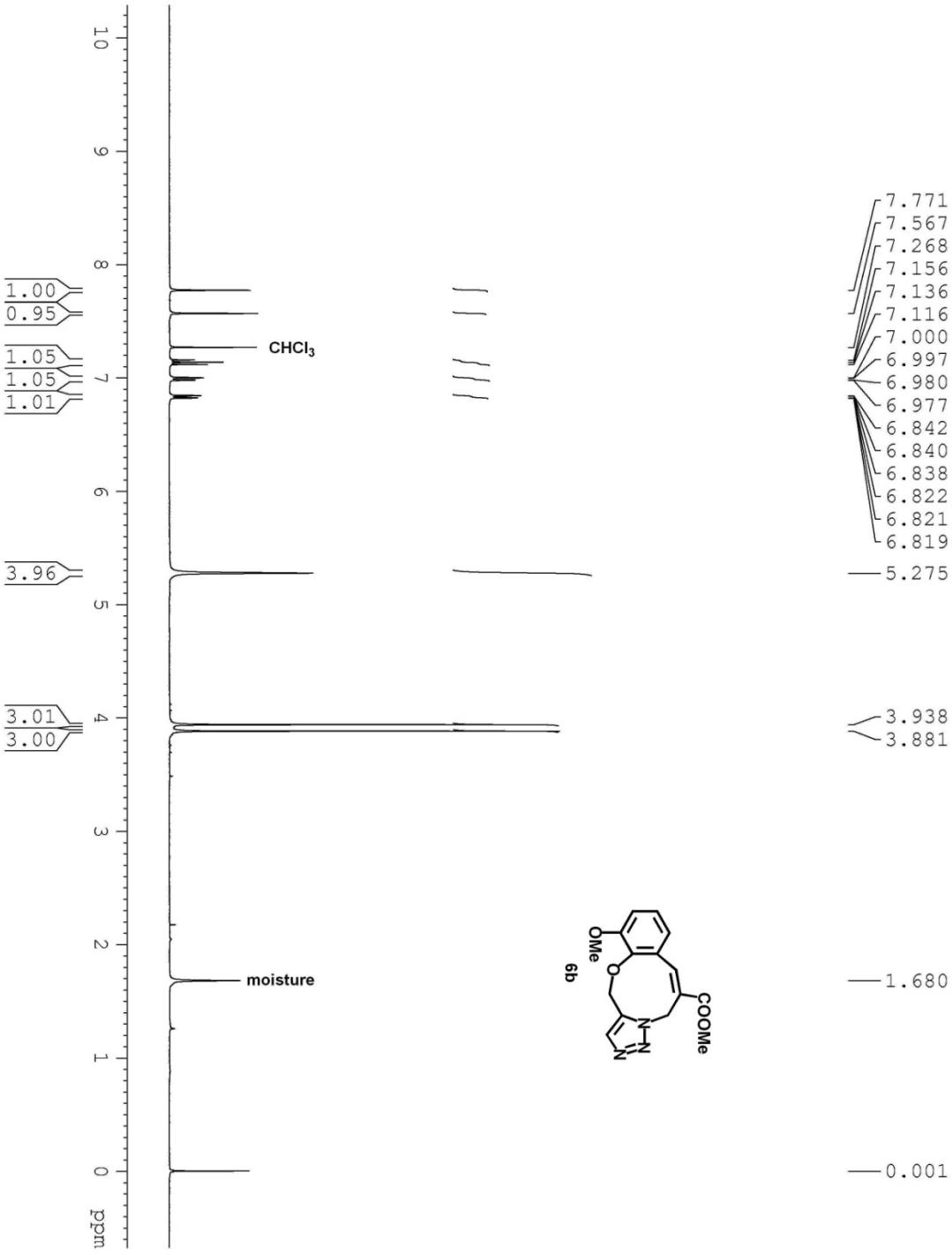
157.16
140.96
133.65
132.68
132.09
131.60
125.93
124.87
124.29
121.44
77.42
77.10
76.78
64.87
52.65
46.46
CDCl3
6a
COOMe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6.838
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6.821
6.819
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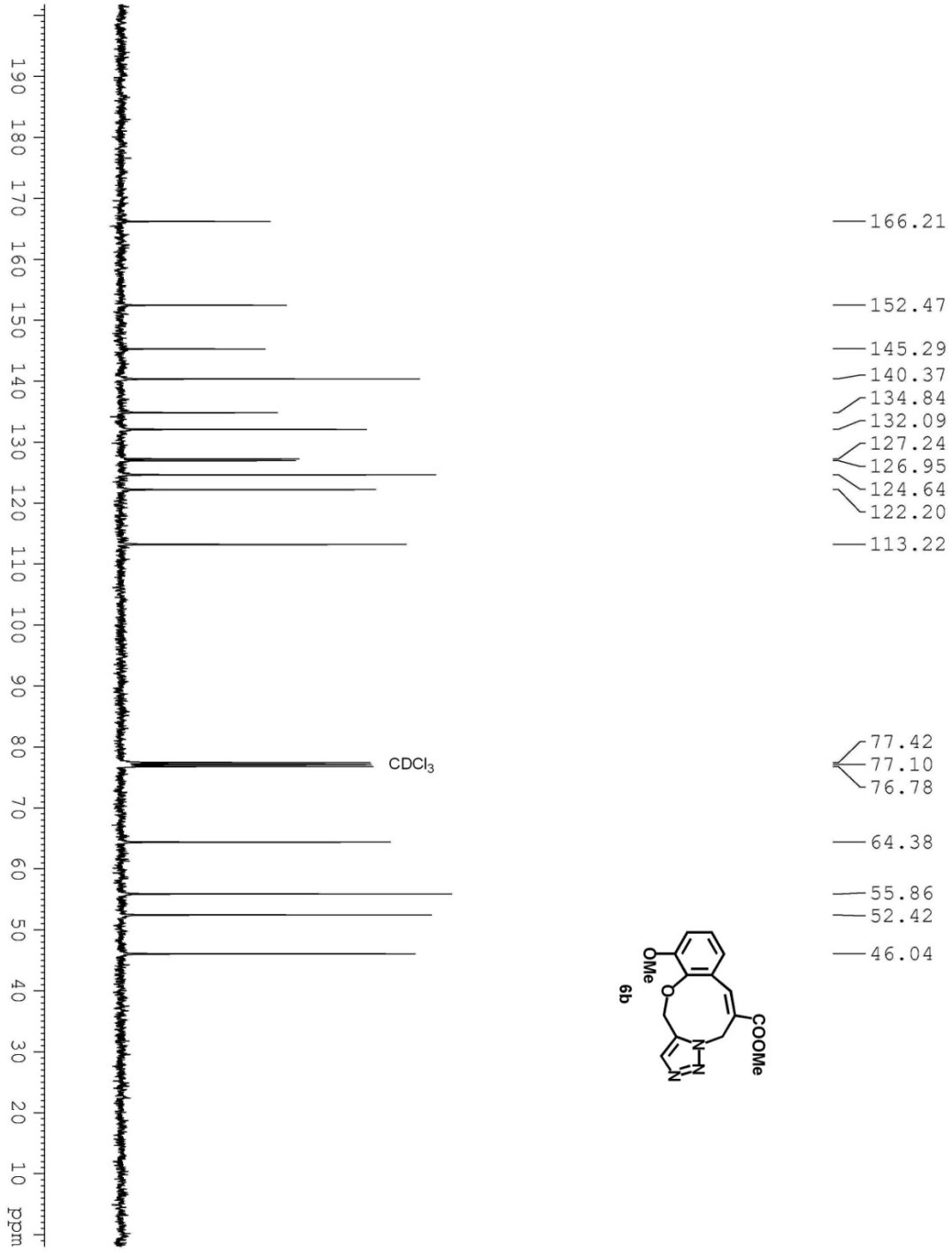
3.938
3.881
1.680
0.001
1.00
0.95
1.05
1.05
1.01
3.96
3.01
3.00
CHCl3
moisture
ppm
OMe
COOMe
6b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127.24
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122.20
113.22
77.42
77.10
76.78
64.38
55.86
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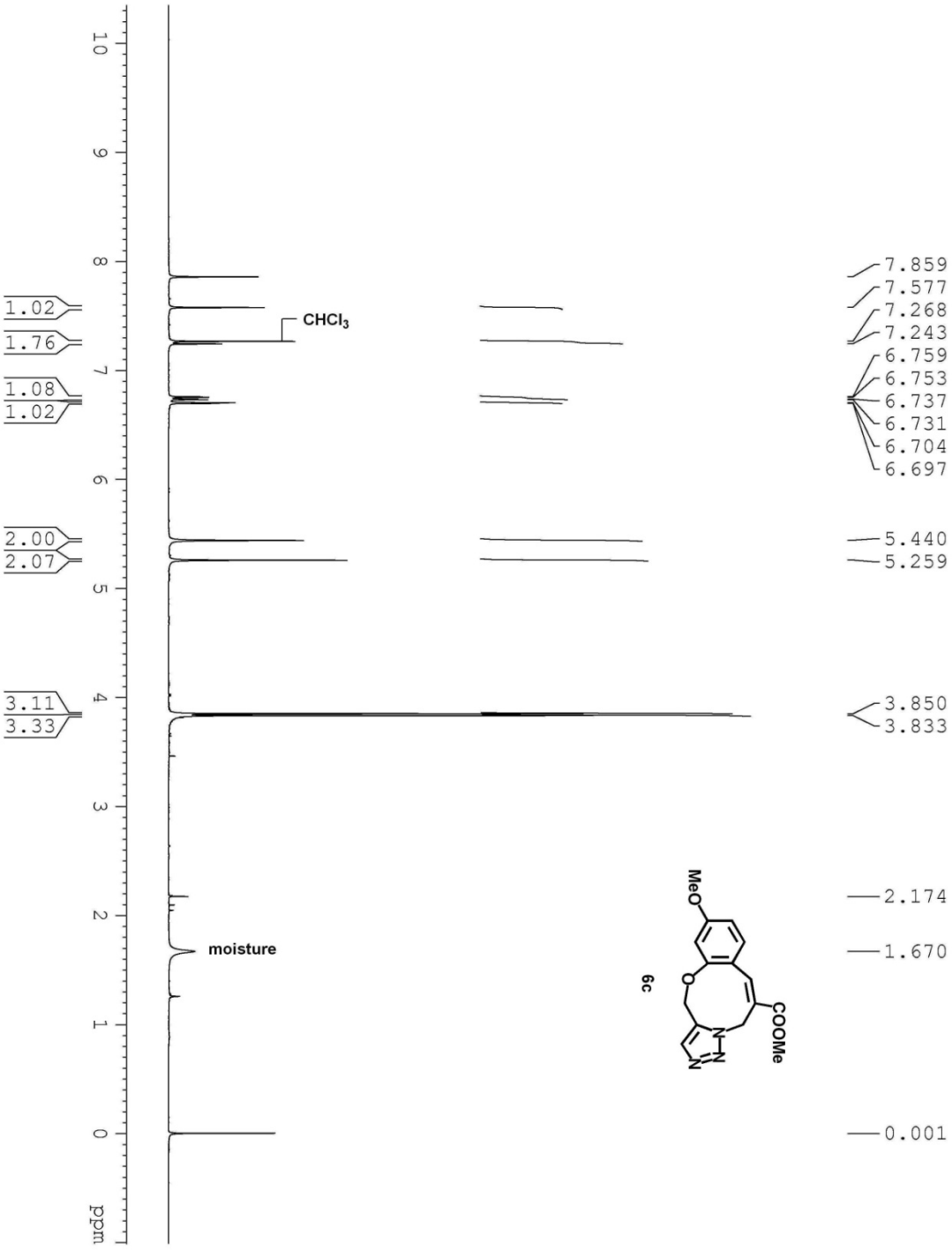
CDCl3
OMe
COOMe
6b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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3.833
2.174
1.670
0.001
1.02
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2.07
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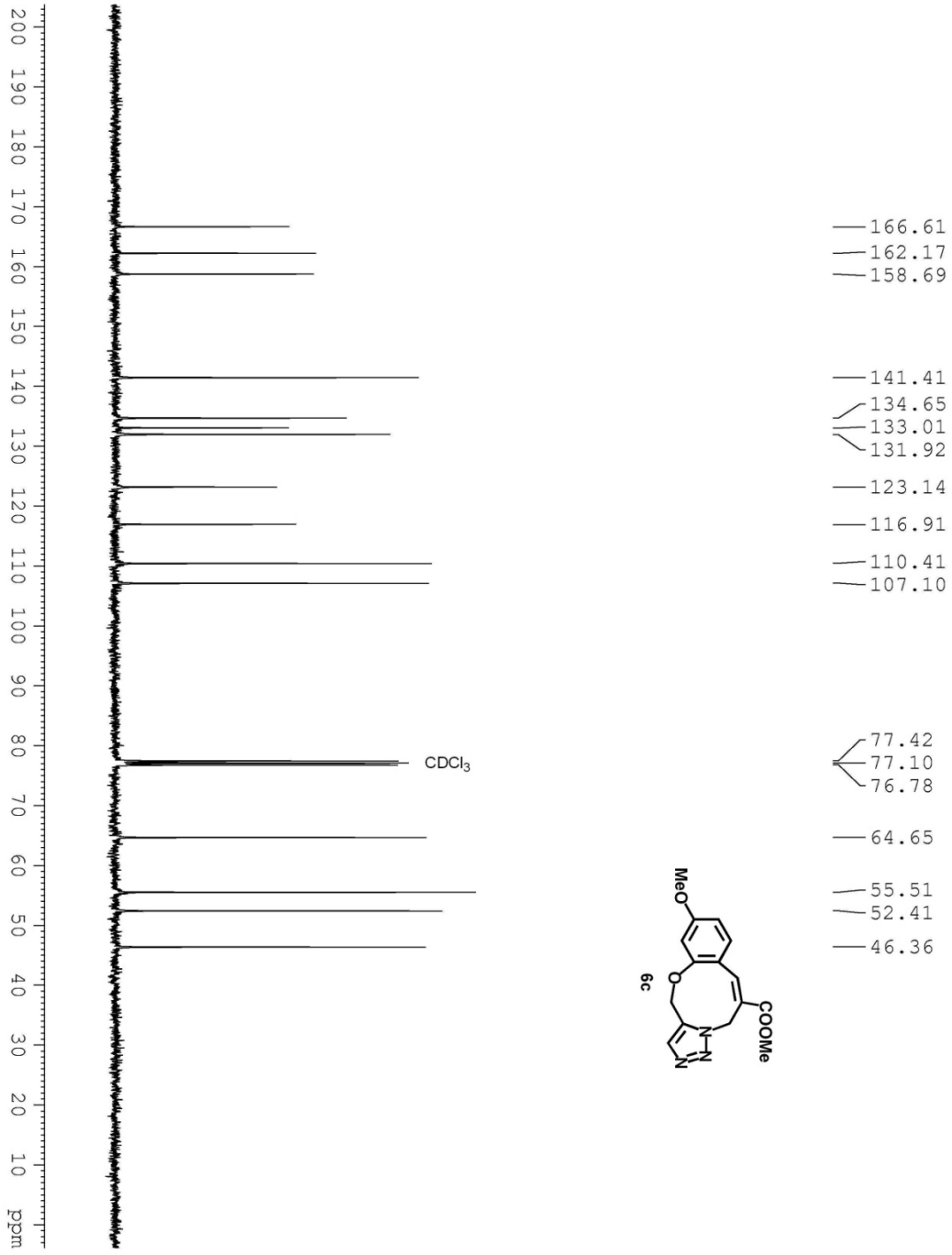
CHCl3
moisture
MeO
COOMe
6c
ppm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76.78
64.65
55.51
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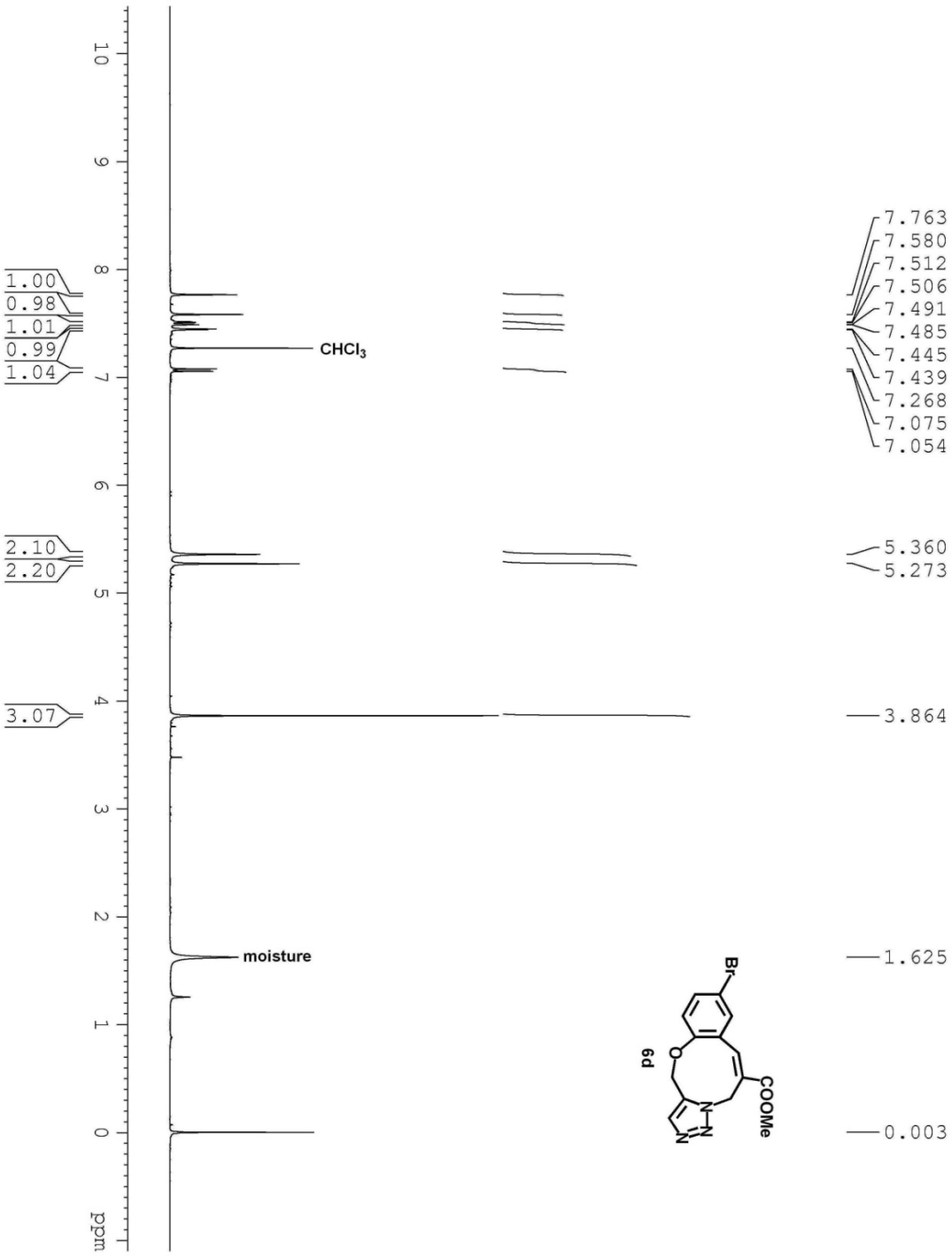
MeO
O
N
N
N
COOMe
6c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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ppm
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7.506
7.491
7.485
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7.439
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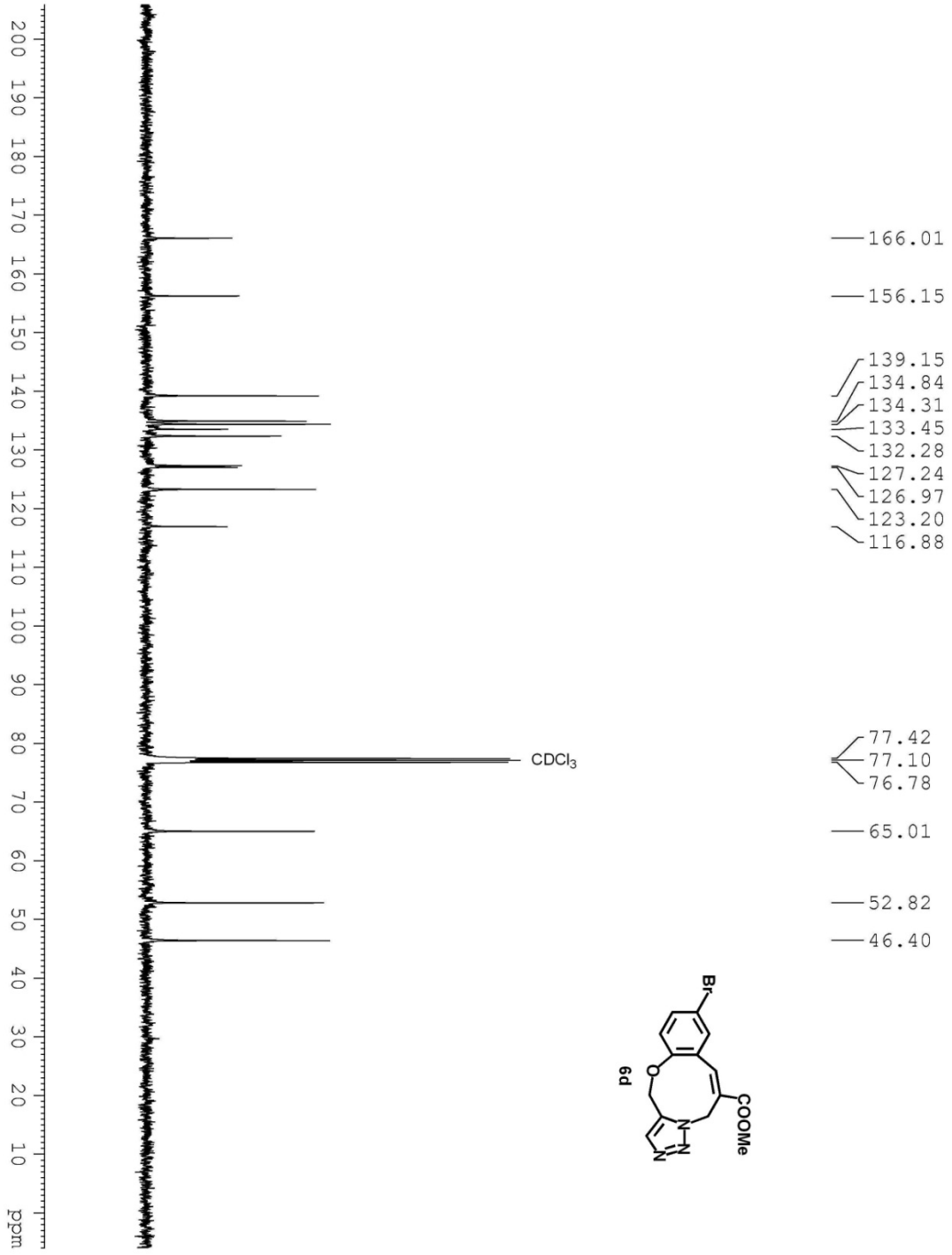
N
COOMe
6d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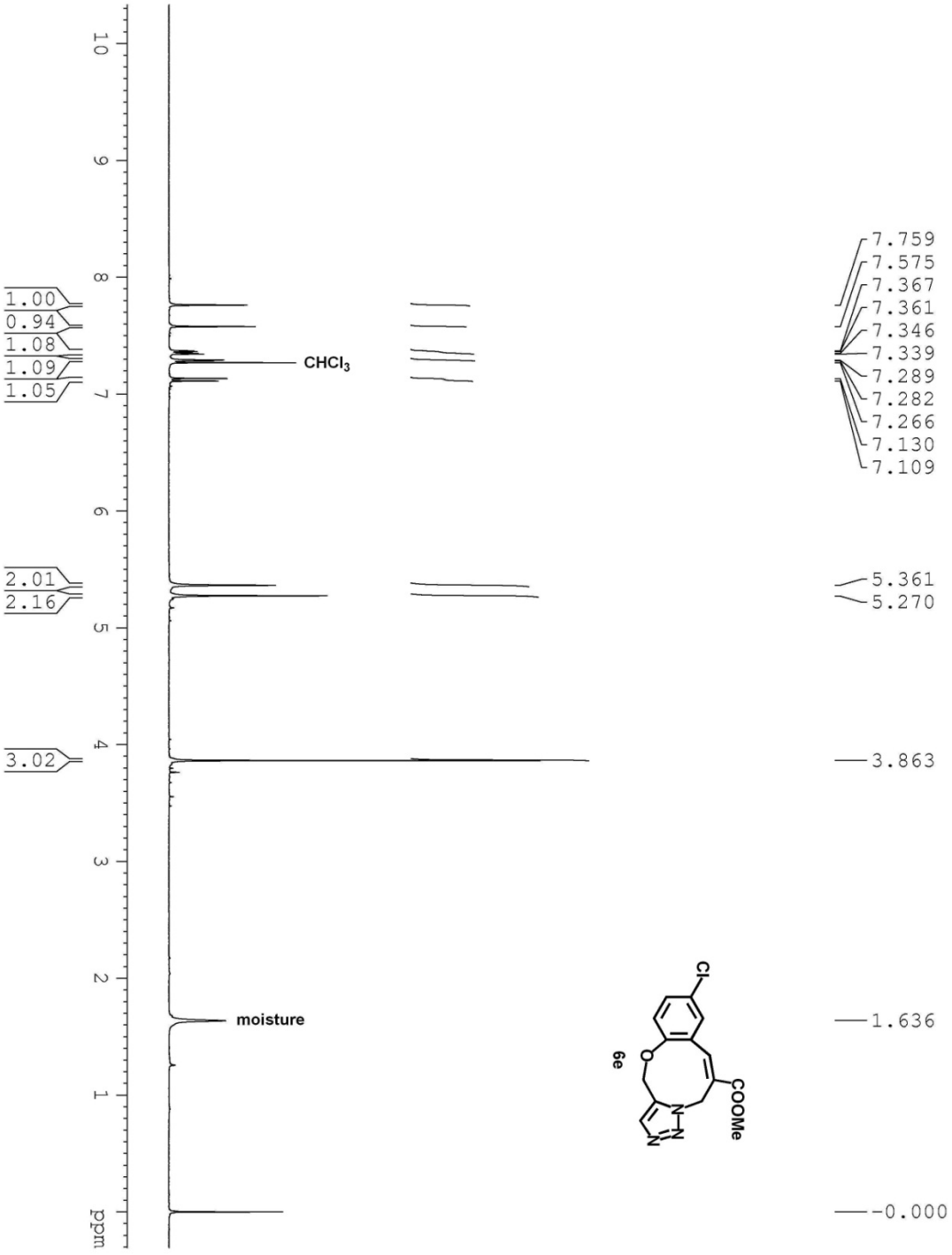
ppm
Br
O
N
N
COOMe
6d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7.289
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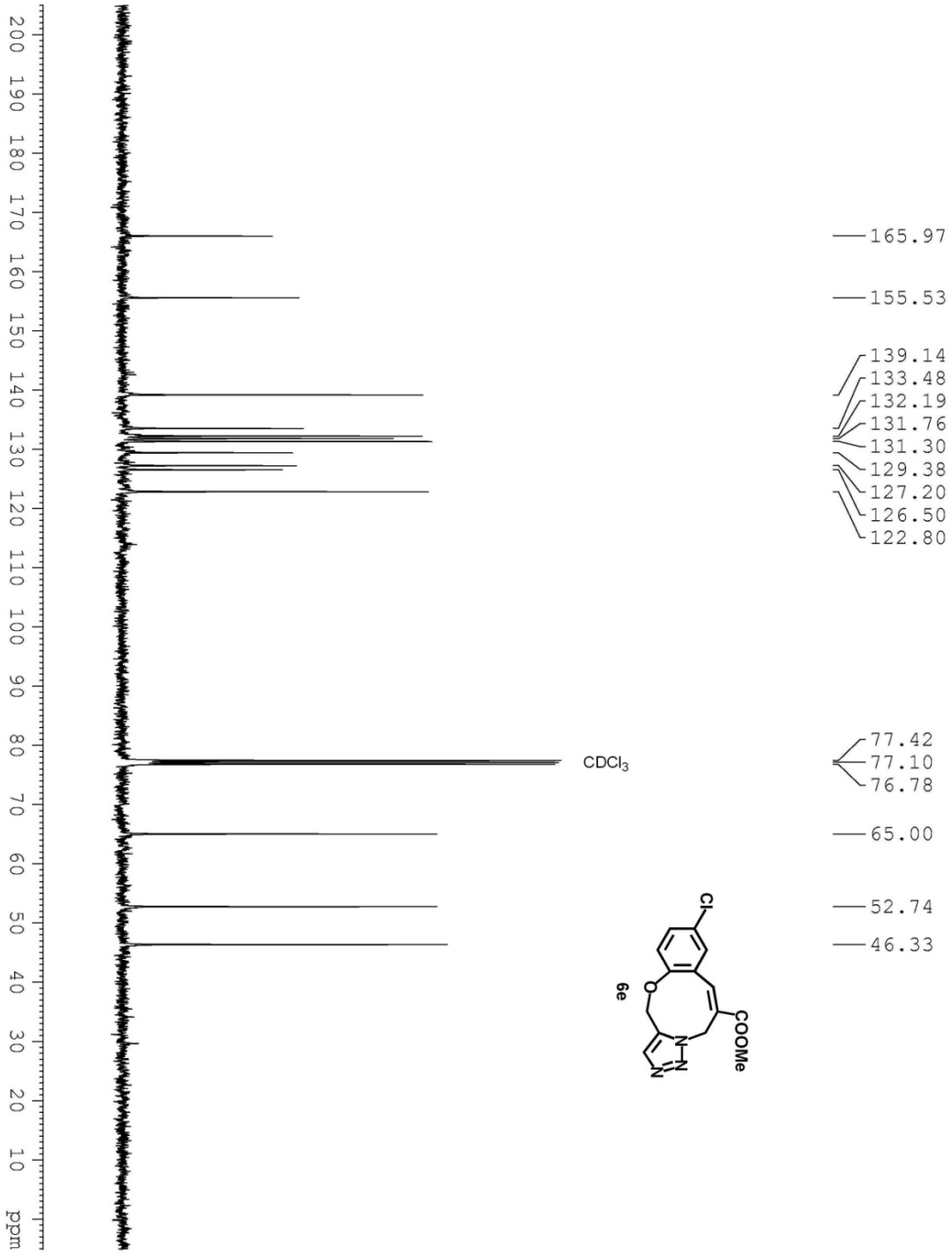
-0.000
ppm
Cl
6e
COOMe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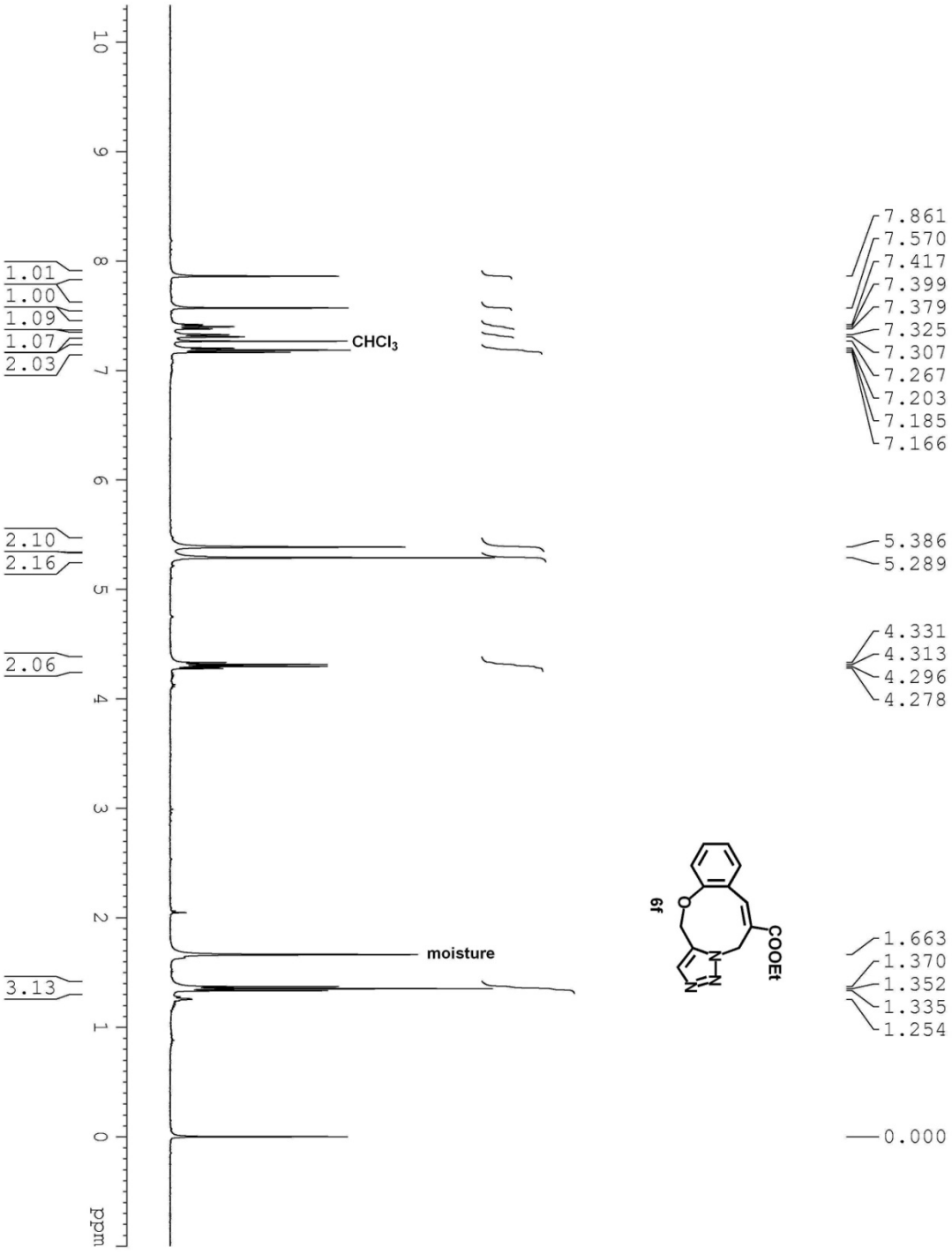
77.10
76.78
65.00
52.74
46.33
CDCl3
Cl
O
N
N
COOMe
6e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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4.313
4.296
4.278
1.663
1.370
1.352
1.335
1.254
0.000
1.01
1.00
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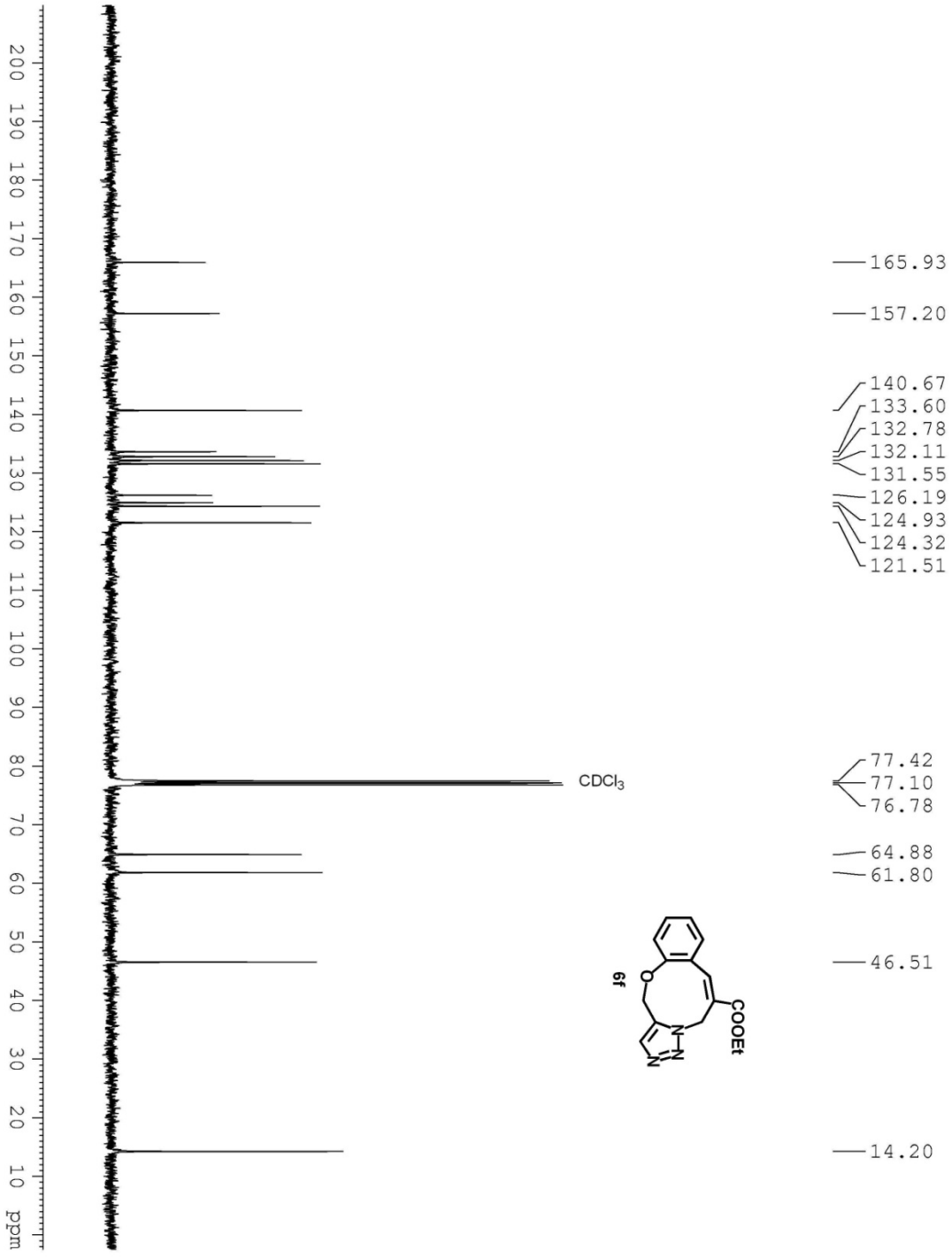
CHCl3
moisture
6f
COOEt
ppm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6f
COOEt
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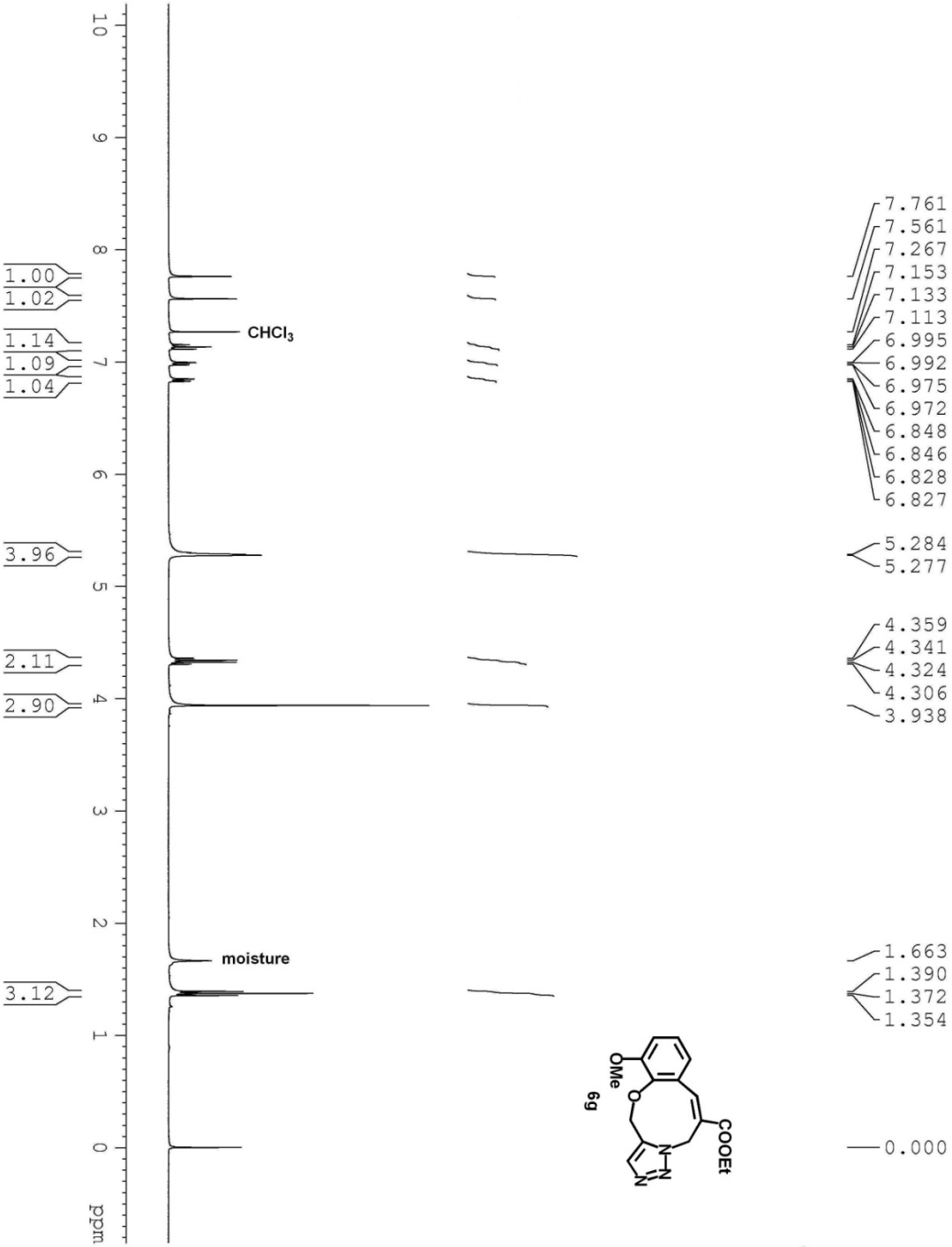
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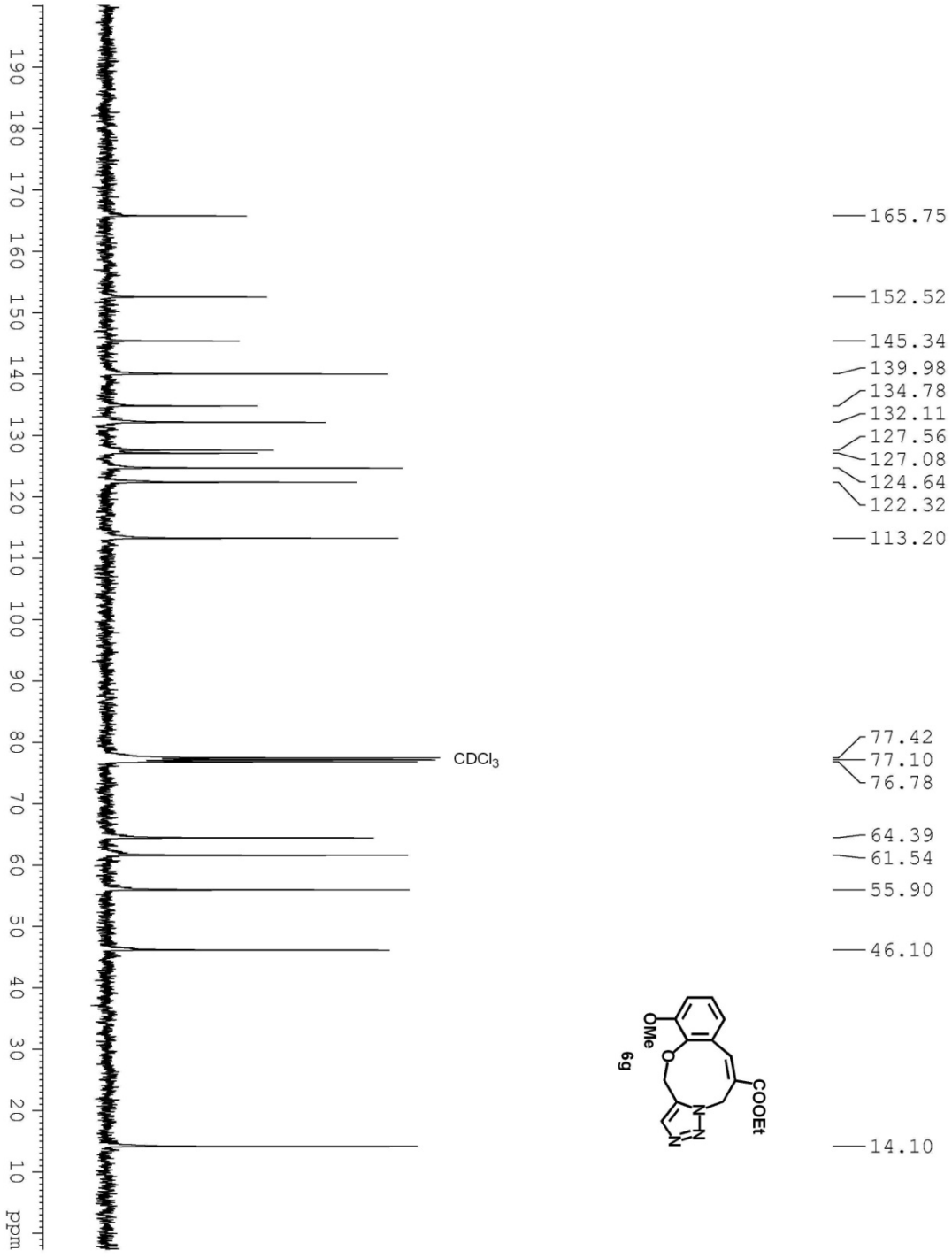
CHCl3
moisture
ppm
OMe
6g
COOEt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76.78
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OMe
COOEt
6g
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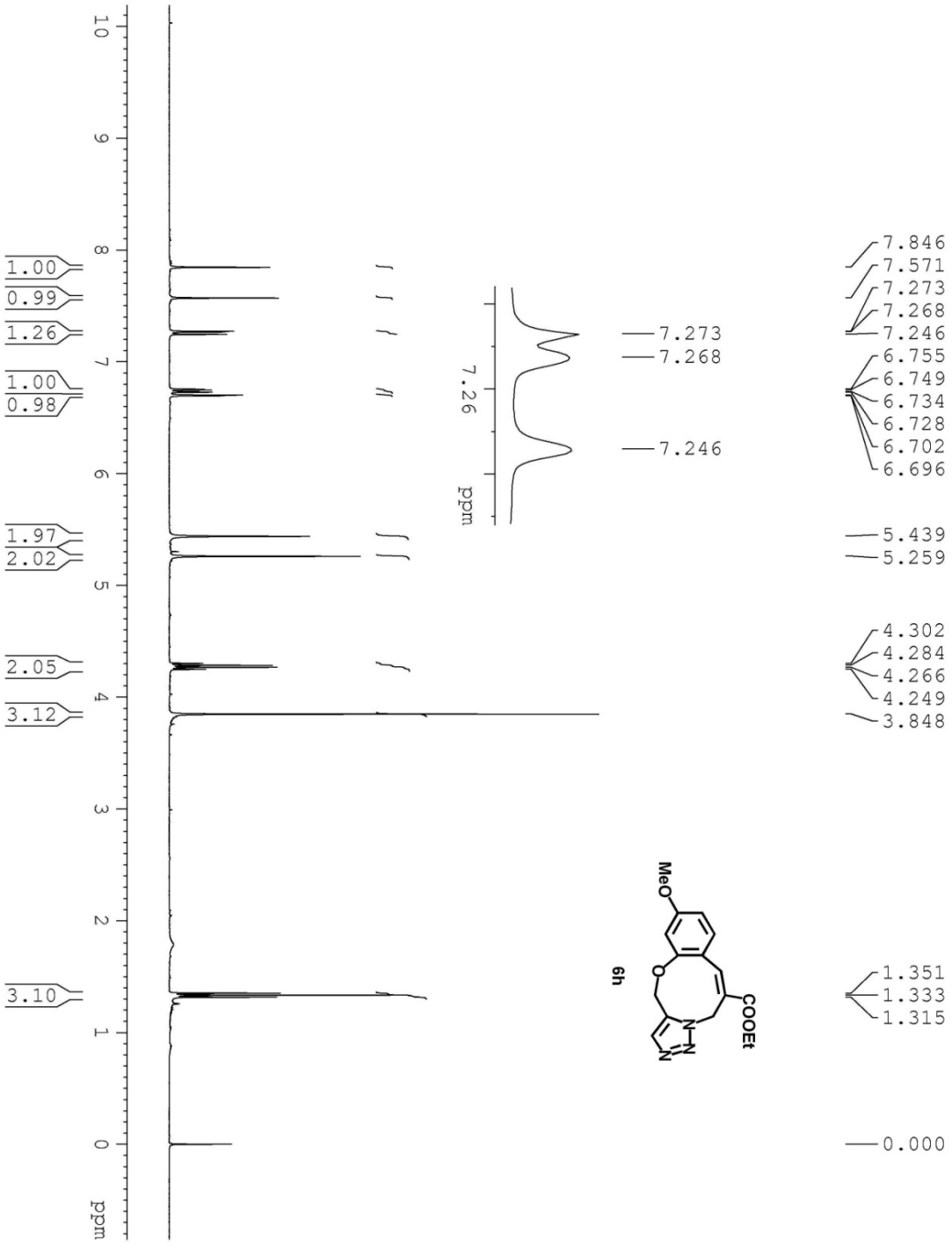
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1.333
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7.273
7.268
7.246
7.26
ppm
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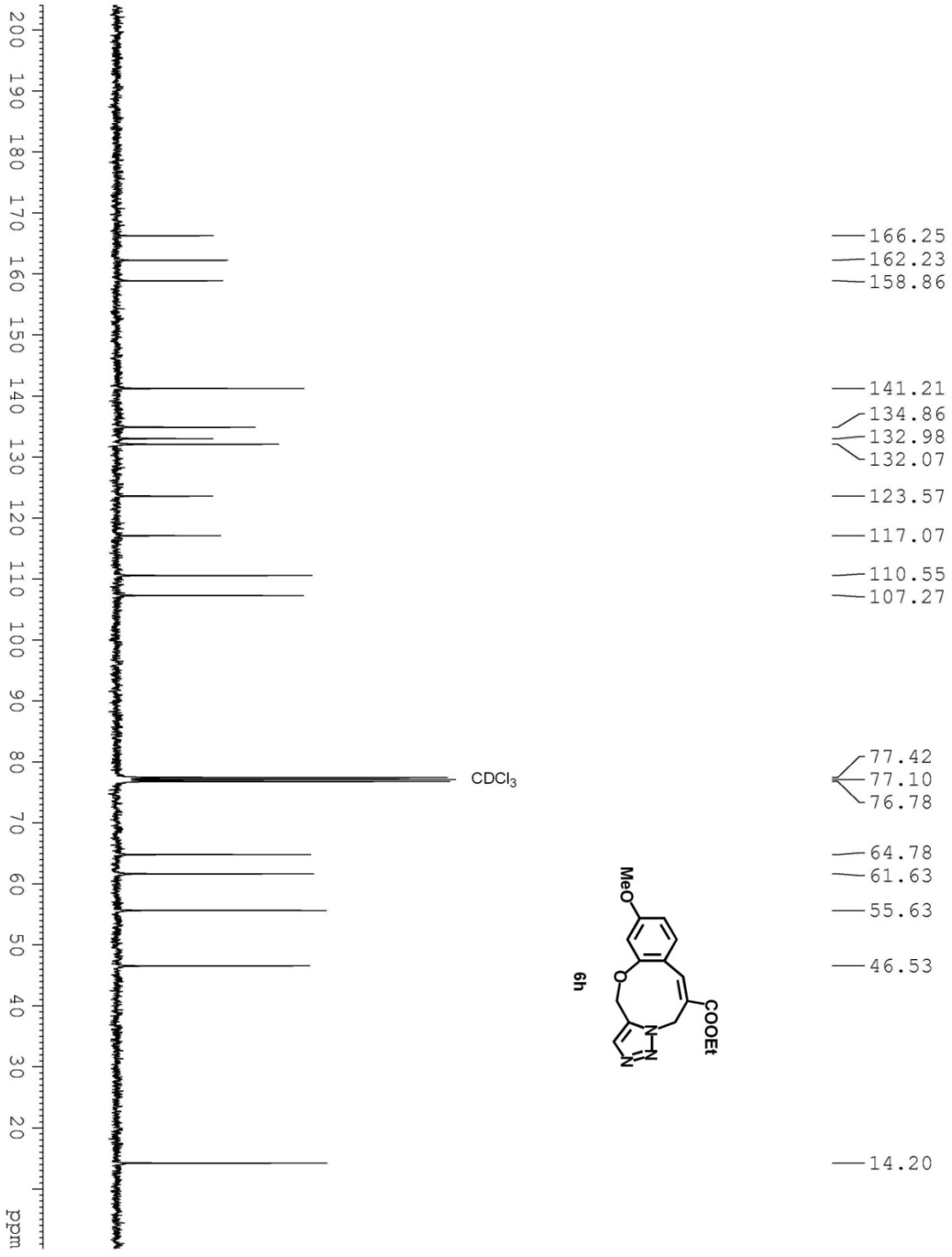
3.12
3.10
MeO
COOEt
6h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76.78
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COOEt
6h
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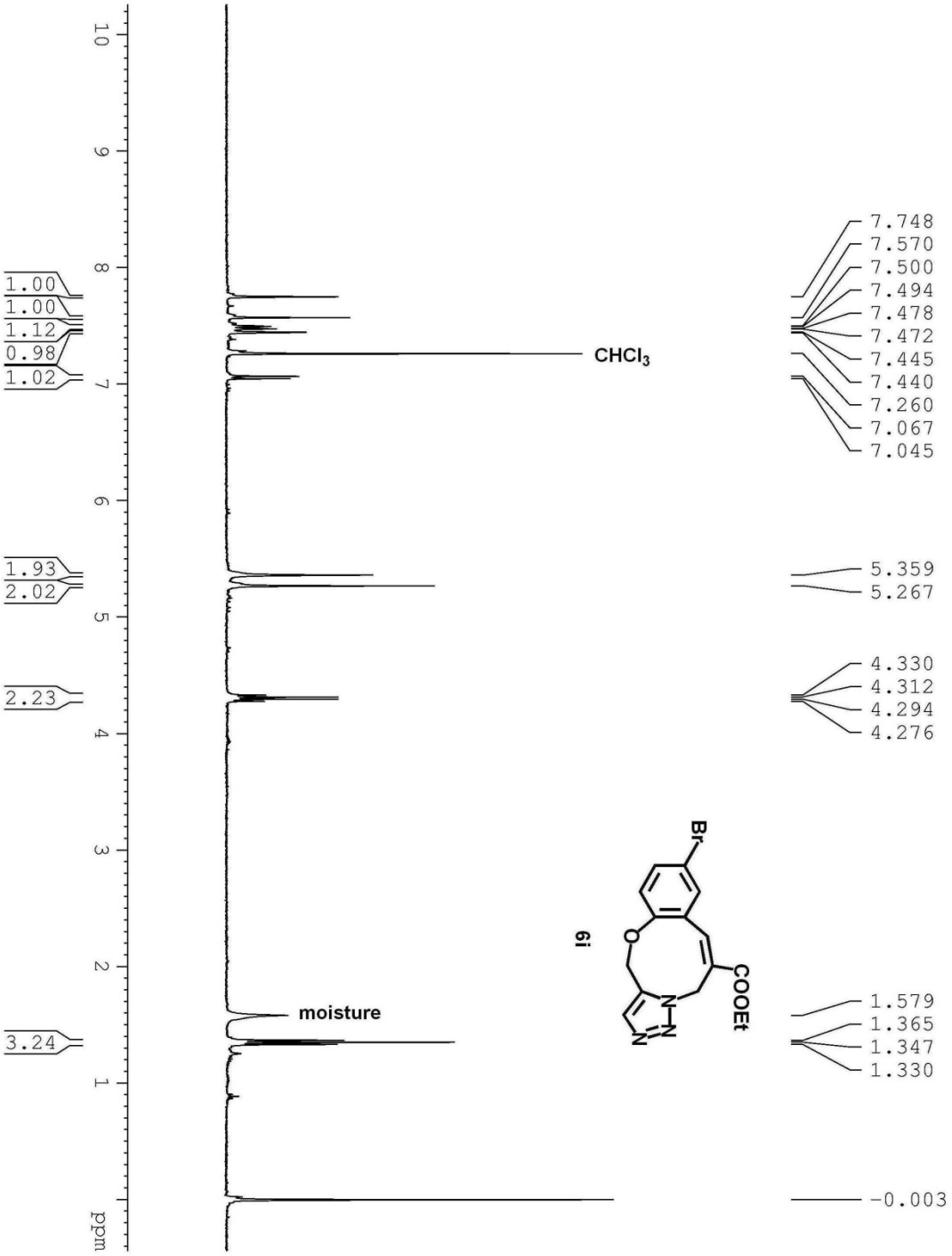
ppm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4.294
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1.365
1.347
1.330
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1.00
1.00
1.12
0.98
1.02
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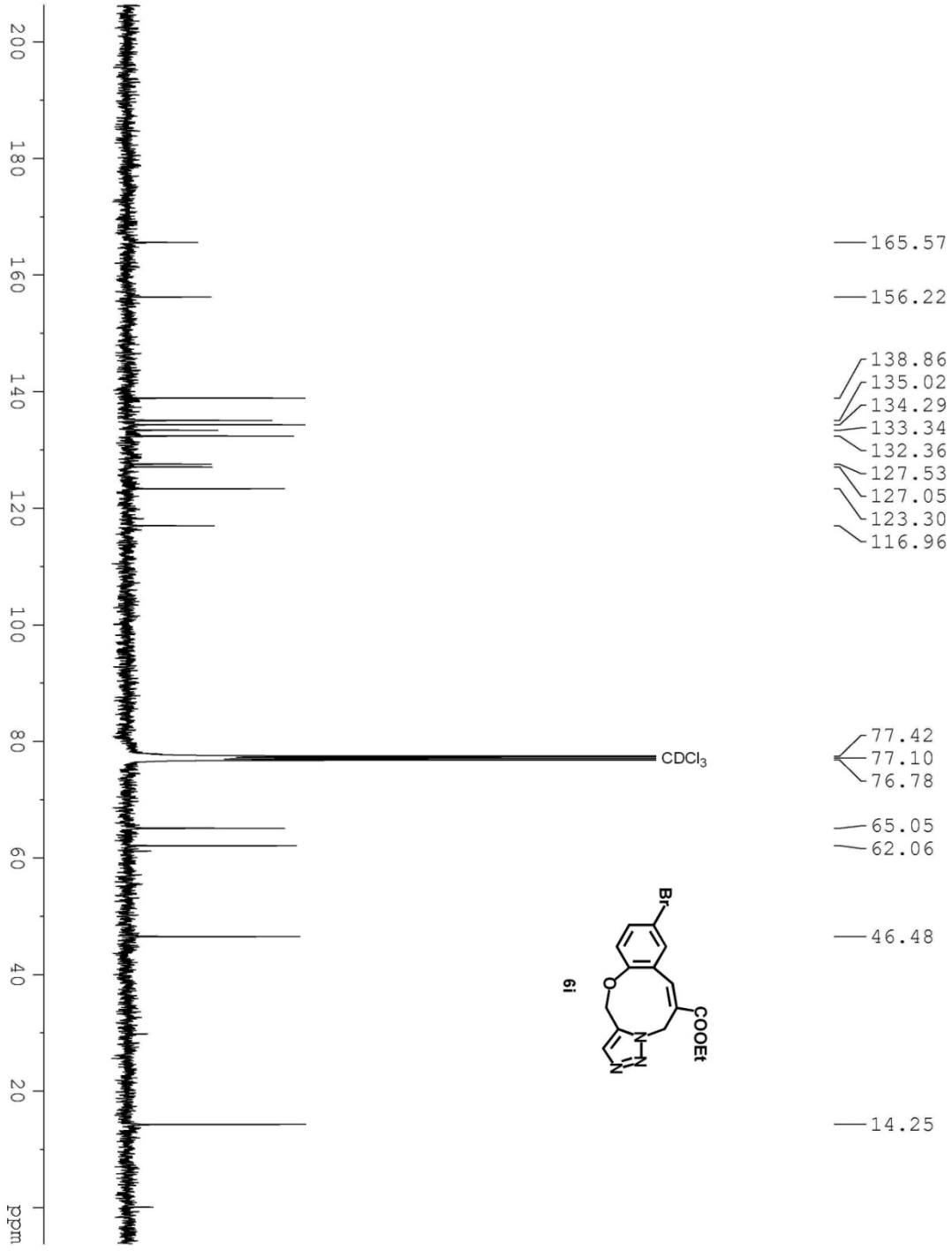
3.24
CHCl3
moisture
ppm
6i
Br
COOEt
O
N
N
N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77.10
76.78
65.05
62.06
46.48
14.25
CDCl3
6i
Br
COOEt
200
180
160
140
120
100
80
60
40
20
ppm

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 6a

```
Bond precision:  C-C = 0.0018 A          Wavelength=0.71073

Cell:           a=19.4754(15)    b=10.3699(8)       c=15.3638(12)
                alpha=90         beta=125.193(1)    gamma=90
Temperature:    25 K
```

	Calculated	Reported
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Space group	C 2/c	C2/c
Hall group	-C 2yc	?
Moiety formula	C14 H13 N3 O3	C14 H13 N3 O3
Sum formula	C14 H13 N3 O3	C14 H13 N3 O3
Mr	271.27	271.27
Dx,g cm-3	1.421	1.421
Z	8	8
Mu (mm-1)	0.103	0.103
F000	1136.0	1136.0
F000’	1136.53	
h,k,lmax	23,12,18	23,12,18
Nref	2475	2475
Tmin,Tmax	0.948,0.960	0.948,0.960
Tmin’	0.948	

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Correction method= EMPIRICAL

Data completeness= 1.000          Theta(max)= 25.920

R(reflections)= 0.0384( 2339)     wR2(reflections)= 0.0958( 2475)

S = 1.051                  Npar= 182
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The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

PLAT005_ALERT_5_G No _iucr_refine_instructions_details in the CIF ? Do !

---

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
0 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
1 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
0 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
0 ALERT type 4 Improvement, methodology, query or suggestion
1 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 01/06/2013; check.def file version of 24/05/2013

Datablock 6a - ellipsoid plot