Indium-mediated diastereoselective allylation reactions: preparation of α-hydroxy and α-amino acids

Jung Gyu Lee,[a,b] Kyung Il Choi,[a] Ae Nim Pae,[a] Hun Yeong Koh,[a] Yonghan Kang[b] and Yong Seo Cho*[a]

[a] *Biochemicals Research Center, Korea Institute of Science and Technology, Cheongryang P.O. Box 131, Seoul 130-650, Korea. E-mail: ys4049@kist.re.kr; Fax: +82-2-958-5189*

[b] *Department of Chemistry College of Sciences, Hanyang University, 1271 Sa-1-dong, Ansan city, Kyunggi-do 425-791, Korea*

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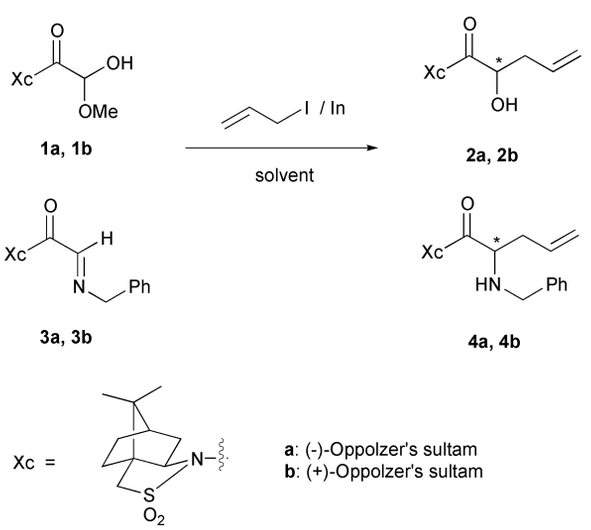
The hemiacetals of (+)- and (−)-*N*-glyoxyloylbornane-10,2-sultam and their imines reacted with allyl iodide in the presence of indium in DMF to give the corresponding α-hydroxy and α-amino camphor sultam derivatives with high diastereoselectivities (86–90% de). This method could be useful for preparation of α-hydroxy and α-amino acids.

Introduction

Optically pure α-hydroxy and α-amino acids are important building blocks in synthetic organic chemistry. A number of methods that have been used to prepare these compounds have been reported.[1] Recently, Kakinuma *et al.* have reported diastereoselective indium mediated allylation using an oxzolidinone auxiliary for the synthesis of vicenisamine and kedarosamine.[2] We previously described the preparation of *tert*-α-hydroxy acids with excellent diastereomeric excesses using α-ketoimides derived from Oppolzer's sultam.[3] In this paper, we report the asymmetric allylation of (+)- and (−)-*N*-glyoxyloylbornane-10,2-sultam and their imines in the presence of indium (Scheme 1).

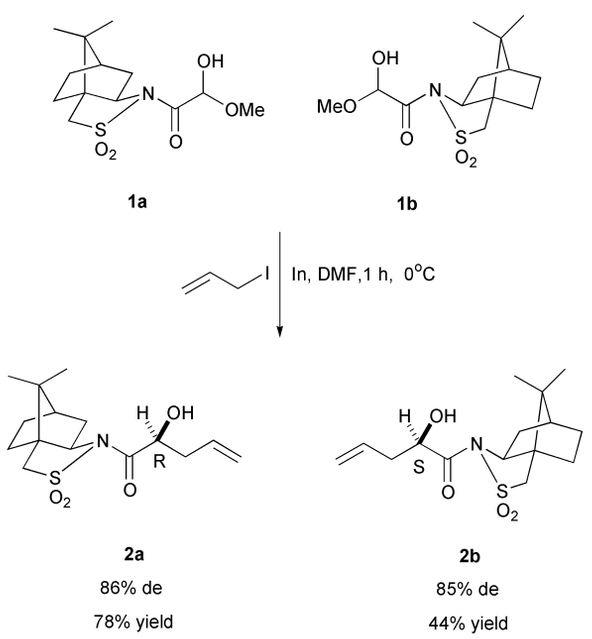


Scheme 1

Results and discussion

Hemiacetals of (−)- and (+)-*N*-glyoxyloylbornane-10,2-sultam (**1a** and **1b**) were prepared by known methods.[4,5] Firstly, the reaction of (−)-*N*-glyoxyloylbornane-10,2-sultam (**1a**) with allyl bromide and indium in 25% aqueous THF was carried out to give the corresponding homoallyl alcohol in 40% yield and 42% de. For optimization of the reaction, we examined the allylation of (−)-hemiacetal **1a** with allyl bromide or allyl iodide in the presence of indium, and varied the solvents used *e.g.* 25% aqueous THF, 20% aqueous EtOH and anhydrous DMF. The reactions were also performed at various temperatures from −30 °C to room temperature. From these permutations the highest diastereoselectivity was observed when the reaction was carried out using allyl iodide in DMF at 0 °C.

Within 1 h the reaction gave the homoallyl alcohol **2a** in 78% yield and 86% de, as determined by HPLC analysis employing either a Daicel Chiral OD or AD column. In the case of (+)-hemiacetal **1b**, homoallyl alcohol **2b** was obtained in 44% yield and 85% de under the same reaction conditions (Scheme 2).



Scheme 2

Each allylation reaction of aldehyde **5a** and optically pure hemiacetal **6a**, prepared by recrystallization,[6] exhibited the same diastereoselectivity as the reaction with the diastereomeric mixture of **1a** under the same conditions. These results

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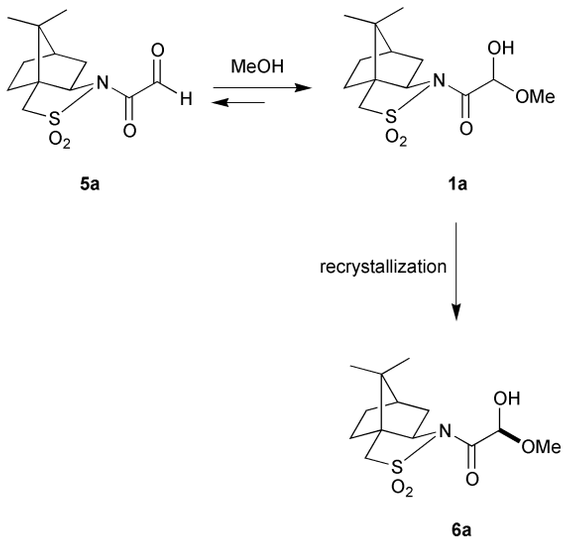


Scheme 3

suggest that the allylation reaction proceeds *via* aldehyde **5a** transformed from hemiacetal **1a** or **6a** (Scheme 3).

The absolute configuration of the newly generated chiral center in compound **2a** could be deduced as having a (*S*)-configuration by comparing the optical rotation of synthesized **8** with the known (*R*)-2-hydroxypentanoic acid **9**[7] ($[\alpha]_D^{20}$ = −4.40, *c* = 1.0 in $CHCl_3$) (Scheme 4). The optical rotation of **8** showed $[\alpha]_D^{20}$ = +4.80 (*c* = 0.39 in $CHCl_3$). 2-Hydroxypentanoic acid **8** was prepared by hydrolysis using lithium hydroxide in aqueous THF, followed by hydrogenation using palladium–charcoal. For the structure identification, compound **7** was transformed into methyl ester **10** by treatment with (trimethylsilyl)diazomethane.

The allylation reactions of imines **3a** and **3b** which were prepared from the reaction of benzylamine with the hemiacetals of (−)- and (+)-*N*-glyoxyloylbornane-10,2-sultam **1a** and **1b** were also examined using the same reaction conditions as the allylations of hemiacetals **1a** and **1b**. The allylation reactions of imines **3a** and **3b** smoothly proceeded to give the corresponding homoallylic amines **4a** and **4b** in 80% and 66% yields with high diastereoselectivity, 90% and 88% de, respectively (Scheme 5).

In order to determine the absolute configuration of the new chiral centers in compounds **4a** and **4b**, we prepared compound **11** from **4b** and optically pure L-2-aminopent-4-enoic acid, respectively (Scheme 6).[8] The optical rotation of **11**, prepared from **4a**, showed $[\alpha]_D^{20}$ = −25.5 (*c* = 0.22 in $CHCl_3$). Although it showed a little deviation from the optical rotation of compound **11** which was prepared from L-2-aminopent-4-enoic acid (**13**) ($[\alpha]_D^{20}$ = −35.0, *c* = 0.14 in $CHCl_3$), the absolute configuration of the new chiral center in compound **4a** could be assigned as having (*S*)-configuration.

This high diastereoselectivity of allylation reactions might be explained by the conventional six-membered transition state formed by the chelation of an oxygen atom of sulfur oxide and the nitrogen of imines **3a** and **3b** (oxygen of carbonyl group in cases of **1a** and **1b**) with indium (Fig. 1).

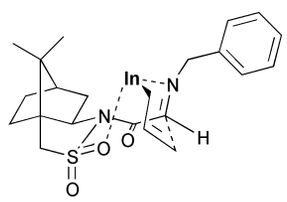


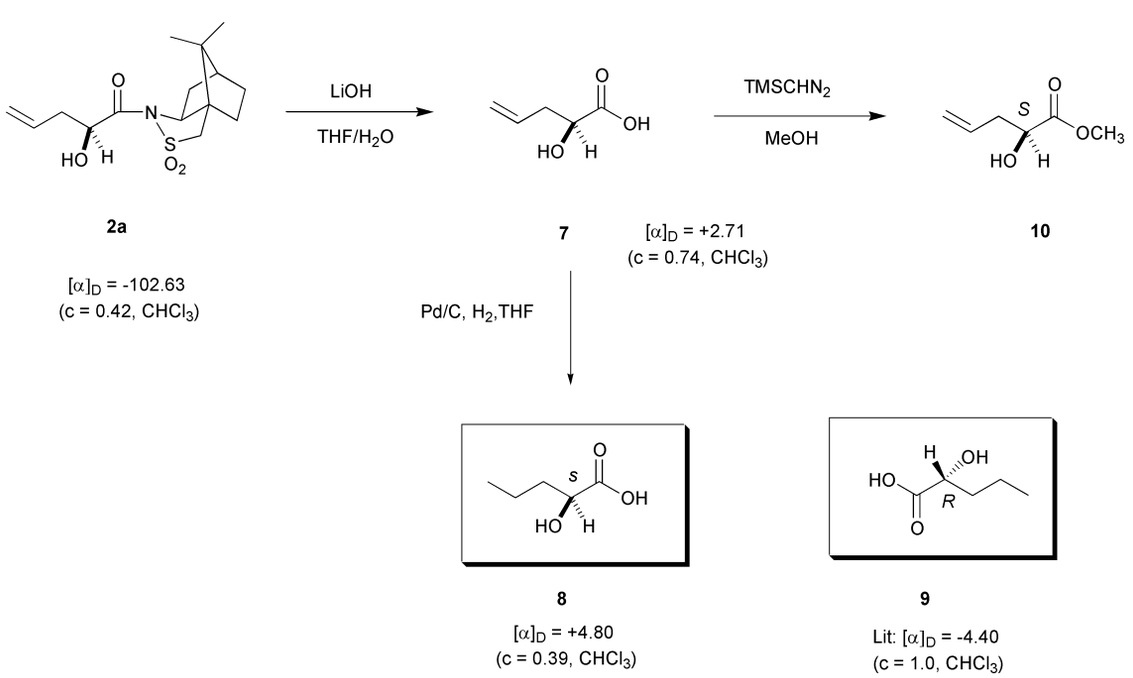
Fig. 1

In summary, (+) or (−)-*N*-glyoxyloylbornane-10,2-sultam and their imines reacted with allyl iodide in the presence of indium in DMF to give the corresponding α-hydroxy and α-amino camphor† sultam derivatives with high diastereoselectivities 86–90% de.

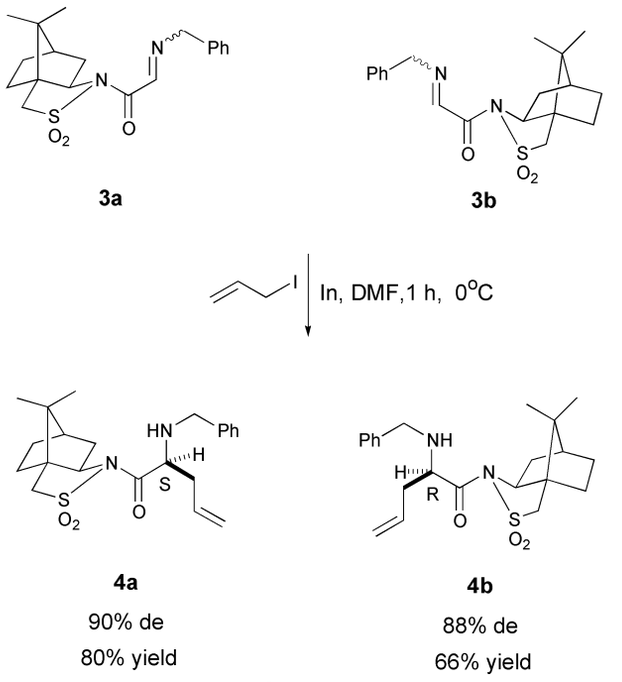
Experimental

All starting materials were obtained commercially from Aldrich or prepared by known methods. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$, unless otherwise stated, on a Bruker Avance DPX-300 NMR spectrometer with tetramethylsilane as internal standard. Specific optical rotations were measured on a Autopol III Rudolph research instrument and are in units of 10^{-1} deg cm^2 g^{-1}. All NMR shifts were measured in parts per million (ppm).

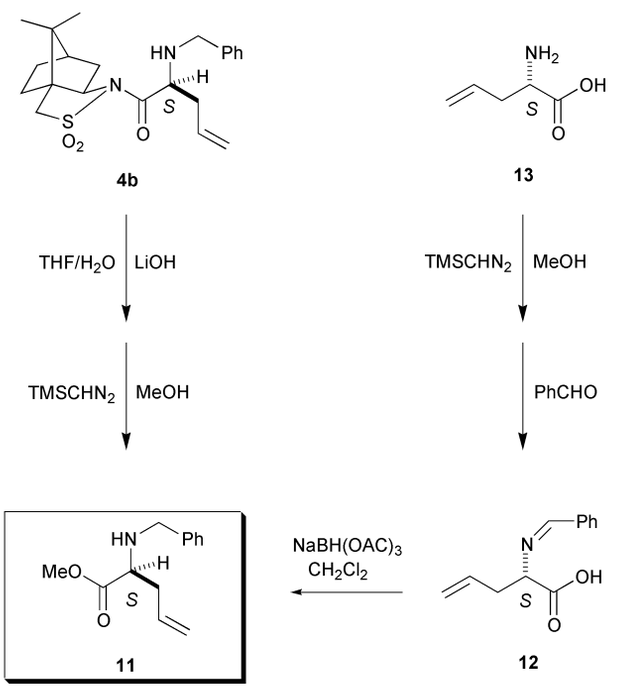
† The IUPAC name for camphor is bornan-2-one.



Scheme 4



Scheme 5



Scheme 6

General procedure for the allylation of the hemiacetal (2*R*,2′*R*)-*N*-(2′-hydroxypent-4′-enoyl)bornane-10,2-sultam (2a)

To a solution of (2*R*)-*N*-glyoxyloylbornane-10,2-sultam **1a** (348 mg, 1.15 mmol) in DMF (5 mL) were added allyl iodide (578 μL, 3.44 mmol) and indium powder (263 mg, 2.29 mmol). The solution was stirred at 0 °C for 1 h. H_2O was added to the reaction mixture which was then extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. Flash chromatography of the residue gave the product **2a** (279 mg, 78%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (m, 1H), 5.03 (m, 2H), 4.71 (m, 1H), 3.82 (m, 1H), 3.38 (d, 2H, J = 3.8 Hz), 2.39 (m, 2H), 1.96–1.77 (m, 5H), 1.33–1.25 (m, 2H), 1.02 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.65, 132.48, 119.27, 70.80, 65.39, 53.31, 49.31, 48.23, 44.96, 40.26, 38.59, 33.11, 26.84, 21.08, 20.27; HRMS (CI, M^+ + H) calcd for $C_{15}H_{24}O_4NS$ 314.1426, found 314.1433; IR (KBr) ν/cm^{-1} 3426, 2960, 1696, 1651 cm^{-1}; mp = 105 °C.

(2*R*,2′*S*)-*N*-(2′-Hydroxypent-4′-enoyl)bornane-10,2-sultam (2b)

Following the procedure used for **2a**, (2*S*)-*N*-glyoxyloylbornane-10,2-sultam **1b** (555 mg, 1.83 mmol) was treated with allyl iodide (922 mg, 5.49 mmol) and indium (420 mg, 3.66 mmol) to afford **2b** (250 mg, 44%).

2b: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.67 (m, 1H), 5.03 (t, 2H, J = 7.91 Hz), 4.71 (m, 1H), 3.82 (q, 1H), 3.38 (d, 2H, J = 3.82 Hz), 2.39 (m, 2H), 1.96–1.77 (m, 5H), 1.33–1.25 (m, 2H), 1.02 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ = 174.65, 132.48, 119.27, 70.80, 65.39, 53.31, 49.31, 48.23, 44.96, 40.26, 38.59, 33.11, 26.84, 21.08, 20.27; HRMS (CI, M^+ + H) calcd for $C_{15}H_{24}O_4NS$ 314.1426, found 314.1429; FT-IR (KBr, $CHCl_3$) ν/cm^{-1} 3426, 2960, 1696, 1651; $[\alpha]_D^{20}$ = −102.6 (c = 0.42, $CHCl_3$).

(*R*)-Methyl 2-hydroxyvalerate (10)

To a solution of 2-hydroxypent-4-enoic acid **7** (74 mg, 0.64 mmol) in methanol (3 mL) was added (trimethylsilyl)diazomethane 2.0 M in hexane (478 μL). After stirring for 1 h, the reaction mixture was concentrated and purified by column chromatography (pentane : ether = 5 : 1) to give the product (46 mg, yield = 55%).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.80 (m, 1H), 5.16 (q, 2H), 4.27 (q, 1H), 3.78 (s, 3H), 2.85 (d, J = 5.95 Hz), 2.56 (m, 1H), 2.45 (m, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ = 175.25, 132.86, 119.18, 70.43, 52.92, 39.06; FT-IR (KBr, $CHCl_3$) ν/cm^{-1} 3426, 2960, 1696, 1651; $[\alpha]_D^{20}$ = + 21.48 (c = 0.12, $CHCl_3$).

General procedure for the allylation of the imine (2*R*,2′*S*)-*N*-(2′-benzylaminopent-4′-enoyl)bornane-10,2-sultam (4a)

To a solution of (2*R*)-*N*-glyoxyloylbornane-10,2-sultam **1a** (300 mg, 0.99 mmol) in methylene chloride (5 mL) was added anhydrous Na_2SO_4 and benzylamine (119 μL, 1.09 mmol). After stirring for 4 h, the reaction mixture was filtered and concentrated under reduced pressure. To a solution of the residue (**3a**) in DMF (5 mL) was added allyl iodide (498 mg, 2.97 mmol) and indium (227 mg, 1.98 mmol) at 0 °C. After stirring for 1 h H_2O was added to the reaction mixture which was then extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. Flash chromatography of the residue gave the product **4a** (398 mg, yield = 80%).

4a: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.23 (m, 5H), 5.75 (m, 1H), 5.00 (t, 2H, J = 11.32 Hz), 4.04 (t, 1H, J = 5.94 Hz), 3.91 (q, 1H), 3.59 (dd, 2H, J = 12.68 and 12.71 Hz), 3.41 (d, 2H, J = 5.63 Hz), 2.42 (m, 2H), 2.01–1.81 (m, 5H), 1.37–1.11 (m, 2H), 1.09 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ = 175.58, 140.50, 133.79, 128.68, 128.56, 127.33, 118.63, 65.41, 61.28, 53.55, 52.47, 48.97, 48.20, 45.00, 39.21, 38.77, 33.23, 26.89, 21.17, 20.31; HRMS (CI, M^+ + H) calcd for $C_{22}H_{31}N_2O_3S$ 403.2055, found 403.2042; FT-IR (KBr, $CHCl_3$) ν/cm^{-1} = 3346, 2958, 1692, 1651; $[\alpha]_D^{20}$ = −6.84 (c = 2.11, $CHCl_3$).

(2*R*,2′*R*)-*N*-(2′-Benzylaminopent-4′-enoyl)bornane-10,2-sultam (4b)

Following the procedure used for **4a**, to a solution of (2*S*)-*N*-glyoxyloylbornane-10,2-sultam **1b** (30.5 mg, 0.10 mmol) in methylene chloride (1 mL) was added anhydrous Na_2SO_4 and benzyl amine (12 μL, 0.11 mmol). After 4 h the reaction mixture was filtered and concentrated. To a solution of the residue (**3b**) in DMF (1 mL) was added allyl iodide (28 μL, 0.30 mmol) and indium (23 mg, 0.20 mmol) to afford **4b** (27 mg, 66 %).

4b: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (m, 5H), 5.75 (m, 1H), 5.00 (m, 2H), 4.04 (t, 1H, J = 5.94 Hz), 3.91 (q, 1H), 3.59 (dd, 2H, J = 12.68 and 12.71 Hz), 3.41 (d, 2H, J = 5.63 Hz), 2.42 (m, 2H), 2.01–1.81 (m, 5H), 1.37–1.11 (m, 2H), 1.09 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.58, 140.50, 133.79, 128.68, 128.56, 127.33, 118.63, 65.41, 61.28, 53.55,

52.47, 48.97, 48.20, 45.00, 39.21, 38.77, 33.23, 26.89, 21.17, 20.31; IR (KBr) ν/cm^{-1} 3346, 2958, 1692, 1651.

(2*S*)-2-Benzylaminopent-4-enoic acid methyl ester (11)

To a solution of (2*R*,2′*S*)-*N*-(2′-benzylaminopent-4′-enoyl)-bornane-10,2-sultam (**4a**) in 3.9 mL of H_2O–THF (1 : 2) was added lithium hydroxide monohydrate (88 mg, 2.10 mmol). After stirring at rt for 20 h the sultam was recovered from the reaction mixture by extraction with methylene chloride. The aqueous layer was evaporated and the residue was purified on a Amberlite IR 120 (Plus) ion exchange (acidic) resin to give the 2-benzylaminopent-4-enoic acid (30 mg, 0.15 mmol). To a solution of the residue in 2.5 mL of methanol–benzene (2 : 7) was added (trimethylsilyl)diazomethane, 2.0 M solution in hexane (110 μL, 0.22 mmol). After stirring for 4 h, the reaction mixture was evaporated and purified by column chromatography to give (*S*)-2-benzylaminopent-4-enoic acid methyl ester **11** (26 mg, yield = 80%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (m, 5H), 5.67 (m, 1H), 5.01 (q, 2H), 3.75 (d, 1H, J = 13.0 Hz), 3.64 (s, 3H), 3.58 (d, 1H, J = 13.0 Hz), 3.31 (t, 1H, J = 6.5 Hz), 2.36 (t, 2H, J = 6.8 Hz), 1.81 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.49, 140.04, 133.98, 128.81, 128.67, 127.51, 118.49, 60.62, 52.39, 52.12, 38.12; HRMS (CI, $M^+ + H$) calcd for $C_{13}H_{18}O_2N$ 220.1338, found 220.1346; IR (KBr) ν/cm^{-1} 3334, 3033, 1736, 1655; $[\alpha]_D^{20}$ = −25.5 (c = 0.22 in $CHCl_3$).

Acknowledgements

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