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Application of directed metallation in synthesis. Part 3: Studies in the synthesis of (±)-semivioxanthin and its analogues☆

Sukanta Kamila, Chandrani Mukherjee, Sasanka S. Mondal and Asish De*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700-032, India

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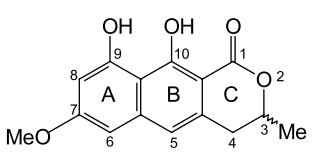
Abstract—The synthesis of several analogues of (±)-semivioxanthin including five thiophene analogues, using directed metalation are reported. The strategy consisted of the synthesis of functionalized naphthalene or benzo[*b*]thiophene as building blocks followed by annelation of the pyrone. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Semivioxanthin (**1**) is a naturally occurring linear naphthopyrone with a stereogenic centre at C-3. Both of its enantiomeric forms occur in nature and have antifungal properties. (+)-Semivioxanthin has 3-*R* configuration and was isolated[2] from the culture filtrate of *Penicillium citreoviride* while the other isomer was isolated[3] from *Cryptospirosis abietina* and, in addition to being fungicidal, is a defoliant[3] and also possesses abscisic[3] properties. Although its biological activities make it an interesting synthetic target, there are only a few reports on synthetic studies on semivioxanthin and its analogues. Racemic semivioxanthin was synthesized by Yamaguchi[4] and Deshpande[5] using a polyketide approach and condensation of a pyrone with a polysubstituted benzene, respectively. More recently Deshpande[6] obtained 35% yield of (−)-semivioxanthin during the synthesis of (+)-orthosporine. Tatsuta and Nakata[7] reported the conversion of one of the products of intramolecular aldolisation of a polyketide lactone to the linear naphthopyrone (**2**) related to semivioxanthin.



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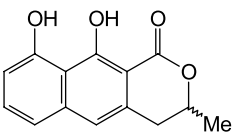

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Our aim was to develop a common strategy towards the synthesis of racemic semivioxanthin and its analogues and we intended to use for this purpose, the methodology of heteroatom directed *ortho*-metallation[8] commonly termed 'directed metallation'. The use of directed metallation in organic synthesis has been amply reviewed.[8] One of the many ramifications of this methodology is its usefulness in the annelation of a ring on to an existing aromatic or heteroaromtic core, of which there are many examples[8–10] including those reported from this laboratory. While designing the analogues, the principal structural features of the natural product viz. the linear naphthopyrone skeleton, oxygenated substituents in the aromatic rings and the methyl substituent in the lactone ring were meant to be preserved while allowing variations of the positions of the oxygenated functionalities and replacement of each of the benzene rings in turn with thiophene, following the general principle of bioisosterism.[11] A preliminary account[10] of our work was published earlier.

2. Results and discussion

It was envisaged to synthesize suitably functionalized naphthalene or benzo[*b*]thiophene as building blocks followed by annelation of the pyrone ring through acid mediated cyclization of an *ortho*-allyl tertiary benzamide. This strategy was fairly successful in most of the cases, except the two reported below. Thus our attempt to obtain the natural product, as envisaged in Scheme 1, met with limited success.

Commercially available dimethylresorcilic acid (**3**) was converted into its diethylamide (**4**) followed by regioselective introduction of an allyl group *ortho*- to the amide function by metallation-transmetallation,[12,13] under carefully controlled conditions. Use of *s*-BuLi even slightly in

☆ For Part 2 see Ref. 1.

Keywords: semivioxanthin; naphthopyrone; benzothienopyrone; directed metallation.

* Corresponding author. Tel.: +91-33-473-4971x246/253; fax: +91-33-473-2805; e-mail: ocad@mahendra.iacs.res.in

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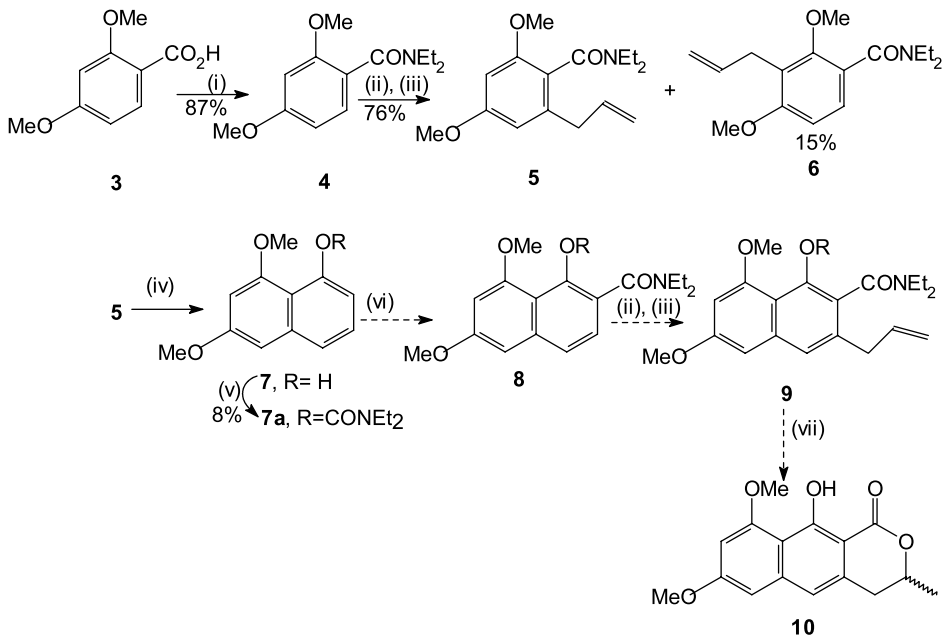
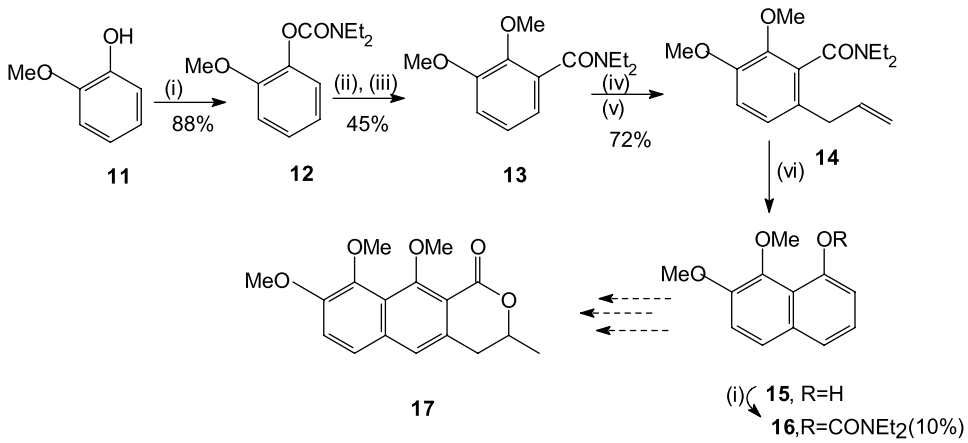


Scheme 1. *Reagents*: (i) $SOCl_2$/benzene/reflux/*N*,*N*-diethylamine, (ii) *s*-BuLi (2.2 equiv.)/THF/CuBr–Me_2S/−78°C, (iii) Allyl bromide(2 equiv.), (iv) LDA (1.5 equiv.)/THF/−78°C or MeLi (2 equiv.)/THF/0°C, (v) NaH/THF/$ClCONEt_2$, (vi) *s*-BuLi/TMEDA/THF/−78°C/$ClCONEt_2$, (vii) 6N HCl/reflux.

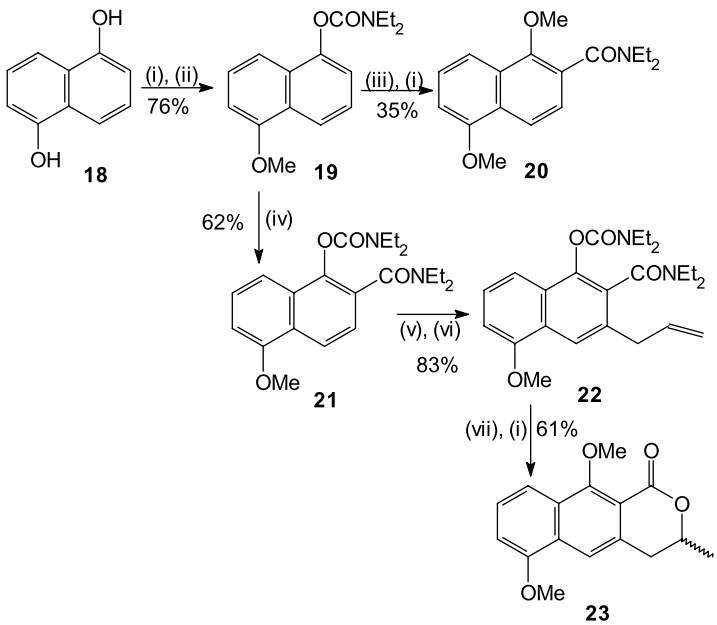
excess of 2.2 equiv. led to a mixture containing the undesired regioisomer **6**. Cyclisation of **5** to 1-hydroxy-6,8-dimethoxynaphthalene (**7**) with LDA or MeLi[14] was easily accomplished. Its conversion to the *O*-carbamate (**7a**) by reacting with *N*,*N*-diethylcarbamyl chloride under standard reaction conditions (K_2CO_3/acetone or NaH/THF) was, however, disappointing. The extremely poor yield of **7a** (8%) made it unsuitable as an intermediate for the three subsequent steps proposed in Scheme 1 and all our attempts to increase the yield of **7a** were unsuccessful.

A similar problem was encountered during the synthesis of the analogue **17** of semivioxanthin starting from guiacol (**11**) (Scheme 2) because of the poor conversion of **15** to the key intermediate **16** (10%). The *O*-carbamate **12** underwent smooth anionic *ortho*-Fries rearrangement[15] and subsequent O-methylation, introduction of allyl function *ortho*- to the amide group followed by cyclisation afforded **15** in reasonable yield.

Analogues **23** and **29** of semivioxanthin (Schemes 3 and 4), were, however, successfully synthesized by the same type of route. In both the cases the *O*-carbamate functions in the naphthalenic intermediates are free from any steric interaction with methoxy substituents in the *peri*-position. In Scheme 3 the two hydroxy functions of 1,5-dihydroxy-naphthalene **18** were sequentially converted to methoxy and *O*-carbamate. The resulting compound **19** underwent selective deprotonation *ortho*- to the *O*-carbamate function under standard directed metallation conditions (*s*-BuLi/TMEDA/THF/−78°C). The deprotonated species underwent anionic *ortho*-Fries rearrangement when left at room temperature for 12 h and the resulting salicylamide was subjected to *O*-methylation to afford **20**. Alternatively the deprotonated species could be quenched with *N*,*N*-diethylcarbamylchloride to afford **21**. Attempts to introduce an allyl function *ortho*- to the tertiary amide in **20** led to an intractable mixture containing among others *N*,*N*-diethyl-1-allyloxy-5-methoxy-2-carboxamide, presumably resulting



Scheme 2. *Reagents*: (i) NaH/THF/$ClCONEt_2$/rt, (ii) *s*-BuLi/TMEDA/THF/−78°C, (iii) K_2CO_3/MeI/acetone, (iv) *s*-BuLi/THF/CuBr–Me_2S/−78°C, (v) Allyl bromide (2.5 equiv.), (vi) LDA (1.5 equiv.)/THF/−78°C or MeLi (2 equiv.)/THF/0°C.



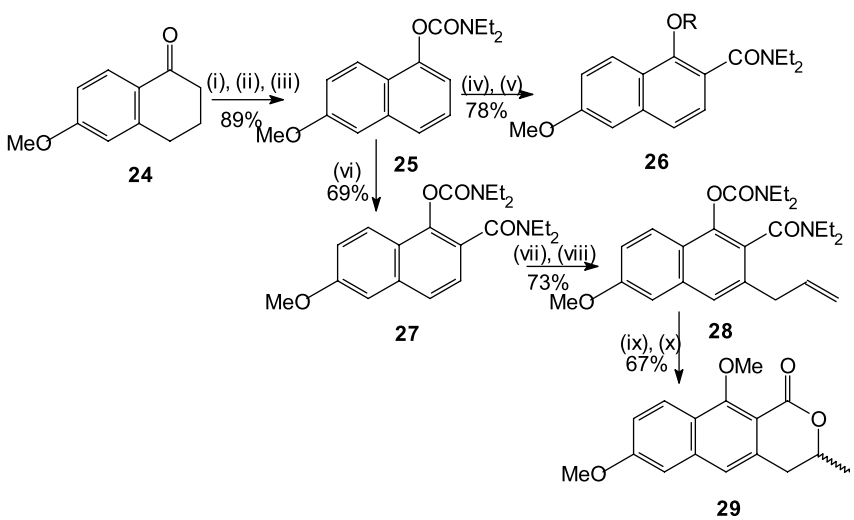
Scheme 3. *Reagents*: (i) K_2CO_3 (1.2 equiv.)/MeI(1.1 equiv.)/acetone/reflux, (ii) NaH/THF/ClCONEt$_2$/rt, (iii) *s*-BuLi/TMEDA/THF/−78°C, (iv) *s*-BuLi/TMEDA/THF/−78°C/ClCONEt$_2$, (v) *s*-BuLi/THF/CuBr−Me_2S/−78°C, (vi) Allyl bromide, (vii) 6N HCl/reflux/36 h.

from demethylation and subsequent O-allylation. An allyl group was successfully introduced *ortho*- to the tertiary amide function in **21** and the resulting compound **22** was cyclized.[16]

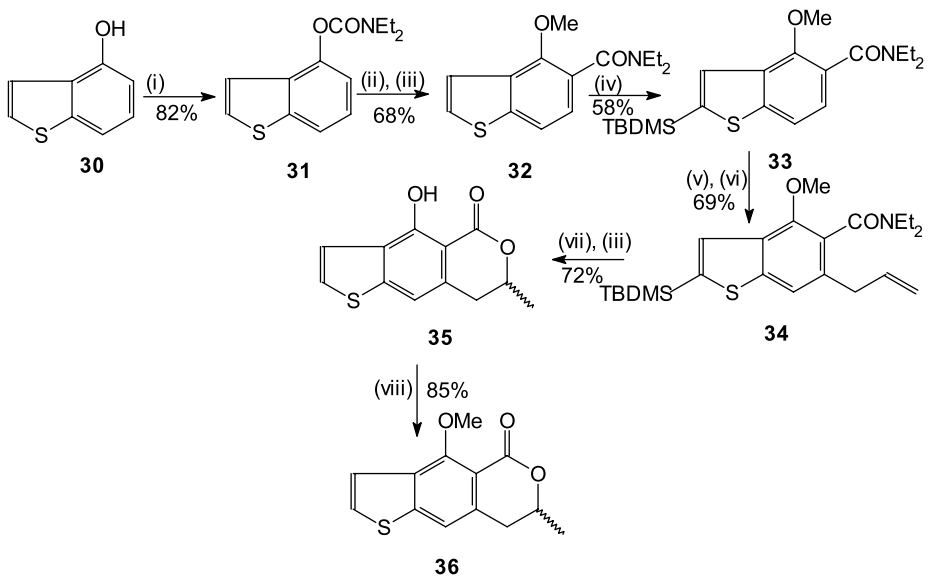
The drastic reaction conditions needed for cyclization[16] (heating under reflux with 6N HCl for 36 h) resulted in the hydrolysis of the *O*-carbamate and the somewhat labile phenolic compound was O-methylated to afford **23** in 61% yield.

The synthesis of **29** (Scheme 4) started from 6-methoxy-1-tetralone (**24**) which was converted into the *O*-carbamate **25**. Deprotonation *ortho*- to the *O*-carbamate function took place under standard directed metallation conditions and subsequent anionic *ortho*-Fries rearrangement generated the salicylamide which was converted to the OMOM derivative **26** (R=MOM). Introduction of allyl function *ortho*- to the tertiary amide group in **26** (R=MOM) was not possible because of the hydrolysis of the OMOM function and subsequent O-allylation. The deprotonated species generated from **25** was quenched with *N*,*N*-diethylcarbamylchloride to afford **27** in 69% yield. Introduction of allyl function *ortho*- to the tertiary amide group in **27** afforded **28** which was subsequently cyclized with hot HCl. The *O*-carbamate function was hydrolysed during cyclization as in the previous case and the crude phenolic compound was O-methylated to afford **29**.

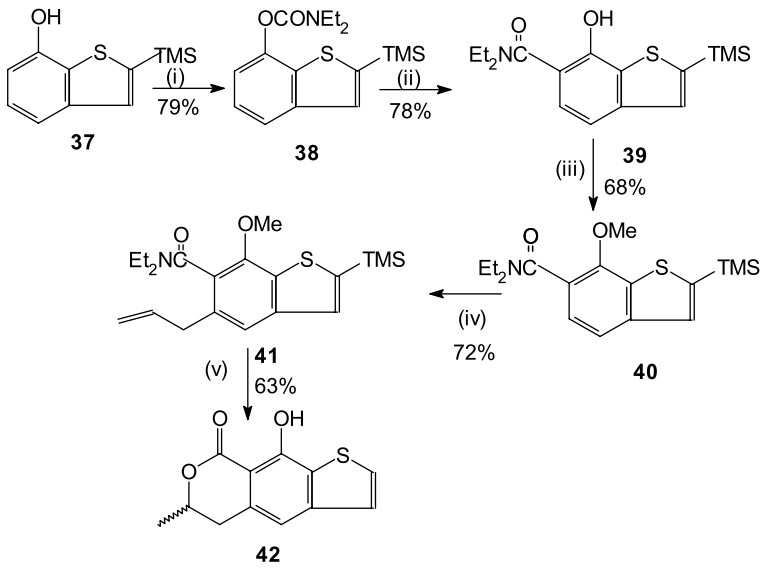
The thiophene analogues **36**, **42**, **49**, **50** and **55** of semivioxanthin were also synthesized (Schemes 5–8) in which the A and B rings of the natural product were



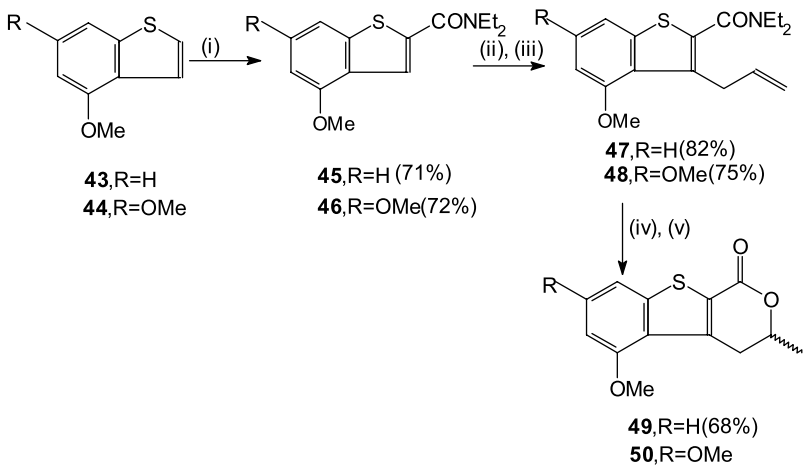
Scheme 4. *Reagents*: (i) Br_2/CCl_4, (ii) Li_2CO_3/LiBr/DMF/△,[17] (iii) NaH/THF/ClCONEt$_2$/rt, (iv) *s*-BuLi/THF/TMEDA/−78°C, (v) NaH/THF/MOMCl, (vi) *s*-BuLi/TMEDA/THF/ClCONEt$_2$, (vii) *s*-BuLi/THF/CuBr−Me_2S, (viii) Allyl bromide, (ix) 6N HCl/reflux/55 h, (x) K_2CO_3/MeI/acetone.



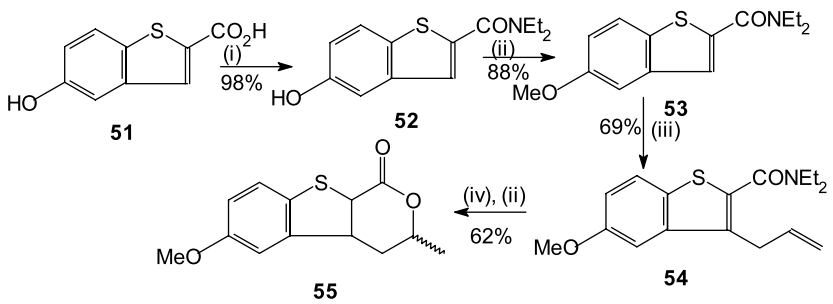
Scheme 5. *Reagents*: (i) NaH/THF/ClCONEt$_2$, (ii) *s*-BuLi/TMEDA/THF/−78°C, (iii) K_2CO_3/MeI/acetone, (iv) *s*-BuLi/TMEDA/THF/−78°C/TBDMSCl, (v) *s*-BuLi/THF/−78°C/CuBr–Me_2S, (vi) Allyl bromide, (vii) 6N HCl/reflux/55 h. (viii) K_2CO_3/MeI/acetone.



Scheme 6. *Reagents*: (i) NaH/THF/ClCONEt$_2$/rt, (ii) *s*-BuLi(2.5 equiv.)/TMEDA/THF/−78°C−rt, (iii) K_2CO_3 (1.2 equiv.)/Acetone/MeI, (iv) *s*-BuLi (2.5 equiv.)/CuBr–Me_2S/ Allyl bromide (3 equiv.)/THF, (v) 6N HCl/reflux/ 51 h.



Scheme 7. *Reagents*: (i) *s*-BuLi/TMEDA/THF/−78°C/ClCONEt$_2$, (ii) *s*-BuLi/THF/−78°C/CuBr–Me_2S, (iii) Allyl bromide, (iv) 6N HCl/reflux/56–60 h, (v) K_2CO_3/MeI/acetone.



Scheme 8. *Reagents*: (i) $SOCl_2$/benzene/diethylamine/reflux, (ii) K_2CO_3/acetone/MeI, (iii) *s*-BuLi/THF/−78°C/ CuBr−Me_2S/allyl bromide, (iv) 6N HCl/reflux/39 h.

replaced in turn by thiophene. Readily available functionalized benzo[*b*]thiophenes[1] were used as starting materials in these syntheses. In the analogues **36** and **42**, ring A comprised thiophene while in the analogues **49**, **50** and **55** ring B comprised thiophene.

In the first step of the synthesis of **36** (Scheme 5), 4-hydroxybenzo[*b*]thiophene[18] (**30**) was converted into its *O*-carbamate (**31**). The latter was subjected to anionic *ortho*-Fries rearrangement followed by O-methylation of the resulting salicylamide. After silyl protection of the free α-position of the thiophene ring,[7] an allyl function was introduced in the 6-position of **33** through usual sequences. Demethylation with concomittant desilylation was observed during cyclisation of **34** (hot 6N HCl, 55 h) and the slightly labile phenolic cyclized product **35** was characterized as its methyl ether **36**.

Compounds **42**, **49**, **50** and **55** were synthesized following the same synthetic methodology (Schemes 6–8) starting from 7-hydroxybenzo[*b*]thiophene[1] (**37**), 4-methoxybenzo[*b*]thiophene (**43**),[1,19] 4,6-dimethoxybenzo[*b*]thiophene (**44**)[1] and 5-hydroxybenzo[*b*]thiophene-2-carboxylic acid (**51**),[20] respectively. The tricyclic phenolic compound **42** obtained from the cyclization of **41** was notably stable in contrast to similar compounds reported in this paper and did not need conversion to its methyl ether for characterization. The yield of compound **50** (49%) can be calculated from the peak heights in the NMR spectrum [δ_H (300 MHz, $CDCl_3$) 6.31 (1H, d, *J*=2.07 Hz, C-8), 6.08 (1H, d, *J*=2.07 Hz, C-6), 5.09–5.11 (1H, m, C-3), 3.68 (3H, s, −OMe), 3.64 (3H, s, −OMe), 3.51–3.30 (2H, m, C-4), 1.42 (3H, d, *J*=6.10 Hz, $-CH_3$). The IR spectrum showed carbonyl absorption at 1720 cm^{-1}]. However trace impurities present along with this product which could not be separated thereby preventing the preparation of analytically pure sample.

3. Conclusion

This work is another demonstration of the effectiveness of the methodology of directed metallation as a synthetic tool, which enabled us to synthesize a number of analogues of semivioxanthin, designed through variation of its structure permissible under the general principle of bioisosterism. Work is currently in progress towards the synthesis of the natural product and overcoming the difficulties in the synthesis of analogues **10** and **17**.

4. Experimental

4.1. General

Commercially available solvents were distilled prior to use. Light petroleum ether (bp 60–80°C) was used for column chromatography. Anhydrous sodium sulfate was used as drying agent. THF, *n*-hexane, cyclohexane were dried by the usual sodium-benzophenone-ketyl method. ^1H and ^{13}C NMR spectra (300 MHz) were recorded in $CDCl_3$ solution on Bruker DPX-300 spectrometer. Chemical shifts (δ) are expressed in ppm using tetramethylsilane as internal standard. Coupling constant (*J*) values are given in Hz. Melting points (uncorrected) were recorded in open capillaries on a hot stage apparatus. IR spectra were recorded on a FTIR-8300, SHIMADZU spectrometer, for solids in potassium bromide discs and for liquids by placing a thin layer of the sample between two potassium bromide discs. *n*-BuLi and *s*-BuLi were prepared in our laboratory by reacting lithium dispersion with 1-chlorobutane in *n*-hexane (in the case of *n*-BuLi) or 2-chlorobutane in cyclohexane (in the case of *s*-BuLi). Molecularisation of lithium was done either by heating the lithium in heavy paraffin liquid and then vigorous stirring with a mechanical stirrer or under sonication.

4.1.1. *N*,*N*-Diethyl-2,4-dimethoxybenzamide (4). The acid (**3**) (3.2 g, 0.0018 mmol), thionyl chloride (HAZARD) (7.8 mL) and dry benzene (HAZARD) (100 mL) were heated at reflux under stirring for 2 h. Solvent and excess thionyl chloride were removed under vacuum and the crude acid chloride (3.6 g, 0.0018 mmol) was dissolved in benzene (40 mL). Diethylamine (5.6 mL, 0.0054 mmol) in dry benzene (15 mL) was added to the reaction mixture at 0°C, under magnetic stirring. After the addition was complete, the reaction mixture was stirred for 2 h at 0°C and then 8 h at room temperature. After removal of benzene under reduced pressure, the residue was extracted with dichloromethane. The organic layer was thoroughly washed with 5% sodium hydrogencarbonate, then with 5% HCl and finally with water. Removal of solvent after drying the organic layer afforded **4** which was purified by column chromatography (ethyl acetate–light petroleum (1:9)). Colorless viscous liquid (3.6 g, 87%); (Found: C, 65.84; H, 8.15; N, 5.95. $C_{13}H_{19}O_3N$ requires C, 65.82; H, 8.01; N, 5.90%]; ν_{max} ($CHCl_3$) 1614 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.05 (1H, d, *J*=8 Hz, C-6), 6.42 (1H, dd, *J*=2.1, 8 Hz, C-5), 6.39 (1H, d, *J*=2.1 Hz, C-3), 3.74 (3H, s, −OMe), 3.72 (3H, s, −OMe), 3.48 (2H, q, *J*=7.2 Hz, $-CH_2CH_3$), 3.10 (2H, q,

J=7.2 Hz, $-CH_2CH_3$), 1.16 (3H, t, J=6.9 Hz, $-CH_2CH_3$), 0.98 (3H, t, J=6.9 Hz, $-CH_2CH_3$); δ_C (300 MHz, $CDCl_3$) 167.7, 160.1, 155.4, 127.2, 118.6, 103.5, 97.4, 54.3, 54.2, 41.7, 37.8, 12.8, 11.7.

4.1.2. *N*,*N*-Diethyl-5-methoxybenzo[*b*]thiophene-2-carboxamide (53). 5-Hydroxybenzo[*b*]thiophene-2-carboxamide was prepared from 5-hydroxybenzo[*b*]thiophene-2-carboxylic acid in the same way as **4**. The hydroxy group of the carboxamide (1.8 g, 0.000718 mmol) was methylated by the usual procedure (K_2CO_3/acetone/MeI) to afford compound **53** which was purified by column chromatography (ethyl acetate–light petroleum (1:3)). Pale yellow gummy liquid (1.7 g, 88%); (Found: C, 63.79; H, 6.26; N, 5.16. $C_{14}H_{17}O_2NS$ requires C, 63.85; H, 6.51; N, 5.31%); ν_{max} (KBr) 1620 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.69 (1H, d, J=9 Hz, C-7), 7.41 (1H, s, C-3), 7.24 (1H, d, J=2.4 Hz, C-4), 7.04 (1H, dd, J=2.4, 9 Hz, C-6), 3.87 (3H, s, –OMe), 3.56 (4H, q, J=6 Hz, $-CH_2CH_3$), 1.27 (6H, t, J=9 Hz, $-CH_2CH_3$); δ_C (300 MHz, $CDCl_3$) 164.2, 157.6, 139.7. 138.8, 132.4, 123.9, 122.8, 116.1, 106.0, 55.4, 42.0, 14.0.

4.1.3. *N*,*N*-Diethyl-2,4-dimethoxy-6-allylbenzamide (5). *s*-BuLi (2.2 equiv., 4.6 mL) was slowly added by syringe to a solution of the substrate (1 g, 0.000421 mmol) in dry THF (10 mL) at −78°C followed by CuBr–Me_2S (2 equiv., 1.7 g) after 1 h. The temperature of the reaction mixture was allowed to rise between −10°C to −15°C and kept at that temperature for 30 min. After cooling the reaction mixture to −78°C allylbromide (2 equiv., 0.73 mL) was added. After 1 h at −78°C the reaction mixture was allowed to attain room temperature and filtered through a pad of silica gel which was washed with ethyl acetate. The organic layer was washed with water and dried. Removal of solvent afforded **5** which was purified by column chromatography (ethyl acetate–light petroleum (1:4)). Colorless gummy liquid (0.88 g, 76%); (Found: C, 69.38; H, 8.40; N, 5.01. $C_{16}H_{23}O_3N$ requires C, 69.31; H, 8.30; N, 5.05%); ν_{max} ($CHCl_3$) 1631 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.27 (1H, d, J=2.0 Hz, C-5), 6.22 (1H, d, J=2 Hz, C-3), 5.76–5.85 (1H, m, $-CH_2-CH=CH_2$), 4.92–5.01 (2H, m, $-CH_2-CH=CH_2$), 3.67 (3H, –OMe), 3.65 (3H, s, –OMe), 2.96–3.35 {6H, m, $-CH_2-CH=CH_2$, $-CON(CH_2CH_3)_2$}, 1.12 {3H, t, J=7.1 Hz, $-CON(CH_2CH_3)_2$}, 0.91 {3H, t, J=7.1 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 167.9, 160.5, 156.4, 138.7, 136.2, 118.9, 116.2, 105.5, 96.1, 55.3, 55.1, 42.6, 38.3, 37.1, 13.6, 12.6. This procedure is followed for the synthesis of all other allyl compounds.

4.1.4. *N*,*N*-Diethyl-2,3-dimethoxy-6-allylbenzamide (14). Purified by column chromatography (ethyl acetate–light petroleum (1:3)). Gummy liquid (72%). (Found: C, 69.30; H, 8.26; N, 5.00. $C_{16}H_{23}O_3N$ requires C, 69.31; H, 8.30; N, 5.05%); ν_{max} ($CHCl_3$) 1632 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.93 (1H, d, J=8.4 Hz, C-5), 6.84 (1H, d, J=8.4 Hz, C-6), 5.89–5.92 (1H, m, $-CH_2-CH=CH_2$), 5.03–5.11 (2H, m, $-CH_2-CH=CH_2$), 3.84 (3H, s, –OMe), 3.81 (3H, s, –OMe), 3.07–3.77 {4H, m, $-CON(CH_2CH_3)_2$}, 1.24 {3H, t, J=7.2 Hz, $-CON(CH_2CH_3)_2$}, 1.06 {3H, t, J=7.2 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 167.4, 150.7, 144.4, 136.6, 131.9, 128.8, 124.8, 115.9, 112.1, 61.3, 55.6, 42.8, 38.4, 36.2, 13.6, 12.5.

4.1.5. *N*,*N*-Diethyl-1-carbamyloxy-3-allyl-5-methoxynaphthalene-2-carboxamide (22). Purified by column chromatography (ethyl acetate–light petroleum (2:3)). Gummy liquid (85%); [Found: C, 69.68; H, 8.0; N, 6.8. $C_{24}H_{32}O_4N_2$ requires C, 69.9; H, 7.76; N, 6.79%]; ν_{max} ($CHCl_3$) 1708, 1629 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.01 (1H, s, C-4), 7.36 (1H, dd, J=8.4, 7.5 Hz, C-7), 7.28 (1H, d, J=8.4 Hz, C-8), 6.8 (1H, d, J=7.5 Hz, C-6), 6.12–5.9 (1H, m, $-CH_2-CH=CH_2$), 5.2–5.13 (2H, m, $-CH_2-CH=CH_2$), 3.97 (3H, s, –OMe), 3.1–3.6 {10H, m, $-CH_2-CH=CH_2$, $-OCON(CH_2CH_3)_2$, $-CON(CH_2CH_3)_2$}, 1.0–1.3 {12H, m, $-OCON(CH_2CH_3)_2$, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 167.4, 155.5, 153.8, 143.5, 136.5, 133.8, 128.8, 128.0, 126.8, 126.7, 120.1, 117.2, 114.4, 105.0, 55.9, 43.2, 42.7, 42.5, 38.6, 37.7, 14.7, 13.9, 13.8, 13.1.

4.1.6. *N*,*N*-Diethyl-1-carbamyloxy-3-allyl-6-methoxynaphthalene-2-carboxamide (28). Purified by column chromatography (ethyl acetate–light petroleum (3:7)). Viscous liquid (73%); [Found: C, 69.87; H, 7.74; N, 6.76. $C_{24}H_{32}O_4N_2$ requires C, 69.9; H, 7.76; N, 6.79%]; ν_{max} ($CHCl_3$) 1721 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.60 (1H, d, J=9 Hz, C-8), 7.46 (1H, s, C-4), 7.11 (1H, dd, J=2.4, 9 Hz, C-7), 7.06 (1H, d, J=2.4 Hz, C-5), 5.9–6.12 (1H, m, $-CH_2-CH=CH_2$), 5.06–5.26 (2H, m, $-CH_2-CH=CH_2$), 3.89 (3H, s, –OMe), 3.1–3.6 {10H, m, $-CH_2-CH=CH_2$, $-OCON(CH_2CH_3)_2$, $-CON(CH_2CH_3)_2$}, 1.01–1.32 {12H, m, $-OCON(CH_2CH_3)_2$, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 167.4, 158.7, 153.8, 143.9, 136.4, 135.9, 135.3, 126.2, 124.7, 123.9, 122.3, 119.5, 117.3, 105.9, 55.7, 43.1, 42.7, 42.5, 38.6, 37.4, 14.7, 14.0, 13.8, 13.1.

4.1.7. *N*,*N*-Diethyl-4-methoxy-6-allyl-2-*tert*-butyldimethylsilyl[1]benzo[*b*]thiophene-5-carboxamide (34). Purified by column chromatography (ethyl acetate–light petroleum (2:3)). Gummy liquid (69%); [Found: C, 66.35; H, 8.3; N, 3.17. $C_{22}H_{33}O_2NSSi$ requires C, 66.14; H, 8.44; N, 3.35%]; ν_{max} (KBr) 1624 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.52 (1H, s, C-3), 7.51 (1H, s, C-7), 5.93–6.02 (1H, m, $-CH_2-CH=CH_2$), 5.09–5.16 (2H, m, $-CH_2-CH=CH_2$), 3.99 (3H, s, –OMe), 3.62 {2H, q, J=7.2 Hz, $-CON(CH_2CH_3)_2$}, 3.35–3.46 (2H, m, $-CH_2-CH=CH_2$), 3.14 {2H, q, J=7.2 Hz, $-CON(CH_2CH_3)_2$}, 1.31 {3H, t, J=7.2 Hz, $-CON(CH_2CH_3)_2$}, 1.04 {3H, t, J=7.2 Hz, $-CON(CH_2CH_3)_2$}, 0.97 {9H, s, $-Si(CH_3)_2C(CH_3)_3$}, 0.36 (6H, s, $-Si(CH_3)_2C(CH_3)_3$}; δ_C (300 MHz, $CDCl_3$) 167.8, 150.3–114.0, 62.4, 43.2, 38.8, 37.1, 26.1, 13.6, 12.8, −5.2.

4.1.8. *N*,*N*-Diethyl-5-allyl-7-methoxy-2-trimethylsilylbenzo[*b*]thiophene-6-carboxamide (41). Purified by column chromatography (ethyl acetate–light petroleum (3:7)). Colorless viscous oil (72%); [Found: C, 64.10; H, 7.83; N, 3.9. $C_{20}H_{29}O_2NSSi$ requires C, 64.00; H, 7.73; N, 3.73%]; ν_{max} ($CHCl_3$) 1629 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 7.44 (1H, s, C-3), 7.41 (1H, s, C-4), 5.88–5.97 (1H, m, $-CH_2-CH=CH_2$), 5.01–5.11 (2H, m, $-CH_2-CH=CH_2$), 4.04 (3H, s, –OMe), 3.25–3.46 {6H, m, $-CH_2-CH=CH_2$, $-CON(CH_2CH_3)_2$}, 1.03 {3H, t, J=9 Hz, $-CON(CH_2CH_3)_2$}, 1.29 {3H, t, J=6 Hz, $-CON(CH_2CH_3)_2$}, 0.38 {9H, s, $-Si(CH_3)_2C(CH_3)_3$}. δ_C (300 MHz, $CDCl_3$) 150.3, 145.6, 139.0, 136.0, 134.2, 132.8, 127.8, 125.7, 117.8, 116.4, 62.4, 42.8, 39.1, 36.8, 16.6, 13.6, 12.5, 0.1.

4.1.9. *N*,*N*-Diethyl-3-allyl-4-methoxybenzo[*b*]thiophene-2-carboxamide (47). Purified by column chromatography (ethyl acetate–light petroleum (2:3)). Gummy liquid (81%); [Found: C, 67.19; H, 6.67; N, 4.8. $C_{17}H_{21}O_2NS$: C, 67.32; H, 6.93; N, 4.62%]; ν_{max} ($CHCl_3$) 1623 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.3 (1H, d, *J*=8 Hz, C-7), 7.2 (1H, dd, *J*=8, 7.8 Hz, C-6), 6.69 (1H, d *J*=7.8 Hz, C-5), 5.93–6.02 (1H, m, $-CH_2-CH{=}CH_2$), 4.85–4.97 (2H, m, $-CH_2-CH{=}CH_2$), 3.84 (3H, s,–OMe), 3.23–3.71 {6H, m, $-CH_2-CH{=}CH_2$, $-CON(CH_2CH_3)_2$}, 1.01–1.21{6H, m, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 164.5, 156.2, 140.5, 136.5, 132.6, 129.6, 127.7, 125.4, 114.3, 114.2, 104.5, 54.7, 33.3, 12.6.

4.1.10. *N*,*N*-Diethyl-3-allyl-4,6-dimethoxybenzo[*b*]thiophene-2-carboxamide (48). Purified by column chromatography (ethyl acetate–light petroleum (3:7)). Yellowish viscous liquid (75%); [Found: C, 64.9; H, 7.1; N, 4.6. $C_{18}H_{23}O_3NS$: C, 64.86; H, 6.9; N, 4.2%]; ν_{max} ($CHCl_3$) 1631 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.75 (1H, d, *J*=1.9 Hz, C-7), 6.32 (1H, d, *J*=1.9 Hz, C-5), 5.88–6.0 (1H, m, $-CH_2-CH{=}CH_2$), 4.84–4.96 (2H, m, $-CH_2-CH{=}CH_2$), 3.8 (3H, s, –OMe), 3.78 (3H, s, –OMe), 3.16–3.70 {6H, m, $-CH_2-CH{=}CH_2$, $-CON(CH_2CH_3)_2$}, 0.97–1.18 {6H, m, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 171.1, 159.4, 157.5, 142.4, 137.5, 133.5, 131.2, 129.2, 115.1, 97.0, 96.6, 56.0, 55.7, 34.0, 30.1, 11.3.

4.1.11. *N*,*N*-Diethyl-3-allyl-5-methoxybenzo[*b*]thiophene-2-carboxamide (54). Purified by column chromatography (ethyl acetate–petroleum ether (3:7)). Gummy liquid (69%); [Found: C, 67.35; H, 6.98; N, 4.79. $C_{17}H_{21}O_2NS$: C, 67.32; H, 6.93; N, 4.62%]; ν_{max} ($CHCl_3$) 1624 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 6.67 (1H, d, *J*=9 Hz, C-7), 7.19 (1H, d, *J*=2.4 Hz, C-4), 7.03 (dd, 1H, *J*=2.4, 9 Hz, C-6), 6.11–5.92 (1H, m, $-CH_2-CH{=}CH_2$), 4.81–5.92 (2H, m, $-CH_2-CH{=}CH_2$), 3.87 (3H, s, –OMe), 3.49–3.62 {6H, m, $-CH_2-CH{=}CH_2$, $-CON(CH_2CH_3)_2$}, 1.25 {6H, t, *J*=6 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 164.7, 157.5, 139.7, 134.8, 133.1, 131.7, 131.2, 123.0, 116.3, 115.0, 105.1, 55.4, 42.2, 31.6, 13.1.

4.1.12. *N*,*N*-Diethyl-2,3-dimethoxybenzamide (13). To a well stirred solution of TMEDA (4 mL, 1.5 equiv.) and THF (50 mL), *s*-BuLi (13.45 mL, 1.5 equiv.) was added at −78°C. Stirring was continued for 40 min when an yellow colour developed. Compound **12** (4 g, 0.00179 mmol) in THF (10 mL) was then added to it at that temperature. The reaction mixture was allowed to attain room temperature and kept at that temperature for 16 h. Usual work up afforded the hydroxy compound which was sufficiently pure for the next step. This crude phenolic compound (3.34 g, 0.001497 mmol) was methylated using K_2CO_3 (2.5 g, 1.2 equiv.) and methyl iodide (4.7 mL, 5 equiv.). Purified by column chromatography (ethyl acetate: petroleum ether (3:17)). Pale yellow liquid (1.57 g, 45%); [Found: C, 65.80; H, 8.18; N, 6.1. $C_{13}H_{19}O_3N$ requires C, 65.79; H, 8.07; N, 5.90%]; ν_{max} ($CHCl_3$) 1627 cm^{-1}; δ_H (300 MHz, $CDCl_3$), 7.07 (1H, dd, *J*=6, 9 Hz, C-5), 6.9 (1H, dd, *J*=3, 9 Hz, C-6), 6.80 (1H, dd, *J*=3, 6 Hz, C-4), 3.88 (3H, s, –OMe), 3.85 (3H, s, –OMe), 3.16 {4H, q, *J*=6 Hz, $-CON(CH_2CH_3)_2$}, 1.14 {6H, t, *J*=6 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 168.3, 152.6, 144.7, 132.4, 124.6, 118.7, 112.5, 61.4, 55.7, 42.9, 38.8, 13.9, 12.8.

4.1.13. *N*,*N*-Diethyl-1,5-dimethoxynaphthalene-2-carboxamide (20). Prepared in the same way as before. Purified by column chromatography (ethyl acetate–light petroleum (1:3)). Gummy liquid (35%); [Found: C, 70.86; H, 7.31; N, 4.87. $C_{17}H_{21}O_3N$ requires C, 70.8; H, 7.3; N, 4.8%]; ν_{max} ($CHCl_3$) 1633 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.04 (d, 1H, *J*=8.6 Hz, C-4), 7.72 (d, 1H, *J*=8.2 Hz, C-8), 7.44 (1H, dd, *J*=8.0, 8.2 Hz, C-7), 7.29 (1H, d, *J*=8.6 Hz, C-3), 6.86 (1H, d, *J*=8.0 Hz, C-6), 4.07 (3H, s, –OMe), 3.9 (3H, s, –OMe), 3.43 {4H, q, *J*=6.6 Hz, $-CON(CH_2CH_3)_2$}, 1.16 {6H, t, *J*=7.14 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 169.5, 156.0, 151.9, 129.3, 127.4, 126.9, 126.9, 124.2, 118.7, 114.9, 105.1, 63.1, 55.9, 43.4, 39.5, 14.4, 13.2.

4.1.14. *N*,*N*-Diethyl-1-methoxymethylene-6-methoxynaphthalene-2-carboxamide (26). Purified by column chromatography (ethyl acetate–light petroleum (1:4)). Colorless viscous liquid (78%); [Found: C, 68.41; H, 7.35; N, 4.48. $C_{18}H_{23}O_4$ requires C, 68.13; H, 7.25; N, 4.41%]; ν_{max} ($CHCl_3$) 1627 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.15 (1H, d, *J*=8.1 Hz, C-8), 7.53 (1H, d, *J*=8.4 Hz, C-3), 7.29 (1H, d, *J*=8.4 Hz, C-4), 7.19 (1H, dd, *J*=2.5, 9.1 Hz, C-7), 7.12 (1H, d, *J*=2.5 Hz, C-5), 5.19 (2H, s, $-OCH_2OCH_3$), 3.92 (3H, s, $-OCH_2OCH_3$), 3.5 (3H, s, –OMe), 3.1–3.5 {4H, m, $-CON(CH_2CH_3)_2$}, 1.28 {3H, t, *J*=7.2 Hz, $-CON(CH_2CH_3)_2$}, 1.03 {3H, t, *J*=7.2 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 169.6, 158.9, 149.7, 136.7, 125.8, 125.0, 124.6, 124.0, 123.7, 119.6, 106.2, 101.0, 58.2, 55.7, 43.5, 39.5, 14.4, 13.3.

4.1.15. *N*,*N*-Diethyl-4-methoxybenzo[*b*]thiophene-5-carboxamide (32). Purified by column chromatography (ethyl acetate–light petroleum (1:3)). Colorless liquid (68%); [Found: C, 63.65; H, 6.61; N, 5.45. $C_{14}H_{17}O_2NS$ requires C, 63.85; H, 6.51; N, 5.31%]; ν_{max} ($CHCl_3$) 1635 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.78 (1H, d, *J*=8.7 Hz, C-6), 7.46 (1H, d, *J*=5.4 Hz, C-3), 7.13 (1H, d, *J*=5.4 Hz, C-2), 7.03 (1H, d, *J*=8.7 Hz, C-7), 3.88 (3H, s, –OMe), 3.45 {4H, q, *J*=7.8 Hz, $-CON(CH_2CH_3)_2$}, 1.64 {6H, t, *J*=6.9 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 167.8, 150.4, 145.6, 139.0, 132.9, 127.9, 125.7, 117.9, 116.5, 62.4, 38.5, 36.8, 12.8, 12.1.

4.1.16. *N*,*N*-Diethyl-7-methoxy-2-trimethylsilylbenzo[*b*]thiophene-6-carboxamide (40). Purified by column chromatography (ethyl acetate–light petroleum (3:7)). Colorless gummy liquid (68%); [Found: C, 61.00; H, 7.56; N, 4.19. $C_{17}H_{25}O_2NSSi$ requires C, 60.89; H, 7.46; N, 4.17%]; ν_{max} ($CHCl_3$) 1596 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.55 (1H, d, *J*=8.1 Hz, C-5), 7.46 (1H, s, C-3), 7.19 (1H, d, *J*=8.1 Hz, C-4), 4.05 (3H, s, –OMe), 3.50 {4H, q, *J*=6 Hz, $-CON(CH_2CH_3)_2$}, 1.15 {6H, t, *J*=9 Hz, $-CON(CH_2CH_3)_2$}, 0.39 (9H, s, $-SiMe_3$); δ_C (300 MHz, $CDCl_3$) 153.7, 146.6, 144.0, 142.7, 136.6, 131.5, 120.6, 117.1, 62.4, 42.9, 42.6, 14.8, 13.8, 0.1.

4.1.17. *N*,*N*-Diethyl-4-methoxy-2-*tert*-butyldimethylsilylbenzo[*b*]thiophene-5-carboxamide (33). Synthesized from **32** following the general procedure using *tert*-butyldimethylsilylchloride (TBDMSCl) as electrophile. Purified

by column chromatography (ethyl acetate: light petroleum (3:7)). Colorless viscous liquid (58%); [Found: C, 63.94; H, 8.04; N, 3.81. $C_{20}H_{31}NO_2Ssi$ requires C, 63.61; H, 8.28; N, 3.71%]; ν_{max} ($CHCl_3$) 1630 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.63 (1H, d, J=8.4 Hz, C-6), 7.59 (1H, s, C-3), 7.18 (1H, d, J=8.4 Hz, C-7), 4.02 (3H, s, –OMe), 3.64 {2H, q, J=7.8 Hz, $-CON(CH_2CH_3)_2$}, 3.16 {2H, q, J=7.8 Hz, $-CON(CH_2CH_3)_2$}, 1.30 {3H, t, J=6.9 Hz, $-CON(CH_2CH_3)_2$}, 1.04 {3H, t, J=6.9 Hz, $-CON(CH_2CH_3)_2$}, 0.98 {9H, s, $-Si(CH_3)_2C(CH_3)_3$}, 0.37 {6H, s, $-Si(CH_3)_2C(CH_3)_3$}; δ_C (300 MHz, $CDCl_3$) 167.7, 150.2, 145.3, 139.2, 132.9, 127.7, 125.5, 117.3, 115.5, 62.4, 38.4, 36.3, 12.7, 12.1, −5.2.

4.1.18. *N,N*-Diethyl-1-carbamyloxy-2-methoxybenzene (12). Compound **11** (5 g, 0.004 mmol) was converted to the corresponding *O*-carbamate by the usual procedure using NaH (2.4 g, 1.5 equiv.), $ClCONEt_2$ (5.06 mL, 1 equiv.). Purified by column chromatography (ethyl acetate: light petroleum (1:9)); Gummy liquid (7.9 g, 88%); [Found: C, 64.32; H, 7.81; N, 4.94. $C_{12}H_{17}O_3N$ requires C, 64.57; H, 7.62; N, 6.27 %]; ν_{max} ($CHCl_3$) 1686 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.06 (2H, dd, J=1.4, 9.0 Hz, C-6, C-7), 6.87 (2H, dd, J=1.4, 9 Hz, C-3, C-4), 3.72 (3H, s, –OMe), 3.36 {4H, q, $-CON(CH_2CH_3)_2$}, 1.21 {6H, t, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 152.4, 150.1, 139.1, 124.4, 121.6, 118.8, 116.7, 54.0, 40.5, 40.3, 11.7.

4.1.19. *N,N*-Diethyl-1-carbamyloxy-7,8-dimethoxynaphthalene (16). Prepared in the same way as **12**. Purified by column chromatography (ethyl acetate–light petroleum (3:7)); Yellowish oil (10%); [Found: C, 67.0; H, 6.83; N, 4.41. $C_{17}H_{21}O_4N$ requires C, 67.32; H, 6.93; N, 4.62 %]; ν_{max} ($CHCl_3$) 1694 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.59 (2H, d, J=8.6 Hz, C-2, C-4), 7.52 (2H, dd, J=7.5, 8.6 Hz, C-3, C-5), 7.10 (1H, d, J=7.5 Hz, C-6), 3.93 (3H, s, –OMe), 3.88 (3H, s, –OMe), 3.52 {4H, q, J=6 Hz, $-OCON(CH_2CH_3)_2$}, 1.23 {6H, t, J=9 Hz, $-OCON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 154.8, 149.6, 146.3, 143.1, 131.8, 125.8, 124.4, 123.3, 120.4, 115.5, 61.1, 56.7, 42.2, 41.6, 13.9, 13.2.

4.1.20. *N,N*-Diethyl-1-carbamyloxy-5-methoxynaphthalene (19). Potassium carbonate (3.87 g, 1 equiv.) was added to a solution of the compound **18** (4.5 g, 0.0028 mmol) in dry acetone (20 mL). After stirring for 3 h the mixture was cooled to 0°C and methyl iodide (1.4 mL, 8 equiv.) in dry acetone (10 mL) was added drop wise at that temperature. After stirring for 2 h at 0°C and 10 h at room temperature, the mixture was filtered, the solvent was removed under reduced pressure and the residue was poured into crushed ice. After extraction with diethyl ether, the organic layer was washed with water and removal of solvent afforded compound **19** which was purified by column chromatography (ethyl acetate–light petroleum (3:7)). Low melting white solid (1.71 g, 40%); [Found: C, 69.81; H, 7.02; N, 5.10. $C_{16}H_{19}O_3N$ requires C, 70.32; H, 6.95; N, 5.12%]; ν_{max} (KBr) 3360 cm^{-1}. δ_H (300 MHz, $CDCl_3$) 7.84 (1H, d, J=8.1 Hz, C-4), 7.74 (1H, d, J=8.0 Hz, C-8), 7.39 (1H, dd, J=7.8, 8.1 Hz, C-3), 7.29 (1H, dd, J=7.8, 8 Hz, C-7), 6.82 (2H, d, J=7.8 Hz, C-6, C-8), 4.0 (3H, s, –OMe); δ_C (300 MHz, $CDCl_3$) 155.0, 154.3, 147.5, 128.0, 127.3, 125.7, 125.5, 119.1, 113.4, 105.6, 56.9. The free hydroxy group was converted to *O*-carbamate by usual procedure. Purification of the reaction mixture by column chromatography (ethyl acetate–petroleum ether (1:9)) afforded **19** as a yellow solid (76%), mp 65–66°C; [Found C, 70.41; H, 6.98; N, 5.11. $C_{16}H_{19}O_3N$ requires C, 70.32; H, 6.95; N, 5.12%]; ν_{max} (KBr) 1708 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.11 (1H, d, J=8.4 Hz, C-2), 7.37–7.50 (3H, m, C-3, C-4, C-7), 7.29 (1H, dd, J=7.8, 1 Hz, C-8), 6.82 (1H, d, J=7.2 Hz, C-6), 4.0 (3H, s, –OMe), 3.52 {4H, q, J=9 Hz, $-OCON(CH_2CH_3)_2$}, 1.3 {6H, t, J=6 Hz, $-OCON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 155.9, 154.7, 147.6, 129.0, 127.3, 126.7, 125.1, 119.2, 113.9, 104.6, 55.9, 42.7, 42.4, 14.9, 13.8.

4.1.21. *N,N*-Diethyl-1-carbamyloxy-6-methoxynaphthalene (25). Compound **25** was synthesized from commercially available 6-methoxy-α-tetralone (**24**). Bromination (with CuBr) and dehydrobromination (with Li_2CO_3/LiBr/DMF) afforded the 6-methoxy-1-hydroxynaphthalene as white solid (87%). The hydroxy compound (4.16 g, 0.0024 mmol) was converted to *O*-carbamate by the usual procedure as described earlier with NaH (1.43 g, 1.5 equiv.) and freshly distilled *N,N*-diethylcarbamylchloride (4.35 mL, 1.2 equiv.) and THF as solvent. Crystallisation with ether–petroleum ether afforded **25** as an yellowish solid (5.9 g, 90%), mp 83–85°C; [Found: C, 70.35; H, 6.79; N, 4.88. $C_{16}H_{19}O_3N$ requires C, 70.32; H, 6.95; N, 5.12%]; ν_{max} ($CHCl_3$) 1629 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.81 (1H, d, J=8.9 Hz, C-8), 7.58 (1H, d, J=8.0 Hz, C-4), 7.4 (1H, dd, J=7.8, 8 Hz, C-3), 7.11–7.17 (3H, m, C-2, C-5, C-7), 3.9 (3H, s, –OMe), 3.51 {4H, q, J=9 Hz, $-OCON(CH_2CH_3)_2$}, 1.30 {6H, t, J=6 Hz, $-OCON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 173.2, 160.1, 158.6, 137.6, 125.8, 124.8, 120.8, 118.1, 116.7, 108.8, 106.1, 55.7, 42.6, 13.8.

4.1.22. *N,N*-Diethyl-4-carbamyloxybenzo[*b*]thiophene (31). Prepared in the same way as **12**. Purified by column chromatography (ethyl acetate–light petroleum (1:9)). Colorless viscous liquid (82%); [Found: C, 62.56; H, 6.37; N, 5.72. $C_{13}H_{15}O_2NS$ requires C, 62.62; H, 6.06; N, 5.61%]; ν_{max} (KBr) 1700 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.76 (1H, d, J=8.1 Hz, C-5), 7.38 (2H, dd, J=2, 8 Hz, C-6, C-7), 7.24 (1H, d, J=5.02, C-3), 7.07 (1H, d, J=5.02, C-2), 3.66–3.2 {4H, m, $-OCON(CH_2CH_3)_2$}, 1.54–1.10 {6H, m, $-OCON(CH_2CH_3)_2$}.

4.1.23. *N,N*-Diethyl-7-carbamyloxy-2-trimethylsilylbenzo[*b*]thiophene (38). Prepared in the same way as compound **12**. Purified by column chromatography (ethyl acetate–light petroleum (1:3)), light yellow oil (79%); [Found: C, 59.78; H, 7.06; N, 4.42. $C_{16}H_{23}O_2NSSi$ requires C, 59.81; H, 7.16; N, 4.36%]; ν_{max} ($CHCl_3$) 1625 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.53 (1H, d, J=7.8 Hz, C-6), 7.36 (1H, s, C-3), 7.24 (1H, dd, J=7.8, 7.5 Hz, C-5), 7.08 (1H, d, J=7.5 Hz, C-4), 3.39 {4H, q, J=7.8 Hz, $-OCON(CH_2CH_3)_2$}, 1.20 {6H, t, J=9 Hz, $-OCON(CH_2CH_3)_2$}, 0.28 {9H, s, $-Si(CH_3)_3$}; δ_C (300 MHz, $CDCl_3$) 153.7, 146.5, 143.9, 142.7, 136.6, 131.5, 125.5, 120.6, 117.1, 42.8, 42.5, 14.7, 13.8, 0.1.

4.1.24. *N,N*-Diethyl-1-carbamyloxy-5-methoxynaphthalene-2-carboxamide (21). To a well stirred solution of TMEDA (1.1 mL, 1.5 equiv.), *s*-BuLi (3.92 mL, 2.5 equiv.)

in THF (10 mL) at −78°C compound **19** (1 g, 0.00044 mmol) was added. After stirring the reaction mixture for 40 min at −78°C, freshly distilled *N*,*N*-diethylcarbamylchloride (0.9 mL, 1.5 equiv.) was added and stirring was continued at that temperature for 1 h. After which it was allowed to attain room temperature and was stirred for further 12 h at that temperature. Usual work up with diethyl ether afforded compound **21** which was purified by column chromatography with ethyl acetate: petroleum ether (1:3) as eluant. Viscous liquid (62%); [Found: C, 67.84; H, 7.72; N, 7.48. $C_{21}H_{28}O_4N_2$ requires C, 67.74; H, 7.52; N, 7.52%]; ν_{max} ($CHCl_3$) 1732, 1714 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.16 (1H, d, *J*=8.5 Hz, C-4), 7.43 (2H, d, *J*=6 Hz, C-7, C-8), 7.3 (1H, d, *J*=8.5 Hz, C-3), 6.84 (1H, dd, *J*=4.2, 4.5 Hz, C-6), 3.99 (3H, s, −OMe), 3.47 {8H, q, *J*=6 Hz, $-OCON(CH_2CH_3)_2$, $-CON(CH_2CH_3)_2$}, 1.21 {12H, t, *J*=7.2 Hz, $-OCON(CH_2CH_3)_2$ $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 168.4, 155.8, 153.9, 143.7, 129.6, 128.2, 127.5, 127.0, 122.7, 120.3, 114.4, 105.1, 56.0, 43.2, 42.7, 42.7, 39.0, 14.8, 14.2, 13.8, 13.0. Compound **27**, **45** and **46** were synthesized in the same way.

4.1.25. *N*,*N*-Diethyl-1-carbamyloxy-6-methoxynaphthalene-2-carboxamide (27). Purified by column chromatography (ethyl acetate–light p etroleum (1:3)). Gummy liquid (69%); [Found: C, 67.78; H, 7.58; N, 7.59. $C_{21}H_{28}O_4N_2$ requires C, 67.74; H, 7.52; N, 7.52%]; ν_{max} ($CHCl_3$) 1629 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.77 (1H, d, *J*=9.1 Hz, C-8), 7.6 (1H, d, *J*=8.4 Hz, C-3), 7.29 (1H, d, *J*=8.4 Hz, C-4), 7.18 (1H, dd, *J*=2.5, 9.1 Hz, C-7), 7.12 (1H, d, *J*=2.5 Hz, C-5), 3.89 (3H, s, −OMe), 3.45 {8H, q, *J*=6.9 Hz, $-OCON(CH_2CH_3)_2$, $-CON(CH_2CH_3)_2$}, 1.2 {12H, t, *J*=7.1 Hz, $-OCON(CH_2CH3)_2$, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 168.4, 158.7, 153.9, 144.2, 136.3, 125.5, 124.8, 124.3, 124.0, 123.9, 120.1, 106.2, 55.7, 43.2, 42.7, 42.7, 39.0, 14.8, 14.2, 13.8, 13.0.

4.1.26. *N*,*N*-Diethyl-4-methoxybenzo[*b*]thiophene-2-carboxamide (45). Purified by column chromatography (ethyl acetate–light petroleum (1:3)). Waxy solid (71%); [Found: C, 64.0; H, 6.37; N, 5.16. $C_{14}H_{17}O_2NS$ requires C, 63.85; H, 6.51; N, 5.31%]; ν_{max} ($CHCl_3$) 1618 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.65 (1H, s, C-3), 7.41 (1H, d, *J*=8 Hz, C-7), 7.3 (1H, dd, *J*=8, 8.6 Hz, C-6), 6.74 (1H, d, *J*=8.6 Hz, C-5), 3.9 (3H, s, −OMe), 3.5 {4H, q, *J*=7.08 Hz, $-CON(CH_2CH_3)_2$}, 1.2 {6H, t, *J*=7.1 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 164.6, 155.9, 142.0, 136.8, 130.0, 127.1, 121.3, 116.4, 114.9, 104.8, 55.8, 42.0, 14.2.

4.1.27. *N*,*N*-Diethyl-4,6-dimethoxybenzo[*b*]thiophene-2-carboxamide (46). Yellow crystals (ether–light petroleum) (72%), mp 110–111°C; [Found: C, 61.52; H, 6.51; N, 4.81. $C_{15}H_{19}O_3NS$ requires C, 61.43; H, 6.48; N, 4.77%]; ν_{max} (KBr) 1604 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.55 (1H, s, C-3), 6.86 (1H, d, *J*=1.6 Hz, C-7), 6.38 (1H, d, *J*=1.6 Hz, C-5), 3.9 (3H, s, −OMe), 3.86 (3H, s, −OMe), 3.57 {4H, q, *J*=7.08 Hz, $-CON(CH_2CH_3)_2$}, 1.27 {6H, t, *J*=7.08 Hz, $-CON(CH_2CH_3)_2$}; δ_C (300 MHz, $CDCl_3$) 164.4, 160.3, 156.4, 143.3, 134.4, 124.7, 121.4, 96.5, 96.1, 56.1, 55.8, 42.7, 14.1.

4.1.28. 3,4-Dihydro-3-methyl-6,10-dimethoxy-1-oxo-1*H*-naphtho[2,3-*c*]pyran (23). Compound **22** was heated at reflux for 36 h with 6N HCl. After cooling, saturated solution of ammonium chloride was added and the reaction mixture was extracted with dichloromethane. The organic phase was washed with water, dried and the solvent evaporated. The crude residue consisting of the labile phenolic cyclization product was methylated with methyl iodide in hot dry acetone in the presence of anhydrous potassium carbonate. After filtering the reaction mixture, the filtrate was washed with water, dried, the solvent evaporated and the residue purified by column chromatography (ethyl acetate–light petroleum (2:3)). Low melting white solid (61%); [Found: C, 70.71; H, 6.15. $C_{16}H_{16}O_4$ requires C, 70.58; H, 5.88%]; ν_{max} (KBr) 1714 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.8 (1H, d, *J*=8 Hz, C-9), 7.75 (1H, s, C-5), 7.36 (1H, dd, *J*=7.5, 8.1 Hz, C-8), 6.87 (1H, d, *J*=7.5 Hz, C-7), 4.59–4.65 (1H, m, C-3), 4.1 (3H, s, −OMe), 4.0 (3H, s, −OMe), 3.04–3.07 (2H, m, C-4), 1.51 (3H, d, *J*=4.5 Hz, $-CH_3$); δ_C (300 MHz, $CDCl_3$) 155.3, 134.9, 126.6, 116.4, 115.7, 115.5, 107.3, 107.0, 76.9, 63.7, 56.1, 37.0, 21.1.

4.1.29. 3,4-Dihydro-3-methyl-7,10-dimethoxy-1-oxo-1*H*-naphtho[2,3-*c*]pyran (29). Purified by column chromatography (ethyl acetate–light petroleum (2:3)). Low melting white solid (67%); [Found: C, 70.87; H, 5.98. $C_{16}H_{16}O_4$ requires C, 70.58; H, 5.88%]; ν_{max} (KBr) 1714 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.2 (1H, d, *J*=9.2 Hz, C-9), 7.26 (1H, s, C-5), 7.16 (1H, dd, *J*=2.5, 9 Hz, C-8), 7.03 (1H, d, *J*=2.5 Hz, C-6), 4.61–4.63 (1H, m, C-3), 4.1 (3H, s, −OMe), 3.9 (3H, s, −OMe), 3.0 (2H, d, *J*=6.6 Hz, C-4), 1.51 (3H, d, *J*=6.33 Hz, $-CH_3$); δ_C (300 MHz, $CDCl_3$) 163.5, 160.9, 154.9, 138.9, 136.6, 126.4, 123.7, 120.1, 119.3, 105.6, 74.7, 63.7, 55.8, 36.9, 21.1.

4.1.30. 3,4-Dihydro-3-methyl-9-methoxy-1-oxo-1*H*-[1]benzothieno[5, 6-*c*]pyran (36). White crystals (ether–light petroleum) (85%), mp 105–106°C; [Found: C, 63.05; H, 4.95. $C_{13}H_{12}O_3S$ requires C, 62.86; H, 4.87%]; ν_{max} (KBr) 1707 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.56 (1H, d, *J*=5.4 Hz, C-8), 7.45 (1H, s, C-5), 7.39 (1H, d, *J*=5.4 Hz, C-7), 4.72–4.79 (1H, m, C-3), 4.1 (3H, s, −OMe), 3.02 (2H, d, *J*=5.7 Hz, C-4), 1.52 (3H, d, *J*=6.3 Hz, $-CH_3$); δ_C (300 MHz, $CDCl_3$) 158.9, 146.2, 136.4, 134.8, 126.9, 122.0, 116.3, 113.2, 96.5, 74.7, 63.3, 36.9, 21.0.

4.1.31. 3,4-Dihydro-3-methyl-5-methoxy-1-oxo-1*H*-[1]benzothieno[2,3-*c*]pyran (49). White crystals (CCl_4–petroleum ether) (68%), mp 136–140°C; [Found: C, 63.1; H, 5.1. $C_{13}H_{12}O_3S$ requires C, 62.9; H, 4.8%]; ν_{max} (KBr) 1708 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.71 (1H, d, *J*=8.7 Hz, C-8), 7.14–7.08 (2H, m, C-6, C-7), 4.84–4.94 (1H, m, C-3), 3.9 (3H, s −OMe), 2.89–3.19 (2H, m, C-4), 1.63 (3H, d, *J*=6.24 Hz, $-CH_3$); δ_C (300 MHz, $CDCl_3$) 157.8, 142.4, 137.9, 136.0, 124.6, 119.2, 105.1, 76.9, 55.6, 30.5, 20.9.

4.1.32. 3,4-Dihydro-3-methyl-6-methoxy-1-oxo-1*H*-[1]benzothieno[2,3-*c*]pyran (55). White crystals (62%) (CCl_4–petroleum ether), mp 128–130°C; [Found: C, 63.12; H, 5.2. $C_{13}H_{12}O_3S$ requires C, 62.9; H, 4.8%]; ν_{max} (KBr) 1701 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.78 (1H, d *J*=8.7 Hz, C-8), 7.19 (1H, d, *J*=2.4 Hz, C-5), 7.15 (1H, dd, *J*=2.4, 8.7 Hz, C-7), 4.87–4.94 (1H, m, C-3), 3.9 (3H, s, −OMe), 2.89–3.20 (2H, m, C-4), 1.6 (3H, d, *J*=6.0 Hz, $-CH_3$); δ_C

(300 MHz, $CDCl_3$) 158.4, 142.4, 137.9, 136.0, 124.6, 119.2, 105.1, 76.9, 56.0, 30.8, 21.2.

4.1.33. 3,4-Dihydro-3-methyl-9-hydroxy-1-oxo-1*H*-[1]benzothieno[6,5-*c*]pyran (42). White solid (63%) (CCl_4–light petroleum), mp 137–138°C; [Found: C, 61.42; H, 4.1. $C_{12}H_{10}O_3S$ requires C, 61.53; H, 4.27%]; ν_{max} (KBr) 1710 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 11.92 (1H, s, –O*H*), 7.6 (1H, d, *J*=6 Hz, C-6), 7.34 (1H, d, *J*=6 Hz, C-7), 7.17 (1H, s, C-5), 4.72–4.79 (1H, m, C-3), 3.02 (2H, d, *J*=9 Hz, C-4),1.59 (3H, d, *J*=6.0 Hz, $-CH_3$); δ_C (300 MHz, $CDCl_3$) 158.9, 146.2, 136.4, 134.8, 126.4, 122.0, 116.3, 113.2, 96.5, 7.7, 36.9, 21.0.

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