Green Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: X. Cao and Y. Zhang, *Green Chem.*, 2016, DOI: 10.1039/C6GC00163G.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/greenchem

ROYAL SOCIETY OF CHEMISTRY View Article Online
DOI: 10.1039/C6GC00163G

Journal Name

ARTICLE

Palladium Catalyzed Direct Benzylation/Allylation of Malonates with Alcohols -- *in-situ* C-O Bond Activation

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

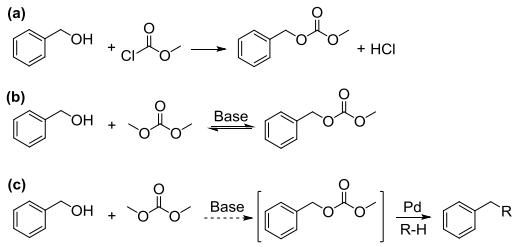
www.rsc.org/

Xueqin Cao[a] and Yugen Zhang[a,*]

High step- and atomic-economy are the endless pursuit in organic and pharmaceutical synthesis. Herein, a new method for directly coupling of benzyl/allyl alcohols with malonates via palladium catalyzed Tsuji-Trost type reaction was developed. The reaction was carried in organic carbonate solvent which would activate alcohols *in situ*, replacing the traditional pre-synthesized carbonates. The new process demonstrated high efficiency, high selectivity and high generality. A wide variety of mono-substituted and bis-substituted malonates were selectively produced under different conditions, and it represents a more step- and atom-economic and environmentally benign synthetic protocol.

The use of naturally abundant and environmentally benign hydroxyl group in organic synthesis has drawn much attention as it represents a more green and step- and atomic-economic synthesis.[1-3] Palladium-catalyzed Tsuji-Trost type benzylation and allylation reactions are efficient and widely used synthetic approaches in organic synthesis, especially for C-C bond formations.[4,5] Typically, in this type of reaction, a benzyl/allyl halide/acetate/carbonate/phosphonate is used as activated alcohol with proper leaving group to react with nucleophile in chemo- and stereoselective way.[6] These activated alcohol reagents require an additional synthetic step as compared to the use of alcohols directly and yet generate stoichiometric amounts of waste during the coupling reaction. In this context, the development of new method to directly apply alcohols as electrophiles for benzylation/allylation of nucleophiles under mild and environmental benign conditions would be highly desirable.[7] Herein, it is demonstrated that benzyl/allyl alcohols can act as effective electrophiles in palladium-catalyzed C-C bond formation reactions in which the C-O bonds are *in-situ* activated by organic carbonate. The direct transformation of alcohol represents a more step- and atom-economic and environmentally benign protocol.

Dimethyl carbonate is stable and represents a low-cost, low toxicity and easy availability solvent.[8] Organic carbonates are also considered as green solvents as they are completely biodegradable and can be synthesized from carbon dioxide.[9] Carbonate protected/activated benzyl/allyl alcohols were typically synthesized by the reaction of alcohols and chloroformate (scheme 1(a)). While, it is also known that there is an equilibrium between alcohol and carbonate under basic condition, scheme 1(b).[10] The formation of benzyl carbonate will activate the benzylic C-O bond and make benzyl alcohol an active electrophile.[11] With that, it is proposed to directly apply alcohols as electrophiles for the C-C coupling reactions in carbonate solvents. The equilibrium in scheme 1 would be pushed to right side as carbonate intermediate is converted to the coupling product (scheme 1(c)).



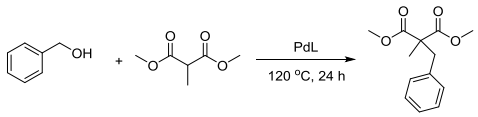
Scheme 1. (a) Typical synthetic method for alcohol protection and activation with carbonate; (b) Equilibrium between alkyl alcohol and carbonate; (c) Hypothesis for directly applying alcohol as electrophile for C-C coupling reaction.

The alkylation of active methylene compounds is a fundamental reaction in organic synthesis, and has usually been carried out under basic condition.[12] The above hypothesis is firstly tested in the reaction of palladium-catalyzed benzylation/allylation of malonates. Typically, benzylation of 2-substituted malonates was carried by using benzyl carbonates and base with palladium/phosphine catalyst under heating condition.[13] Herein, benzyl alcohol was used instead of benzyl carbonate in the reaction. Control reaction for benzyl alcohol and dimethyl methylmalonate (DMMM) with Pd-dppp (diphenylpropylphosphine) catalyst and NaO^{t}Bu in N,N'-dimethylformaldehyde (DMF) did not give any product and starting materials were fully recovered (Table 1, entry 14). When Cs_2CO_3 was used as base, a lousy result was obtained with low selectivity toward benzylated manolate (29%) (Table 1, entry 15). This result indicates that inorganic carbonate could also have equilibrium with benzyl alcohol to form benzyl methyl carbonate. However, this equilibrium is not useful for synthetic application. Subsequently, the reaction mediate was changed to

[a] Dr. X. Cao, Dr. Y.G. Zhang.
Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, The Nanos, Singapore 138669, Singapore. E-mail: ygzhang@ibn.a-star.edu.sg
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

dimethylcarbonate (DMC). In this case, almost quantitative amount of benzylated DMMM was obtained when 2 mol% of $Pd(OAc)_2$, 4.8 mol% of dppp and 2 equiv. of base were applied (Table 1, entry 6). A control reaction with methyl-benzylcarbonate as starting material (Kuwano's method[13]) was also carried and 75% yield of benzylated DMMM was obtained. It indicates that the *in-situ* generated benzylcarbonate intermediate could be more active in the reaction with DMMM. Further condition optimization showed that bi-dentate phosphine ligands gave better results than other ligands (Table 1, entries 1-6). NaO^tBu and Cs_2CO_3 gave better results among those bases have been tested (Table 1, entries 6-11). The reaction can also be carried in the mixture solvents of DMC and Tol or DMF with the yield of product decreased 17-28% (Table 1, entries 12-13). With the optimized conditions in hand (Table S1), substrate scope was then screened.

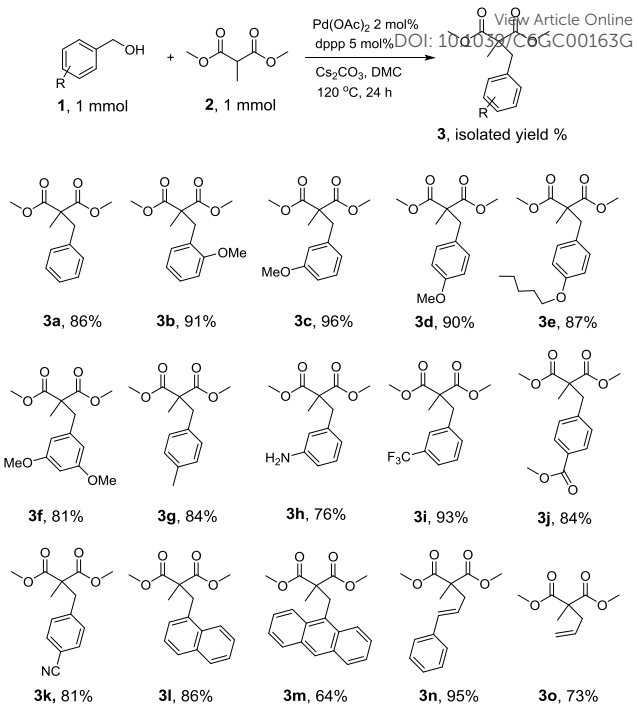
Table 1. Reaction conditions screening for the benzylation of DMMM.[a]



Entry	Ligand, mol%	Base (equiv.)	Sol.	Yield[b] %
1	dba[c]	Cs_2CO_3 (2)	DMC	80
2	Ph_3P[d]	Cs_2CO_3 (2)	DMC	60
3	P_2Ph_5, 4.8	Cs_2CO_3 (2)	DMC	79
4	PPh_2CH_3, 4.8	Cs_2CO_3 (2)	DMC	20
5	dcype, 4.8	Cs_2CO_3 (2)	DMC	83
6	dppp, 4.8	Cs_2CO_3 (2)	DMC	**90**
7	dppp, 4.8	NaO^tBu (2)	DMC	87
8	dppp, 4.8	KOH (2)	DMC	47
9	dppp, 4.8	K_2CO_3 (2)	DMC	57
10	dppp, 4.8	NaOAc (2)	DMC	30
11	dppp, 4.8	Na_3PO_4 (2)	DMC	72
12	dppp, 4.8	Cs_2CO_3 (2)	DMC/Tol	73
13	dppp, 4.8	Cs_2CO_3 (2)	DMC/DMF	62
14	dppp, 4.8	NaO^tBu (2)	DMF	0
15	dppp, 4.8	Cs_2CO_3 (2)	DMF	29

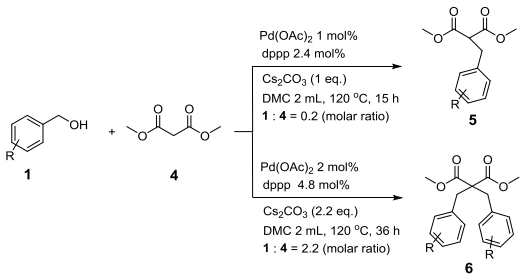
[a] General reaction conditions: Benzyl alcohol (1 mmol), DMMM (1 mmol), $Pd(OAc)_2$ (2 mol%), solvent (2 mL). [b] NMR yield. [c] Tris(dibenzylideneacetone)dipalladium was used as catalyst. [d] $(Ph_3P)_4Pd$ was used as catalyst. dcype = 1,2-bis(dicyclohexylphosphino)ethane.

The scope of the reaction was then investigated with a variety of benzyl alcohols and allyl alcohols (Scheme 2). Benzyl alcohols with electron donating substituents in all 2-, 3-, and 4-position underwent smooth coupling with DMMM to afford substituted malonates (**3b** to **3h**) in good to excellent yields. Electron-deficient benzyl alcohols also underwent smooth coupling reactions to give good to excellent yields (**3i** to **3k**). Bulky substitutions on benzyl alcohols did not affect much of the reaction (**3b**, **3i** and **3m**). Allyl alcohols reacted equivalent good as benzyl alcohols (**3n** and **3o**) in this system.



Scheme 2. Substrate scope of alcohols in palladium catalyzed benzylation/allylation of dimethyl methylmalonate.

Table 2. Palladium catalyzed benzylation/allylation of dimethyl malonate to selectively produce mono-substitued and bis-substituted malonates.

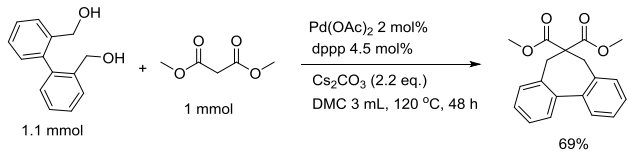


Alcohols	Yield[a] of **5**	Yield[a] of **6**
1a	85	83
1b	93	77[b]
1c	92	61
1d	94	68
1e	69	76[b]
1f	71	73
1g	68	78
1h	<5	0
1i	72	62
1j	60	51[b]
1k	60	60[b]
1l	65	85[b]
1m	62	0
1n	94	90
1o	53[c]	67

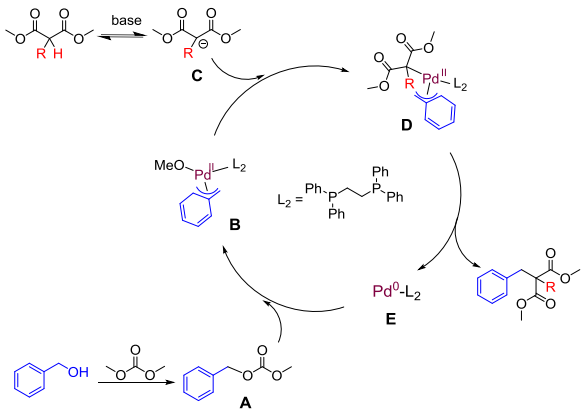
[a] Isolated yields. [b] 48 h. [c] **1**:**4** = 0.67.

With Pd-dppp catalyst, various bases and solvents were further evaluated for the reaction of benzyl alcohol and dimethyl malonate to achieve high chemo-selectivity of mono- or bis-substituted benzyl/allyl malonates (Table S2 and S3). High yield of desired bis-substituted product **6** was obtained with the combination of Cs_2CO_3 and DMC. In contrast, reaction conditions need to be carefully adjusted in order to achieving satisfied yields of mono-substituted products **5** (Table S3). As shown in Table 2, the same alcohol scope was screened for coupling reaction with dimethyl malonate. Both mono-substituted products **5** and bis-substituted products **6** were produced in satisfied yields for most of alcohols under separated reaction conditions. The only exception is alcohol **1h** with amine functionality, very low or no yield was obtained from two reaction systems. There is also no bis-substituted product for alcohol **1m**, due to its huge steric hindrance.

An interesting bis-alcohol substrate (2,2′-Biphenyl-dimethanol) was tested in the reaction conditions for product **6**. As expected, a seven-member ring bis-substituted malonate was synthesized (scheme 3). It may be a useful method for the synthesis other cyclic products. In addition, acetacetic ester also works well in current system (Table S4).



Scheme 3. The synthesis of a seven-member ring bis-substituted malonate.



Scheme 4. Proposed reaction mechanism of palladium catalyzed coupling between alcohols and malonates.

In terms of reaction cycle, three key components were proposed. First of all, benzyl alcohol reacts with dimethyl carbonate under basic condition to form benzyl methyl carbonate **A**. **A** was experimentally observed as a major intermediate during the reaction process. Then, palladium catalyst will undergo oxidative cleavage of C-O bond to form intermediate **B**. Meanwhile, malonate is activated by base to form intermediate **C** which attach to Pd center forming **D**. Following with that, substituted malonate is released via reductive elimination and concurrently, palladium catalyst is regenerated to close the cycle. For allyl alcohol substrates, no allyl methyl carbonate intermediate was observed during the reaction. It may due to the higher activity of allyl alcohol substrates. In fact, control reaction for allyl alcohol and dimethyl methylmalonate (DMMM) with Pd-dppp (diphenylpropylphosphine) catalyst and NaO^{t}Bu in toluene did give significant amount of allyl malonate product.

Conclusions

A new method for directly coupling of benzyl/allyl alcohols with malonates via palladium catalyzed Tsuji-Trost type reaction was developed. The reaction was carried in organic carbonate solvent which would activate alcohols *in situ*. The new process demonstrated high efficiency, high selectivity and high generality. This finding may provide a general method for direct using alcohol in coupling reactions which represents a more step- and atom-economic and environmentally benign synthetic protocol.

Acknowledgements

This work was supported by the Institute of Bioengineering and Nanotechnology (Biomedical Research Council, Agency for Science, Technology and Research (A*STAR), Singapore).

Notes and references

[1] (a) Comprehensive Organic Transformations: A Guide to Functional Group Preparations, 2nd ed.; R. C. Larock, Ed.; Wiley: New York, 1999; (b) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* 2010, **110**, 681; (c) G. Guillena, D. J. Ramón, M. Yus, *Chem. Rev.* 2010, **110**, 1611; (d) A. Watson, J. M. J. Williams, *Science* 2010, **329**, 635; (e) C. Gunanathan, D. Milstein, *Acc. Chem. Res*. 2011, **44**, 588.

[2] (a) O. Debleds, E. Gayon, E. Vrancken, J.-M. Campagne, *Beilstein J. Org. Chem.* 2011, **7**, 866; (b) D.-G. Yu, X. Wang, R.-Y. Zhu, S. Luo, X.-B. Zhang, B.-Q. Wang, L. Wang and Z.-J. Shi, *J. Am. Chem. Soc.*, 2012, **134**, 14638; (c) Z.-C. Cao, D.-G. Yu, R.-Y. Zhu, J.-B. Wei, Z.-J. Shi, *Chem. Commun.*, 2015, **51**, 2683; (d) Q**.** Kang, Y. Zhang, *Green Chem*., 2012, **14,** 1016-1019 .

[3] (a) C. Chuit, H. Felkin, C. Frajerman, G. Roussi and G. Swierczewski, *Chem. Commun.*, 1968, 1604; (b)D. E. Bergbreiter and D. A. Weatherford, *J. Chem. Soc., Chem. Commun.*, 1989, 883; (c) M. Kimura, Y. Horino, R. Mukai, S. Tanaka and Y. Tamaru, *J. Am. Chem. Soc.*, 2001, **123**, 10401; (d) Y. Kayaki, T. Koda and T. Ikariya, *Eur. J. Org. Chem.*, 2004, 4989; (e) B. M. Trost and J. Quancard, *J. Am. Chem. Soc.*, 2006, **128**, 6314; (f) Y.-X. Li, Q.-Q. Xuan, L. Liu, D. Wang, Y.-J. Chen and C.-J. Li, *J. Am. Chem. Soc.*, 2013, **135**, 12536; (g) J. Ye, J. Zhao, J. Xu, Y. Mao and Y. J. Zhang, *Chem. Commun.*,

2013, **49**, 9761; (h) H.-B.Wu, X.-T. Ma and S.-K. Tian, *Chem. Commun.*, 2014, **50**, 219; (i) S. Shirakawa, S. Kobayashi, *Org. Lett.*, 2007, **9**, 311; (j) L. Guo, Y. Liu, W. Yao, X. Leng, Z. Huang, *Org. Lett.*, 2013, **15**, 1144.

1 [4] (a) J. Tsuji, H. Takahashi, A. Morikawa, *Tetrahedron Lett.*, 1965, **6**, 4387; (b) B. M. Trost, T. J. Fullerton, *J. Am. Chem. Soc.*, 1973, **95**, 292; (c) B. M. Trost, L. C. Czabaniuk, *Angew. Chem., Int. Ed.* 2014, **53**, 2826–2851 (d) H. Hikawa, K. Izumi, Y. Ino, S. Kikkawa, Y. Yokoyama, I. Azumaya, *Adv. Synth. Catal.,* 2015, **357**, 1037–1048.

[5] (a) B. M. Trost and L. C. Czabaniuk, *J. Am. Chem. Soc.*, 2012, **134**, 5778; (b) Y. Zhu and V. H. Rawal, *J. Am. Chem. Soc.*, 2012, **134**, 111; (c) T. Mukai, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2010, **12**, 1360; (d) M. F. Grünberg and L. J. Gooßen, *Chem. – Eur. J.*, 2013, **19**, 7334; (e) B. M. Trost and L. C. Czabaniuk, *J. Am. Chem. Soc.*, 2010, **132**, 15534.

[6] (a) J.-Y. Legros and J.-C. Fiaud, *Tetrahedron Lett.*, 1992, **33**, 2509; (b) A. Correa, T. León and R. Martin, *J. Am. Chem. Soc.*, 2014, **136**, 1062; (c) H. M. Wisniewska, E. C. Swift and E. R. Jarvo, *J. Am. Chem. Soc.*, 2013, **135**, 9083; (d) Q. Zhou, H. D. Srinivas, S. Dasgupta and M. P. Watson, *J. Am. Chem. Soc.*, 2013, **135**, 3307; (e) B. L. H. Taylor, E. C. Swift, J. D. Waetzig and E. R. Jarvo, *J. Am. Chem. Soc.*, 2011, **133**, 389; (f) M. R. Harris, M. O. Konev and E. R. Jarvo, *J. Am. Chem. Soc.*, 2014, **136**, 7825; (g) I. M. Yonova, A. G. Johnson, C. A. Osborne, C. E. Moore, N. S. Morrissette and E. R. Jarvo, *Angew. Chem. Int. Ed.*, 2014, **53**, 2422; (h) G. A. Molander and M. D. Elia, *J. Org. Chem.*, 2006, **71**, 9198; (i) L. Ackermann, S. Barfüsser and J. Pospech, *Org. Lett.*, 2010, **12**, 724; (j) T. Mukai, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2010, **12**, 1360; (k) M. R. Harris, L. E. Hanna, M. A. Greene, C. E. Moore and E. R. Jarvo, *J. Am. Chem. Soc.*, 2013, **135**, 3303; (l) Y. Zhu, V. H. Rawal, *J. Am. Chem. Soc.*, 2012, **134**, 111.

[7] (a) T. Maji, K. Ramakumar, J. A. Tunge, *Chem. Commun.*, 2014, **50**, 14045; (b) Y. Gumrukcu, B. de Bruin, J. N. H. Reek, *ChemSusChem*, 2014, **7**, 890; (c) D. Banerjee, R. V. Jagadeesh, K. Junge, H. Junge, and M. Beller, *Angew. Chem. Int. Ed.*, 2012, **51**, 11556.

[8] (a) B. Schäffner, F. Schäffner, S. P. Verevkin, A. Börner, *Chem. Rev.*, 2010, **110**, 4554; (b) P. Tundo, M. Selva, *Acc. Chem. Res.*, 2002, **35**, 706; (c) A. Aouissi, Z. A. Al-Othman, A. Al-Amro, *Int. J. Mol. Sci.* 2010, **11**, 1343-1351.

[9] (a) T. Sakakura and K. Kohno, *Chem. Commun.*, 2009, 1312; (b) M. Honda, M. Tamura, Y. Nakagawa and K. Tomishige, *Catal. Sci. Technol.*, 2014, **4**, 2830; (c) B. Valdurthy, F. Figueras, *Chem. Comm.*, 2004, 734; (d) D. Y. Yu, S. P. Teong and Y. G. Zhang, *Coord. Chem. Rev.,* 2014, **293-294**, 279; (*e*) S. N. Riduan and Y. G. Zhang, *Dalton Trans*. 2010, **39**, 3347; (f) Y. G. Zhang, J. Y. G. Chan, *Energy Environ. Sci.*, 2010, **3**, 408.

[10](a) N. Streidl, R. Branzan, and H. Mayr, *Eur. J. Org. Chem.*, 2010, 4205; (b) M. R. Reithofer, Y. N. Sum, Y. Zhang, Green Chem., 2013, 15, 2086-2090 .

[11] (a) J. D. Weaver, A. Recio III, A. J. Grenning, and J. A. Tunge, *Chem. Rev.*, 2011, **111**, 1846; (b) J. P. Parrish, R. N. Salvatorea and K. W. Junga, *Tetrahedron*, 2000, **56**, 8207; (c) C.-X. Zhuo, C. Zheng, and S.-L. You, *Acc. Chem. Res.*, 2014, **47**, 2558.

[12] (a) R. Kumar and E. V. Van der Eycken, *Chem. Soc. Rev.*, 2013, **42**, 1121; (b) J. Cornella, C. Zarate and R. Martin, *Chem. Soc. Rev.*, 2014, **43**, 8081.

[13] (a) R. Kuwano, Y. Kondo and Y. Matsuyama, *J. Am. Chem. Soc.*, 2003, **125**, 12104. (b) R. Kuwano and Y. Kondo, *Org. Lett.*, 2004, **6**, 3545.

[14] (a) R. Kuwano and M. Yokogi, *Org. Lett.*, 2005, **7**, 945; (b) R. Kuwano and M. Yokogi, *Chem. Commun.*, 2005, 5899; (c) M. Yokogi, R. Kuwano, *Tetrahedron Lett.*, 2007, **48**, 6109; (d) Y. Masuyama, Y. Nakajima, J. Okabe, *Appl. Catal. A: Gen.*, 2010, **387**, 107.

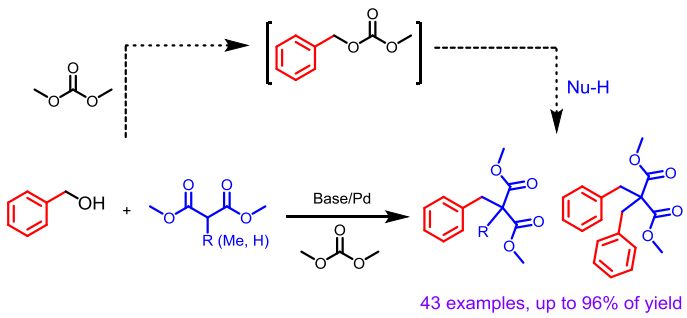
View Article Online
DOI: 10.1039/C6GC00637G

Journal Name ARTICLE

View Article Online
DOI: 10.1039/C6GC00163G

TOC:

A method for directly coupling of benzyl/allyl alcohols with malonates via palladium catalyzed Tsuji-Trost type reaction.



View Article Online
DOI: 10.1039/C6GC00163G

Supporting Information

Palladium Catalyzed Direct Benzylation/Allylation of Malonates with Benzyl-/Allyl-Alcohols – *In Situ* C-O Bond Activation

Xueqin Cao, Yugen Zhang*

Institute of Bioengineering and Nanotechnology
31 Biopolis Way, The Nanos
Singapore 138669
E-mail: ygzhang@ibn.a-star.edu.sg

Table of Contents

View Article Online
DOI: 10.1039/C6GC00163G

1. General Information

All anhydrous solvents were purchased from Sigma-Aldrich and used without further purification. All other reagents were used as received. All reactions were carried out under an argon or nitrogen atmosphere.

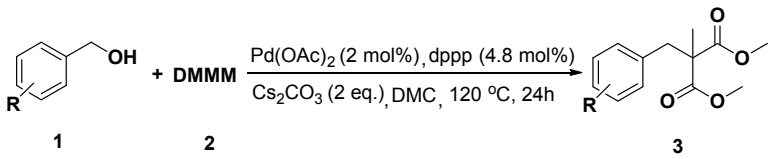
Analytical thin layer chromatography (TLC) was performed using Merck 60 F-254 silica gel plates with visualization by ultraviolet light (254 nm) and/or I_2. Flash column chromatography was carried out on Kieselgel 60 (0.040-0.063 mm) supplied by Merck under positive pressure.

^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on Bruker AV-400 (400 MHz) spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) with the residual solvent peak of tetramethylsilane used as the internal standard at 0.00 ppm. ^{1}H NMR data are reported in the following order: chemical shift, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet), coupling constants (*J*, Hz), integration and assignment. High resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF-QII spectrometer.

Compounds **3a**,[1] **3f**,[2] and **5f** [3] were identified by comparison with their ^{1}H and ^{13}C NMR spectra reported in the literature.

2. Procedure of the benzylation/allylation of DMMM

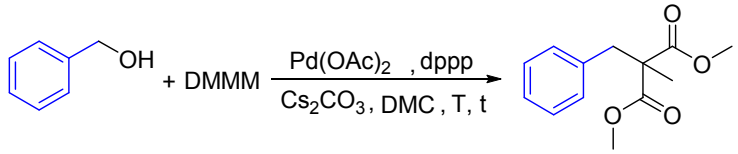
General procedure:



1 2 3

Under nitrogen atmosphere, benzyl alcohol (1.0 mmol), DMMM (1.0 mmol), $Pd(OAc)_2$ (4.5 mg, 20 μmol), dppp (20 mg, 48 μmol), Cs_2CO_3 (652 mg, 2.0 equiv) and dimethylcarbonate (DMC) (2 mL) were combined in a 20 mL headspace vial fitted with a suba seal cap. The mixture was stirred at 120 °C for 24 h, then cooled to room temperature. The mixture was filtered and washed by ethyl acetate. The obtained filtration was evaporated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane) to give the desired product.

Table S1. Reaction conditions screening for the benzylation of DMMM.



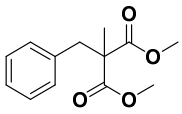
Entry	$Pd(OAc)_2$ mol%	dppp (eq.) mol%	Cs_2CO_3 eq.	DMC mL	Co-solvent mL	T (°C)	t (h)	Yield(%)[a]
1	2	4.8	1	2	-	120	24	79

View Article Online
DOI: 10.1039/C6GC00163G

2	2	4.8	1.5	2	-	120	24	85
3	2	4.8	2	2	-	120	24	90
4	2	4.8	2	2	-	120	16	76
5	2	4.8	2	2	-	120	20	83
6	2	4.8	2	2	-	100	24	29
7	2	4	2	2	-	120	24	85
8	2	2.5	2	2	-	120	24	81
9	1	2	2	2	-	120	24	80
10	2	4.8	2	0.34	Toluene (1)	120	24	< 5
11	2	4.8	2	0.34	DMF (1)	120	24	< 5

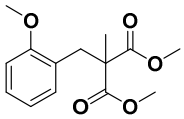
Reaction conditions: Benzyl alcohol (1.0 mmol), DMMM (1.0 mmol). [a] Yield by NMR.

Dimethyl 2-benzyl-2-methylmalonate (3a)



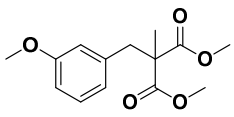
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless solid (203 mg, 86%). Spectroscopic data were in agreement with the published data. [1] **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.30-7.23 (m, 3H, ArH), 7.10-7.07 (m, 2H, ArH), 3.67 (s, 6H, 2 x CH_3), 3.12 (s, 2H, CH_2), 1.22 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.8, 135.9, 130.3, 128.4, 127.2, 54.4, 52.8, 40.7, 19.5; **HRMS** (ESI+) calc. for $C_{13}H_{16}O_4$ $[M+Na]^+$ 259.0941; found 259.0942.

Dimethyl 2-(2-methoxybenzyl)-2-methylmalonate (3b)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless solid (242 mg, 91%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.22 (ddd, J = 8.3, 7.4, 1.8 Hz, 1H, ArH), 7.00 (dd, J = 7.4, 1.8 Hz, 1H, ArH), 6.95 (dd, J = 8.3, 0.8 Hz, 1H, ArH), 6.85 (td, J = 7.4, 1.0 Hz, 1H, ArH), 3.72 (s, 3H, CH_3), 3.66 (s, 6H, 2 x CH_3), 3.17 (s, 2H, CH_2), 1.16 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 172.1, 157.8, 131.5, 128.5, 123.9, 120.2, 110.9, 55.2, 53.8, 52.6, 34.1, 19.2; **HRMS** (ESI+) calc. for $C_{14}H_{18}O_5$ $[M+Na]^+$ 289.1046; found 289.1049.

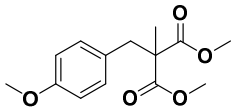
Dimethyl 2-(3-methoxybenzyl)-2-methylmalonate (3c)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (255 mg, 91%). %). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.21-7.17 (m, 1H, ArH), 6.81 (ddd, J = 8.2, 2.6, 0.9Hz, 1H, ArH), 6.67-6.63 (m, 2H, ArH), 3.71 (s, 3H, CH_3), 3.67 (s, 6H, 2 x CH_3), 3.10 (s, 2H, CH_2), 1.23 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.8, 159.5, 137.4, 129.3, 122.5, 115.9, 112.6, 55.3, 54.4, 52.6, 40.6, 19.5; **HRMS** (ESI+) calc. for $C_{14}H_{18}O_5$ $[M+Na]^+$ 289.1046; found 289.1049.

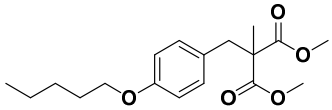
View Article Online
DOI: 10.1039/C6GC00163G

Dimethyl 2-(4-methoxybenzyl)-2-methylmalonate (3d)



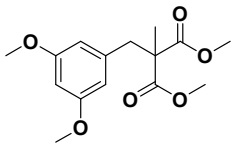
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (239 mg, 90%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.01 (d, J = 8.8Hz, 2H, ArH), 6.83 (d, J = 8.8Hz, 2H, ArH), 3.72 (s, 3H, CH_3), 3.67 (s, 6H, 2 x CH_3), 3.07 (s, 2H, CH_2), 1.22 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.3, 158.4, 131.0, 127.8, 113.5, 55.1, 54.8, 52.4, 40.3, 19.6; **HRMS** (ESI+) calc. for $C_{14}H_{18}O_5$ $[M+Na]^+$ 289.1046; found 289.1051.

Dimethyl 2-methyl-2-(4-(pentyloxy)benzyl)malonate (3e)



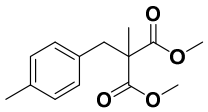
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless liquid (280 mg, 87%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 6.88 (d, J = 8.7Hz, 2H, ArH), 6.81 (d, J = 8.7Hz, 2H, ArH), 3.90 (t, J = 6.5Hz, 2H, CH_2), 3.66 (s, 6H, 2 x CH_3), 3.05 (s, 2H, CH_2), 1.72-1.65 (m, 2H, CH_2), 1.40-1.32 (m, 4H, 2 x CH_2), 1.21 (s, 3H, CH_3), 0.88 (t, J = 7.1Hz, 3H, CH_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.3, 158.0, 130.9, 127.6, 114.0, 67.7, 54.9, 52.4, 40.3, 28.9, 28.1, 22.3, 19.6, 13.9; **HRMS** (ESI+) calc. for $C_{18}H_{26}O_5$ $[M+Na]^+$ 345.1672; found 345.1678.

Dimethyl 2-(3,5-dimethoxybenzyl)-2-methylmalonate (3f)



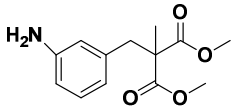
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a white solid (240 mg, 81%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 6.38 (t, J = 2.3 Hz, 1H, ArH), 6.23 (t, J = 2.5 Hz, 2H, ArH), 3.69 (s, 6H, 2 x CH_3), 3.67 (s, 6H, 2 x CH_3), 3.06 (s, 2H, CH_2), 1.24 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.8, 160.4, 138.4, 108.3, 98.8, 55.2, 54.2, 52.7, 40.8, 19.4; **HRMS** (ESI+) calc. for $C_{15}H_{20}O_6$ $[M+Na]^+$ 319.1152; found 319.1160.

Dimethyl 2-methyl-2-(4-methylbenzyl)malonate (3g)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (215 mg, 86%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.08 (d, J = 7.7 Hz, 2H, ArH), 6.97 (d, J = 8.0 Hz, 2H, ArH), 3.67 (s, 6H, 2 x CH_3), 3.08 (s, 2H, CH_2), 2.26 (s, 3H, Ar-CH_3); 1.21 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.7, 136.1, 132.7, 130.0, 128.9, 54.3, 52.6, 40.2, 20.7, 19.3; **HRMS** (ESI+) calc. for $C_{14}H_{18}O_4$ $[M+Na]^+$ 273.1097; found 273.1101.

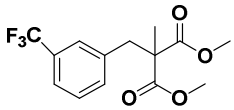
Dimethyl 2-(3-aminobenzyl)-2-methylmalonate (3h)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=2/5) as a light yellow liquid (193 mg, 77%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 6.89 (t, J = 7.7Hz, 1H, ArH), 6.41 (ddd, J = 8.0, 2.2, 0.9Hz, 1H, ArH), 6.26 (t, J = 1.9Hz, 1H, ArH), 6.20 (d, J = 7.5Hz, 1H, ArH), 5.0 (s, 2H, NH_2), 3.67 (s, 6H, 2 x CH_3), 2.96 (s, 2H, CH_2), 1.22 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 172.1, 148.8, 136.3, 128.7, 117.8, 115.7, 112.6, 54.5, 52.6, 41.0, 19.4; **HRMS** (ESI+) calc. for $C_{13}H_{17}NO_4$ $[M+Na]^+$ 274.1050; found 274.1040.

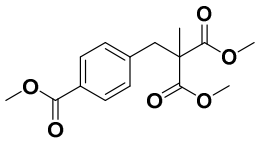
View Article Online
DOI: 10.1039/C6GC00163G

Dimethyl 2-methyl-2-(3-(trifluoromethyl)benzyl)malonate (3i)



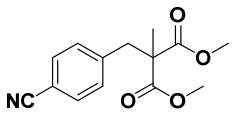
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (283 mg, 93%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.63-7.61 (m, 1H, ArH), 7.53 (td, J = 8.0, 0.6Hz, 1H, ArH), 7.44-7.42 (m, 2H, ArH), 3.67 (s, 6H, 2 x CH_3), 3.25 (s, 2H, CH_2), 1.25 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.5, 137.4, 134.4, 129.3, 129.0 (q, $^2J_{CF}$ = 31Hz), 126.5 (q, $^3J_{CF}$ = 4Hz), 124.3 (q, $^1J_{CF}$ = 272Hz), 123.8 (q, $^3J_{CF}$ = 4Hz), 54.2, 52.6, 40.1, 19.3; **HRMS** (ESI+) calc. for $C_{14}H_{15}F_3O_4$ $[M+Na]^+$ 327.0815; found 327.0818.

Dimethyl 2-(4-(methoxycarbonyl)benzyl)-2-methylmalonate (3j)



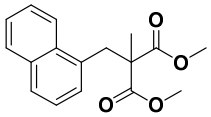
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a white solid (247 mg, 84%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.87 (d, J = 8.4 Hz, 2H, ArH), 7.25 (d, J = 8.4 Hz, 2H, ArH), 3.84 (s, 3H, CH_3), 3.67 (s, 6H, 2 x CH_3), 3.21 (s, 2H, CH_2), 1.24 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.5, 166.2, 141.7, 130.6, 129.2, 128.5, 54.2, 52.7, 52.3, 40.5, 19.4; **HRMS** (ESI+) calc. for $C_{15}H_{18}O_6$ $[M+Na]^+$ 317.0996; found 317.1002.

Dimethyl 2-(4-cyanobenzyl)-2-methylmalonate (3k)



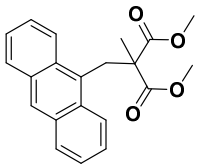
This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/4) as a white solid (212 mg, 81%). %). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.76 (d, J = 8.5 Hz, 2H, ArH), 7.32 (d, J = 8.5 Hz, 2H, ArH), 3.67 (s, 6H, 2 x CH_3), 3.22 (s, 2H, CH_2), 1.23 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.3, 142.0, 132.2, 131.2, 118.8, 110.0, 54.1, 52.7, 40.4, 19.3; **HRMS** (ESI+) calc. for $C_{14}H_{15}NO_4$ $[M+Na]^+$ 284.0893; found 284.0898.

Dimethyl 2-methyl-2-(naphthalen-1-ylmethyl)malonate (3l)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/15) as a colourless sticky liquid (246 mg, 86%). %). **^{1}H NMR** (400 MHz, d_6-DMSO)) δ 7.89-7.82 (m, 3H, ArH), 7.63 (s, 1H, ArH), 7.51-7.46 (m, 2H, ArH), 7.24 (dd, J = 8.4, 1.8Hz, 1H, ArH), 3.70 (s, 6H, 2 x CH_3), 3.31 (s, 2H, CH_2), 1.29 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.7, 133.6, 132.9, 132.1 128.7, 128.4, 127.7, 127.5, 126.3, 125.9, 54.4, 52.7, 40.8, 19.5; **HRMS** (ESI+) calc. for $C_{17}H_{18}O_4$ $[M+Na]^+$ 309.1097; found 309.1098.

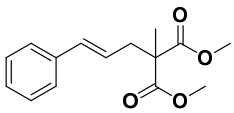
Dimethyl 2-(anthracen-9-ylmethyl)-2-methylmalonate (3m)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/15) as an orange solid (215 mg, 64%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 8.56 (s, 1H, ArH), 8.22-8.20 (m, 2H, ArH), 8.10-8.08 (m, 2H, ArH), 7.38-7.30 (m, 4H, ArH), 4.36 (s, 2H, CH_2), 3.61 (s, 6H, 2 x CH_3), 1.05 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 172.2, 131.1, 131.0, 129.2, 128.7, 127.3, 125.9, 125.1, 124.8, 54.5, 52.9, 30.5, 20.1; **HRMS** (ESI+) calc. for $C_{21}H_{20}O_4$ $[M+Na]^+$ 359.1254; found 359.1260.

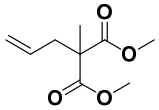
Dimethyl 2-cinnamyl-2-methylmalonate (3n)

View Article Online
DOI: 10.1039/C6GC00163G



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (249 mg, 95%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.37-7.21 (m, 5H, ArH), 6.48 (d, J = 15.2Hz, 1H, =CH), 6.11 (dt, J = 15.6, 7.8Hz, 1H, =CH), 3.67 (s, 6H, 2 x CH_3), 2.69 (dd, J = 7.5, 1.1Hz, 2H, CH_2), 1.36 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.8, 136.7, 133.9, 128.8, 127.6, 126.1, 124.0, 53.5, 52.6, 38.9, 19.7. **HRMS** (ESI+) calc. for $C_{15}H_{18}O_4$ $[M+Na]^+$ 285.1097; found 285.1110.

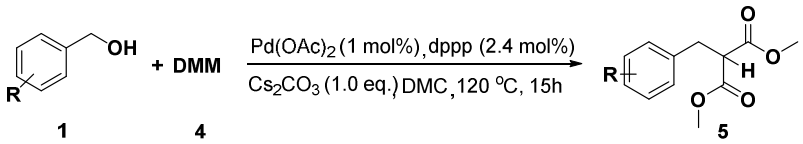
Dimethyl 2-allyl-2-methylmalonate (3o)



This compound was prepared according to general procedure and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (136 mg, 73%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.73-5.62 (m, 1H, =CH), 5.12-5.07 (m, 2H, =CH_2), 3.72 (s, 6H, 2 x CH_3), 2.61 (dt, J = 7.4, 1.1Hz, 2H, CH_2), 1.39 (s, 3H, CH_3); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.3, 132.4, 119.1, 53.4, 52.4, 40.0, 19.7; **HRMS** (ESI+) calc. for $C_9H_{14}O_4$ $[M+Na]^+$ 209.0790; found 209.0793.

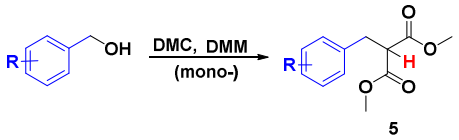
3. Procedure of the benzylation/allylation of DMM

General procedure A:



Under nitrogen atmosphere, benzyl alcohol (1.0 mmol), DMM (5.0 mmol), $Pd(OAc)_2$ (2.3 mg, 10 μmol), dppp (10 mg, 24 μmol), Cs_2CO_3 (326 mg, 1.0 equiv) and DMC (2 mL) were combined in a 20 mL headspace vial fitted with a suba seal cap. The mixture was stirred at 120 °C for 15 h, then cooled to room temperature. The mixture was filtered and washed by ethyl acetate, and the obtained solution was evaporated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane) to give the desired product **5**.

Table S2. Reaction conditions screening for the benzylation of DMM (I).



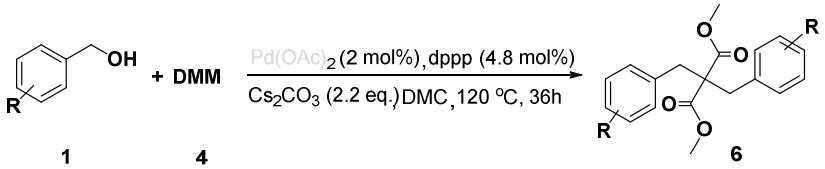
Entry	$Pd(OAc)_2$ (mol%)	dppp (mol%)	Ratio of BnOH/DMM	T(°C)	t(h)	Yield(%)[a] mono-	bis-
1	2	4.8	1:1.2	120	24	38	23
2[b]	2	4.8	1:1.2	120	24	44	20
3[b]	2	4.8	1:3	120	15	70	9

View Article Online
DOI: 10.1039/C6GC00163G

4[b]	2	4.8	1:5	120	15	78	4
5	2	4.8	1:5	120	15	84	6
6	1	2.4	1:5	120	15	86	7
7	1	2.4	1:8	120	15	86	5
8	1	2.4	1:3	120	15	74	11
9	0.5	1.2	1:5	120	15	76	7
10[b]	1	2.4	1:5	120	15	80	6
11	1	2.4	1:5	120	12	78	6
12	1	2.4	1:5	120	18	74	8
13	1	2.4	1:5	110	15	74	6

Reaction conditions: BnOH (1 mmol), Cs_2CO_3 (1.0 eq.), DMC (2 mL). [a]Yield by NMR. [b] Solvent (1 mL DMC + 1 mL Dioxane)

General procedure B:

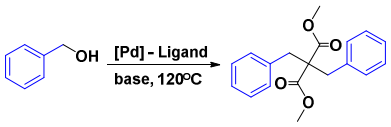


1 4 6

Under nitrogen atmosphere, benzyl alcohol (2.2 mmol), DMM (1.0 mmol), $Pd(OAc)_2$ (4.5 mg, 20 μmol), dppp (20 mg, 48 μmol), Cs_2CO_3 (717 mg, 2.2 equiv) and DMC (2 mL) were combined in a 20 mL headspace vial fitted with a suba seal cap. The mixture was stirred at 120 °C for 36 h, then cooled to room temperature. The mixture was filtered and washed by ethyl acetate, and the obtained solution was evaporated under reduced pressure. The residue was purified by flash column chromatography (EtOAc/hexane) to give the desired product **6**.

View Article Online
DOI: 10.1039/C6GC00163G

Table S3. Reaction conditions screening for the benzylation of DMM (II).

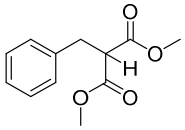


Entry	Base	(eq.)	DMC (mL)	Co-solvent (mL)	t (h)	Yield(%)[a]
1	Cs_2CO_3	(2)	-	Toluene (2)	24	0
2	Cs_2CO_3	(2)	2	-	24	56
3	Cs_2CO_3	(2)	1	-	24	45
4[b]	Cs_2CO_3	(2)	2	-	24	43
5	Cs_2CO_3	(2.2)	2	-	24	67
6	Cs_2CO_3	(2.2)	2	-	29	78
7	Cs_2CO_3	(2.2)	2	-	36	85
8	Cs_2CO_3	(2.5)	2	-	24	54
9	K_2CO_3	(2)	2	-	24	30
10	K_2CO_3	(2.2)	2	-	24	36
11	NaO^tBu	(2)	2	-	24	11
12[c]	Cs_2CO_3	(2)	1	-	24	< 5
13[d]	Cs_2CO_3	(2)	1	-	24	12
14[e]	Cs_2CO_3	(2)	1	-	24	25
15[f]	Cs_2CO_3	(2)	1	-	24	31
16	Cs_2CO_3	(2.2)	1	DMF (1)	24	43
17	Cs_2CO_3	(2.2)	1	DMF (1)	30	46

Reaction conditions: Benzyl alcohol (2.2 mmol), DMM (1.0 mmol), Pd(OAc) (2 mol%), dppp (4.8 mol%), 120 **°C**. [a] Yield by NMR. [b] Pd(OAc) (4 mol%), dppp(10 mol%). [c] TCHP as ligand. [d] DPMP as ligand. [e] dppb as ligand. [f] TPAP as ligand.

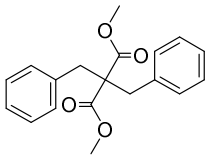
View Article Online
DOI: 10.1039/C6GC00163G

Dimethyl 2-benzylmalonate (5a)



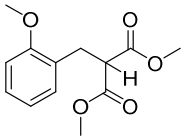
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a colourless liquid (189 mg, 85%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.30-7.19 (m, 5H, ArH), 3.87 (t, J = 8.0 Hz, 1H, CH), 3.60 (s, 6H, 2 x CH_3), 3.08 (d, J = 7.8 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.0, 137.7, 128.8, 128.5, 126.8, 52.8, 52.5, 34.2; **HRMS** (ESI+) calc. for $C_{12}H_{14}O_4$ $[M+Na]^+$ 245.0784; found 245.0775.

Dimethyl 2,2-dibenzylmalonate (6a)



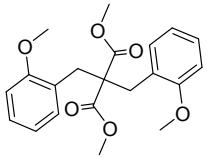
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (259 mg, 83%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.32-7.15 (m, 10H, 2 x ArH), 3.58 (s, 6H, 2 x CH_3), 3.10 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.6, 135.8, 130.1, 128.4, 127.1, 60.0, 52.3, 38.5; **HRMS** (ESI+) calc. for $C_{19}H_{20}O_4$ $[M+Na]^+$ 335.1254; found 335.1248.

Dimethyl 2-(2-methoxybenzyl)malonate (5b)



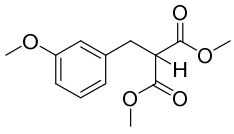
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless liquid (234 mg, 93%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 1H, ArH), 7.13-7.11 (m, 1H, ArH), 6.87-6.82 (m, 2H, ArH), 3.85 (t, J = 8.1 Hz, 1H, CH), 3.83 (s, 3H, Ar-OCH_3), 3.68 (s, 6H, 2 x CH_3), 3.20 (d, J = 7.7 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.1, 157.3, 130.1, 128.5, 125.4, 120.4, 110.7, 55.4, 52.4, 51.0, 29.5; **HRMS** (ESI+) calc. for $C_{13}H_{16}O_5$ $[M+Na]^+$ 275.0890; found 275.0887.

Dimethyl 2,2-bis(2-methoxybenzyl)malonate (6b)



This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless sticky liquid (286 mg, 77%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.20 (td, J = 8.1, 1.7 Hz, 2H, 2 x ArH), 7.02 (dd, J = 7.5, 1.7 Hz, 2H, 2 x ArH), 6.92 (dd, J = 8.2, 0.8 Hz, 2H, 2 x ArH), 7.20 (td, J = 7.4, 1.0 Hz, 2H, 2 x ArH), 3.69 (s, 6H, 2 x Ar-OCH_3), 3.53 (s, 6H, 2 x OCH_3), 3.13 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.9, 157.8, 131.1, 128.2, 124.5, 119.9, 110.3, 58.4, 55.3, 52.4, 33.0; **HRMS** (ESI+) calc. for $C_{21}H_{24}O_6$ $[M+Na]^+$ 395.1465; found 395.1472.

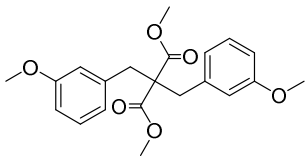
Dimethyl 2-(3-methoxybenzyl)malonate (5c)



This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a colourless liquid (232 mg, 92%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.20-6.74 (m, 4H, ArH), 3.88 (t, J = 8.1 Hz, 1H, CH), 3.72 (s, 3H, Ar-OCH_3), 3.61 (s, 6H, 2 x CH_3), 3.05 (d, J = 7.3 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.0, 159.4, 139.4, 129.4, 120.9, 114.4, 112.3, 55.0, 52.7, 52.5, 34.1; **HRMS** (ESI+) calc. for $C_{13}H_{16}O_5$ $[M+Na]^+$ 275.0890; found 275.0889.

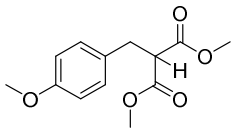
Dimethyl 2,2-bis(3-methoxybenzyl)malonate (6c)

View Article Online
DOI: 10.1039/C6GC00163G



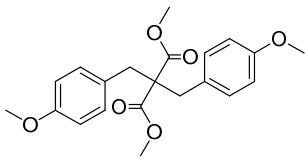
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless sticky liquid (227 mg, 71%). %). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.23 (t, J = 8.0 Hz, 2H, 2 x ArH), 6.83 (ddd, J = 8.3, 2.5, 0.6 Hz, 2H, 2 x ArH), 6.71 (d, J = 7.6 Hz, 2H, 2 x ArH), 6.67 (t, J = 2.0 Hz, 2H, 2 x ArH), 3.72 (s, 6H, 2 x Ar-OCH_3), 3.61 (s, 6H, 2 x CH_3), 3.08 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.6, 159.1, 137.4, 129.4, 122.3, 115.7, 112.5, 59.9, 54.9, 52.5, 38.5; **HRMS** (ESI+) calc. for $C_{21}H_{24}O_6$ $[M+Na]^+$ 395.1465; found 395.1473.

Dimethyl 2-(4-methoxybenzyl)malonate (5d)



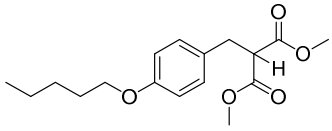
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a colourless liquid (237 mg, 94%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.11 (d, J = 8.8 Hz, 2H, ArH), 6.83 (d, J = 8.8 Hz, 2H, ArH), 3.81 (t, J = 8.0 Hz, 1H, CH), 3.71 (s, 3H, Ar-OCH_3), 3.60 (s, 6H, 2 x CH_3), 3.01 (d, J = 8.0 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.1, 158.2, 130.0, 129.6, 114.0, 55.1, 53.2, 52.5, 33.6; **HRMS** (ESI+) calc. for $C_{13}H_{16}O_5$ $[M+Na]^+$ 275.0890; found 275.0891.

Dimethyl 2,2-bis(4-methoxybenzyl)malonate (6d)



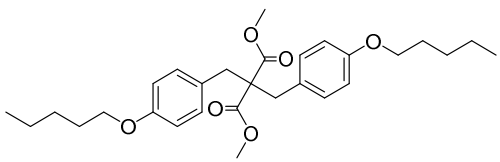
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a white solid (253 mg, 71%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.07 (d, J = 8.8 Hz, 4H, 2 x ArH), 6.81 (d, J = 8.8 Hz, 4H, 2 x ArH), 3.80 (s, 6H, 2 x Ar-OCH_3), 3.66 (s, 6H, 2 x CH_3), 3.16 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.5, 158.5, 131.1, 128.2, 113.7, 60.5, 55.4, 52.1, 38.3; **HRMS** (ESI+) calc. for $C_{21}H_{24}O_6$ $[M+Na]^+$ 395.1465; found 395.1474.

Dimethyl 2-(4-(pentyloxy)benzyl)malonate (5e)



This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless liquid (213 mg, 69%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.09 (d, J = 8.1 Hz, 2H, ArH), 6.81 (d, J = 8.1 Hz, 2H, ArH), 3.90 (t, J = 6.6 Hz, 2H, CH_2), 3.80 (t, J = 8.0 Hz, 1H, CH), 3.60 (s, 6H, 2 x CH_3), 3.01 (d, J = 7.7 Hz, 2H, CH_2), 1.72-1.64 (m, 2H, CH_2), 1.41-1.32 (m, 4H, CH_2 CH_2), 0.88 (t, J = 7.0 Hz, 3H, CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 168.9, 157.3, 130.0, 129.4, 114.3, 67.2, 53.0, 52.2, 33.6, 28.6, 28.0, 22.0, 14.1; **HRMS** (ESI+) calc. for $C_{17}H_{24}O_5$ $[M+Na]^+$ 331.1516; found 331.1523.

Dimethyl 2,2-bis(4-(pentyloxy)benzyl)malonate (6e)

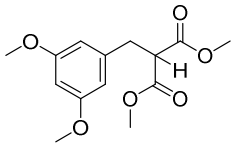


This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless sticky liquid (368 mg, 76%). %). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.04 (d, J = 8.7 Hz, 4H, 2 x ArH), 6.84 (d, J = 8.7 Hz, 4H, 2 x ArH), 3.91 (t, J = 6.5 Hz, 4H, 2 x CH_2), 3.58 (s, 6H, 2 x CH_3), 3.00 (s, 4H, 2 x CH_2), 1.72-1.65 (m, 4H, 2 x CH_2), 1.42-1.30 (m, 8H, 2 x CH_2 CH_2), 0.89 (t, J = 7.1

View Article Online
DOI: 10.1039/C6GC00163G

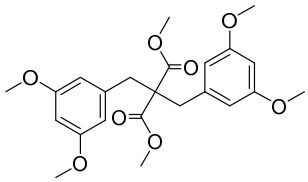
Hz, 6H, 2 x CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.9, 157.8, 131.3, 127.6, 114.3, 67.5, 60.2, 52.4, 37.6, 28.6, 27.9, 22.0, 14.2; **HRMS** (ESI+) calc. for $C_{29}H_{40}O_6$ $[M+Na]^+$ 507.2717; found 507.2724.

Dimethyl 2-(3,5-dimethoxybenzyl)malonate (5f)



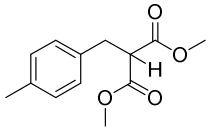
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a colourless liquid (200 mg, 71%). %). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 6.36-6.33 (m, 3H, ArH), 3.88 (t, J = 8.2 Hz, 1H, CH), 3.70 (s, 6H, 2 x Ar-OCH_3), 3.62 (s, 6H, 2 x CH_3), 3.01 (d, J = 8.2 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 168.8, 160.6, 140.1, 106.7, 98.3, 55.2, 52.6, 52.5, 34.3; **HRMS** (ESI+) calc. for $C_{14}H_{18}O_6$ $[M+Na]^+$ 305.0996; found 305.1000.

Dimethyl 2,2-bis(3,5-dimethoxybenzyl)malonate (6f)



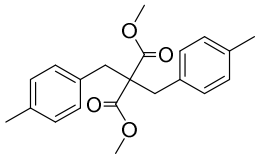
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a white solid (315 mg, 73%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 6.40 (d, J = 2.2 Hz, 2H, 2 x ArH), 6.24 (d, J = 2.2 Hz, 4H, 2 x ArH),3.71 (s, 12H, 4 x Ar-OCH_3), 3.63 (s, 6H, 2 x CH_3), 3.04 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.5, 160.3, 137.8, 108.1, 99.0, 59.6, 55.1, 52.5, 38.6; **HRMS** (ESI+) calc. for $C_{23}H_{28}O_8$ $[M+Na]^+$ 455.1676; found 455.1685.

Dimethyl 2-(4-methylbenzyl)malonate (5g)



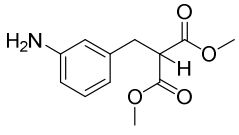
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a colourless liquid (160 mg, 68%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.08 (s, 4H, ArH), 3.83 (t, J = 8.1 Hz, 1H, CH), 3.60 (s, 6H, 2 x CH_3), 3.03 (d, J = 7.5 Hz, 2H, CH_2), 2.25 (s, 3H, Ar- CH_3),; **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.0, 136.0, 134.9, 129.1, 128.7, 52.9, 52.5, 33.8, 20.8; **HRMS** (ESI+) calc. for $C_{13}H_{16}O_4$ $[M+Na]^+$ 259.0941; found 259.0937.

Dimethyl 2,2-bis(4-methylbenzyl)malonate (6g)



This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (265 mg, 78%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.11 (d, J = 7.8 Hz, 4H, 2 x ArH), 7.03 (d, J = 8.0 Hz, 4H, 2 x ArH),3.59 (s, 6H, 2 x CH_3), 3.03 (s, 4H, 2 x CH_2), 2.27 (s, 6H, 2 x Ar-CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.8, 136.3, 132.8, 130.3, 129.2, 60.0, 52.5, 37.9, 20.9; **HRMS** (ESI+) calc. for $C_{21}H_{24}O_4$ $[M+Na]^+$ 363.1567; found 363.1570.

Dimethyl 2-(3-aminobenzyl)malonate (5h)

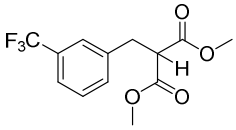


This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/3) as a colourless liquid (12 mg, 5%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 6.89 (t, J = 7.7 Hz, 1H, ArH), 6.40-6.35 (m, 2H, ArH), 6.30 (t, J = 7.5 Hz, 1H, ArH), 5.00 (s, 2H, NH_2), 3.72 (t, J =

View Article Online
DOI: 10.1039/C6GC00163G

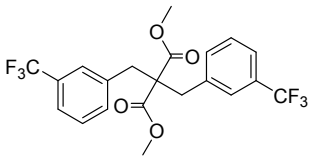
8.0 Hz, 1H, CH), 3.62 (s, 6H, 2 x CH_3), 2.91 (d, J = 8.3 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.1, 148.8, 138.2, 129.1, 116.0, 114.0, 112.5, 53.0, 52.5, 34.5; **HRMS** (ESI+) calc. for $C_{12}H_{15}NO_4$ $[M+Na]^+$ 260.0893; found 260.0888.

Dimethyl 2-(3-(trifluoromethyl)benzyl)malonate (5i)



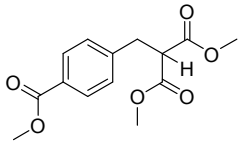
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (209 mg, 72%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.59-7.51 (m, 4H, ArH), 3.99 (t, J = 8.0 Hz, 1H, CH), 3.60 (s, 6H, 2 x CH_3), 3.18 (d, J = 7.3 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.7, 138.5, 132.2, 130.8 (q, $^2J_{CF}$ = 32Hz), 128.9, 125.4 (q, $^3J_{CF}$ = 4Hz), 123.9 (q, $^1J_{CF}$ = 272Hz), 123.6 (q, $^3J_{CF}$ = 4Hz), 53.2, 52.6, 34.3; **HRMS** (ESI+) calc. for $C_{13}H_{13}F_3O_4$ $[M+Na]^+$ 313.0658; found 313.0664.

Dimethyl 2,2-bis(3-(trifluoromethyl)benzyl)malonate (6i)



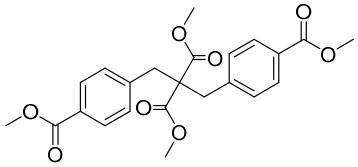
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (278 mg, 62%). %). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.64 (d, J = 7.6 Hz, 2H, 2 x ArH), 7.56 (t, J = 7.8 Hz, 2H, 2 x ArH), 7.49 (d, J = 7.6 Hz, 2H, 2 x ArH), 7.43 (s, 2H, 2 x ArH), 3.57 (s, 6H, 2 x CH_3), 3.25 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.5, 136.7, 133.3, 130.6 (q, $^2J_{CF}$ = 33Hz), 128.7, 126.6 (q, $^3J_{CF}$ = 4Hz), 124.0 (q, $^3J_{CF}$ = 4Hz), 123.9 (q, $^1J_{CF}$ = 272Hz), 60.2, 52.3, 39.5; **HRMS** (ESI+) calc. for $C_{21}H_{18}F_6O_4$ $[M+Na]^+$ 471.1001; found 471.1003.

Dimethyl 2-(4-(methoxycarbonyl)benzyl)malonate (5j)



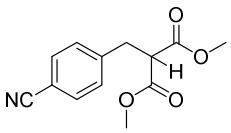
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/3) as a white solid (160 mg, 57%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.88 (d, J = 8.1 Hz, 2H, ArH), 7.37 (d, J = 8.1 Hz, 2H, ArH), 3.95 (t, J = 8.0 Hz, 1H, CH), 3.83 (s, 3H, Ar-$COOCH_3$), 3.61 (s, 6H, 2 x CH_3), 3.16 (d, J = 8.0 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 168.8, 166.1, 143.5, 129.4, 129.3, 128.2, 52.6, 52.3, 52.2, 34.0; **HRMS** (ESI+) calc. for $C_{14}H_{16}O_6$ $[M+Na]^+$ 303.0839; found 303.0846.

Dimethyl 2,2-bis(4-(methoxycarbonyl)benzyl)malonate (6j)



This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a white solid (218 mg, 51%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.4 Hz, 4H, 2 x ArH), 7.21 (d, J = 8.4 Hz, 4H, 2 x ArH), 3.92 (s, 6H, 2 x Ar-$COOCH_3$), 3.65 (s, 6H, 2 x CH_3), 3.27 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 166.8, 141.2, 129.9, 129.5, 128.9, 60.1, 52.3, 52.0, 39.6; **HRMS** (ESI+) calc. for $C_{23}H_{24}O_8$ $[M+Na]^+$ 451.1363; found 451.1371.

Dimethyl 2-(4-cyanobenzyl)malonate (5k)

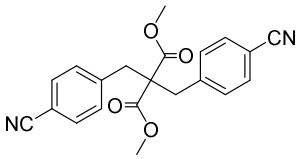


This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/3) as a colourless liquid (148 mg,

View Article Online
DOI: 10.1039/C6GC00163G

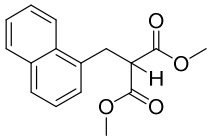
60%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.76 (d, J = 8.8 Hz, 2H, ArH), 7.44 (d, J = 8.8 Hz, 2H, ArH), 3.99 (t, J = 8.0 Hz, 1H, CH), 3.61 (s, 6H, 2 x CH_3), 3.17 (d, J = 8.0 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 168.8, 143.9, 132.6, 130.1, 119.0, 109.8, 52.9, 52.1, 34.1; **HRMS** (ESI+) calc. for $C_{13}H_{13}NO_4$ $[M+Na]^+$ 270.0737; found 270.0729.

Dimethyl 2,2-bis(4-cyanobenzyl)malonate (6k)



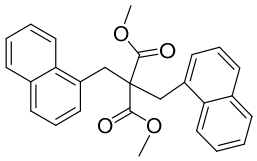
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a a white solid (217 mg, 60%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.69 (d, J = 8.6 Hz, 4H, 2 x ArH), 7.36 (d, J = 8.6 Hz, 4H, 2 x ArH), 3.57 (s, 6H, 2 x CH_3), 3.22 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.0, 141.9, 132.4, 131.2, 118.9, 110.1, 59.8, 52.6; 39.2; **HRMS** (ESI+) calc. for $C_{21}H_{18}N_2O_4$ $[M+Na]^+$ 385.1159; found 385.1161.

Dimethyl 2-(naphthalen-1-ylmethyl)malonate (5l)



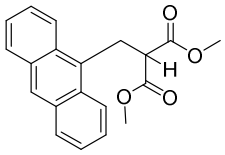
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/6) as a colourless liquid (177 mg, 65%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.88-7.83 (m, 3H, ArH), 7.03 (d, J = 0.7 Hz, 1H, ArH), 7.50-7.45 (m, 2H, ArH), 7.40 (dd, J = 8.5, 1.7 Hz, 1H, ArH), 4.00 (t, J = 8.0 Hz, 1H, CH), 3.60 (s, 6H, 2 x CH_3), 3.26 (d, J = 7.8 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.1, 135.5, 133.2, 132.0, 128.0, 127.63, 127.57, 127.3, 127.1, 126.3, 125.8, 52.7, 52.5, 34.5; **HRMS** (ESI+) calc. for $C_{16}H_{16}O_4$ $[M+Na]^+$ 295.0941; found 295.0939.

Dimethyl 2,2-bis(naphthalen-1-ylmethyl)malonate (6l)



This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a white solid (350 mg, 85%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.93-7.86 (m, 6H, 2 x ArH), 7.74 (s, 2H, 2 x ArH), 7.54-7.49 (m, 4H, 2 x ArH), 7.33 (dd, J = 8.5, 1.8 Hz, 2H, 2 x ArH), 3.62 (s, 6H, 2 x CH_3), 3.33 (s, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.3, 133.6, 133.2, 132.3, 128.9, 128.0, 127.7, 127.6, 127.5, 126.0, 125.6, 60.5, 52.2, 39.6; **HRMS** (ESI+) calc. for $C_{27}H_{24}O_4$ $[M+Na]^+$ 435.1567; found 435.1574.

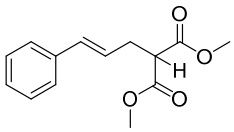
Dimethyl 2-(anthracen-9-ylmethyl)malonate (5m)



This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/6) as a yellow solid (200 mg, 62%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 8.56 (s, 1H, ArH), 8.27-8.24 (m, 2H, ArH), 8.11-8.09 (m, 2H, ArH), 7.60-7.51 (m, 4H, ArH), 4.18 (d, J = 7.8 Hz, 2H, CH_2), 3.87 (t, J = 7.8 Hz, 1H, CH), 3.47 (s, 6H, 2 x CH_3); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.0, 131.2, 129.6, 129.5, 129.3, 127.1, 126.4, 125.3, 124.1, 52.5, 52.4, 26.2; **HRMS** (ESI+) calc. for $C_{20}H_{18}O_4$ $[M+Na]^+$ 345.1097; found 345.1105.

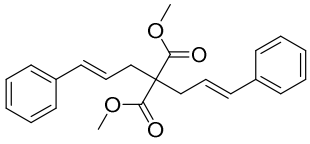
Dimethyl 2-cinnamylmalonate (5n)

View Article Online
DOI: 10.1039/C6GC00163G



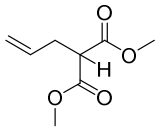
This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/5) as a colourless liquid (219 mg, 94%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.37-7.28 (m, 4H, ArH), 7.25-7.20 (m, 1H, ArH),6.46 (d, J = 16.3 Hz, 1H, = CH), 6.23-6.15 (m, 1H, =CH), 3.73 (t, J = 7.5 Hz, 1H, CH), 3.66 (s, 6H, 2 x CH_3), 2.67 (td, J = 7.3, 1.2 Hz, 2H, CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 169.2, 136.8, 132.2, 128.7, 127.5, 126.1, 125.9, 52.6, 51.1, 32.1; **HRMS** (ESI+) calc. for $C_{14}H_{16}O_4$ $[M+Na]^+$ 271.0941; found 271.0934.

Dimethyl 2,2-dicinnamylmalonate (6n)



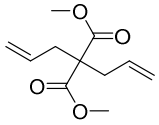
This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless sticky liquid (328 mg, 90%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 7.42-7.40 (m, 4H, 2 x ArH), δ 7.34-7.30 (m, 4H, 2 x ArH), δ 7.26-7.22 (m, 2H, 2 x ArH), 6.52 (d, J = 15.8 Hz, 2H, 2 x = CH), 6.16 (dt, J = 15.8, 8.2 Hz, 2H, 2 x =CH), 3.68 (s, 6H, 2 x CH_3), 2.75 (d, J = 7.4 Hz, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 171.0, 136.7, 134.0, 128.8, 127.6, 126.5, 124.0, 58.1, 52.7, 36.1; **HRMS** (ESI+) calc. for $C_{23}H_{24}O_4$ $[M+Na]^+$ 387.1567; found 387.1571.

Dimethyl 2-allylmalonate (5o)



This compound was prepared according to general procedure A and isolated by flash column chromatography (ethyl acetate/hexane=1/10) as a colourless liquid (91 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.81-5.71 (m, 1H, =CH), 5.14-5.05 (m, 2H, =CH_2), 3.74 (s, 6H, 2 x CH_3), 3.46 (t, J = 7.6 Hz, 1H, CH), 2.67-2.62 (m, 2H, CH_2); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.5, 133.7, 117.8, 52.5, 51.3, 32.8; **HRMS** (ESI+) calc. for $C_8H_{12}O_4$ $[M+Na]^+$ 195.0628; found 195.0630.

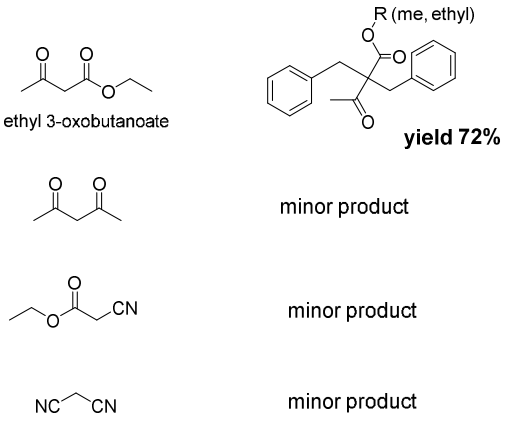
Dimethyl 2,2-diallylmalonate (6o)



This compound was prepared according to general procedure B and isolated by flash column chromatography (ethyl acetate/hexane=1/20) as a colourless liquid (142 mg, 67%). **^{1}H NMR** (400 MHz, d_6-DMSO) δ 5.67-5.58 (m, 2H, 2 x =CH), 5.15-5.09 (m, 4H, 2 x =CH_2), 3.65 (s, 6H, 2 x CH_3), 2.53 (d, J = 8.0 Hz, 4H, 2 x CH_2); **^{13}C NMR** (101 MHz, d_6-DMSO) δ 170.5, 132.4, 119.6, 57.1, 52.5, 36.5; **HRMS** (ESI+) calc. for $C_{11}H_{16}O_4$ $[M+Na]^+$ 235.0941; found 235.0942.

View Article Online
DOI: 10.1039/C6GC00163G

Table S4. Primary screening for other substrates.



Reaction conditions: Benzyl alcohol (2.2 mmol), substrates (1.0 mmol), $Pd(OAc)_2$ (2 mol%), dppp (5 mol%), Cs_2CO_3 (2.2 eq.), DMC (3 mL), 120 °C, 48 h.

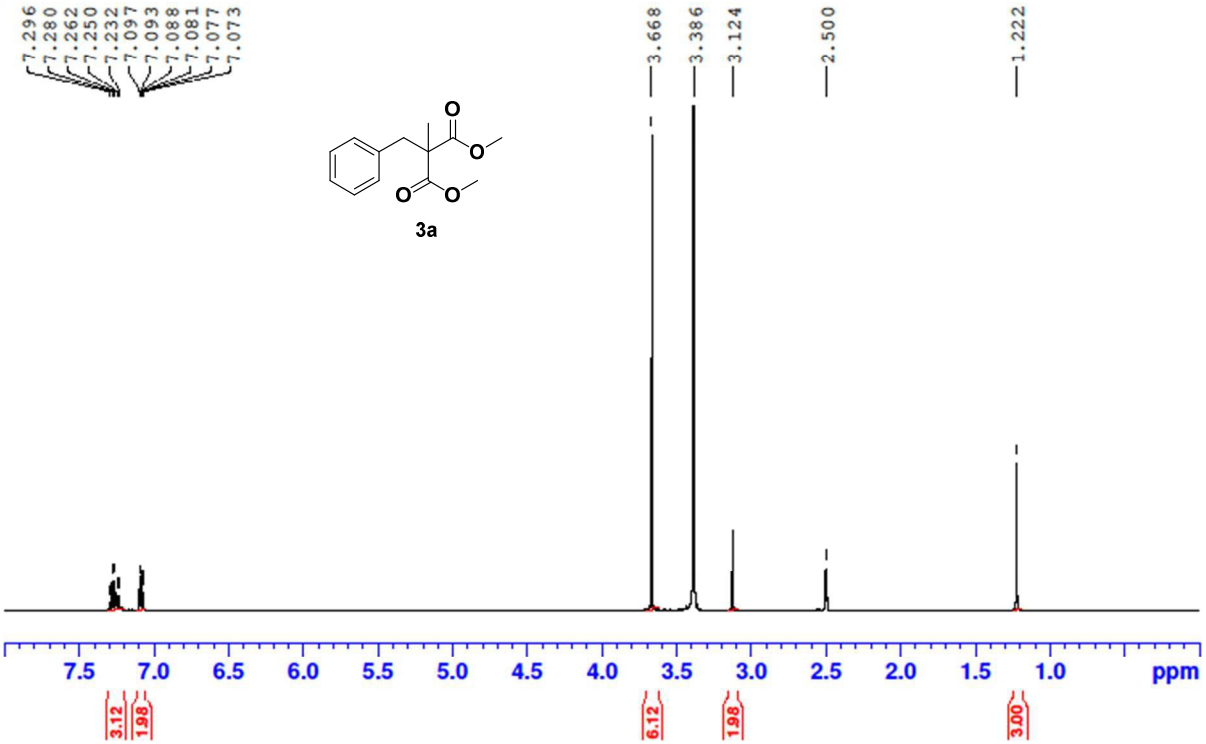
4. References

[1] F. Bjoerkling, J. Boutelje, S. Gatenbeck, K. Hult, T. Norin, P.Szmulik, *Tetrahedron* 1985, **41**, 1347.
[2] E. Fillion, D. Fishlock, A. Wilsily, J. M. Goll. *J. Org. Chem.* 2005, **70**, 1316-1327.
[3] T. Ke, C. R. Wescott, A. M. Klibanov. *J. Am. Chem. Soc.* 1996, **118**, 3366-3374.

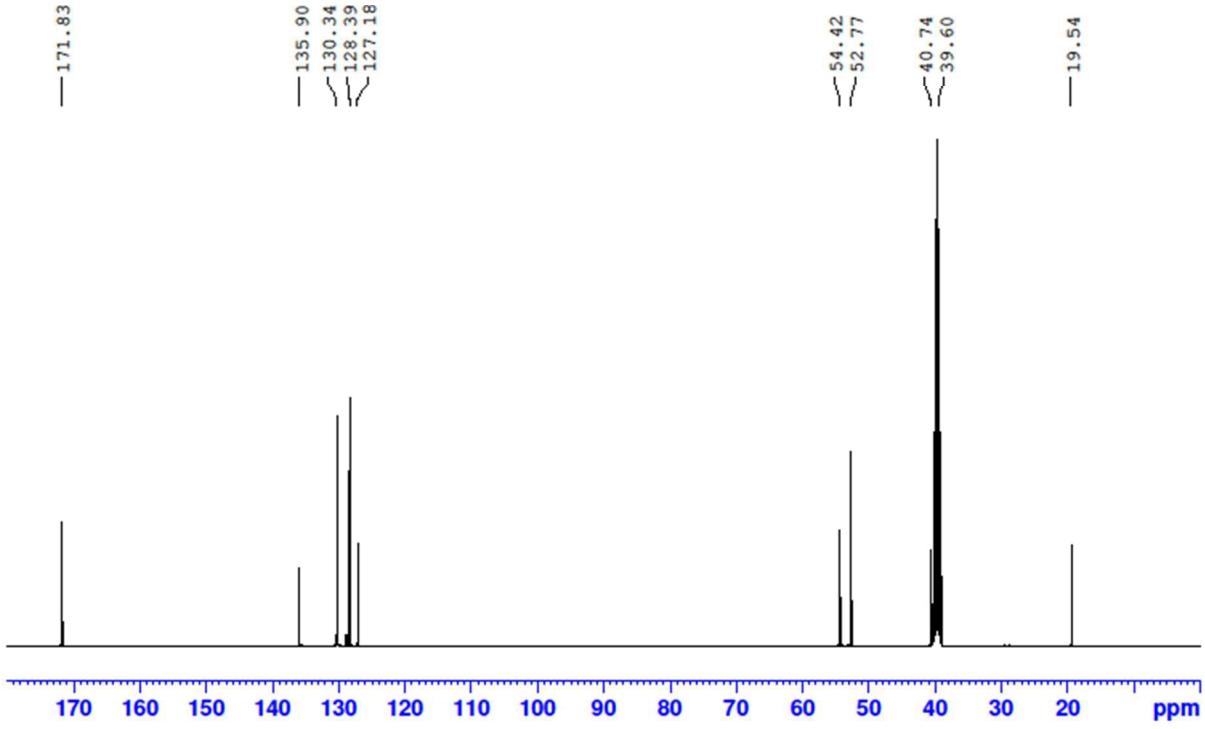
View Article Online
DOI: 10.1039/C6GC00163G

5. ^{1}H and ^{13}C NMR Spectra of malonates

^{1}H NMR, d_6-DMSO, 400 MHz

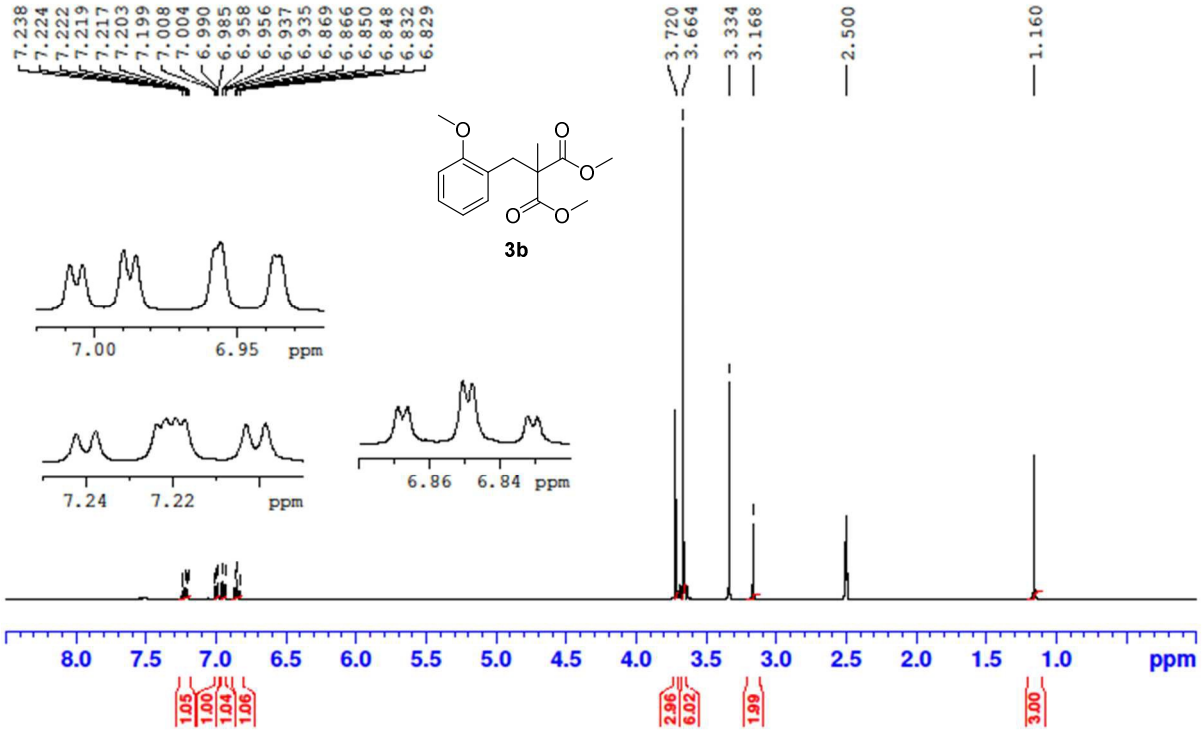


^{13}C NMR, d_6-DMSO, 101 MHz

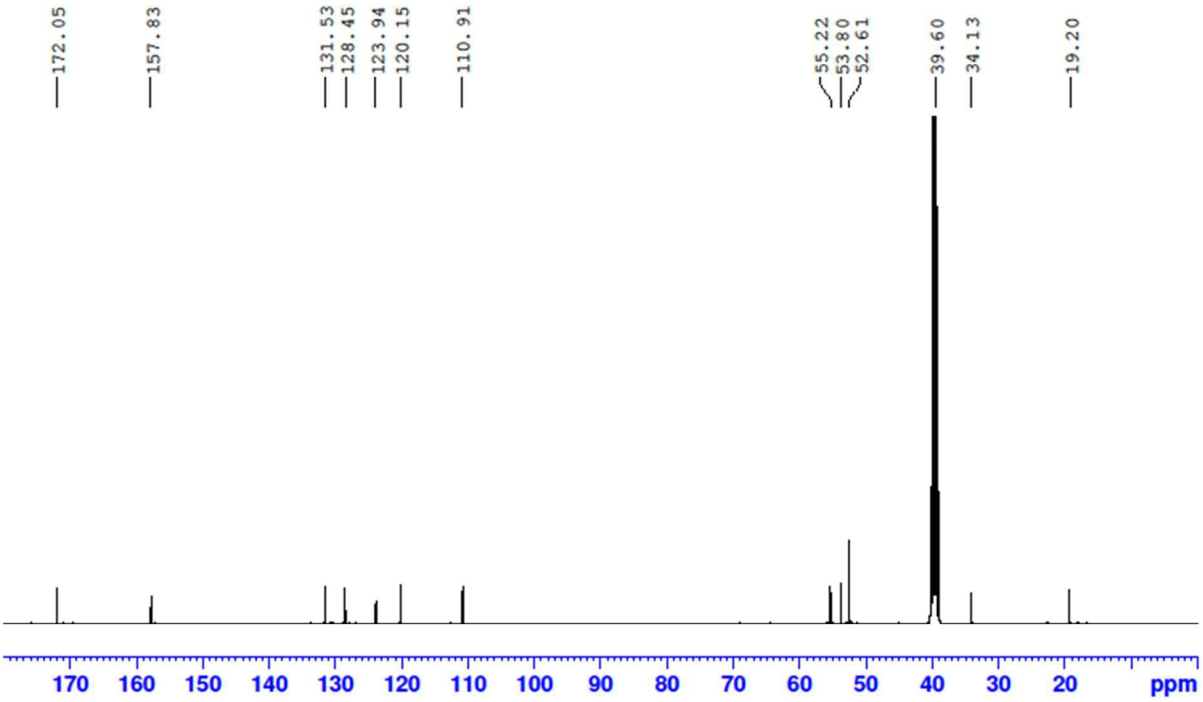


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

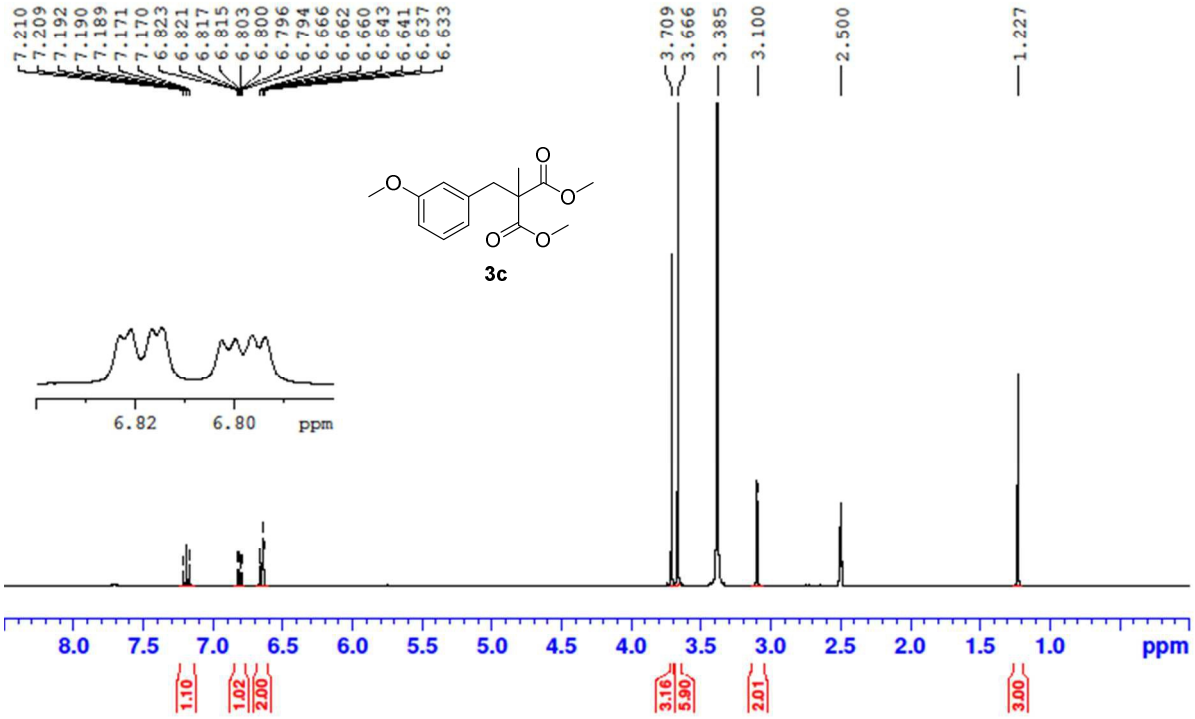


^{13}C NMR, d_6-DMSO, 101 MHz

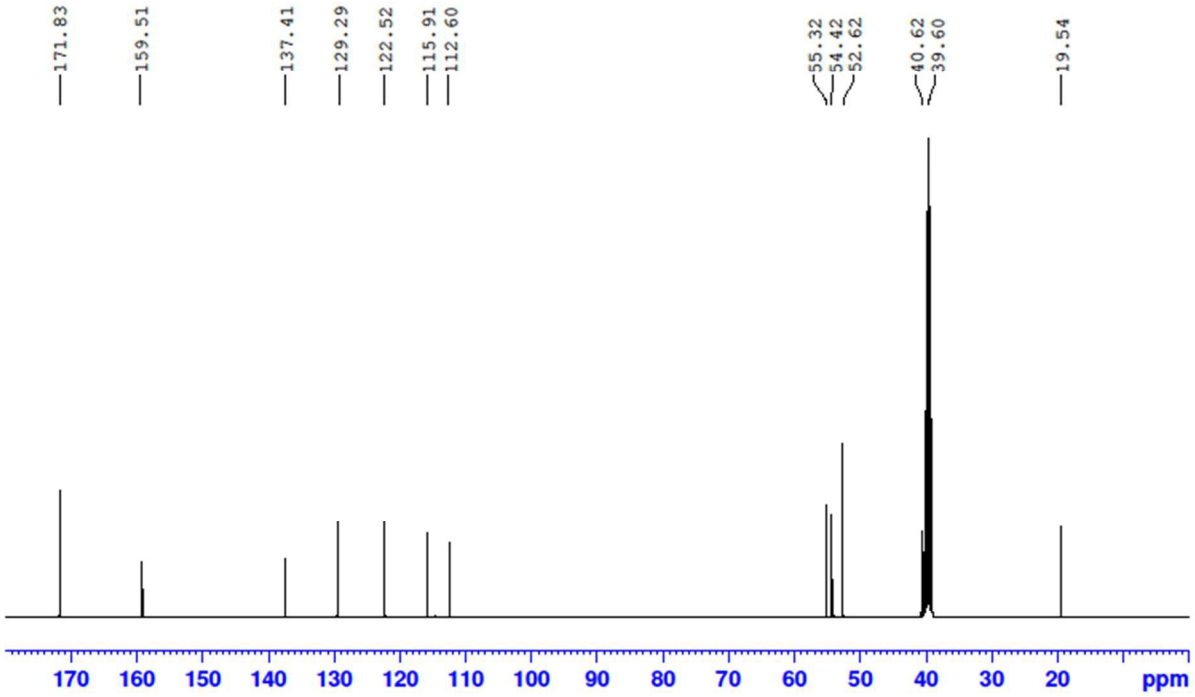


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

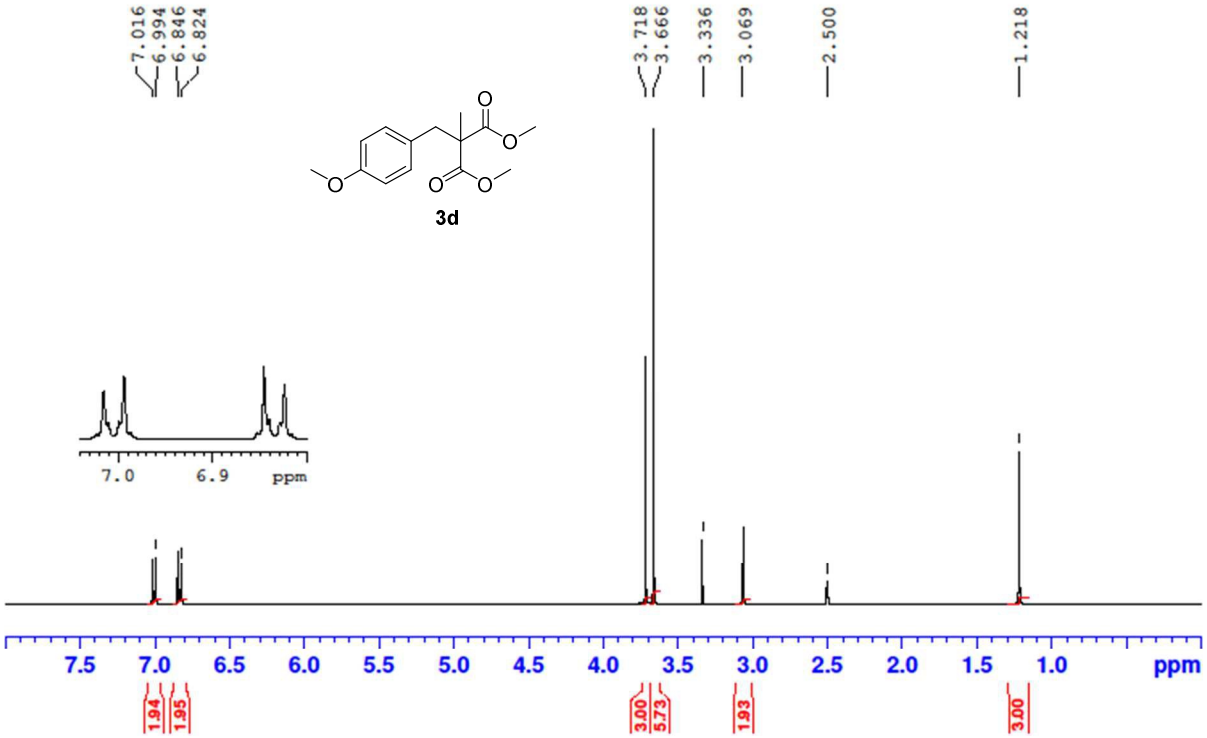


^{13}C NMR, d_6-DMSO, 101 MHz

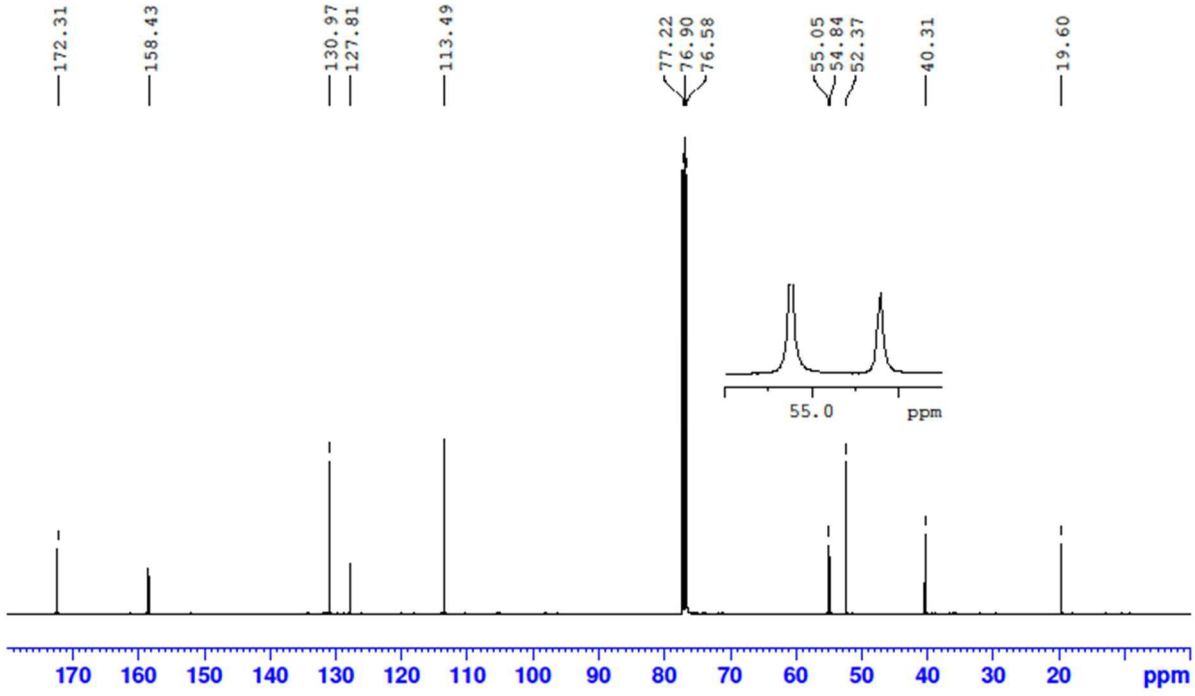


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

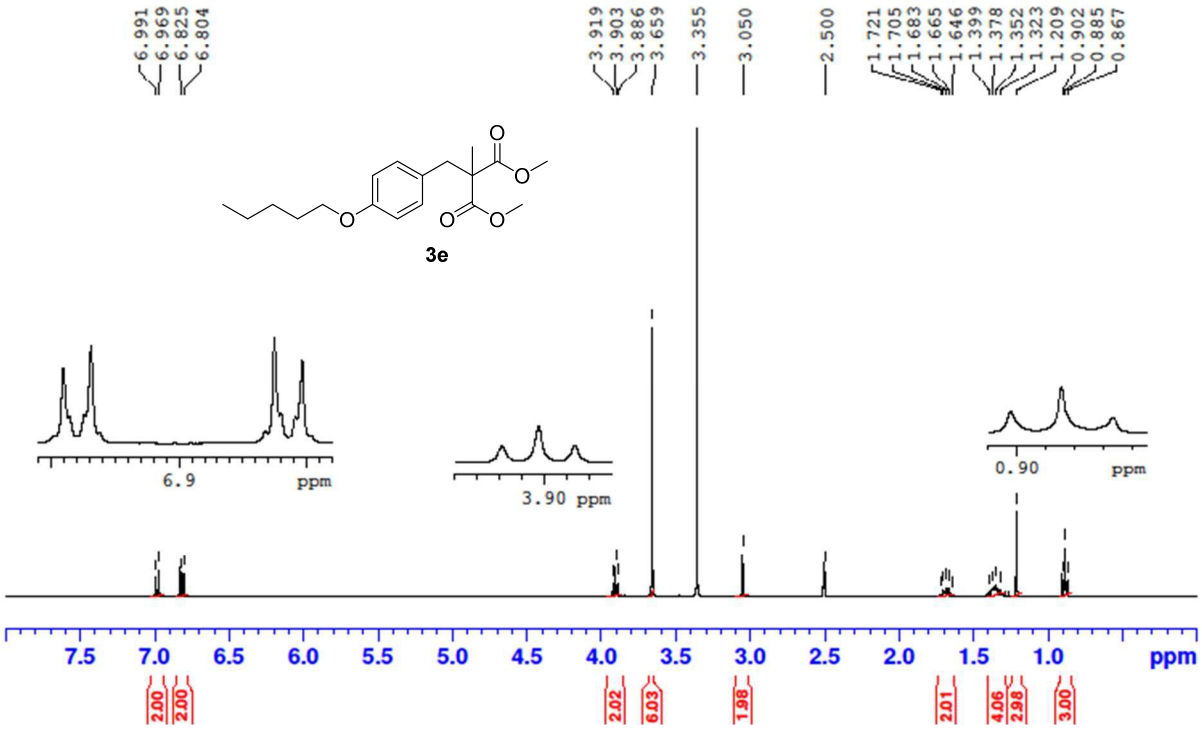


^{13}C NMR, $CDCl_3$, 101 MHz

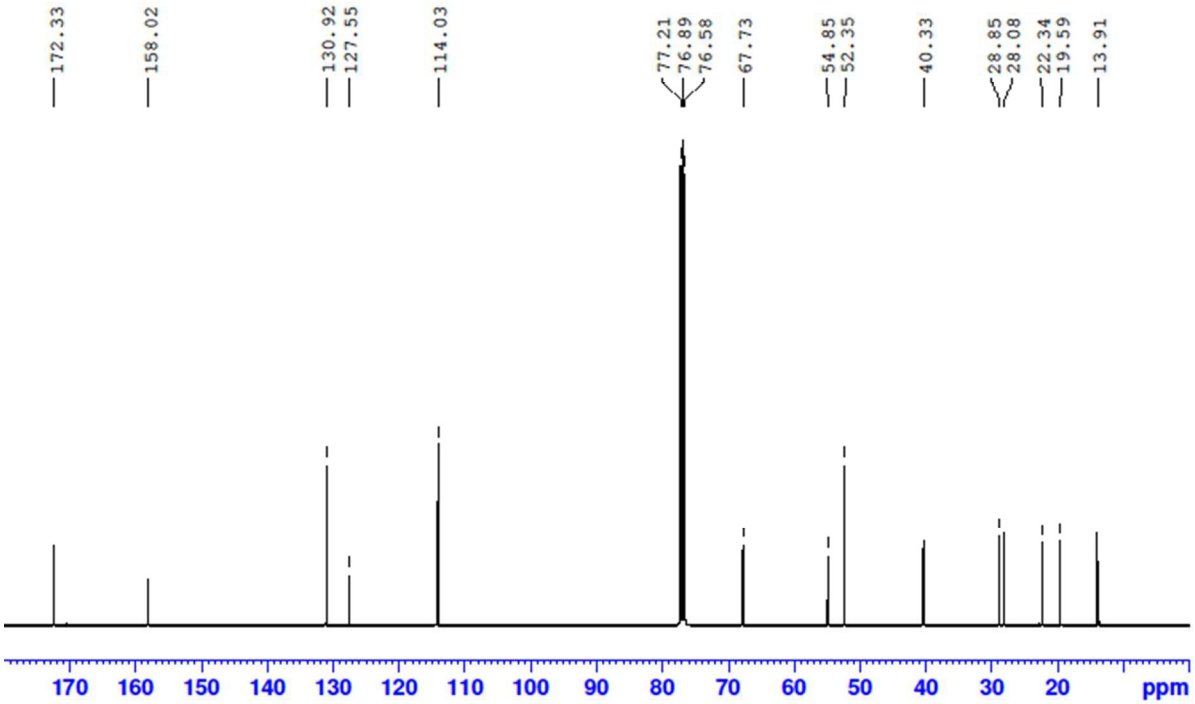


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

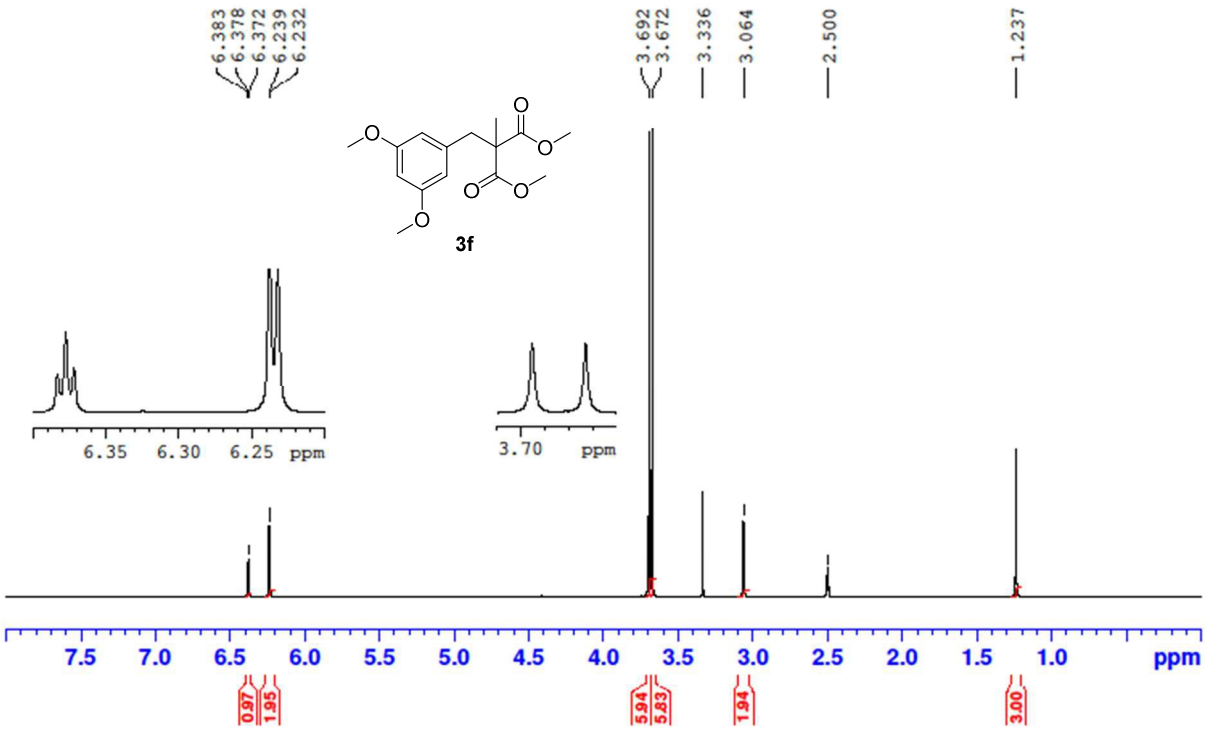


^{13}C NMR, $CDCl_3$, 101 MHz

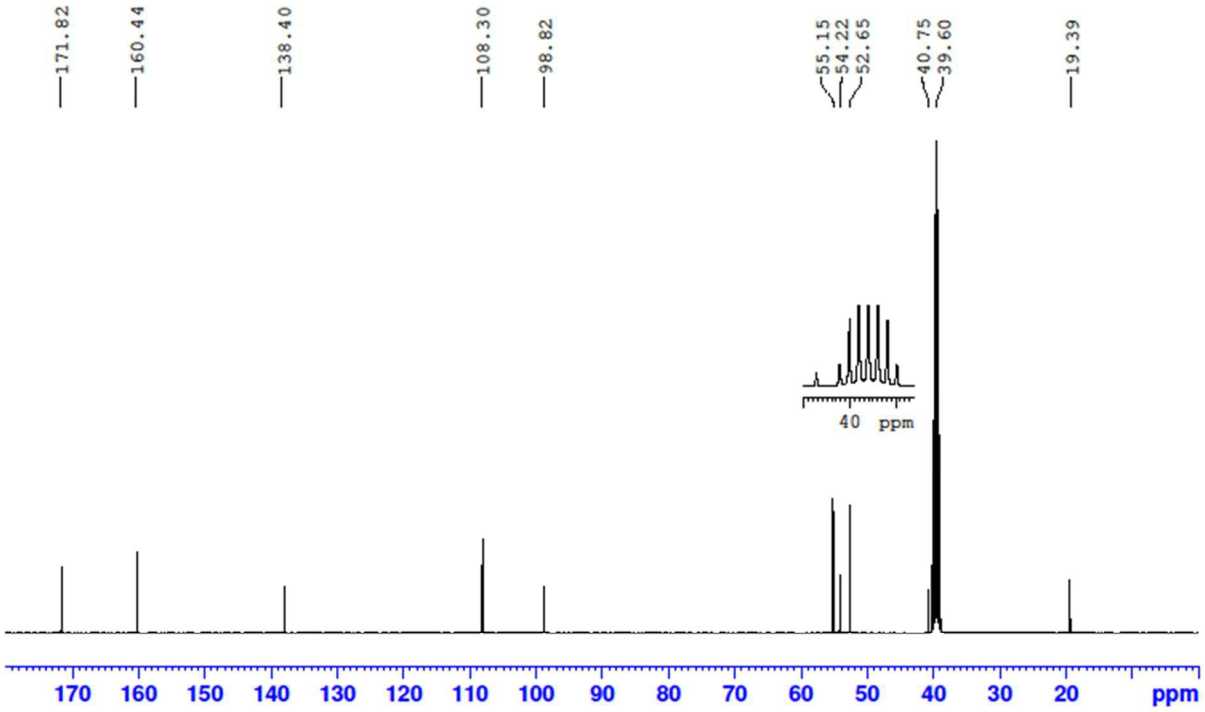


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

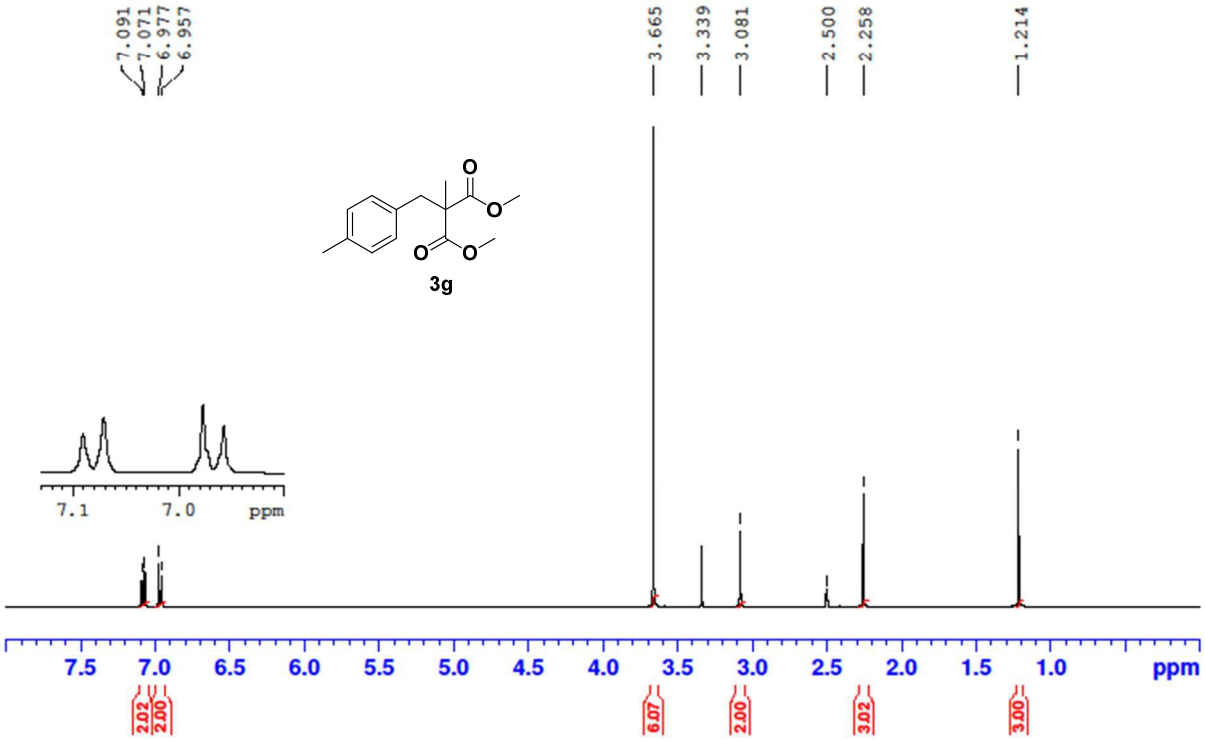


^{13}C NMR, d_6-DMSO, 101 MHz

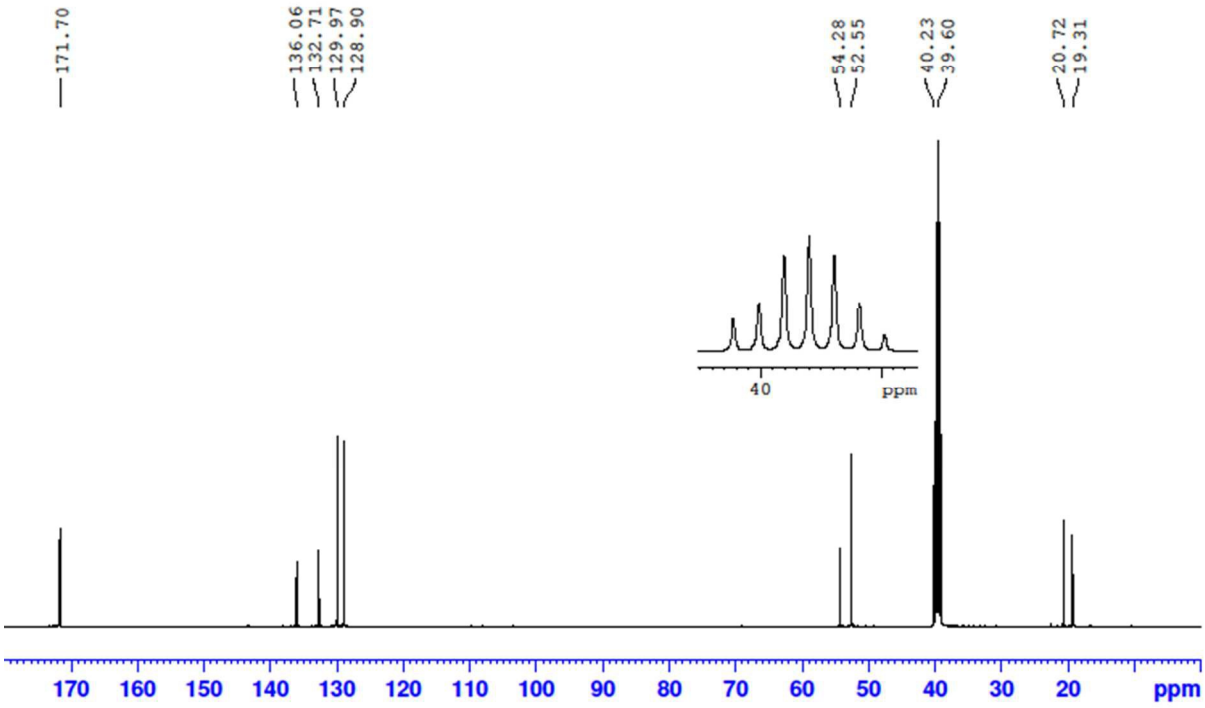


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

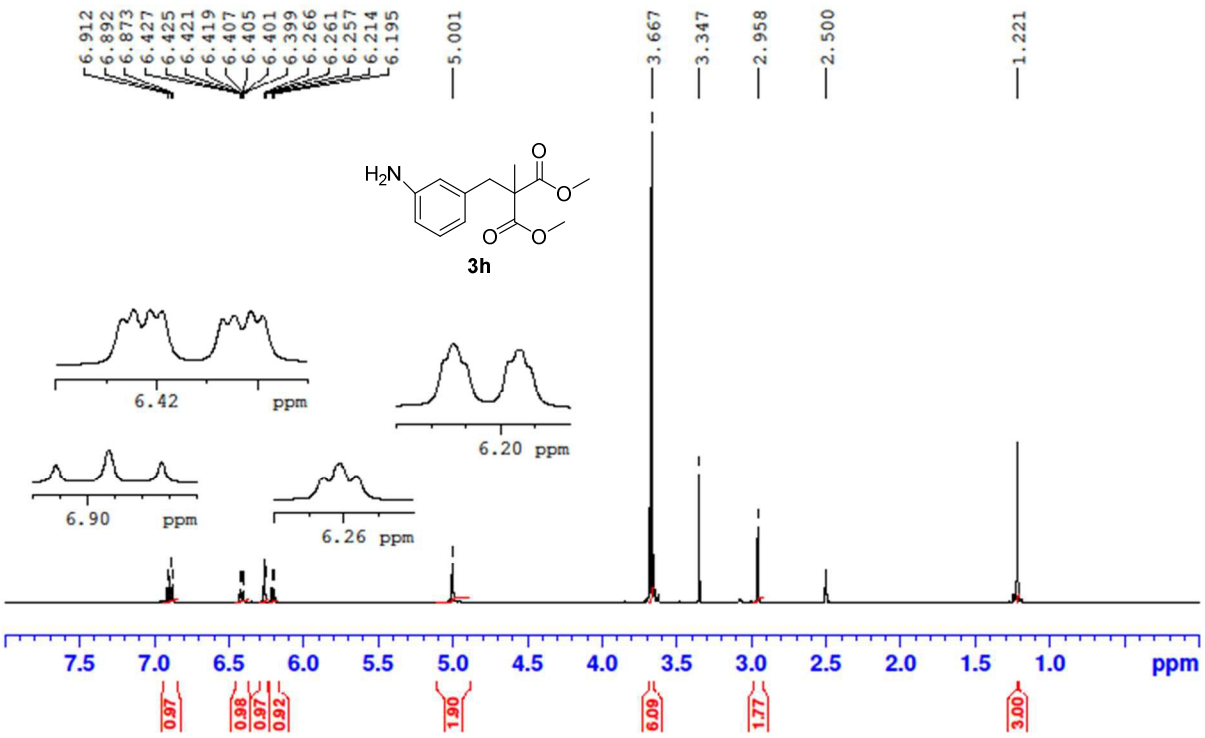


^{13}C NMR, d_6-DMSO, 101 MHz

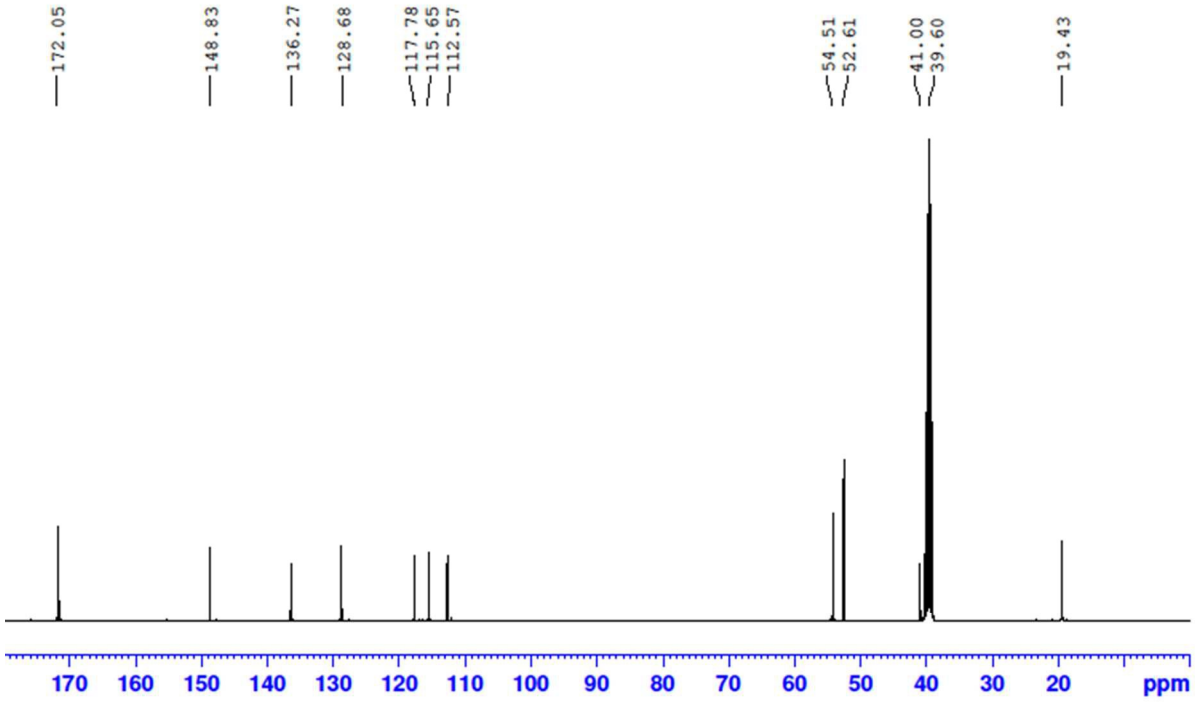


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

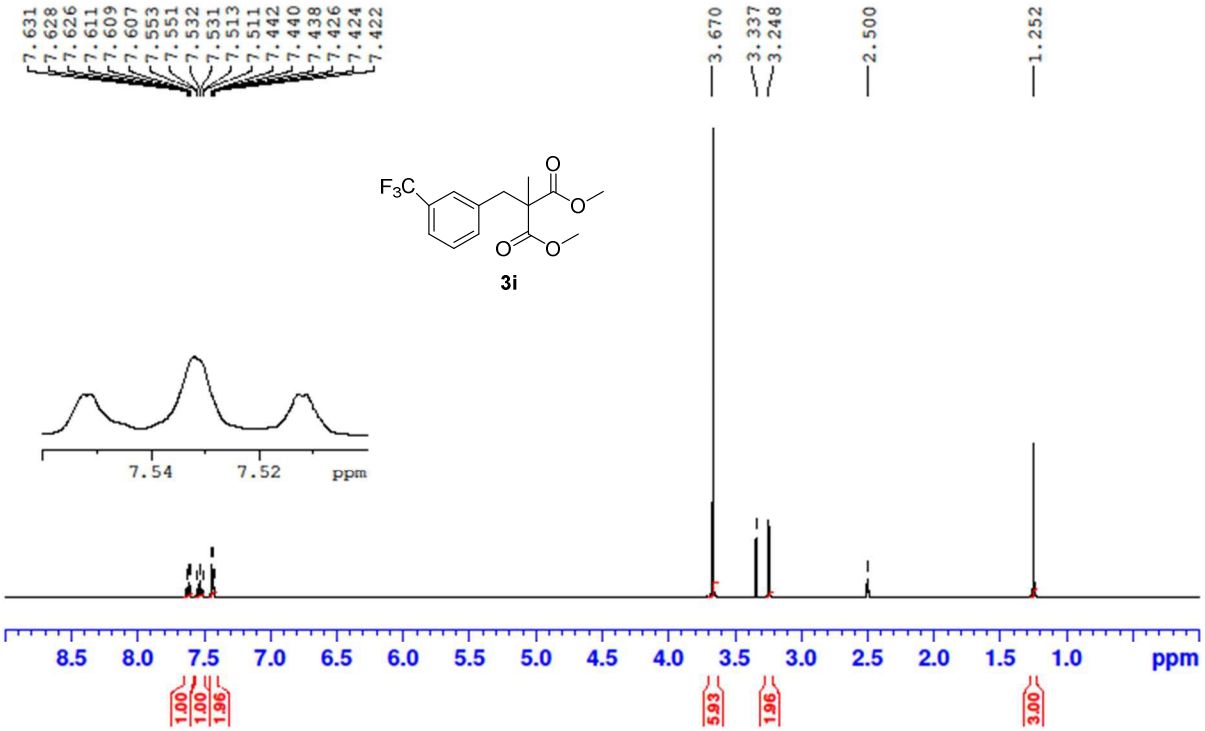


^{13}C NMR, d_6-DMSO, 101 MHz

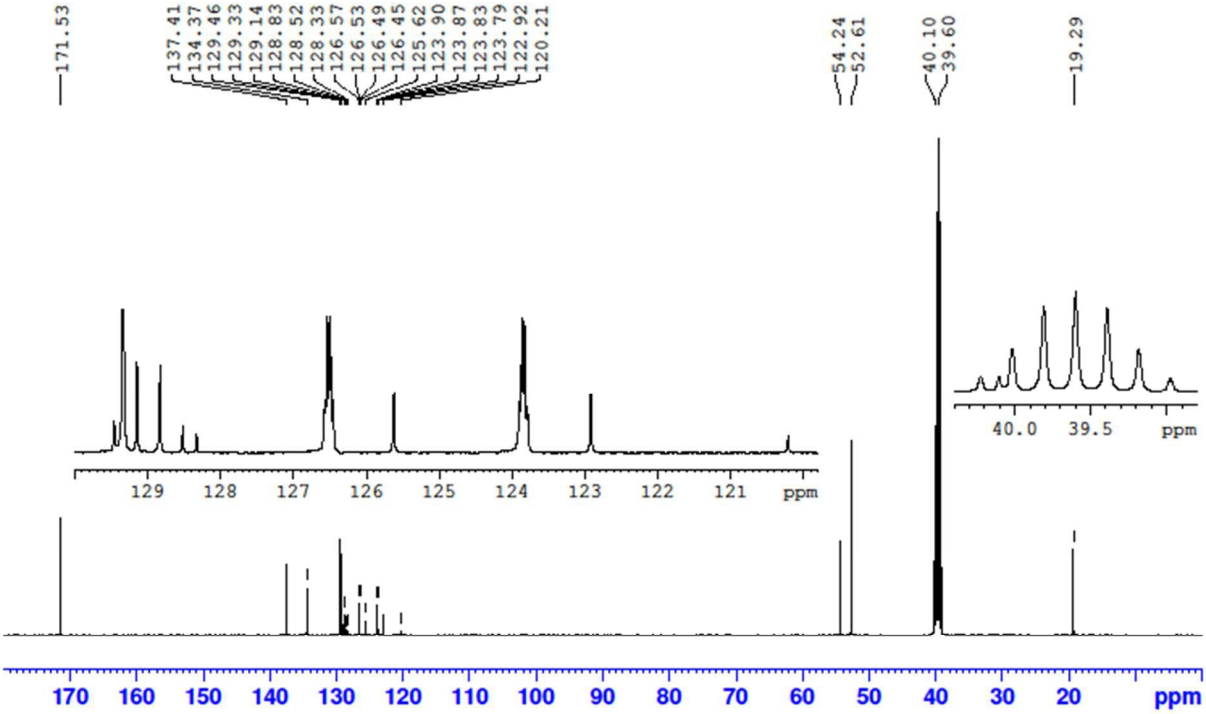


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

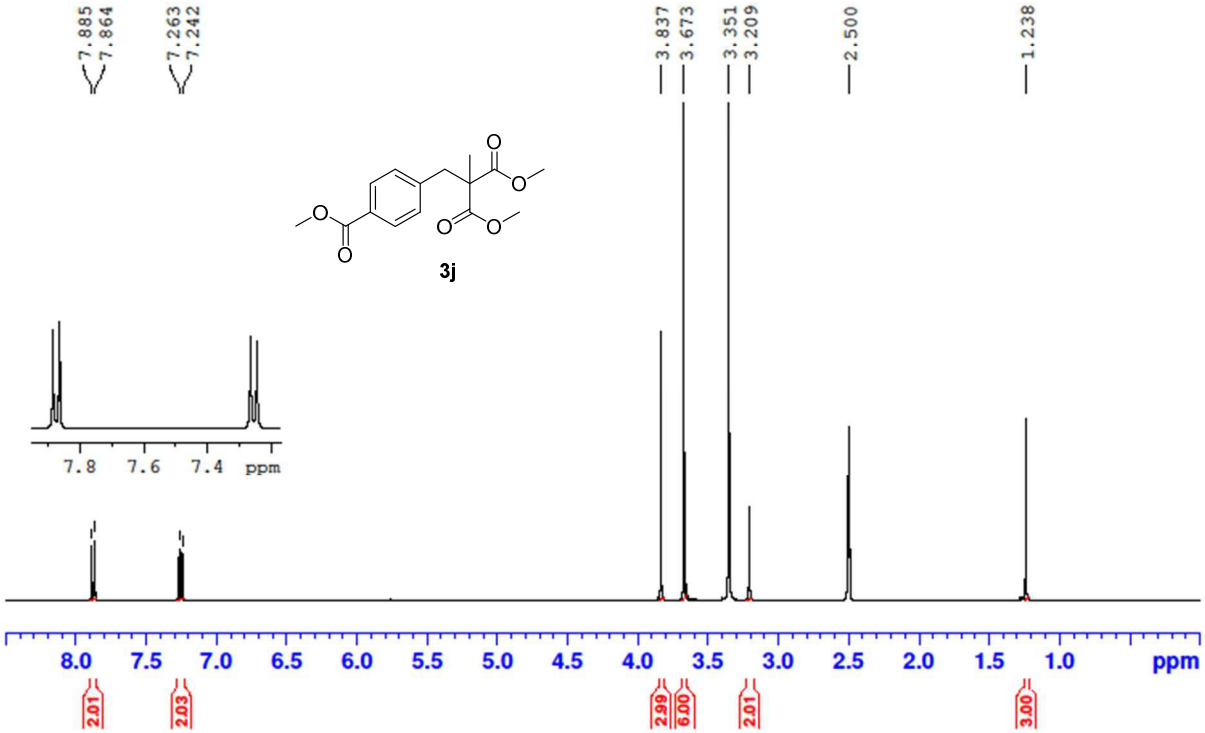


^{13}C NMR, d_6-DMSO, 101 MHz

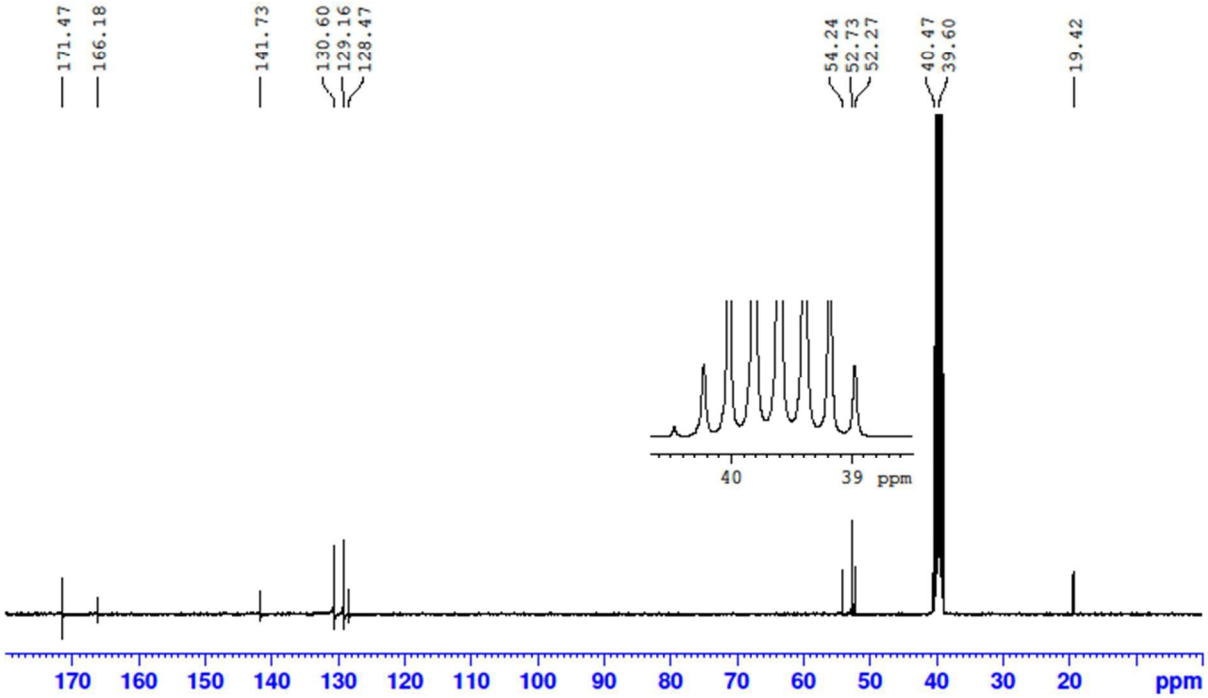


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

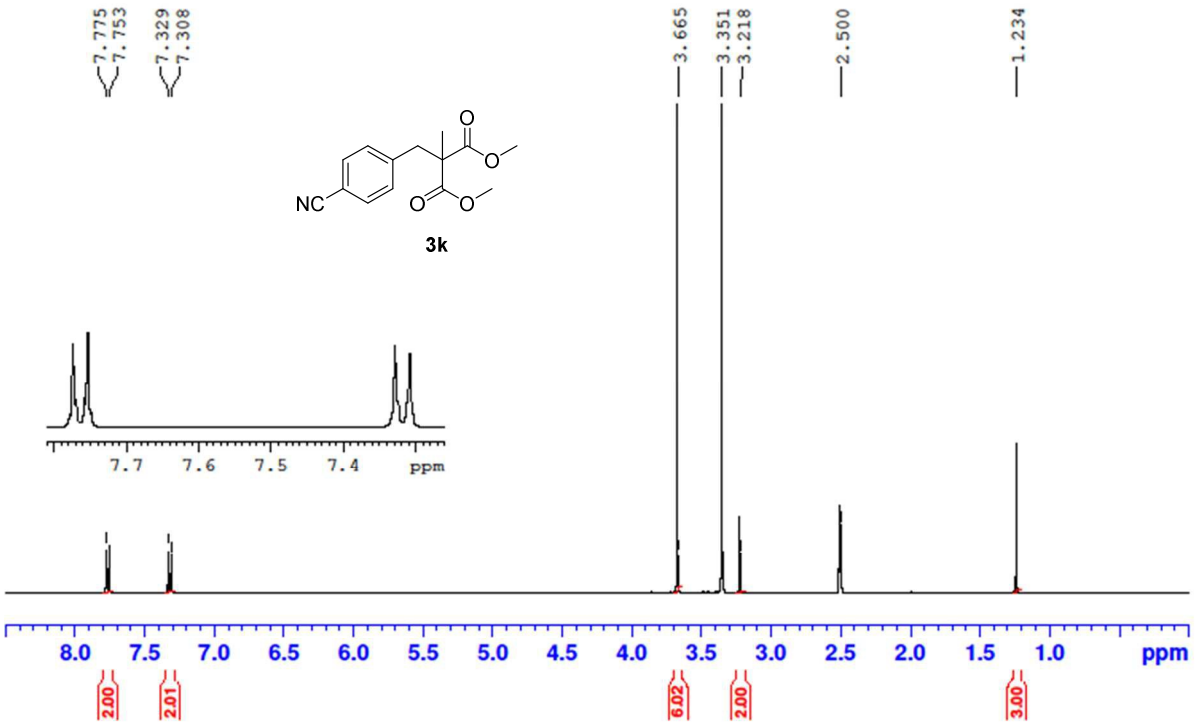


^{13}C NMR, d_6-DMSO, 101 MHz

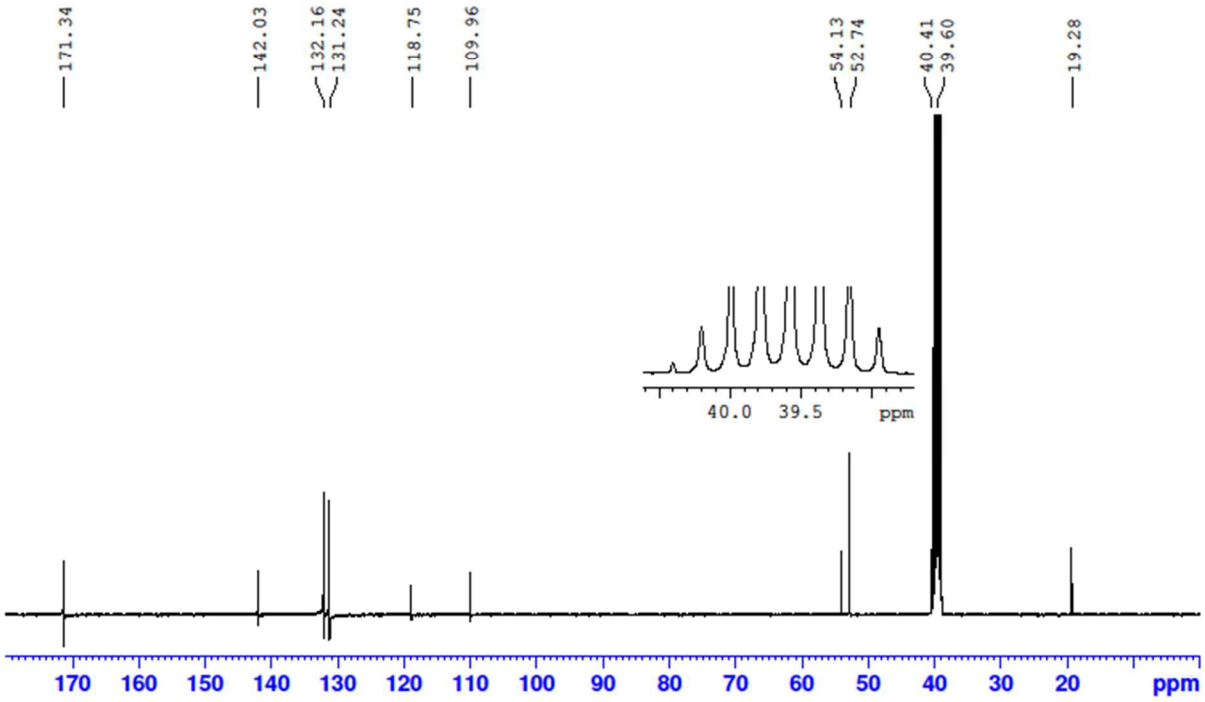


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

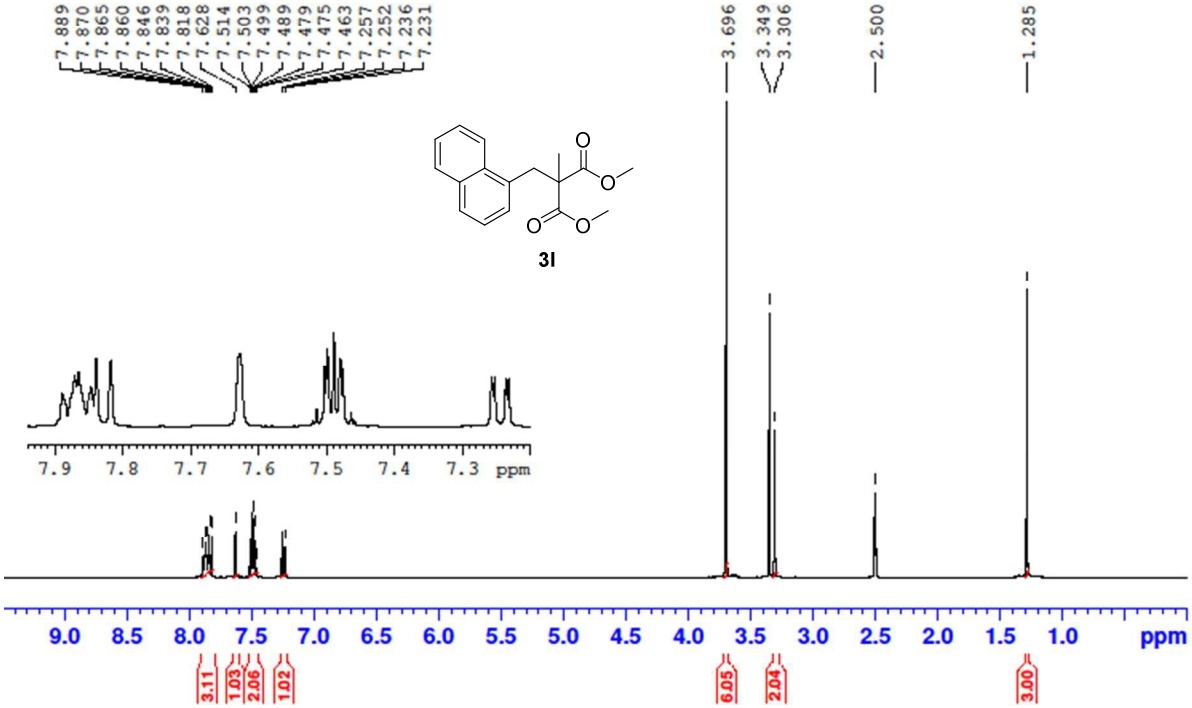


^{13}C NMR, d_6-DMSO, 101 MHz

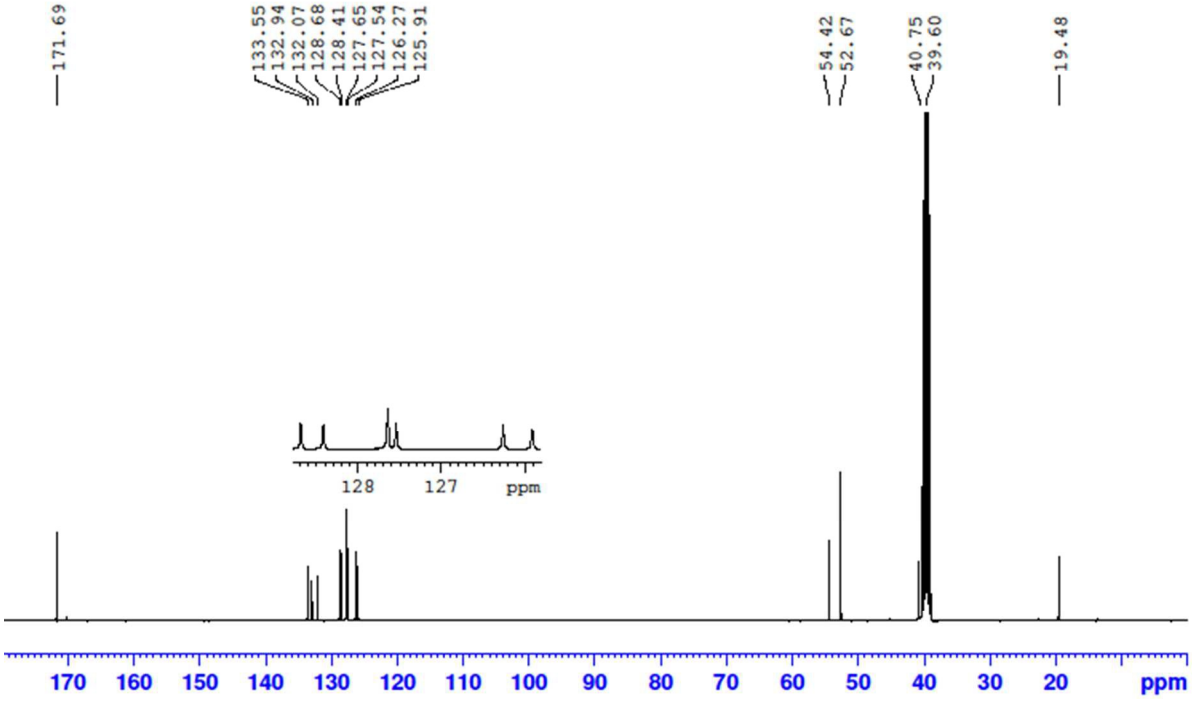


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

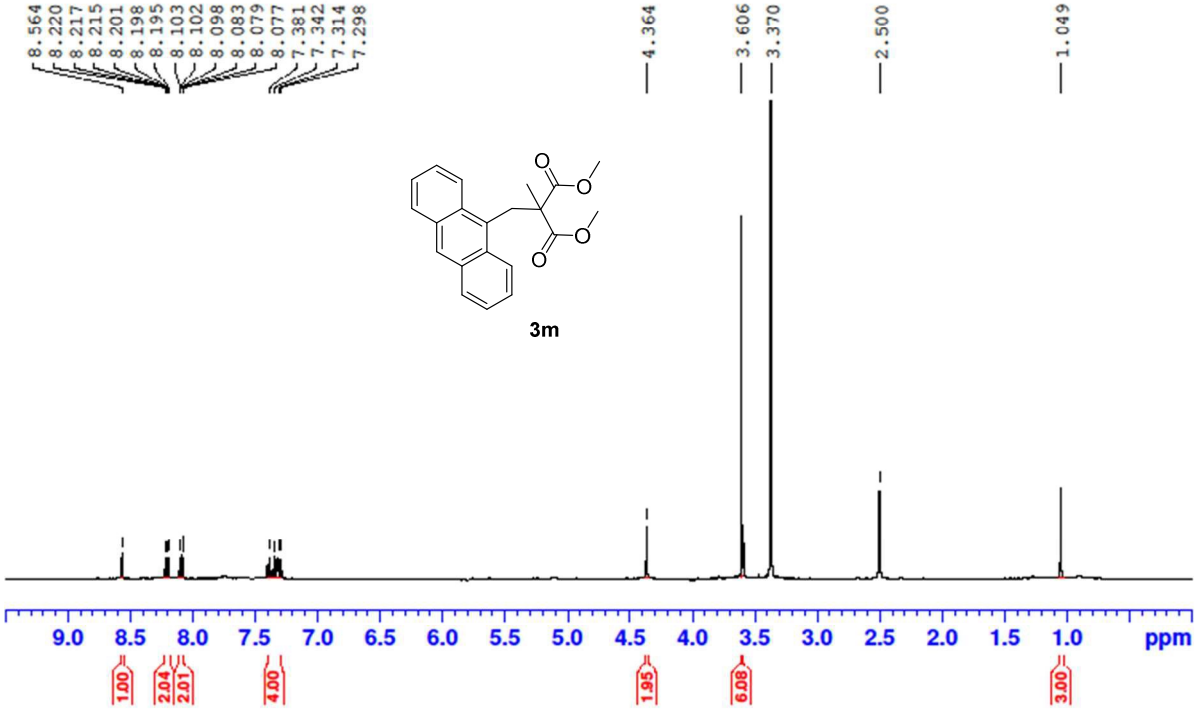


^{13}C NMR, d_6-DMSO, 101 MHz

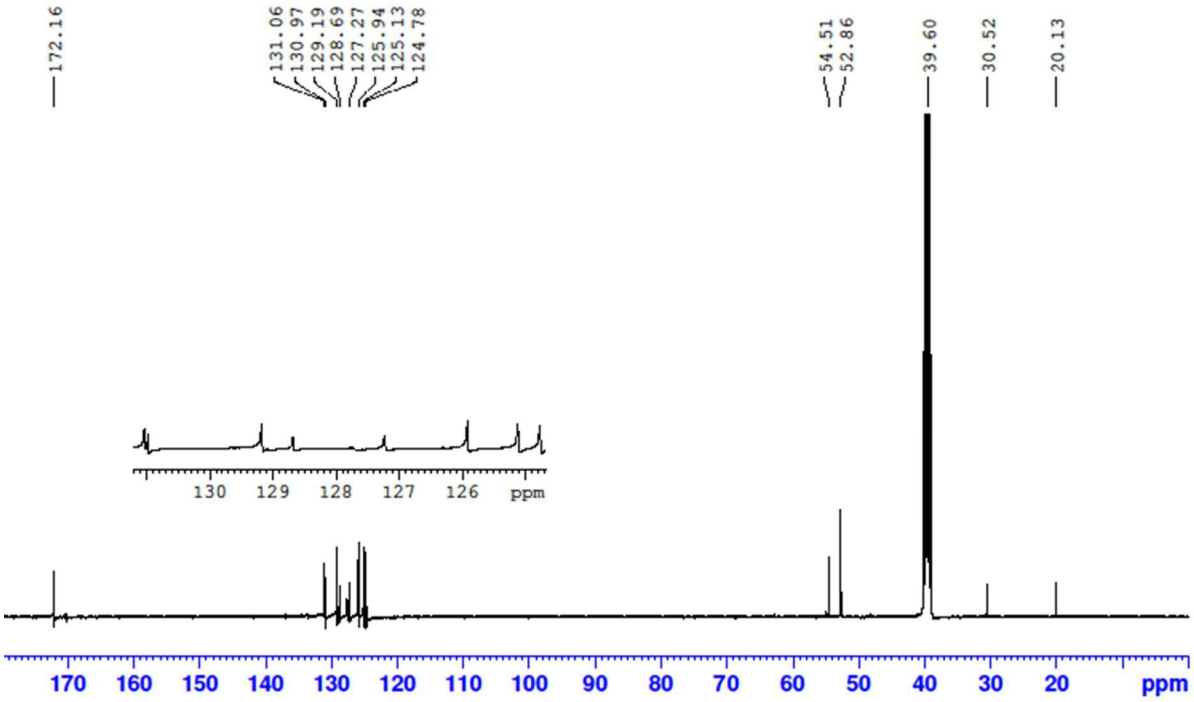


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

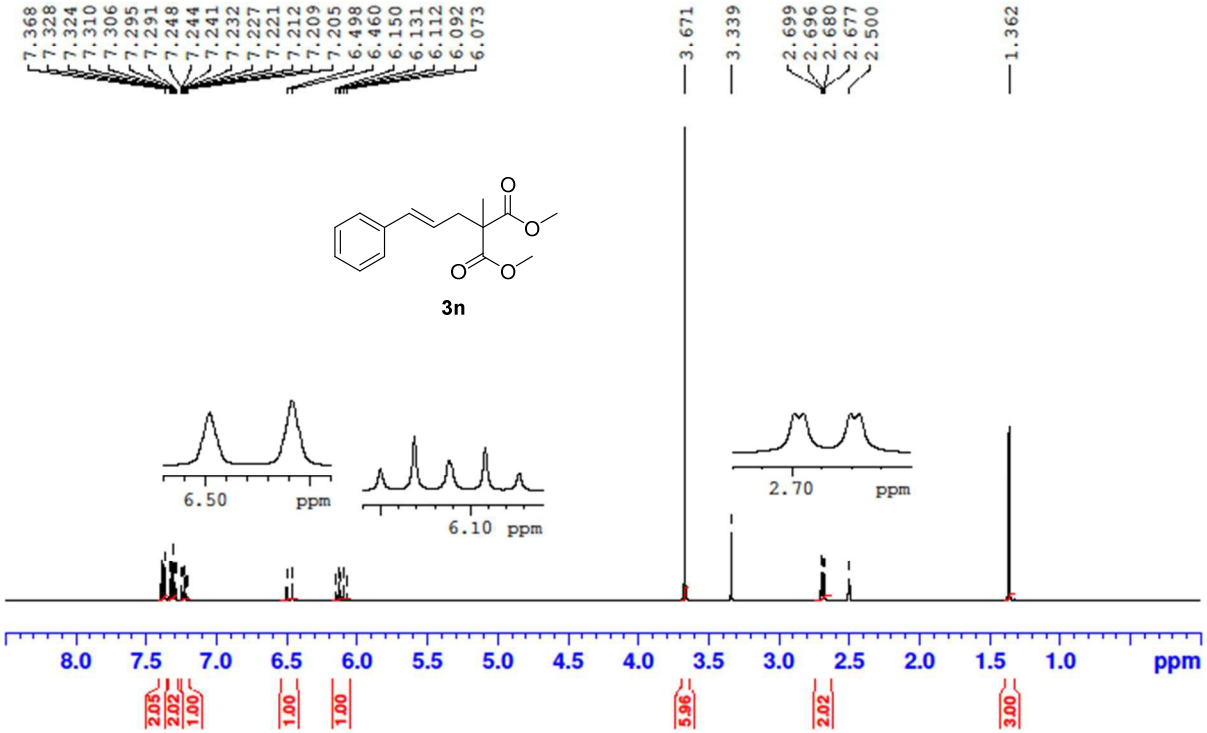


^{13}C NMR, d_6-DMSO, 101 MHz

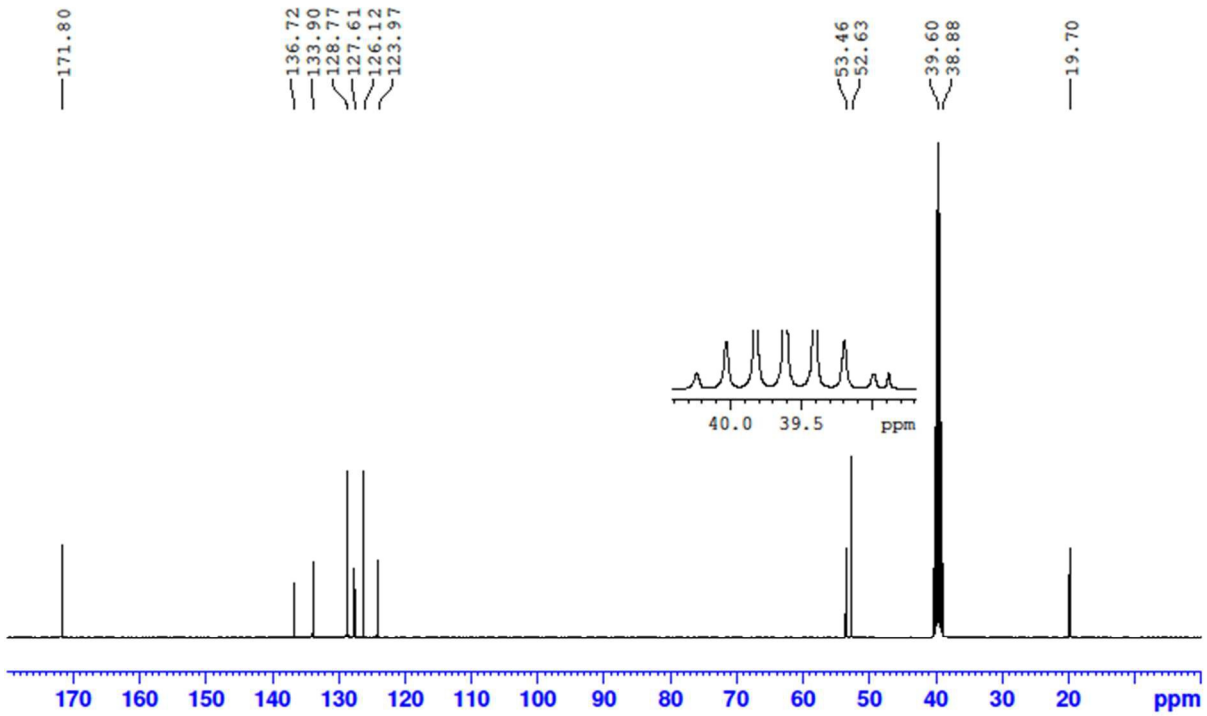


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

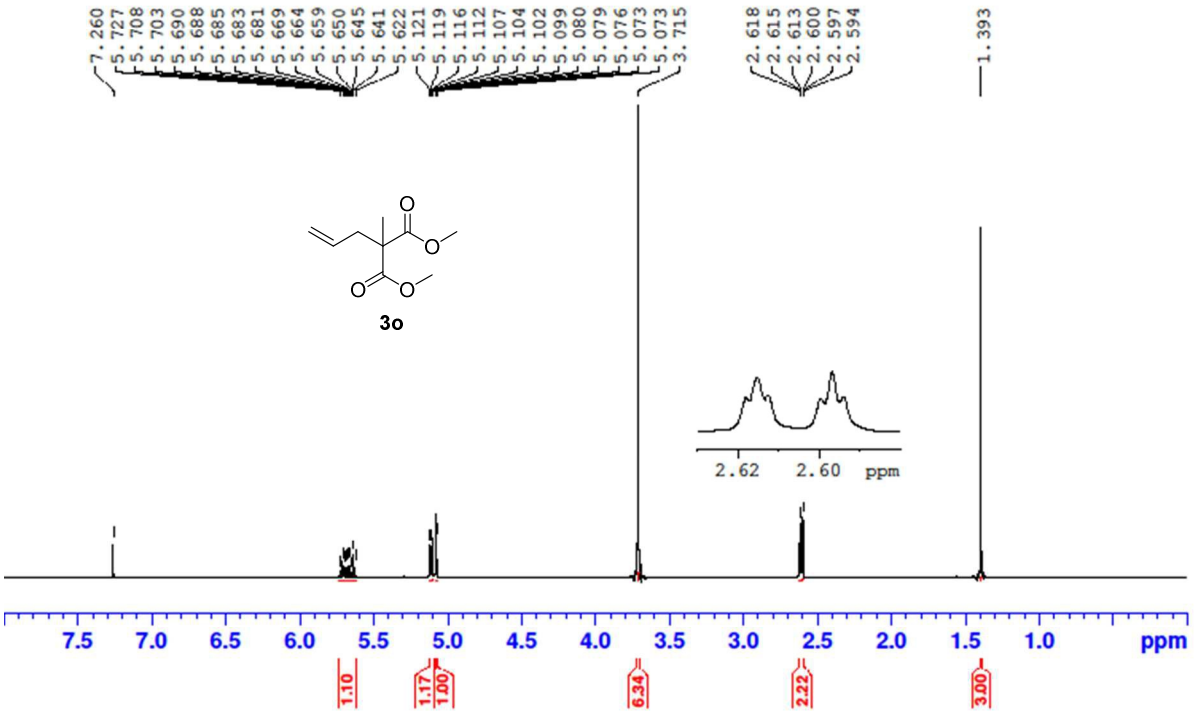


^{13}C NMR, d_6-DMSO, 101 MHz

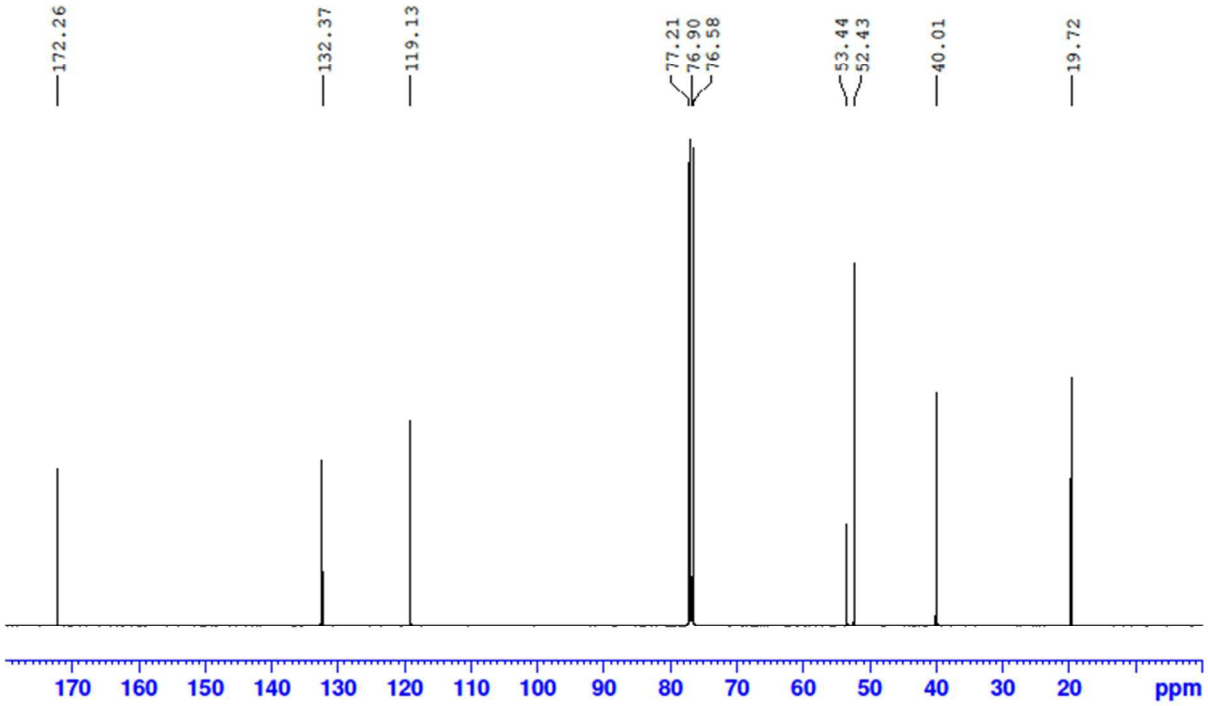


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, $CDCl_3$, 400 MHz

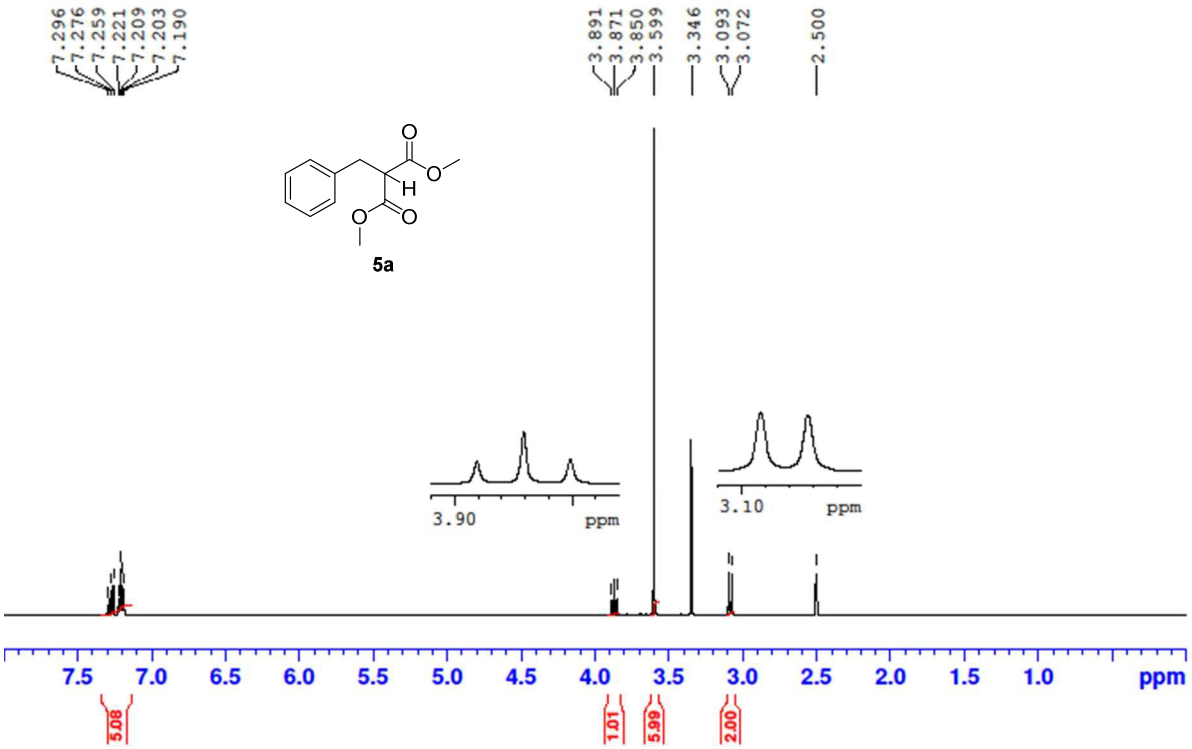


^{13}C NMR, $CDCl_3$, 101 MHz

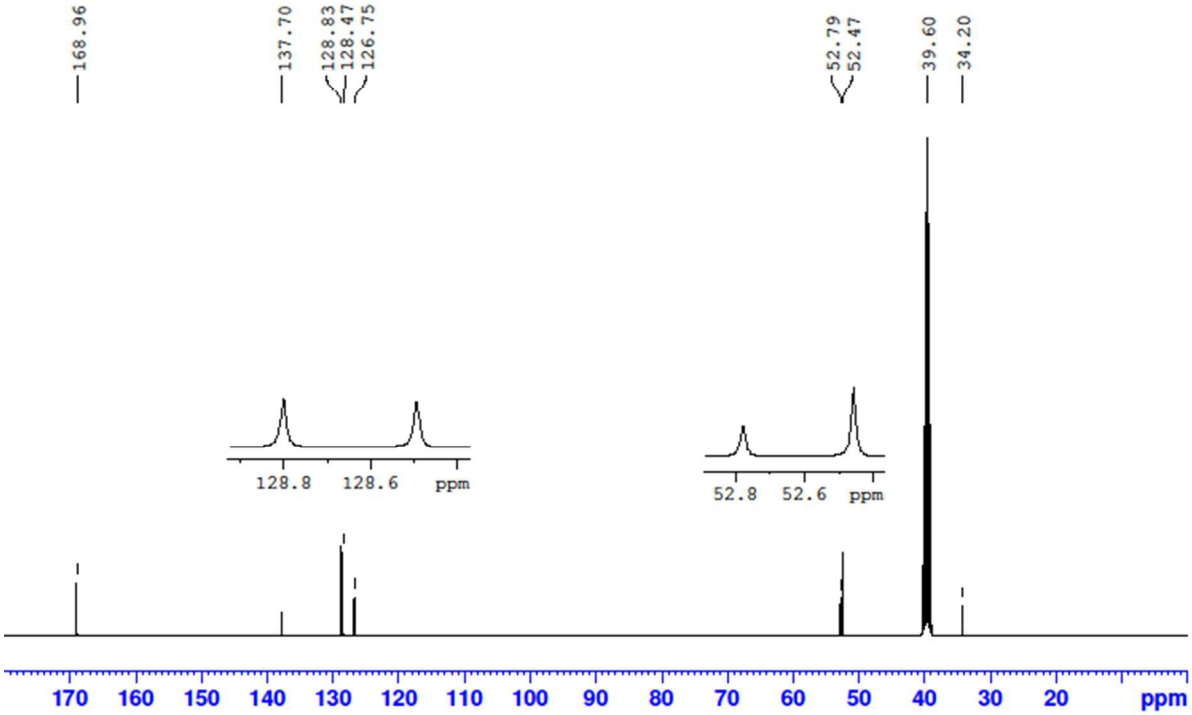


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

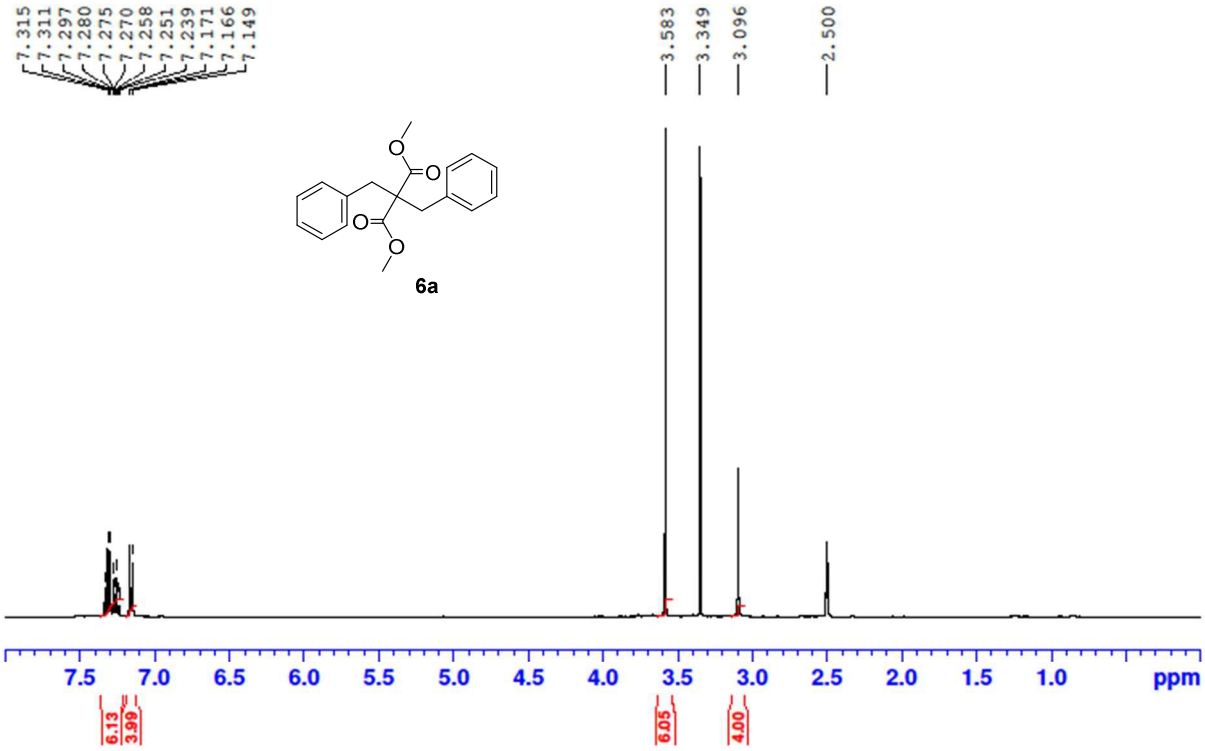


^{13}C NMR, d_6-DMSO, 101 MHz

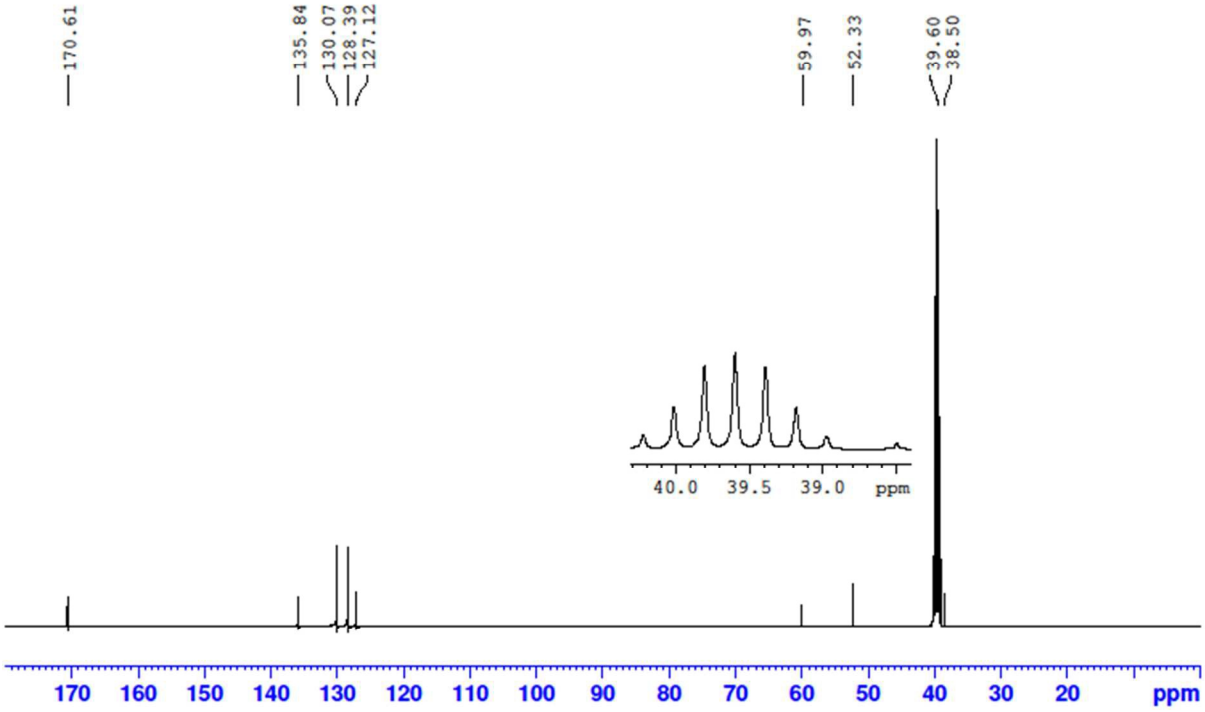


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

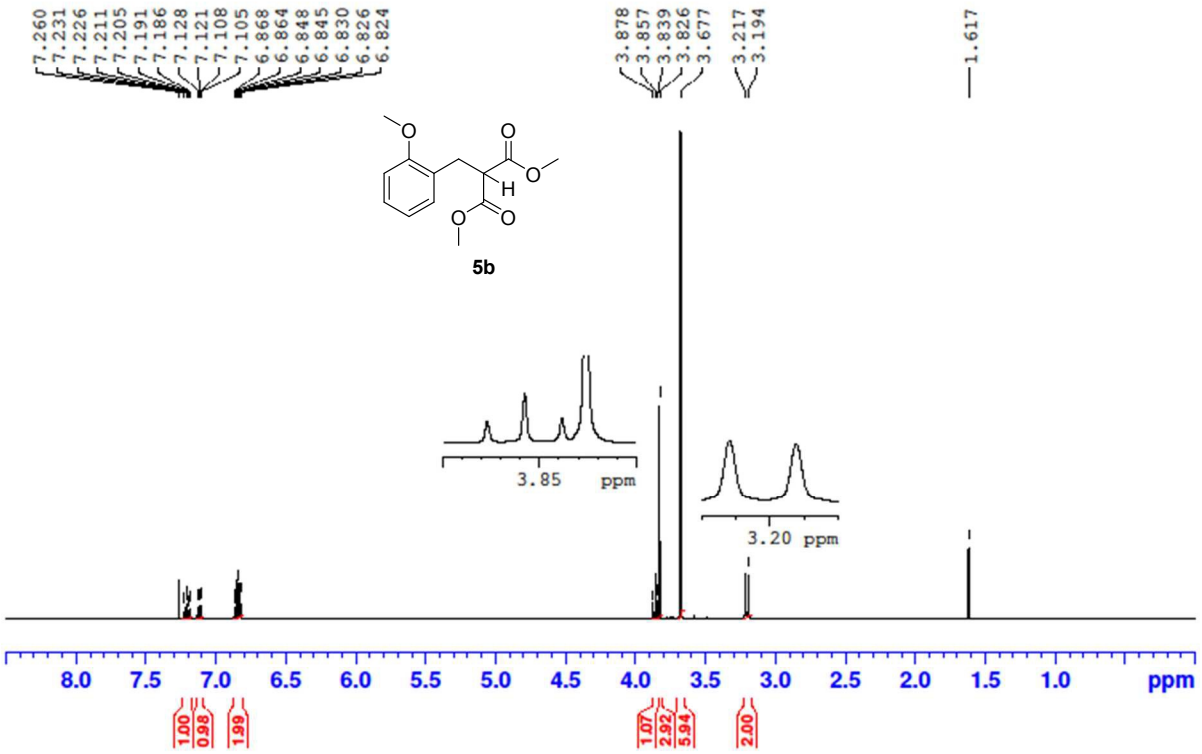


^{13}C NMR, d_6-DMSO, 101 MHz

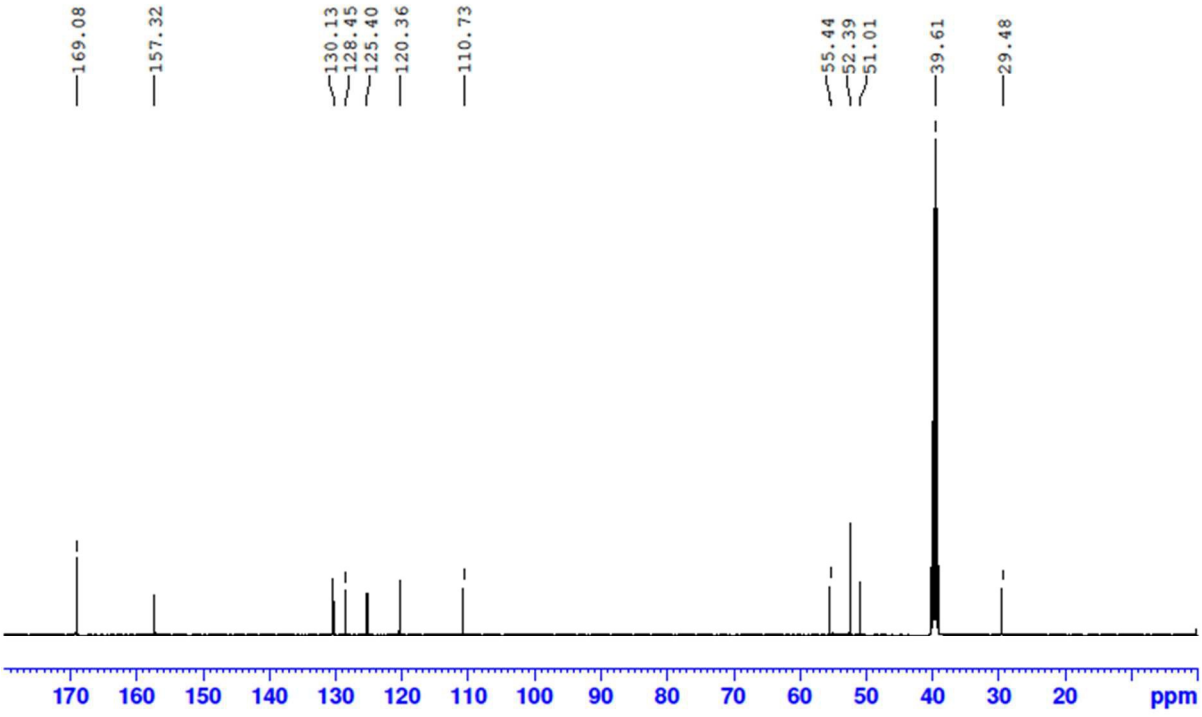


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, $CDCl_3$, 400 MHz

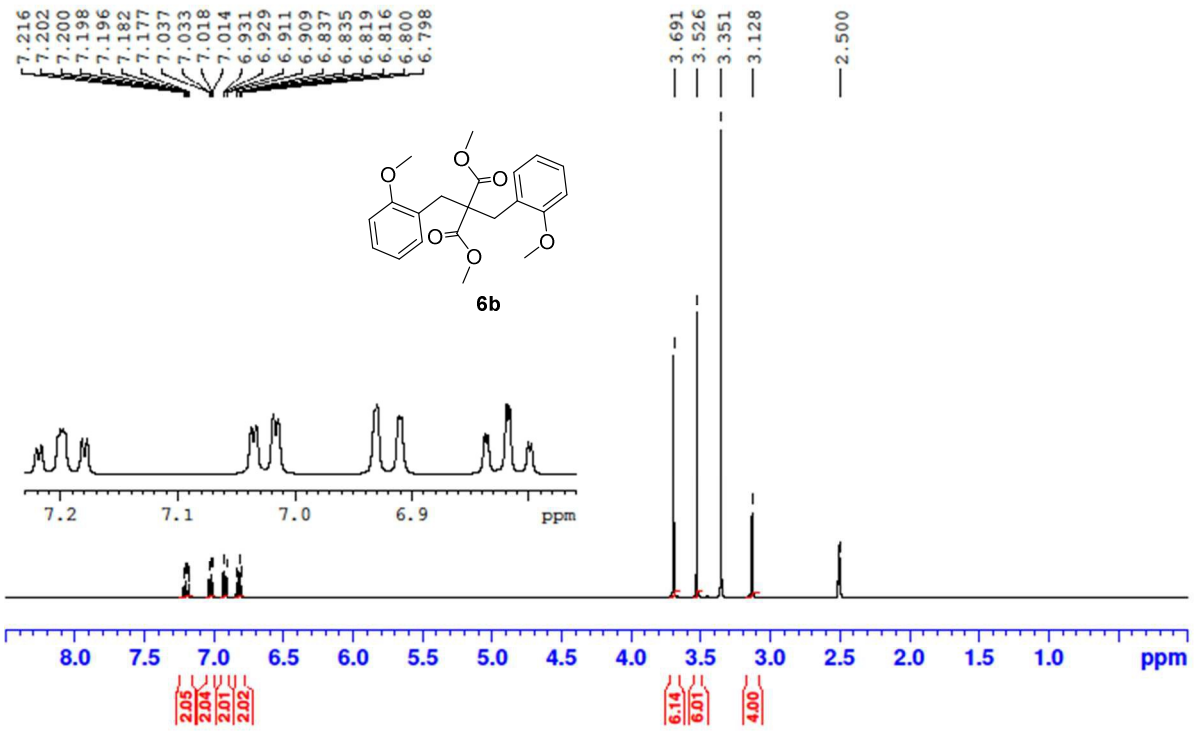


^{13}C NMR, d_6-DMSO, 101 MHz

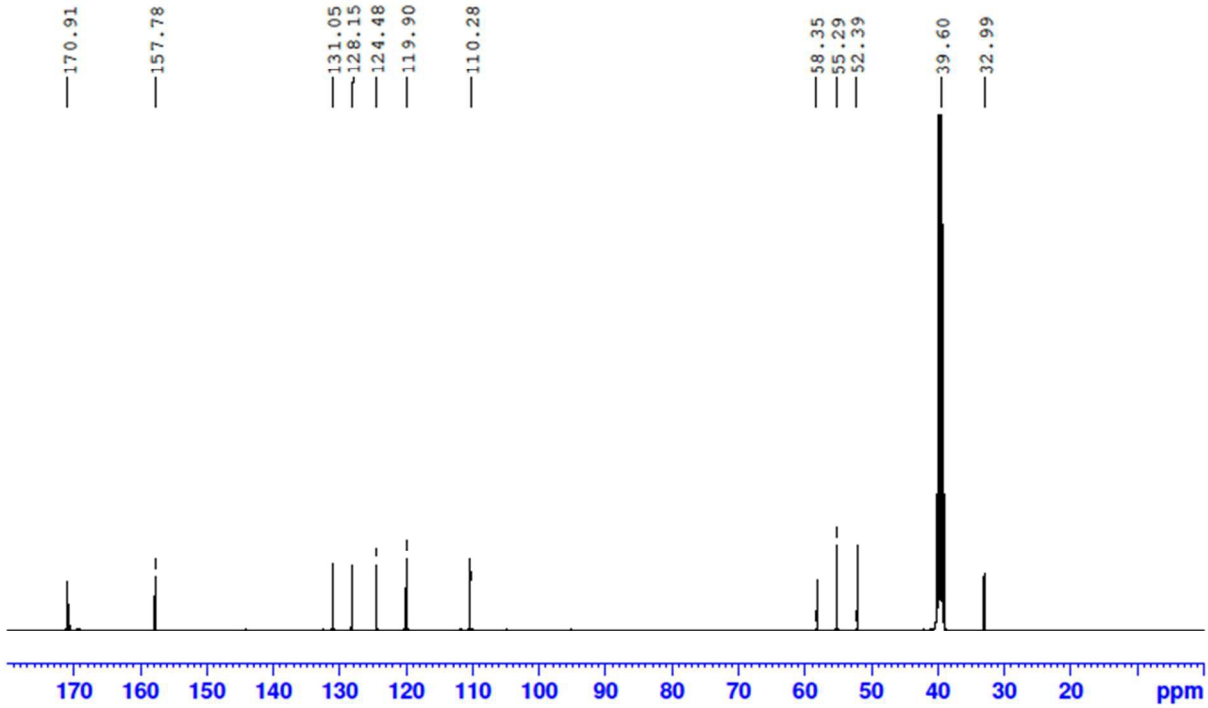


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

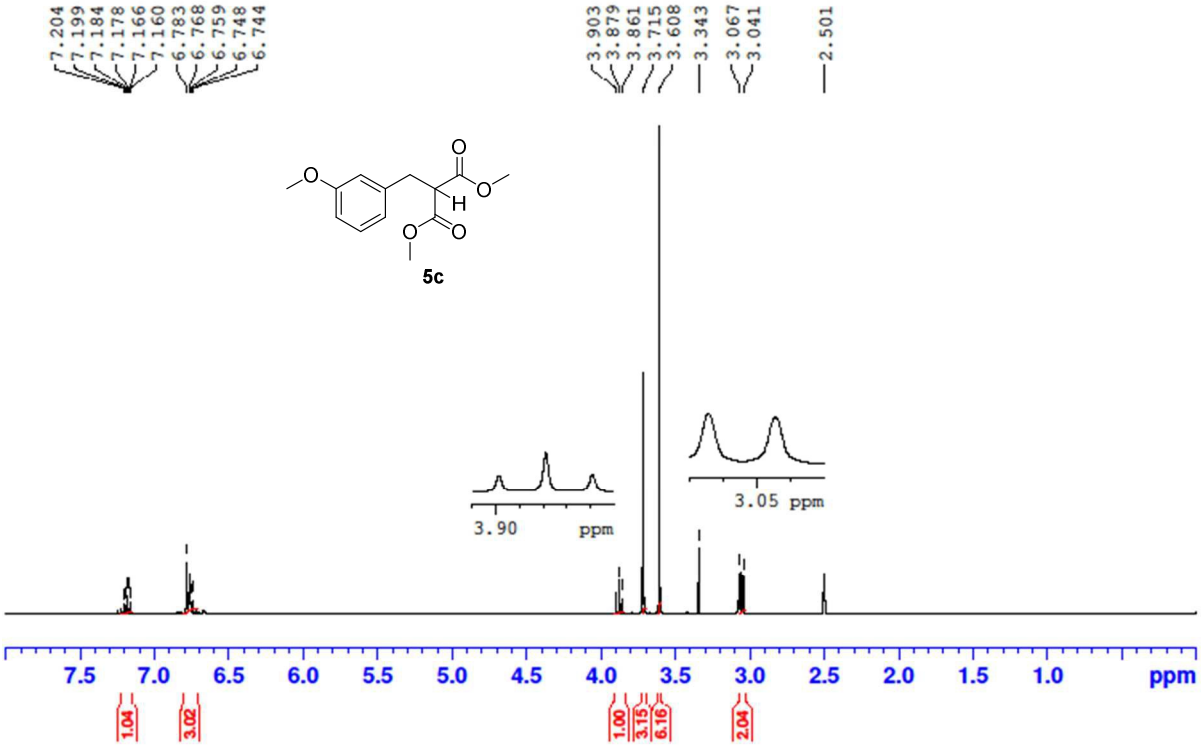


^{13}C NMR, d_6-DMSO, 101 MHz

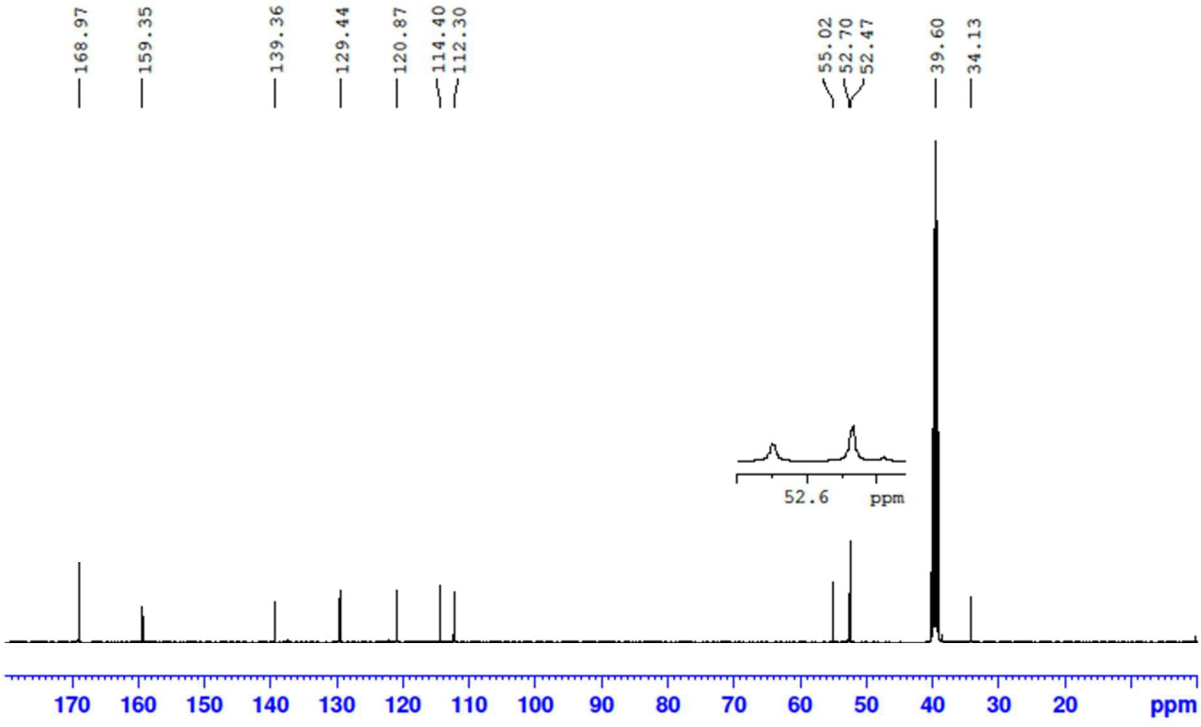


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

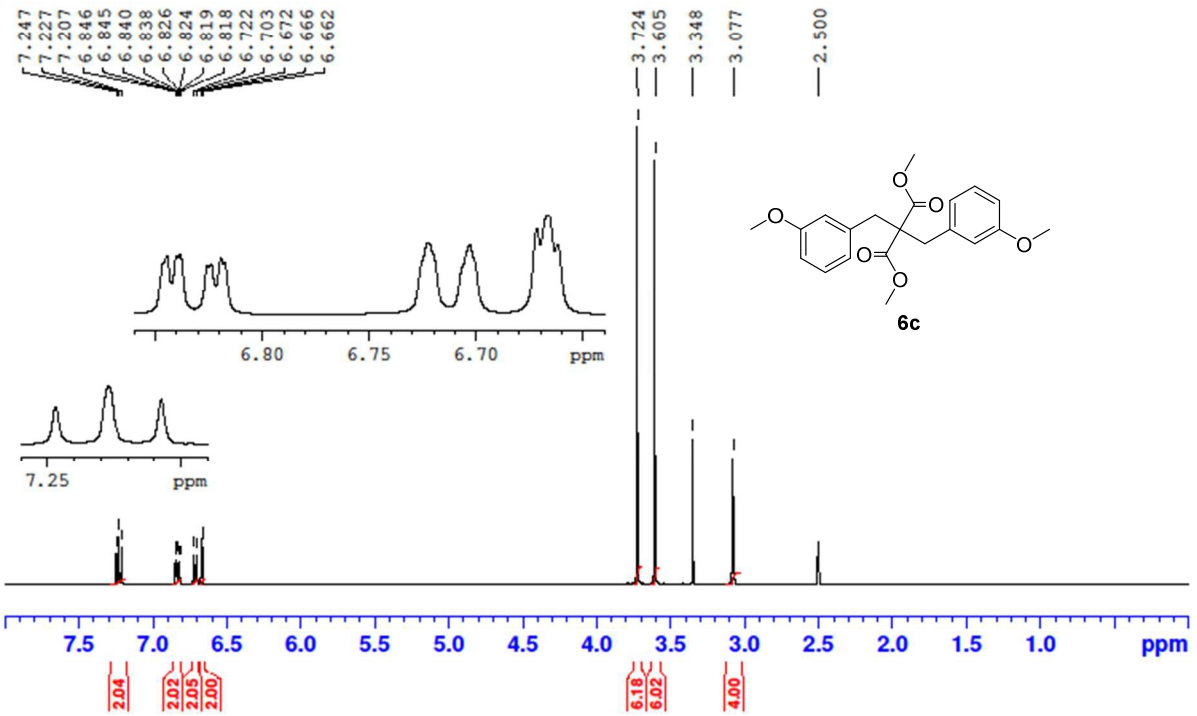


^{13}C NMR, d_6-DMSO, 101 MHz

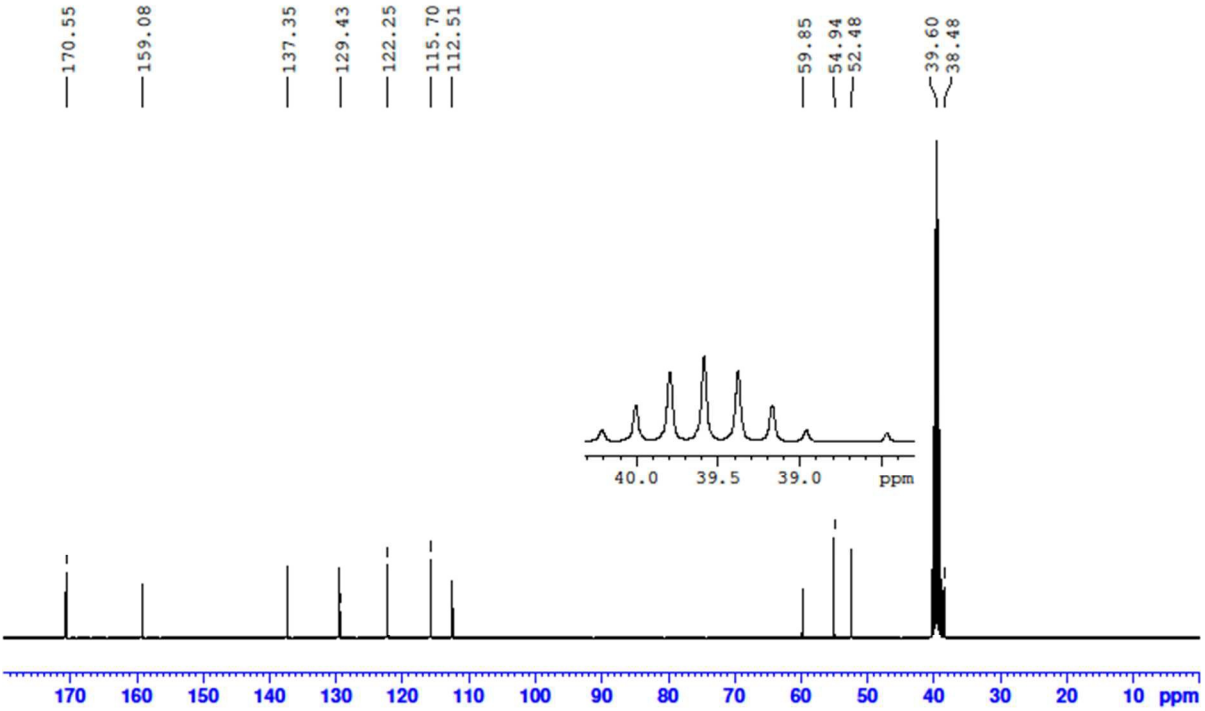


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

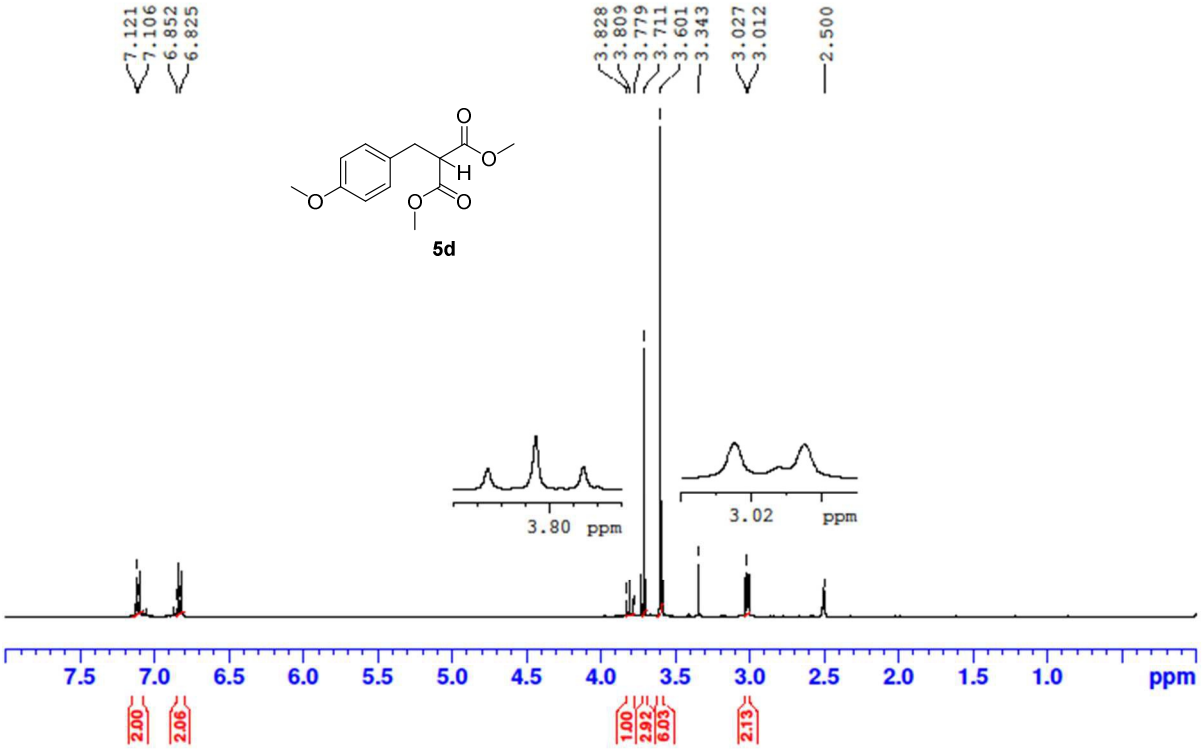


^{13}C NMR, d_6-DMSO, 101 MHz

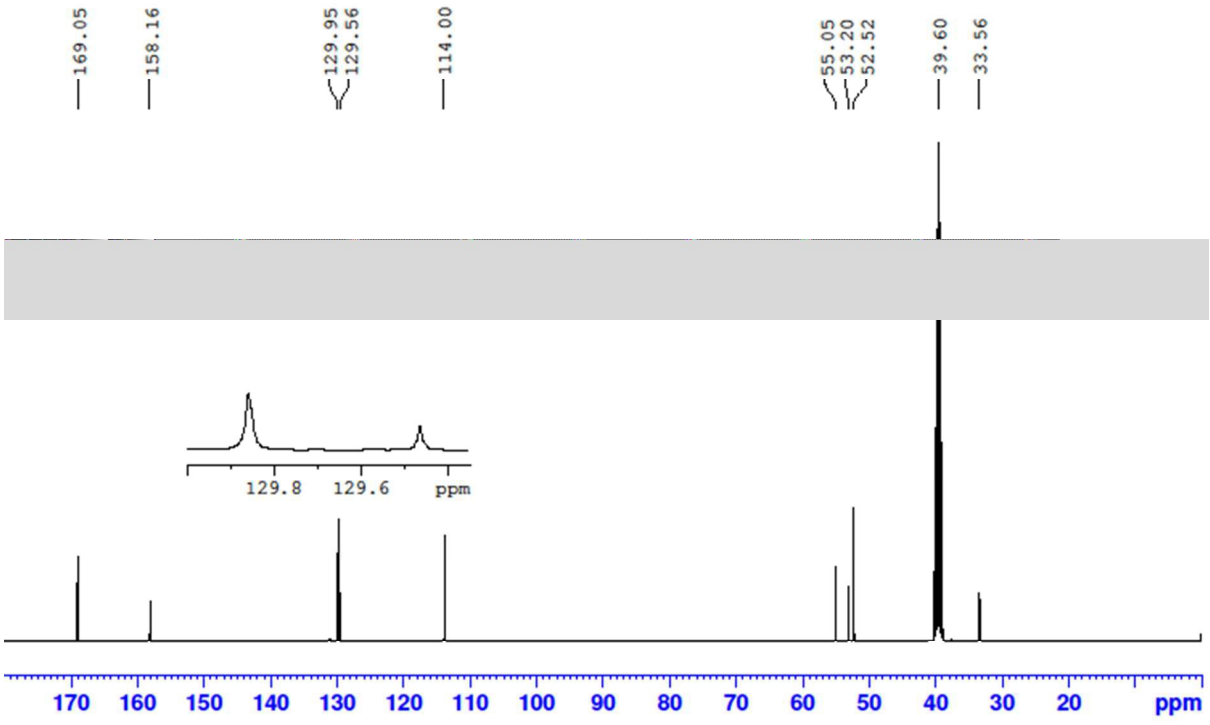


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

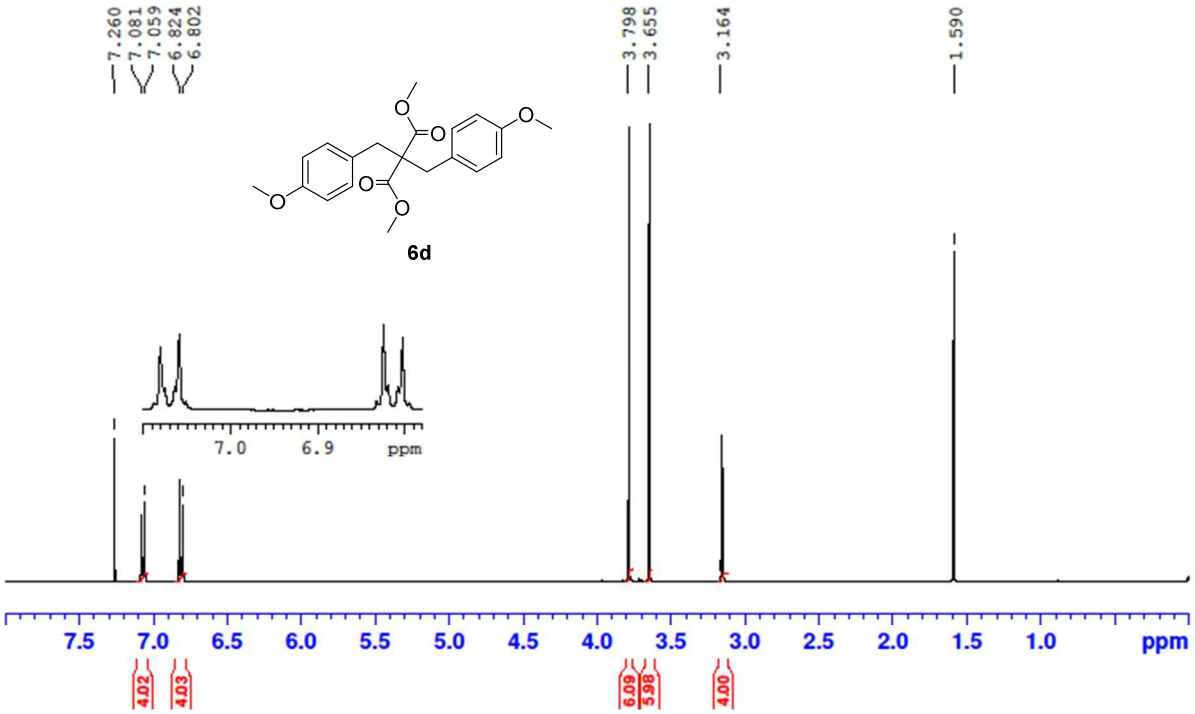


^{13}C NMR, d_6-DMSO, 101 MHz

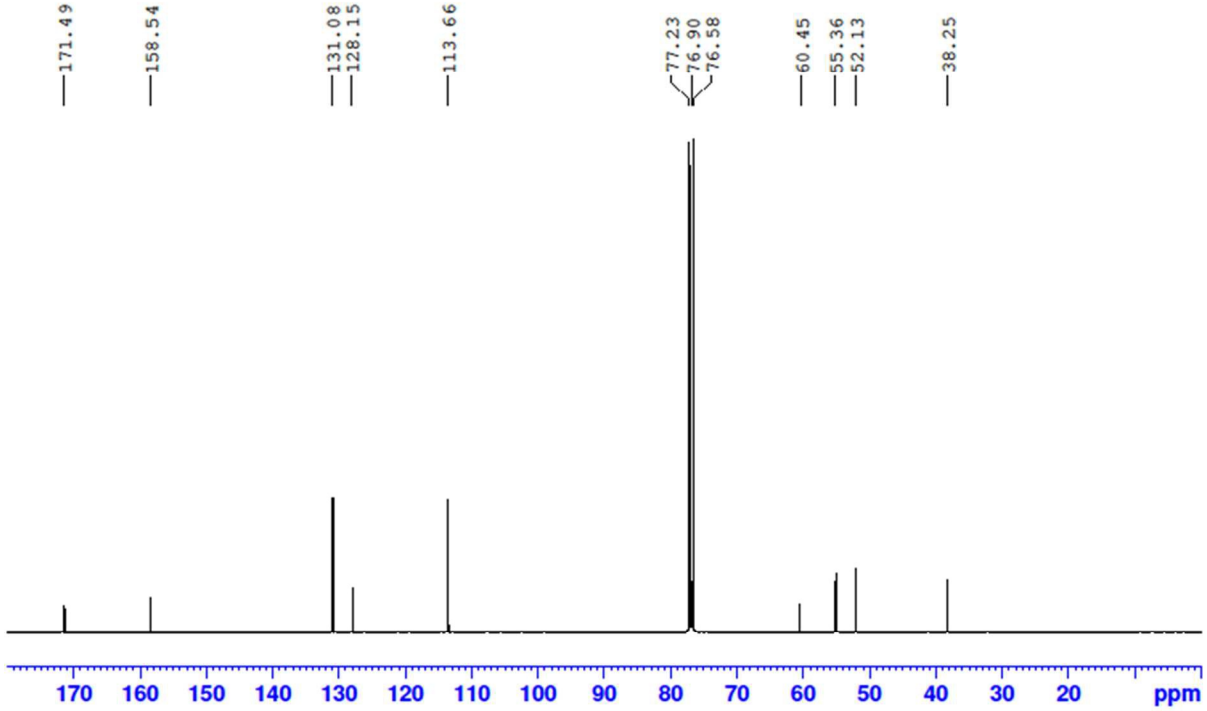


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, $CDCl_3$, 400 MHz

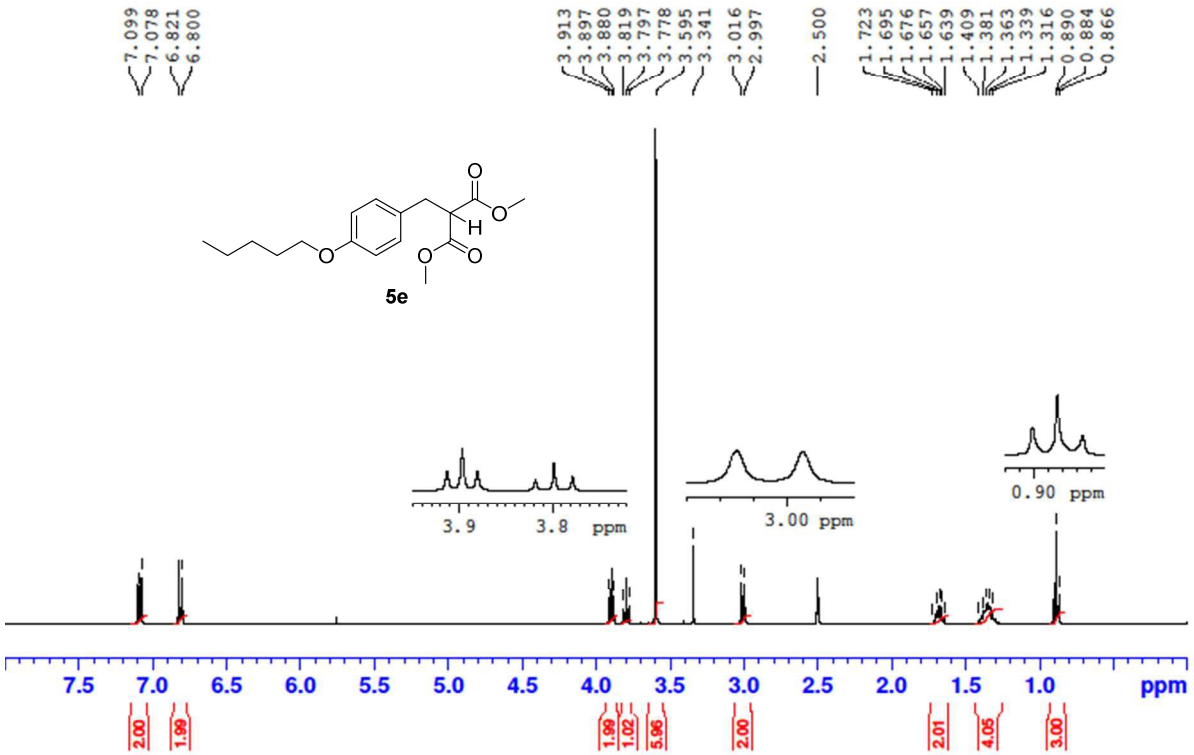


^{13}C NMR, $CDCl_3$, 101 MHz

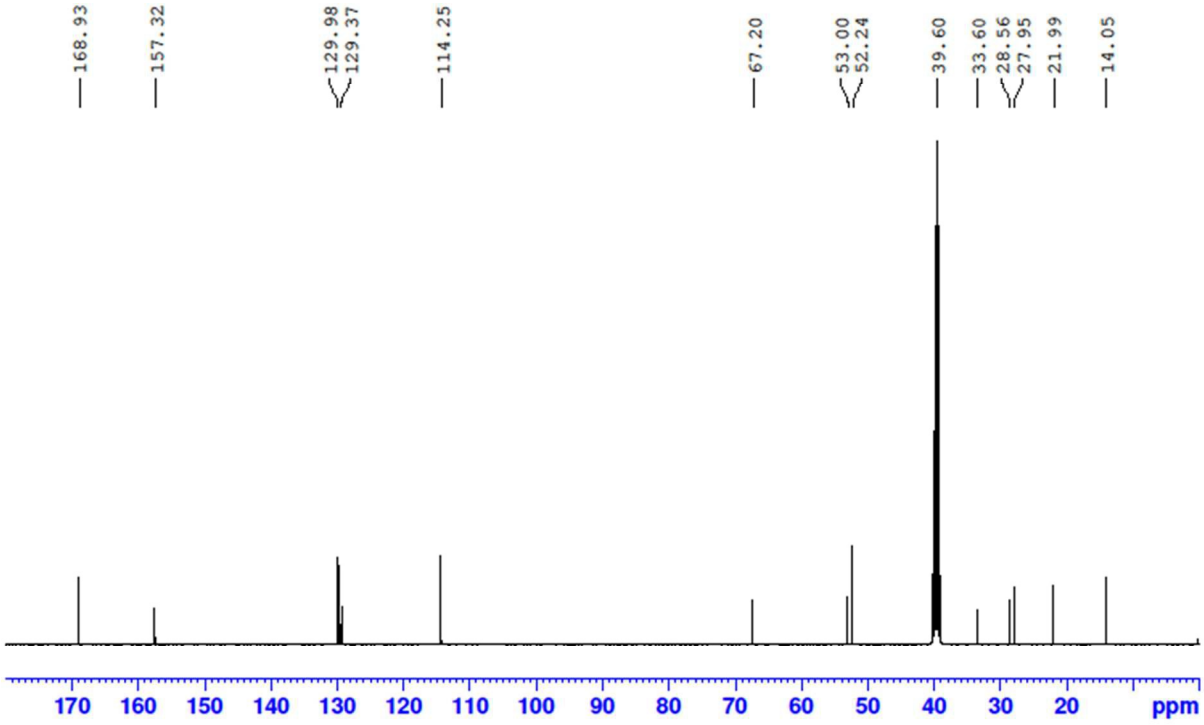


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

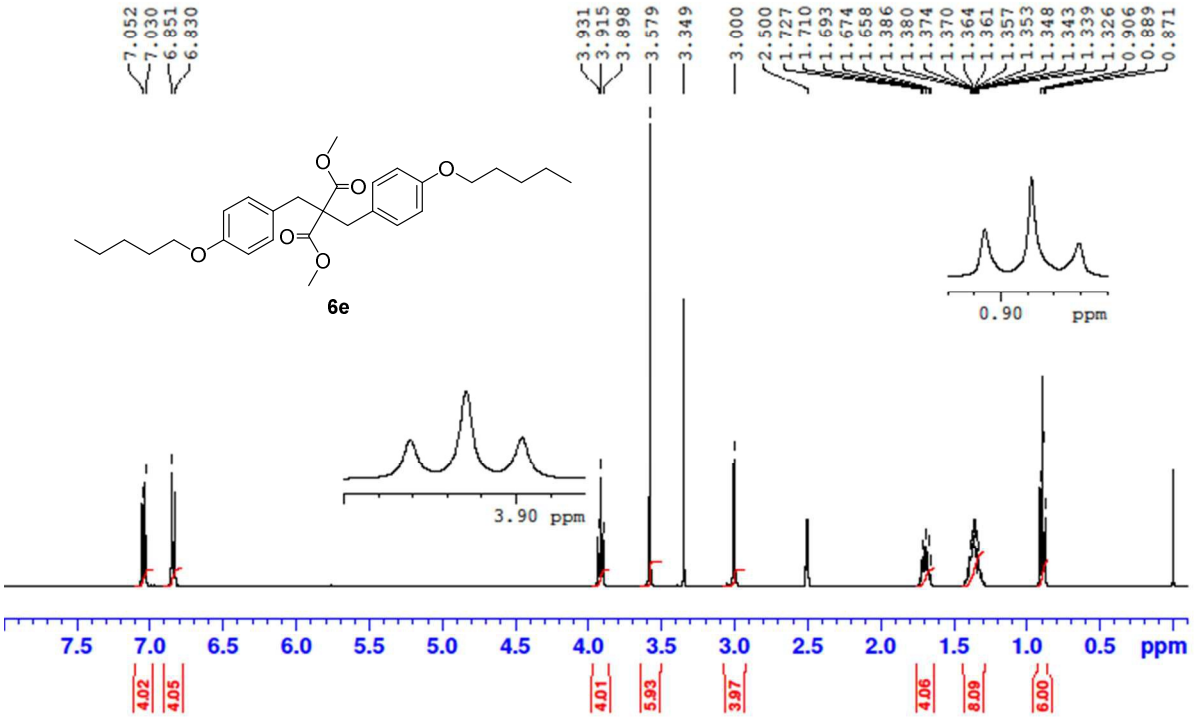


^{13}C NMR, d_6-DMSO, 101 MHz

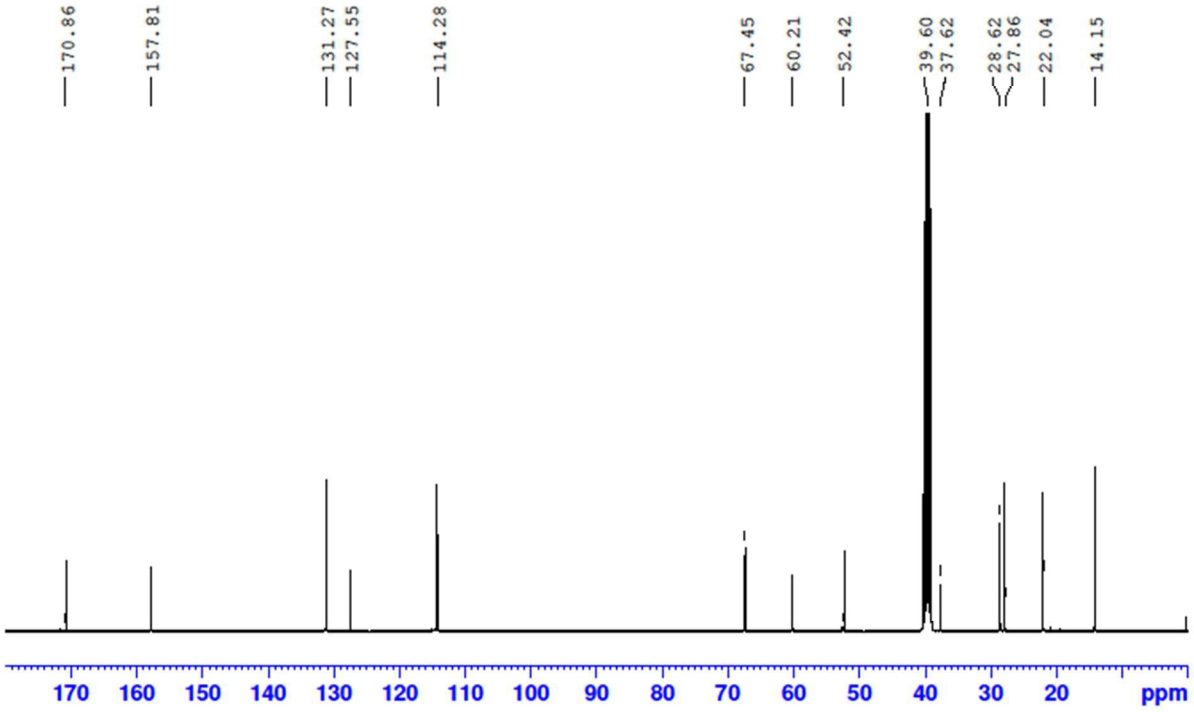


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

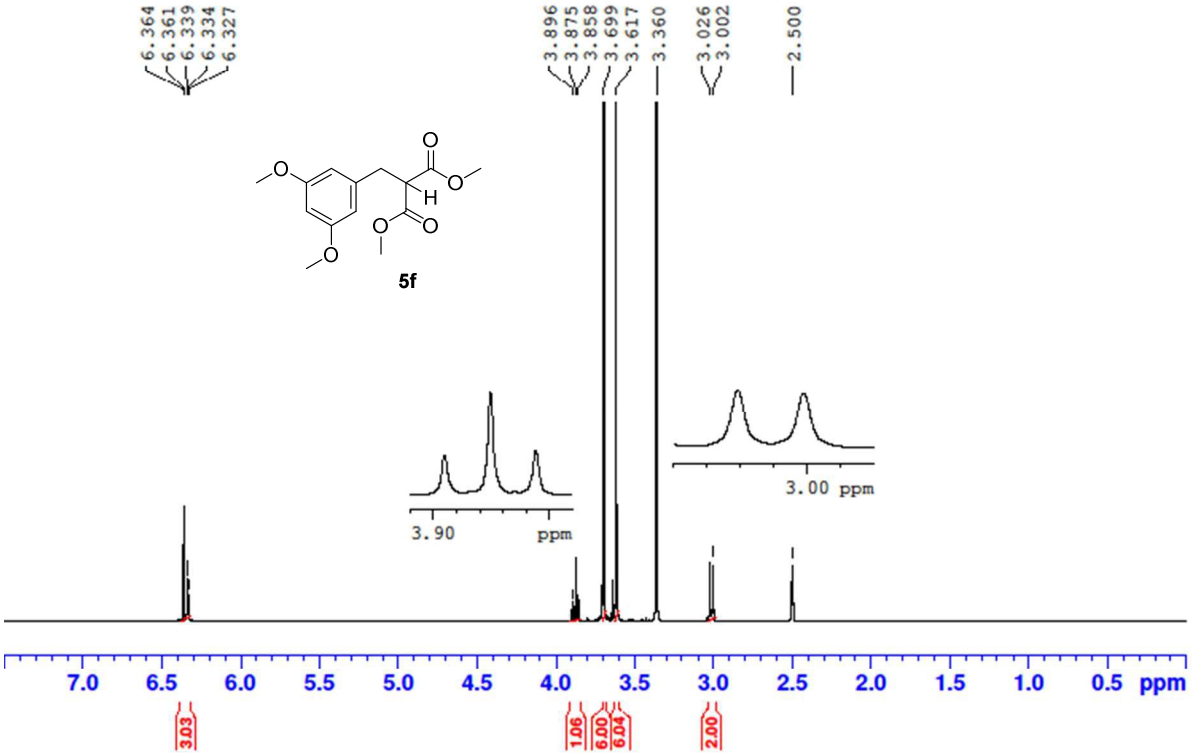


^{13}C NMR, d_6-DMSO, 101 MHz

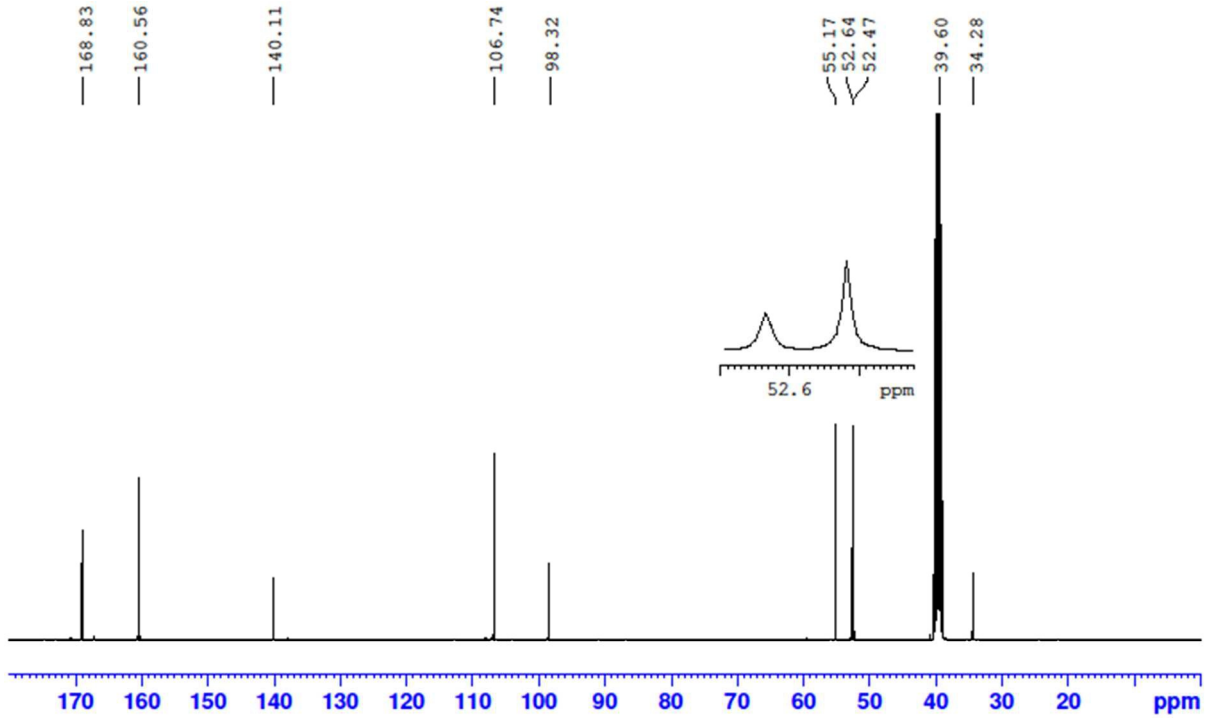


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

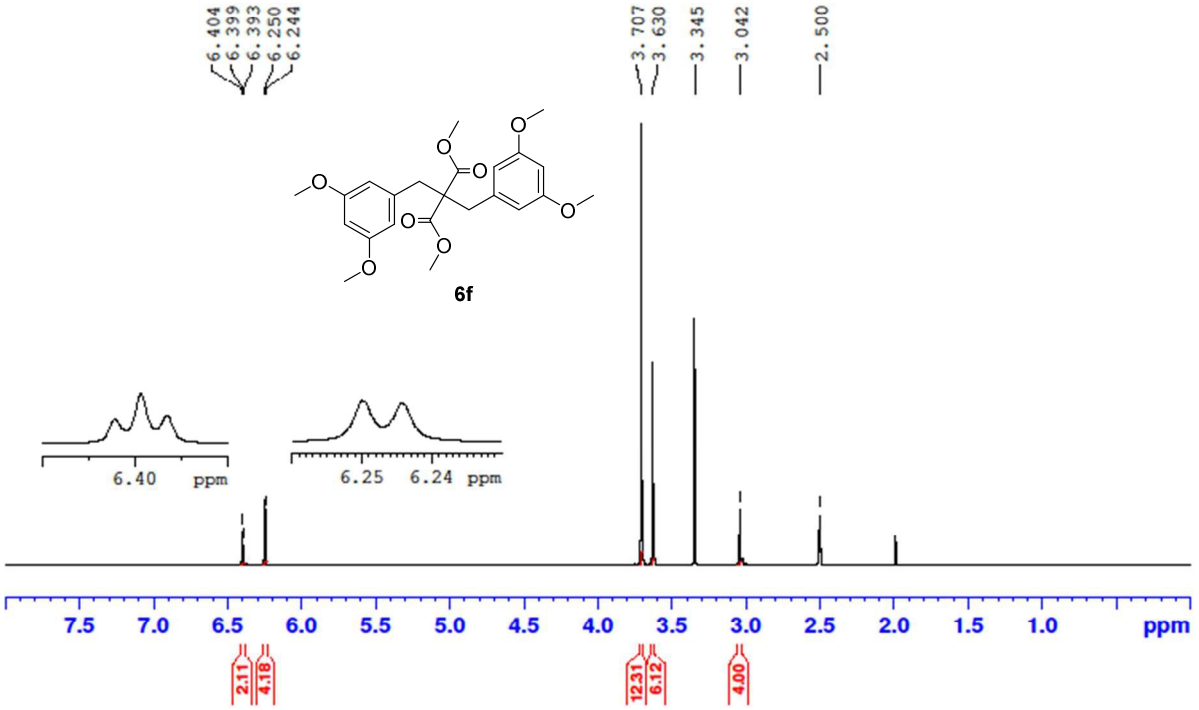


^{13}C NMR, d_6-DMSO, 101 MHz

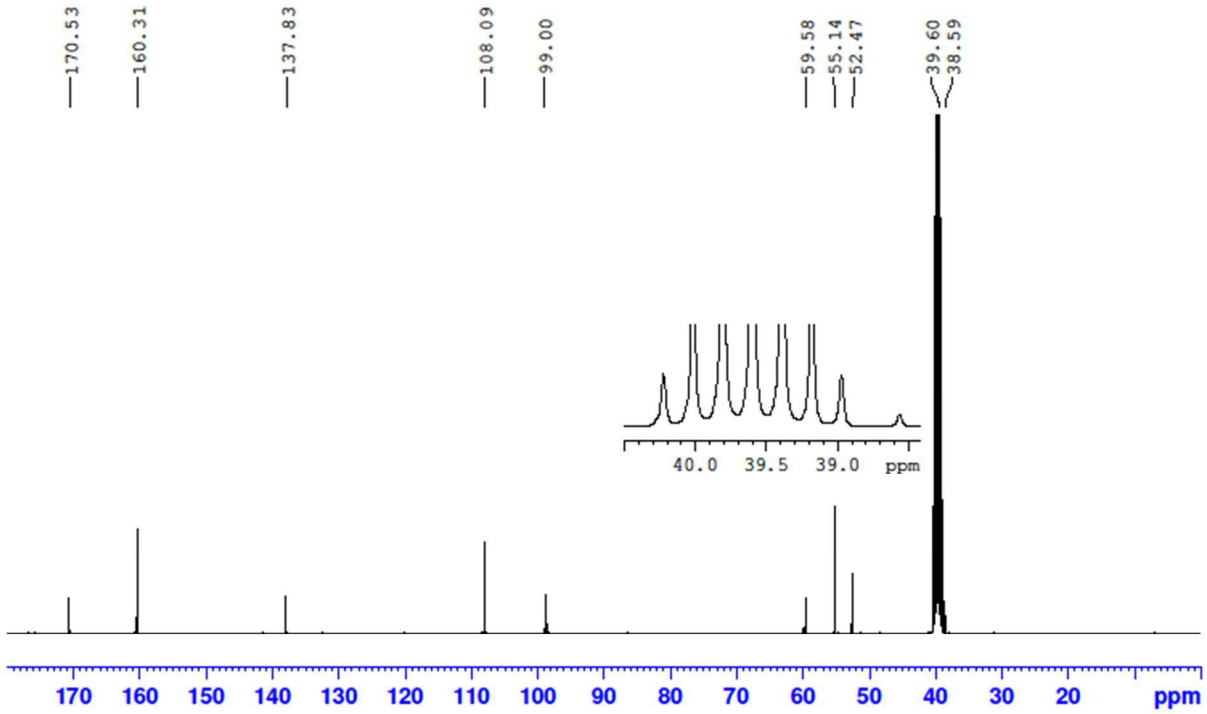


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

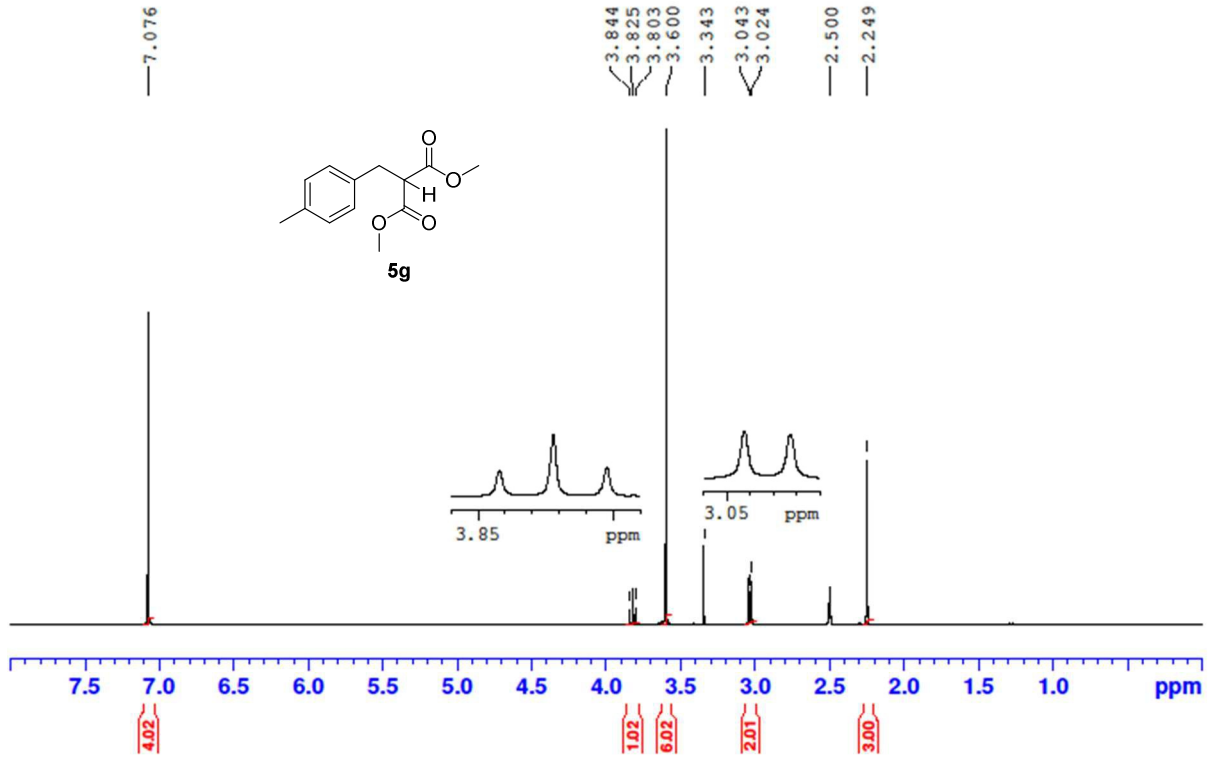


^{13}C NMR, d_6-DMSO, 101 MHz

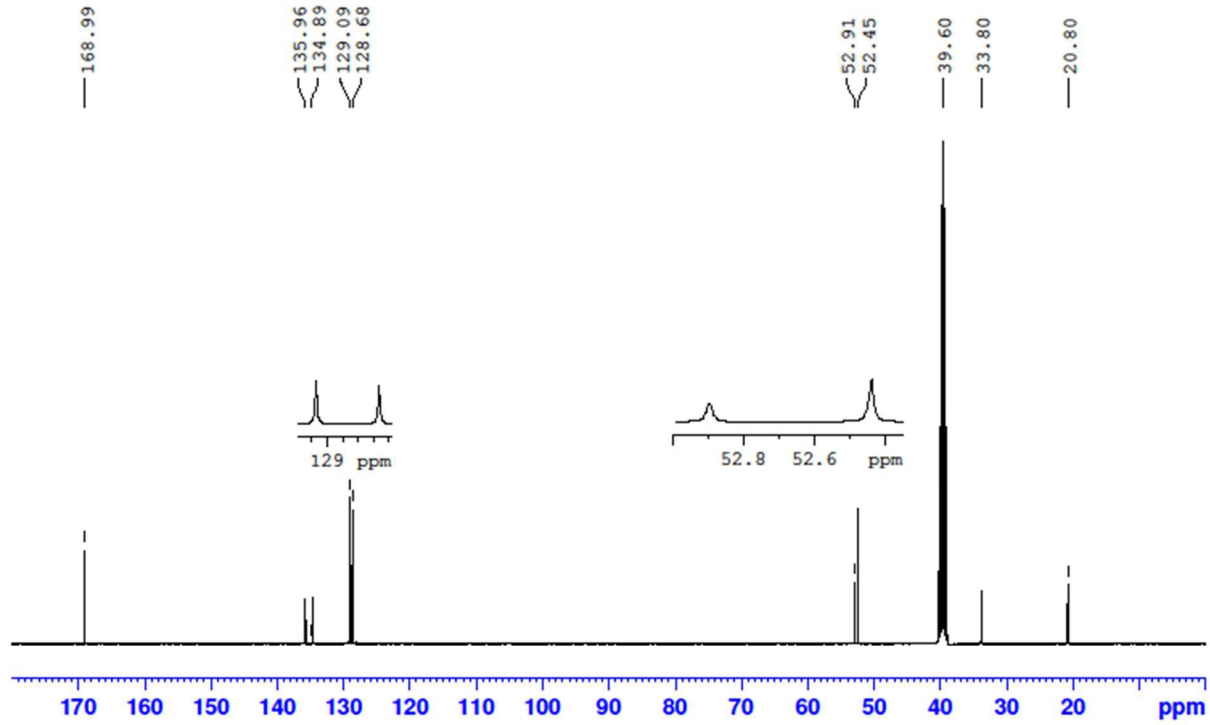


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

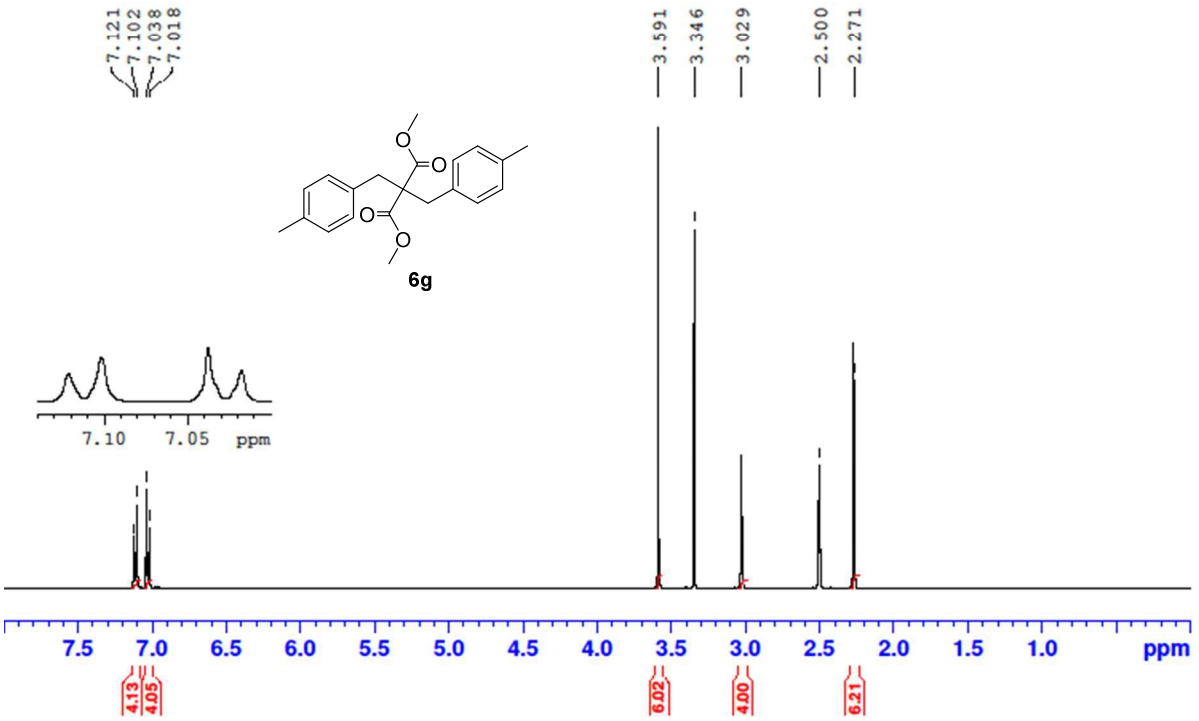


^{13}C NMR, d_6-DMSO, 101 MHz

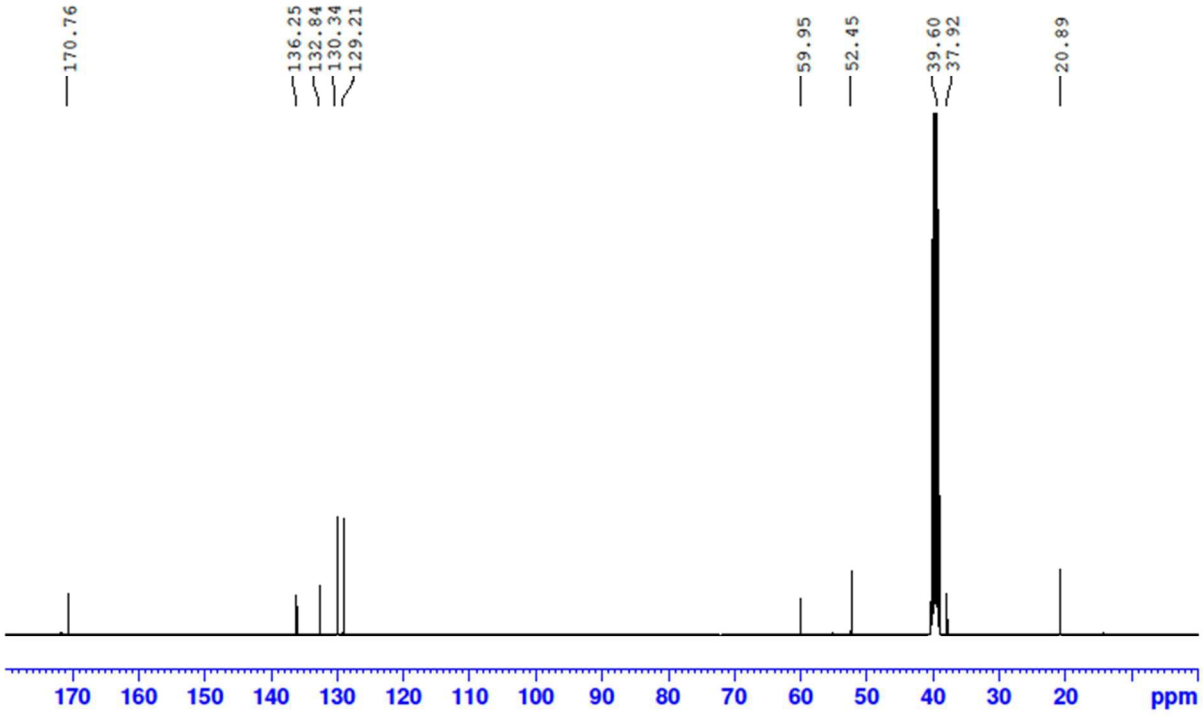


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

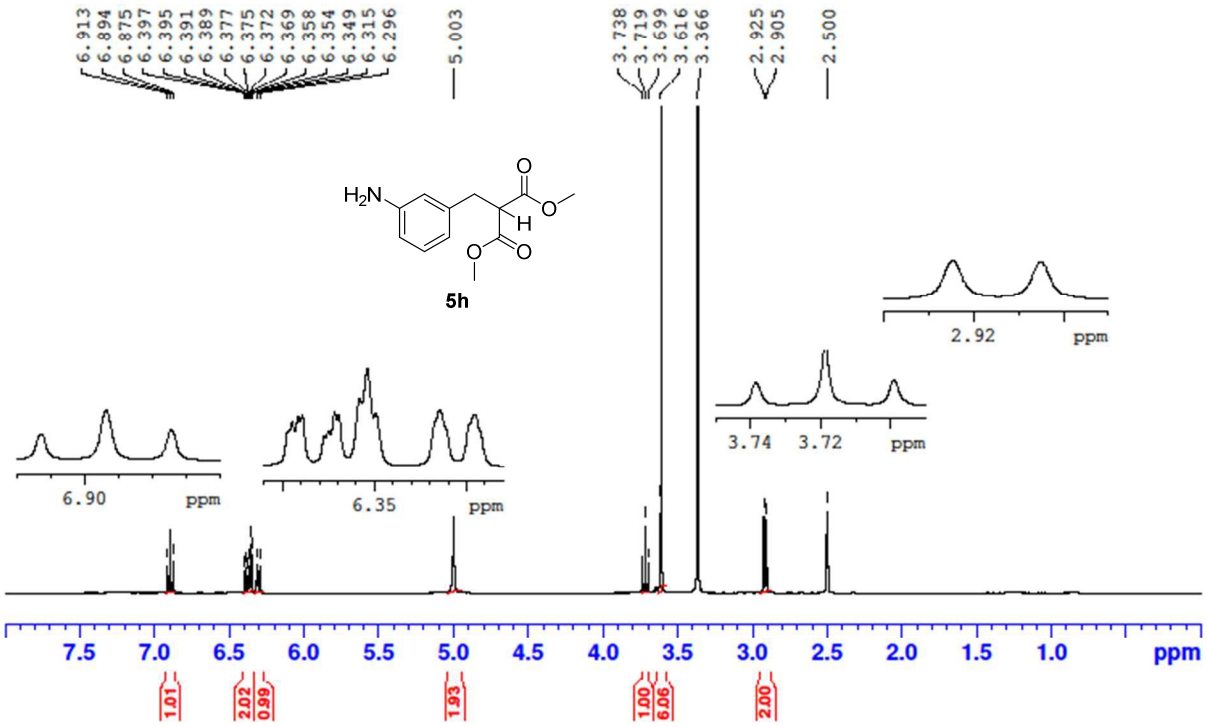


^{13}C NMR, d_6-DMSO, 101 MHz

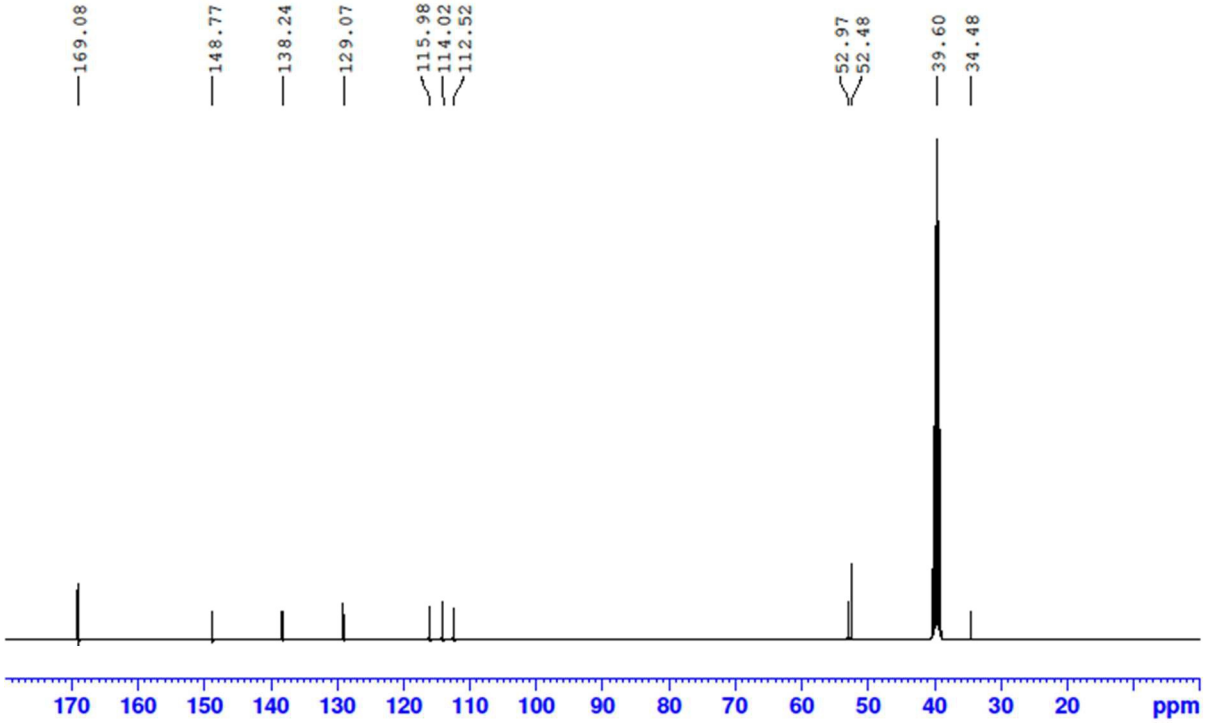


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

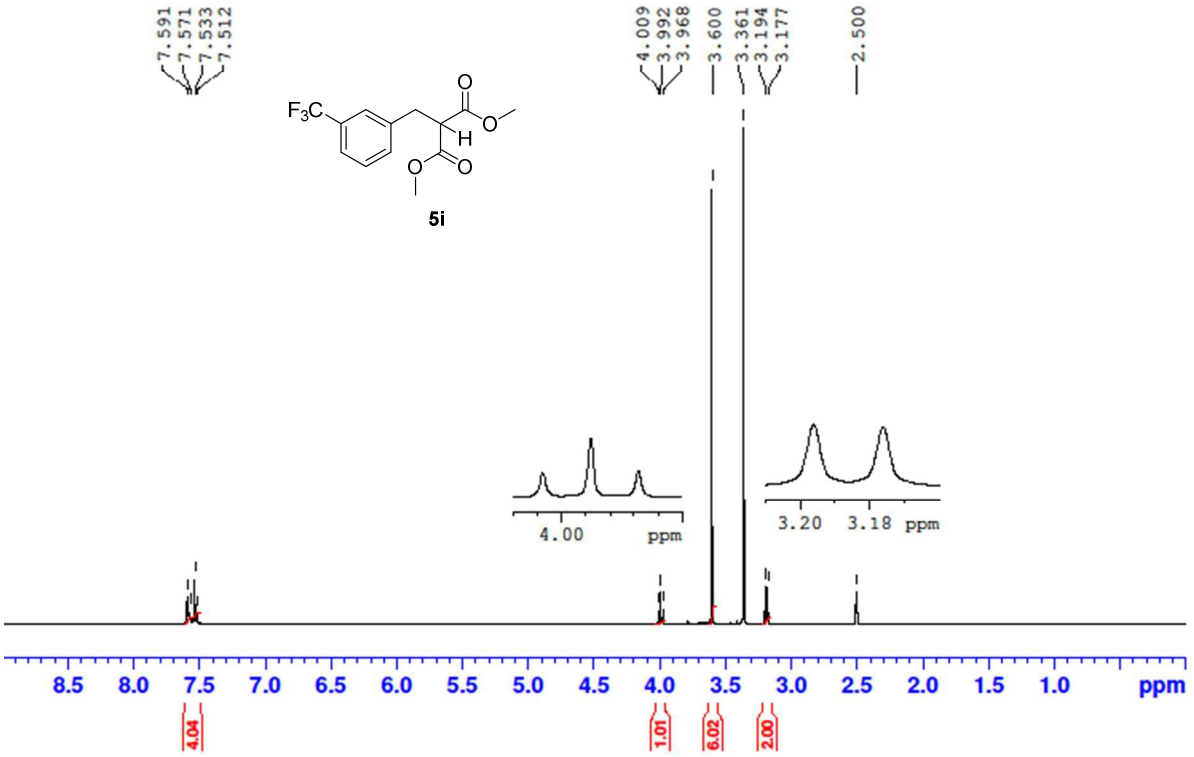


^{13}C NMR, d_6-DMSO, 101 MHz

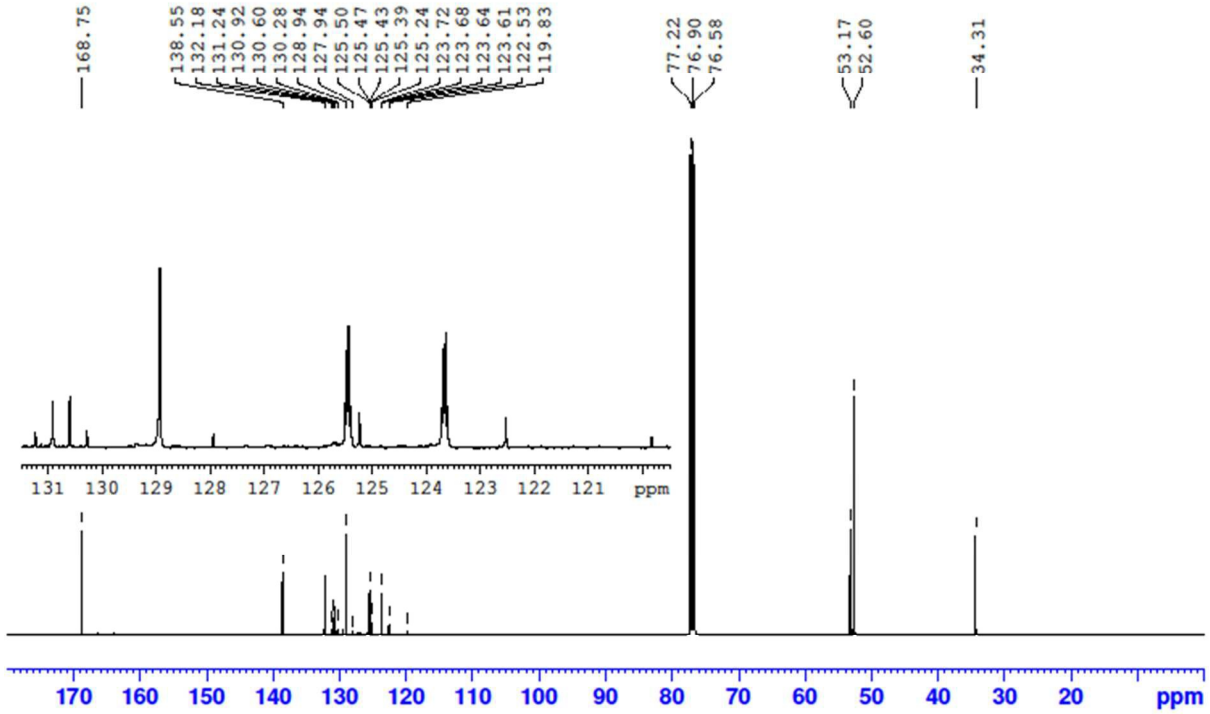


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

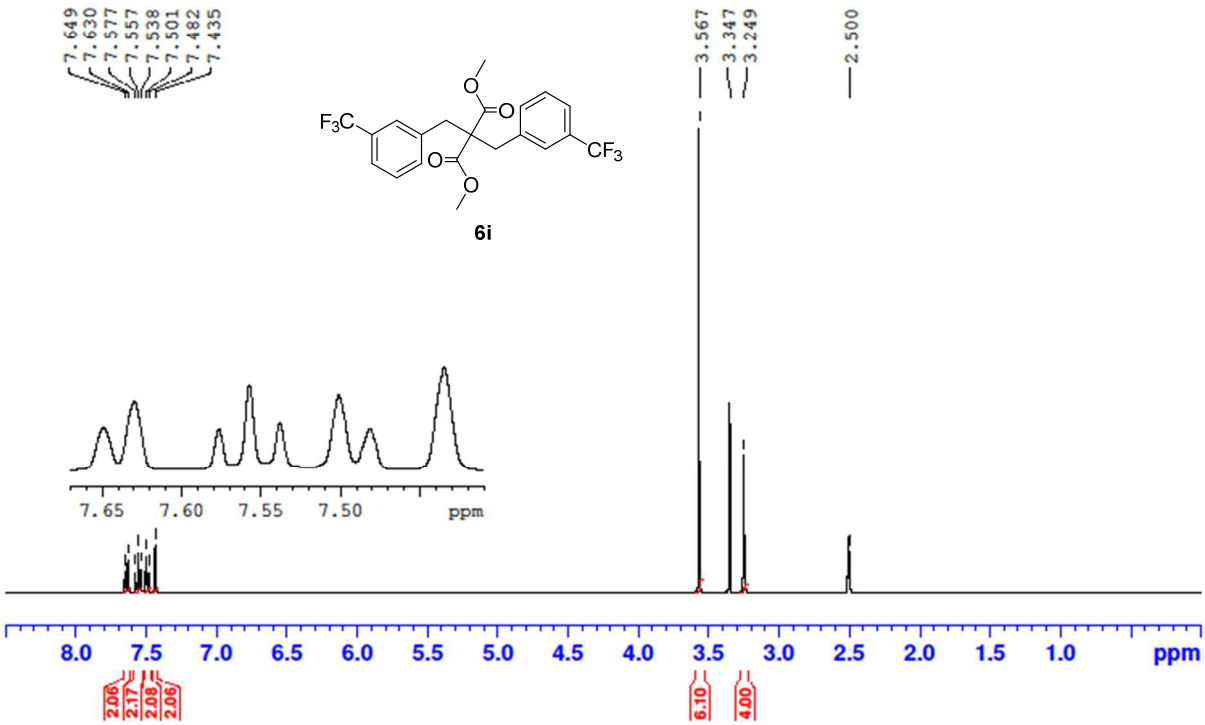


^{13}C NMR, $CDCl_3$, 101 MHz

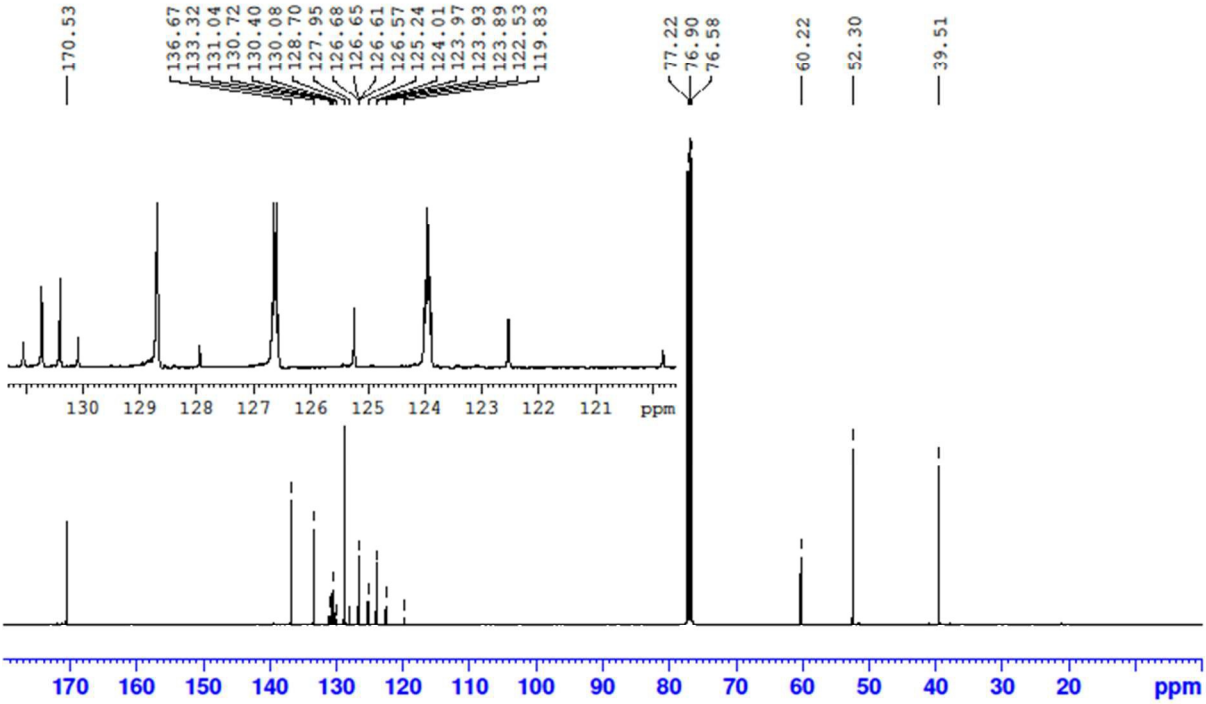


^{1}H NMR, d_6-DMSO, 400 MHz

View Article Online
DOI: 10.1039/C6GC00163G

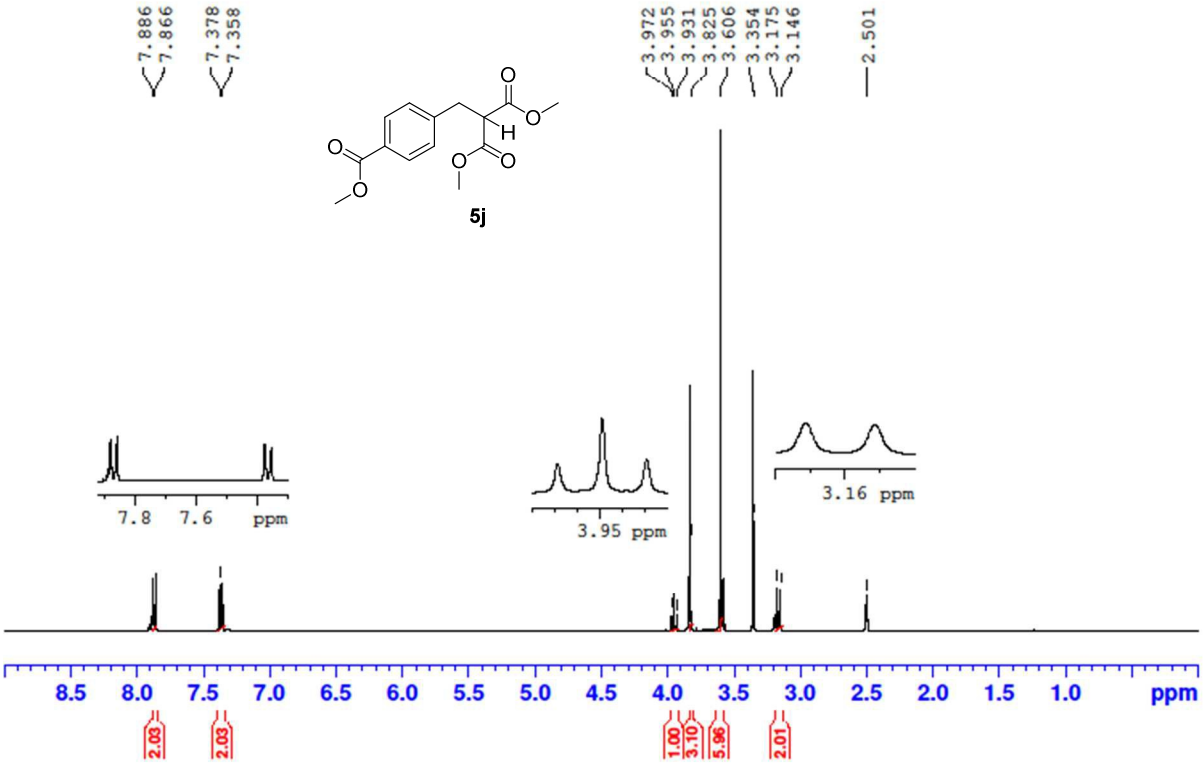


^{13}C NMR, $CDCl_3$, 101 MHz

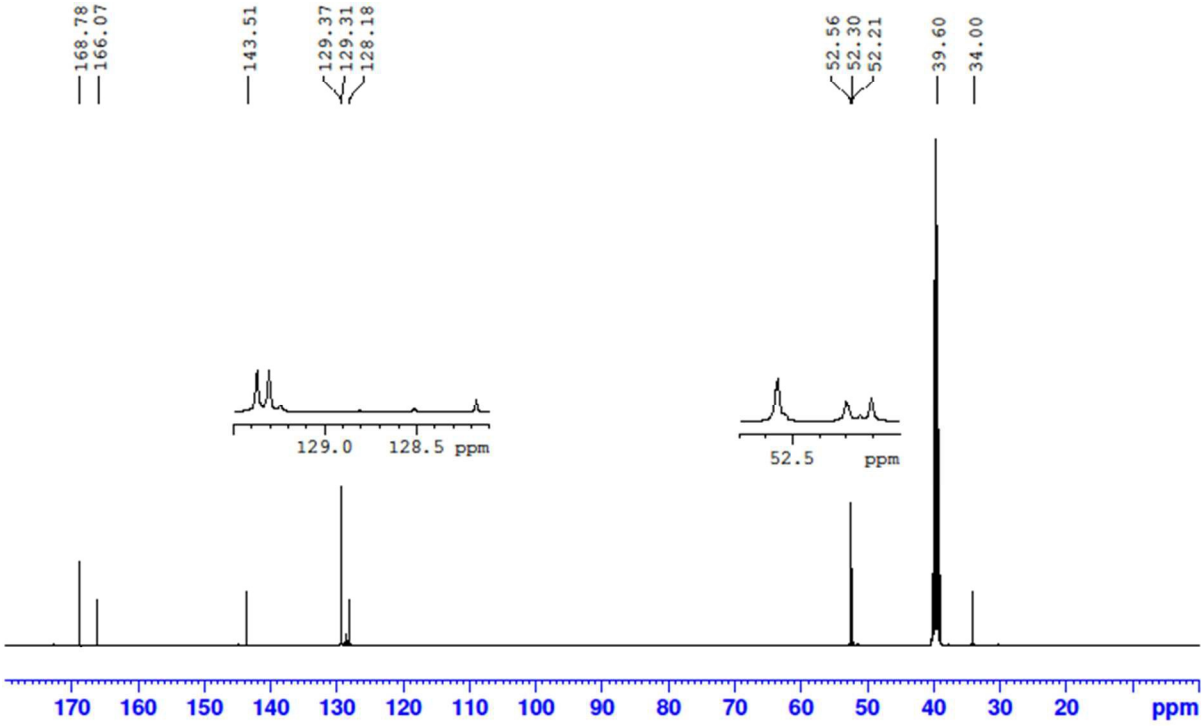


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

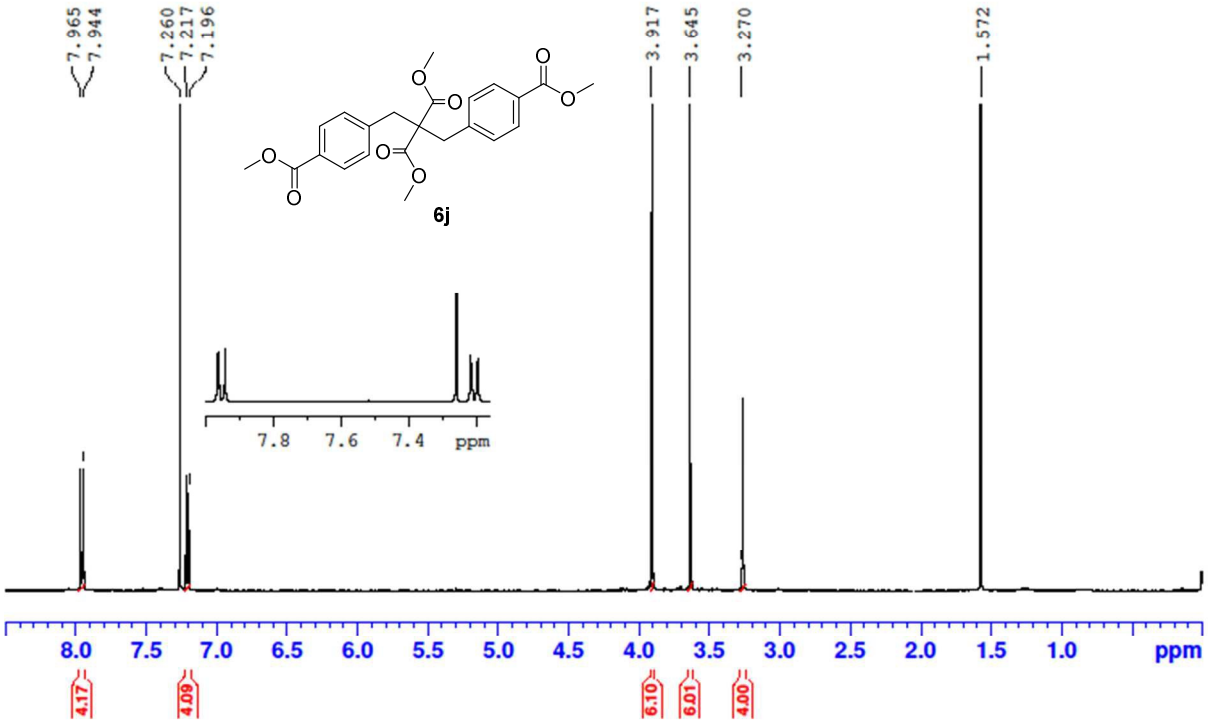


^{13}C NMR, d_6-DMSO, 101 MHz

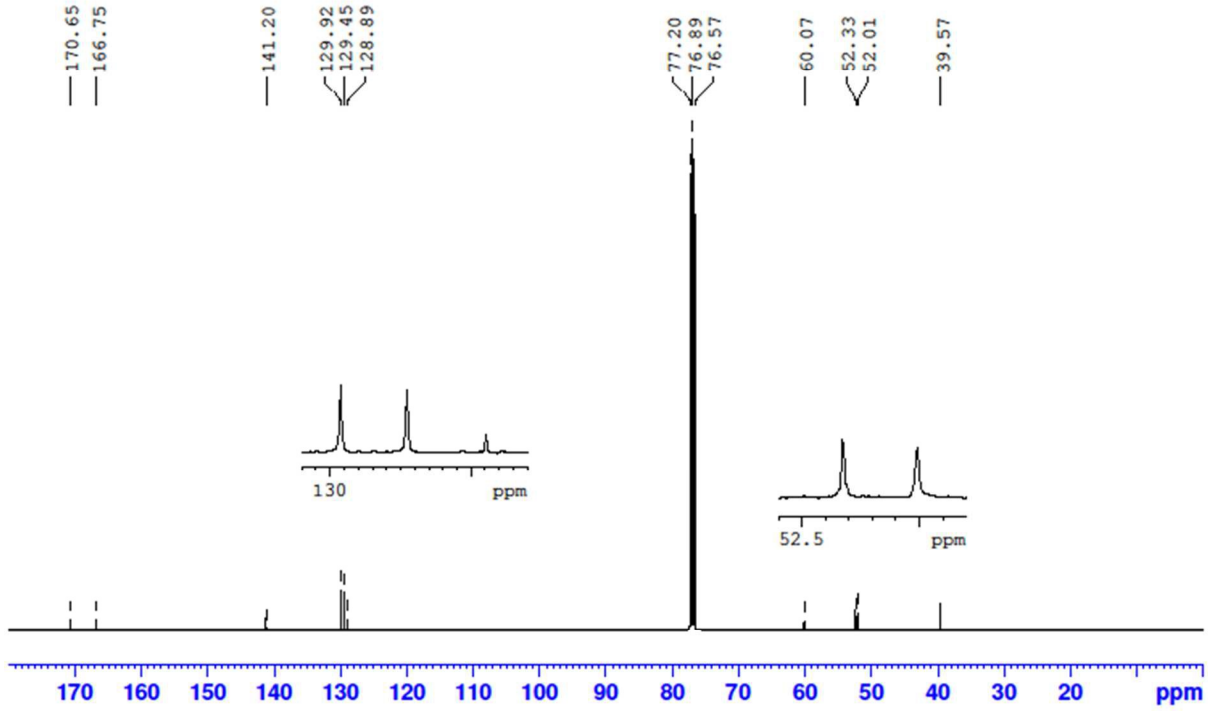


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, $CDCl_3$, 400 MHz

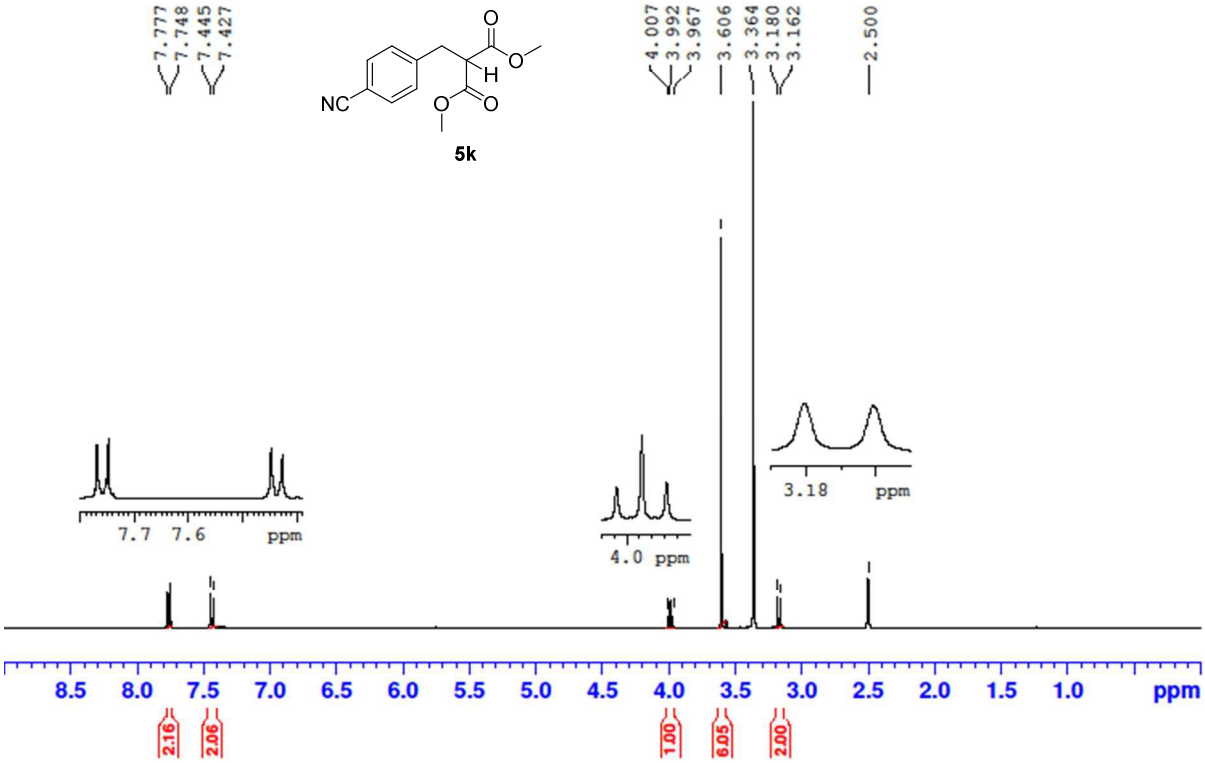


^{13}C NMR, $CDCl_3$, 101 MHz

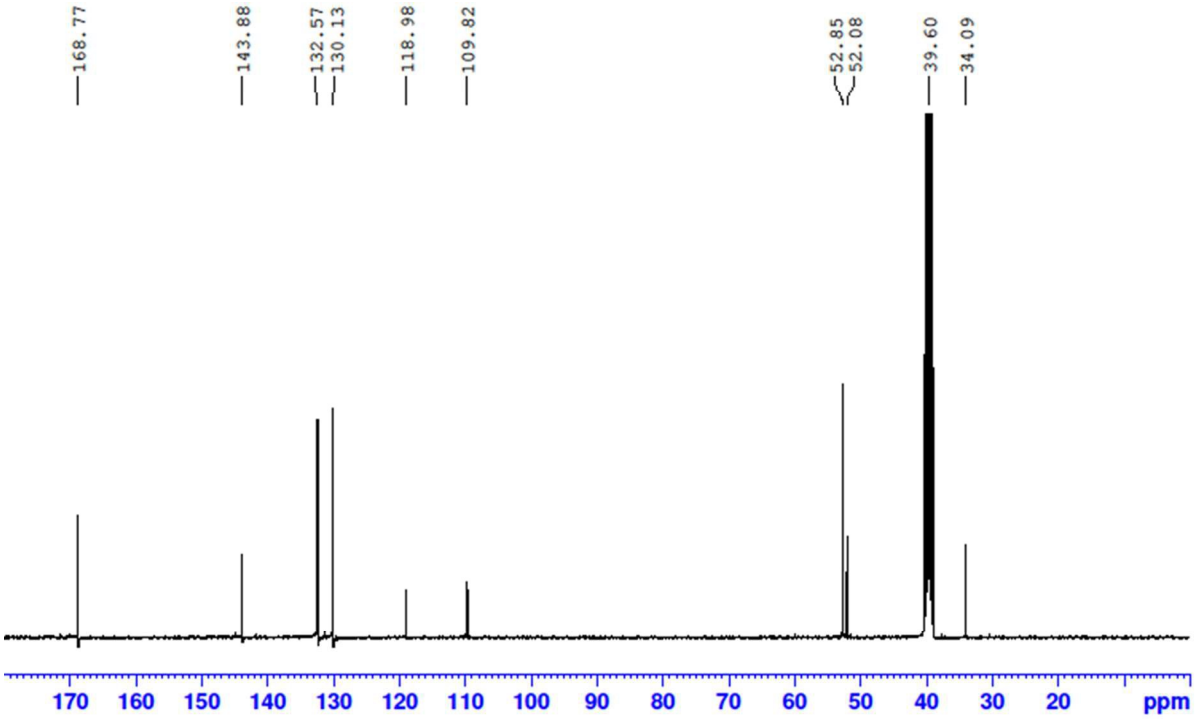


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

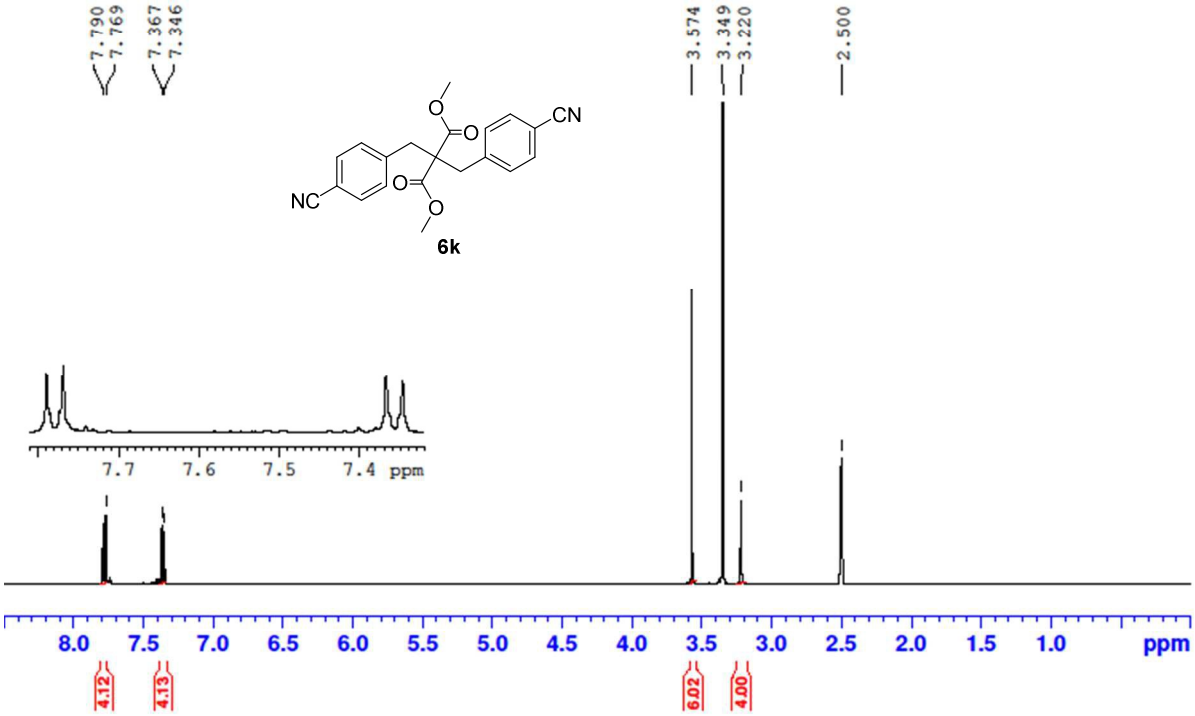


^{13}C NMR, d_6-DMSO, 101 MHz

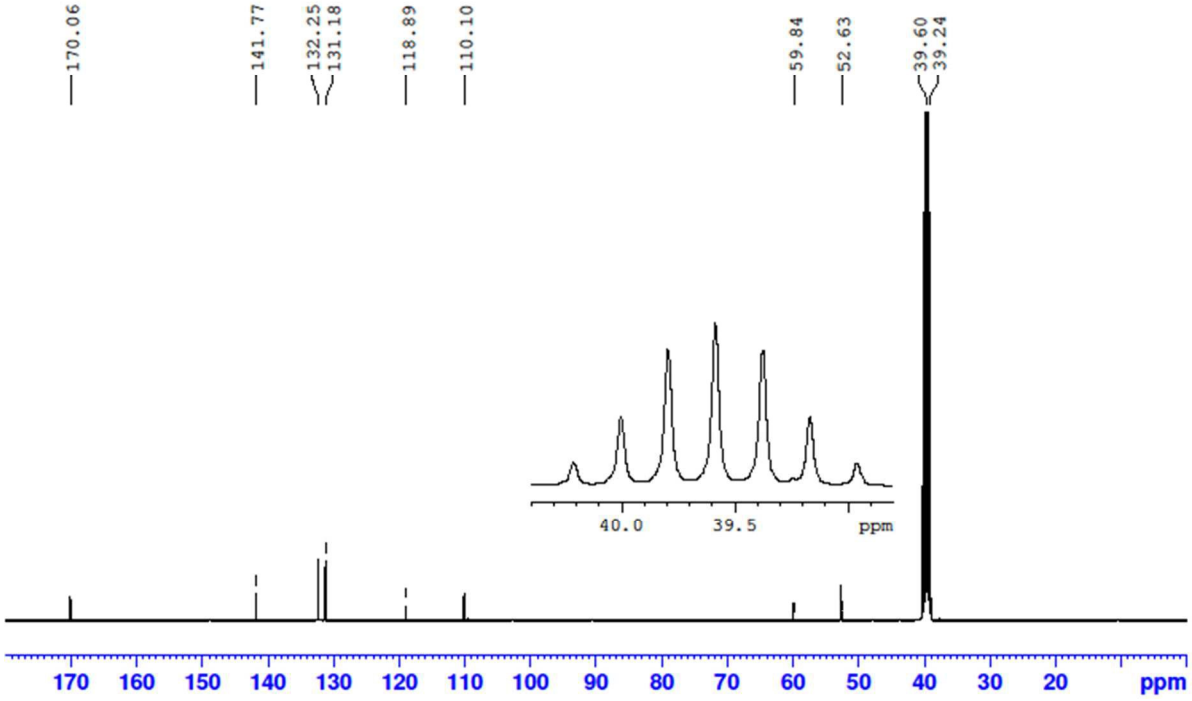


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

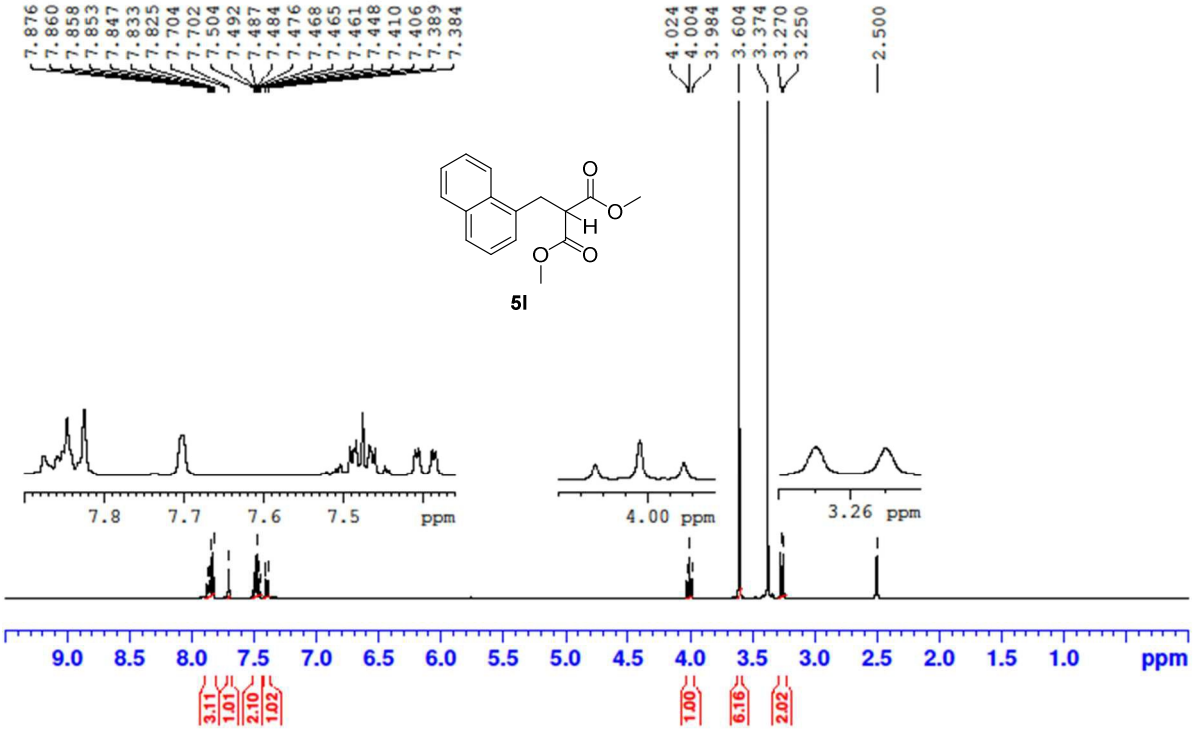


^{13}C NMR, d_6-DMSO, 101 MHz

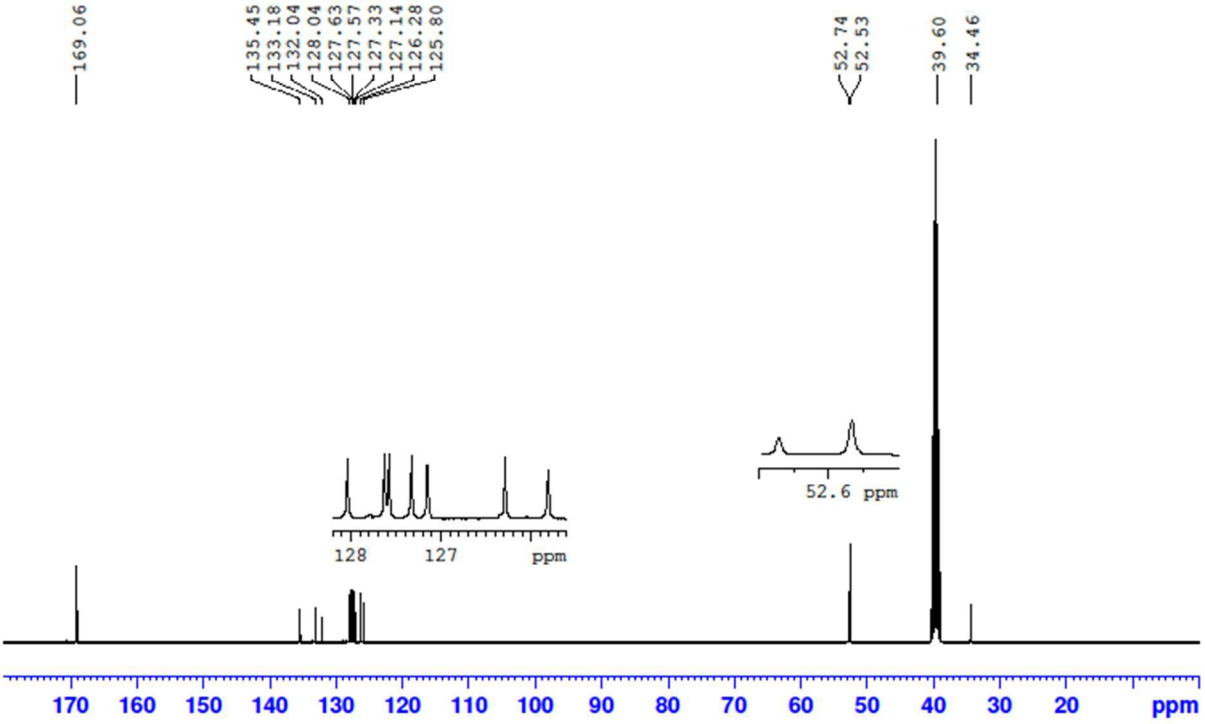


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

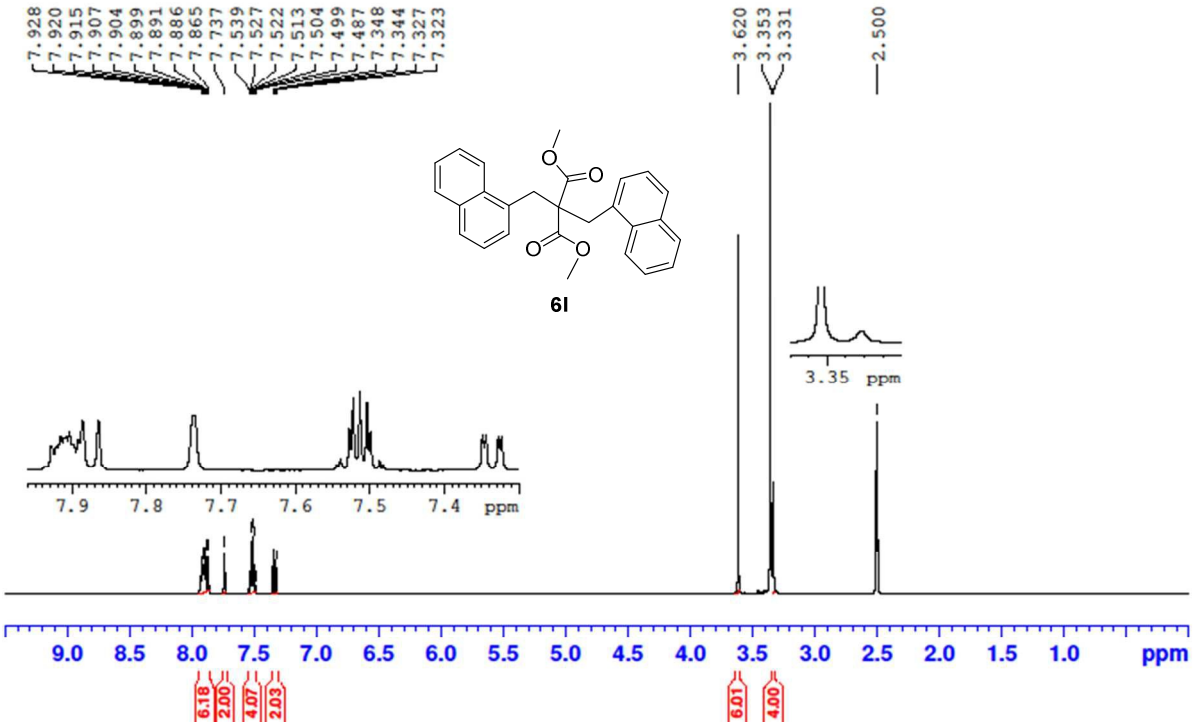


^{13}C NMR, d_6-DMSO, 101 MHz

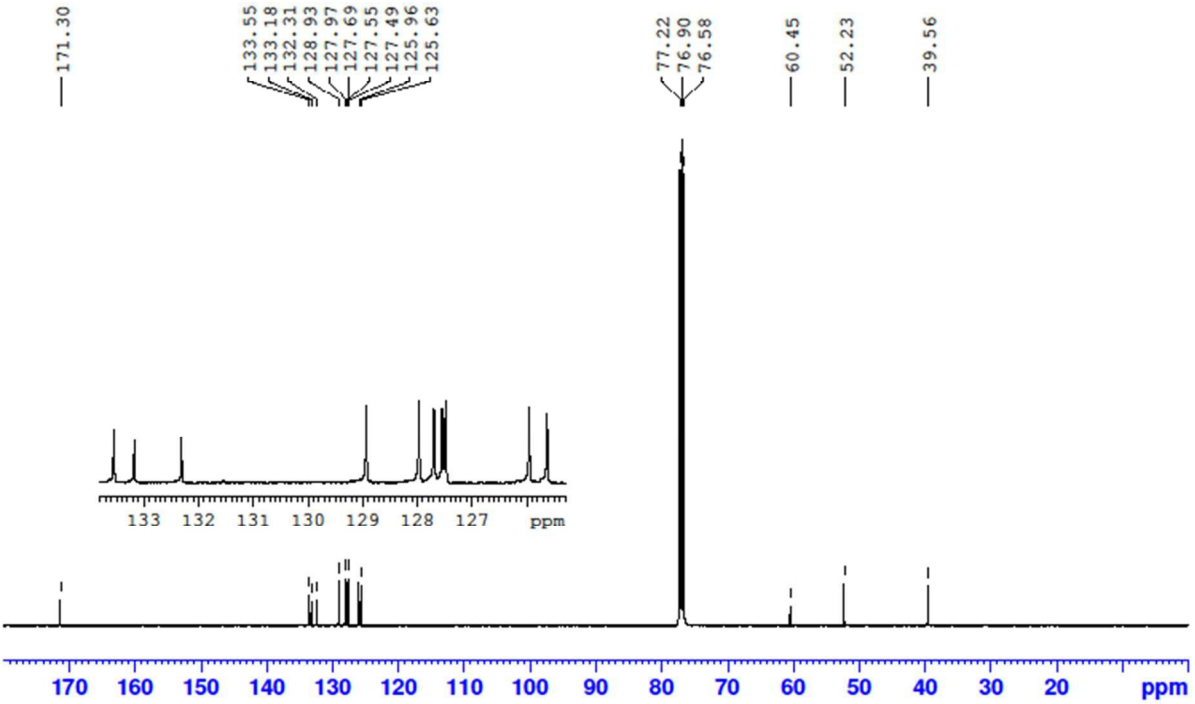


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

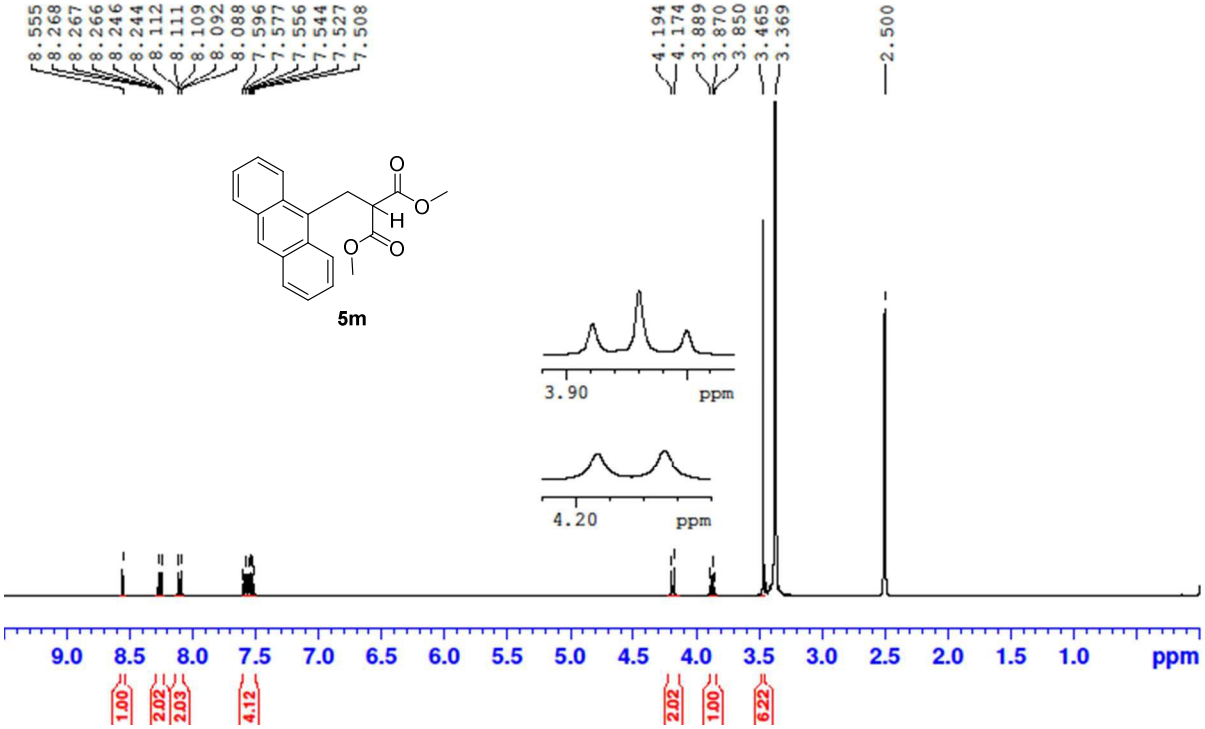


^{13}C NMR, $CDCl_3$, 101 MHz

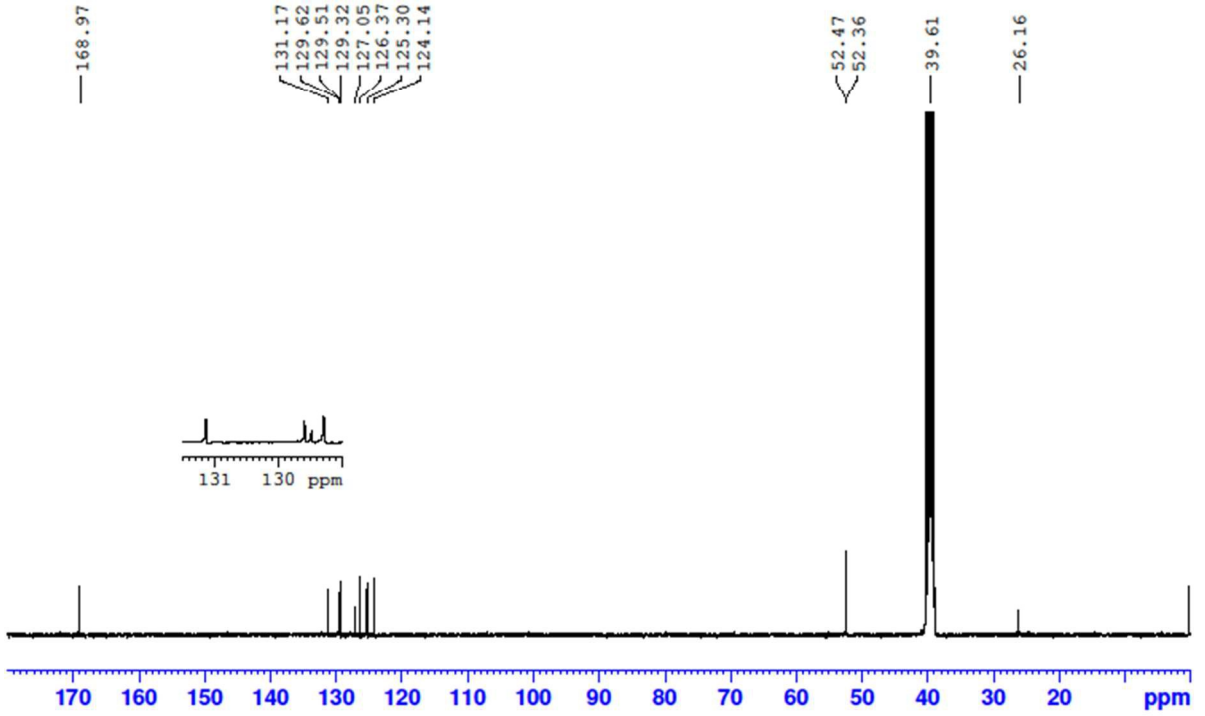


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

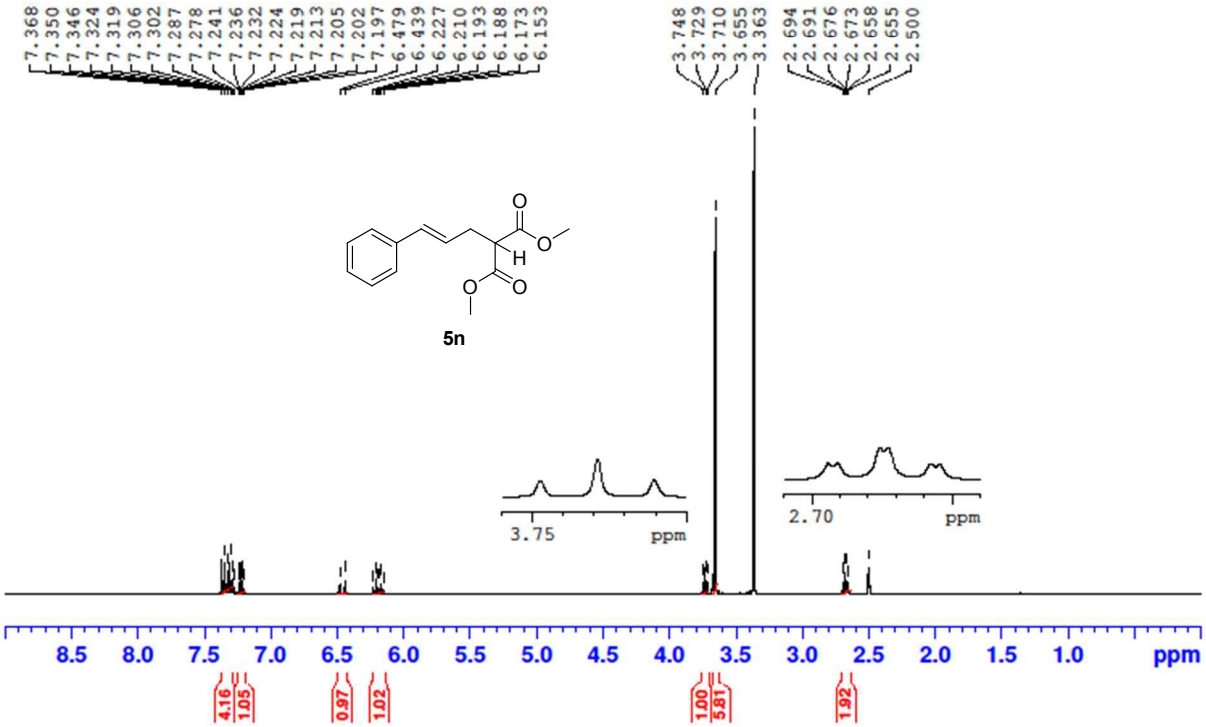


^{13}C NMR, d_6-DMSO, 101 MHz

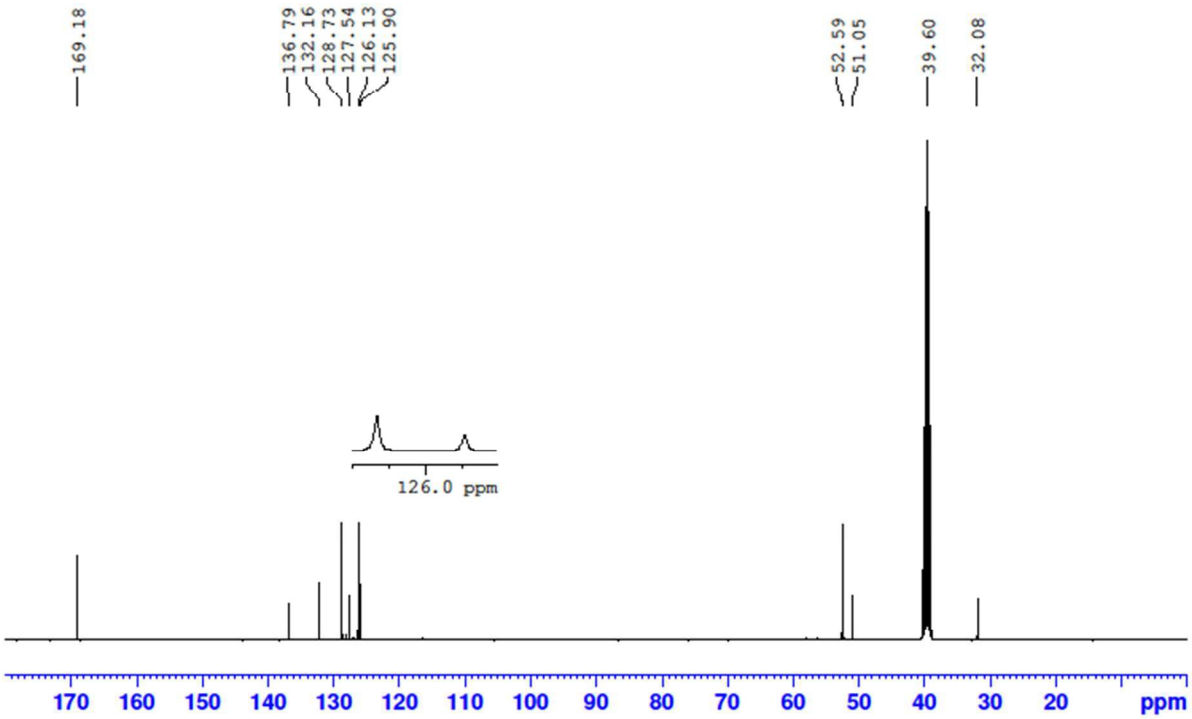


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

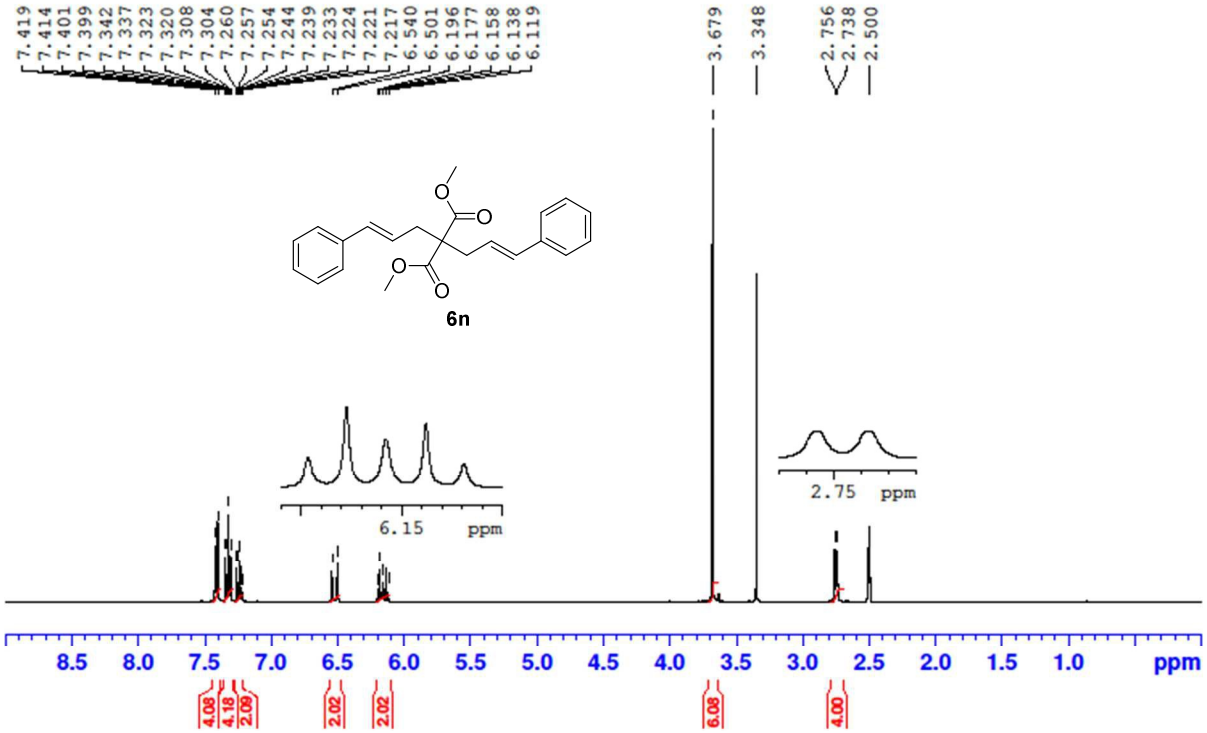


^{13}C NMR, d_6-DMSO, 101 MHz

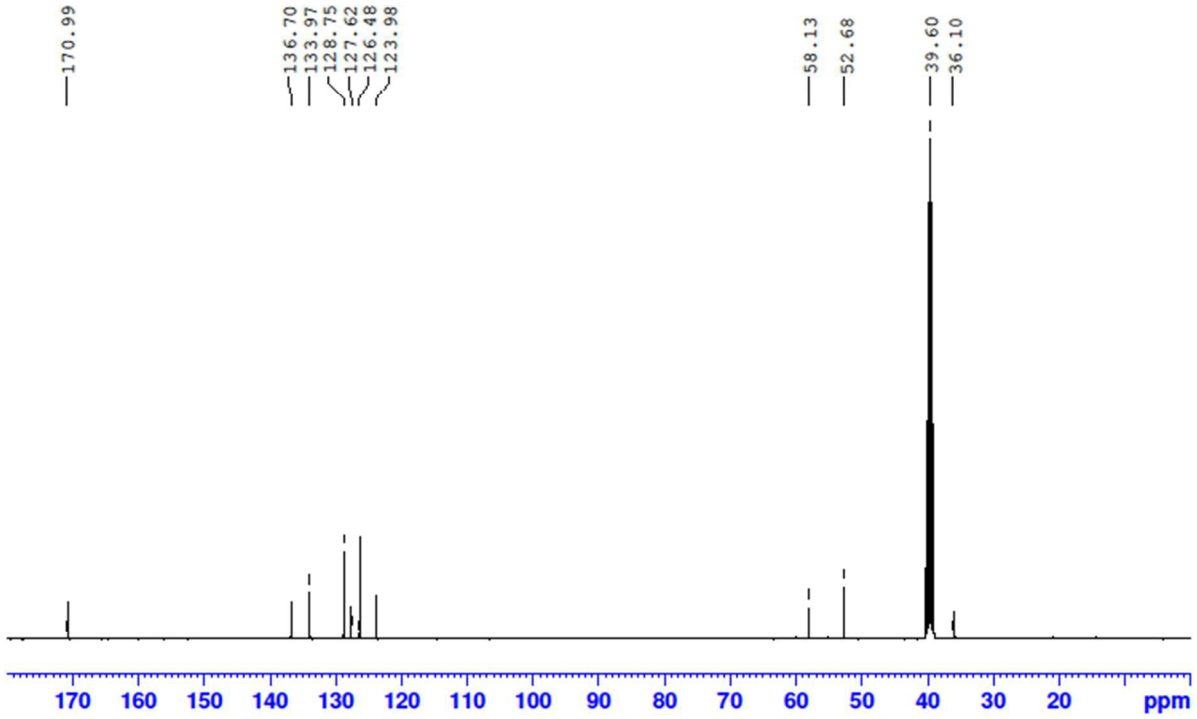


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

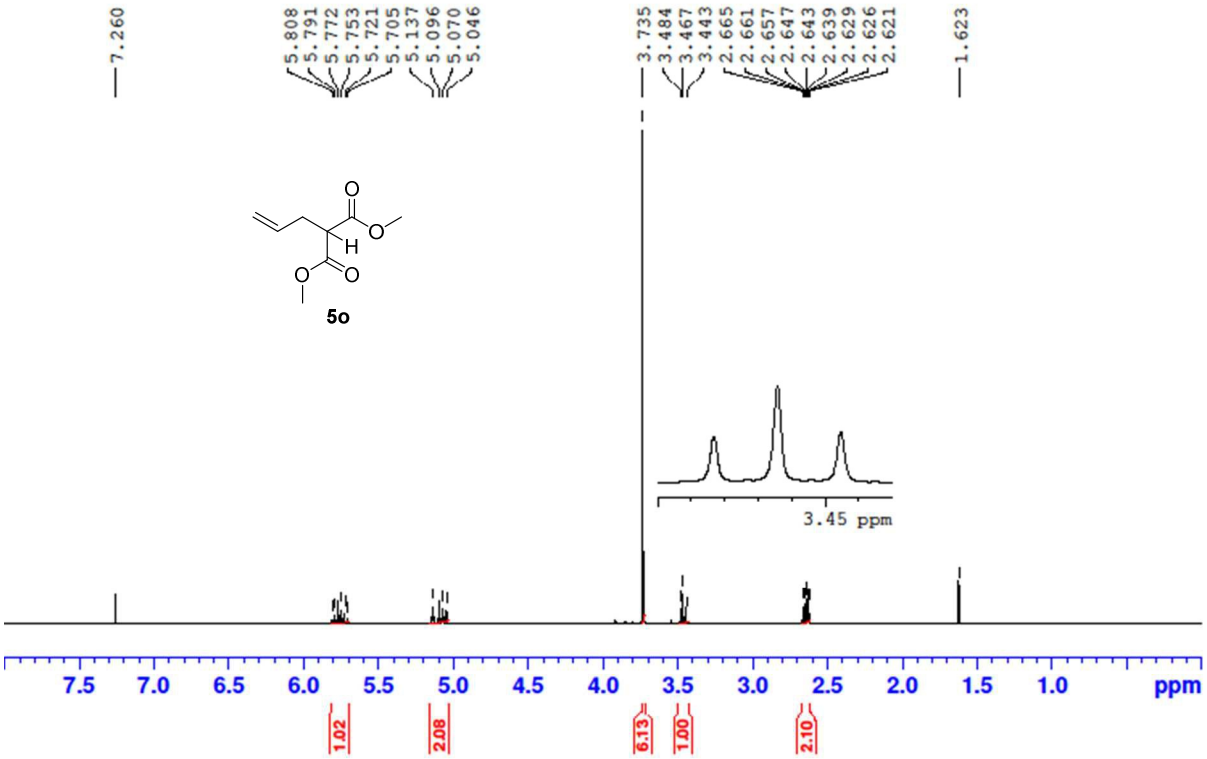


^{13}C NMR, d_6-DMSO, 101 MHz

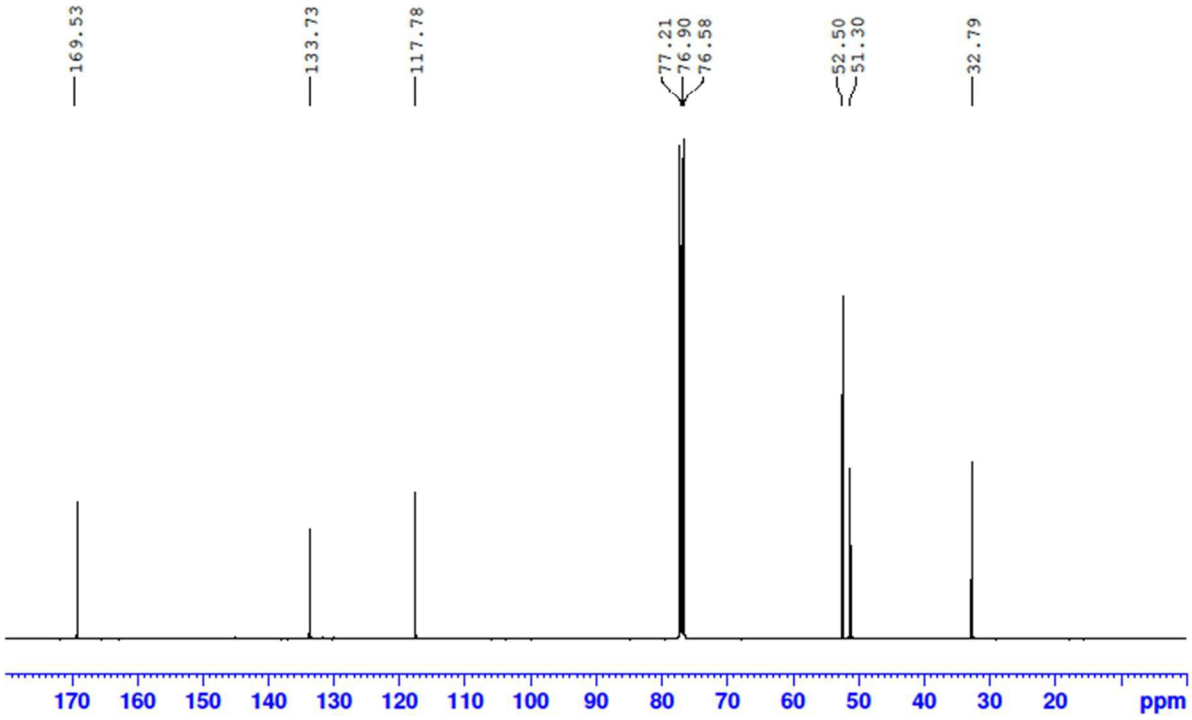


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, $CDCl_3$, 400 MHz

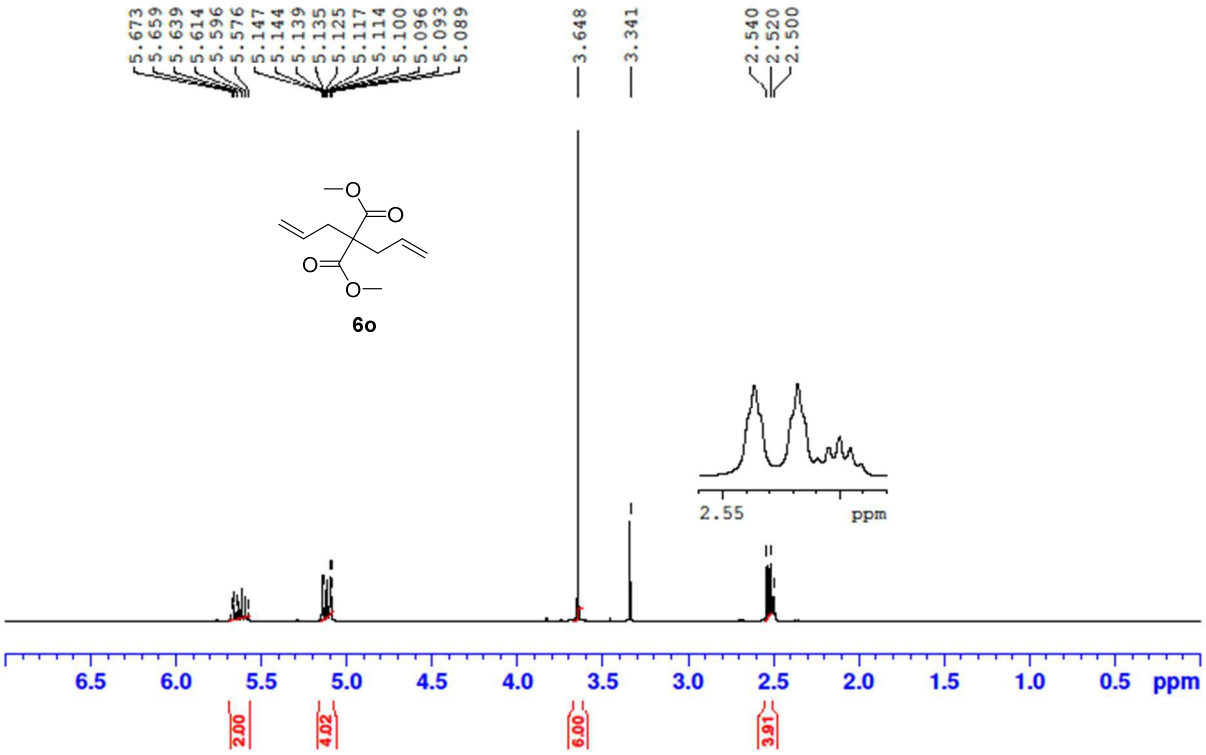


^{13}C NMR, $CDCl_3$, 101 MHz

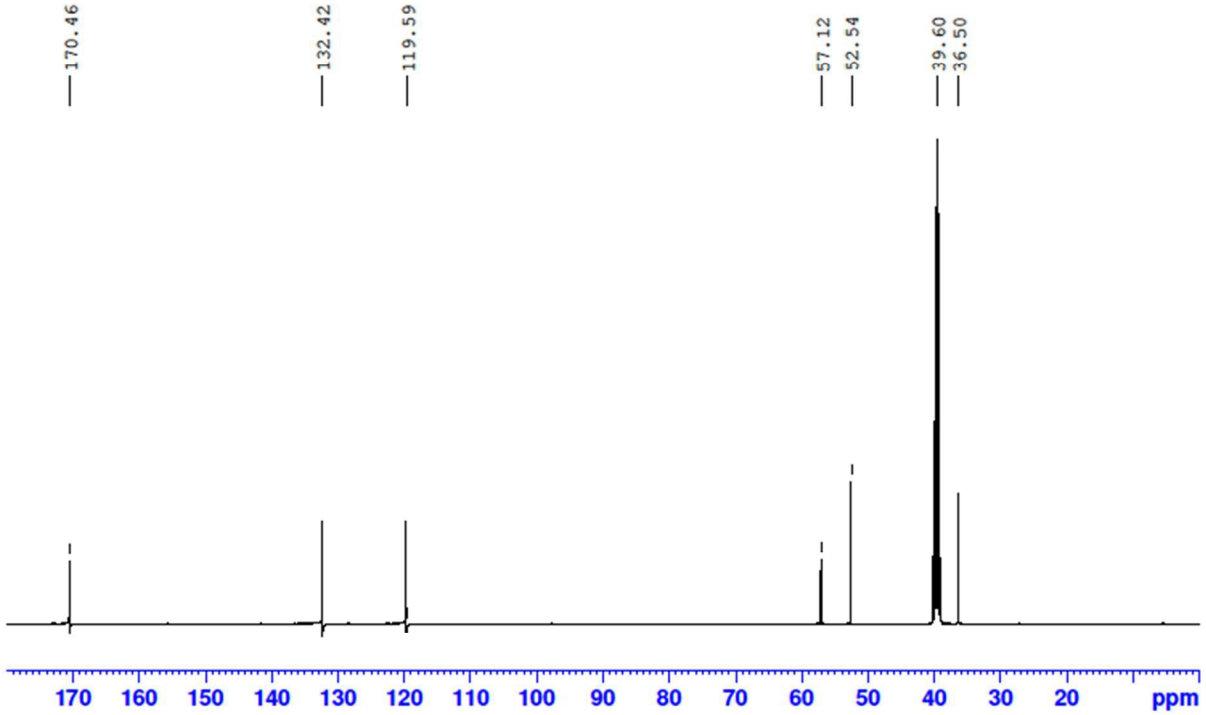


View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz

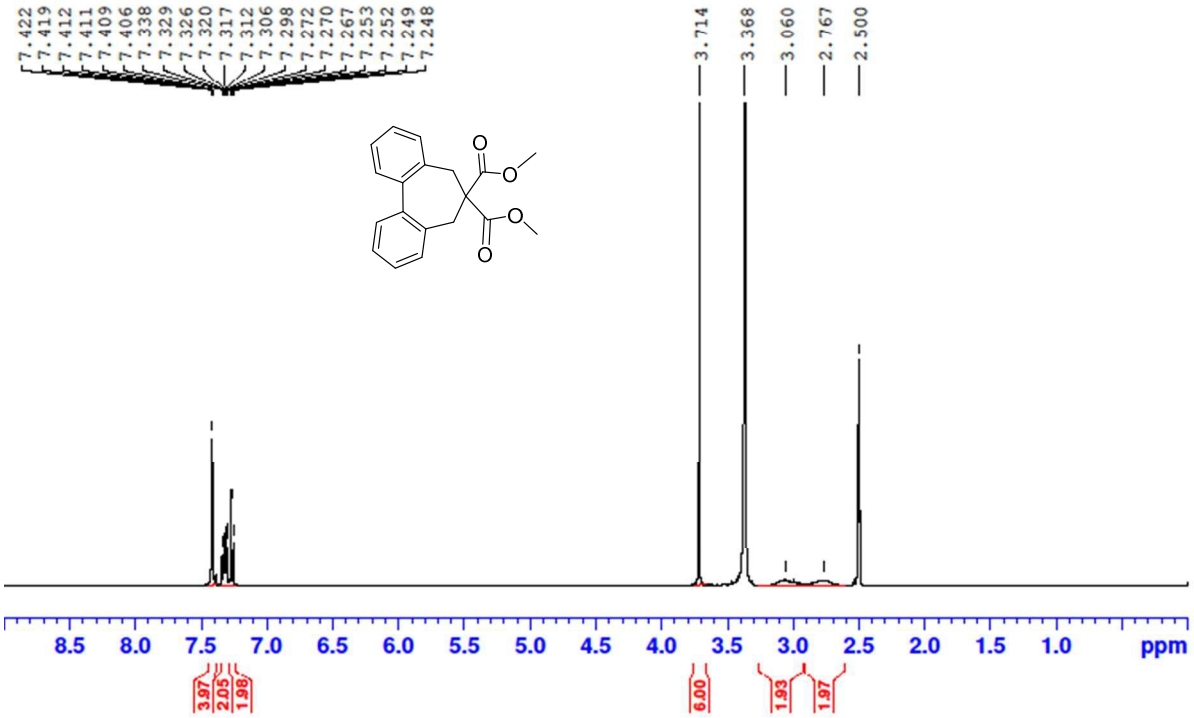


^{13}C NMR, d_6-DMSO, 101 MHz



View Article Online
DOI: 10.1039/C6GC00163G

^{1}H NMR, d_6-DMSO, 400 MHz



^{13}C NMR, d_6-DMSO, 101 MHz