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(*N*,*N*-Diisopropylcarbamoyloxy)-methyl *p*-tolyl sulfone: preparation and application for the syntheses of 1,2-diols

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Dedicated to Professor Qi-Zhuo Wang on the occasion of his 90th birthday

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ABSTRACT

1-(*N*,*N*-Diisopropylcarbamoyloxy)-1-tosyl-methane ($CbOCH_2Ts$, Cb=*N*,*N*-diisopropylcarbamoyl) was readily prepared from *p*-TolSH, paraformaldehyde and CbCl. With the dual activation of CbO- and Ts-substitutions, deprotonation of $CbOCH_2Ts$ could be effected not only by *n*-BuLi, but also by Grignard reagents. Upon deprotonation, the title compound adds to various carbonyl structures. By choosing proper organometallic reagents for consecutive steps, the addition intermediate undergoes in situ conversions to efficiently yield regioselectively *O*-Cb protected and unprotected 1,2-diols.

1. Introduction

1,2-Diols are ubiquitous in natural products and bioactive structures. Regioselectively protected 1,2-diols are frequently encountered intermediates for organic synthesis.[1] For preparation of these structures, many useful methods starting from olefin or carbonyl structures have been devised.[2] These methods generally require laborious multistep conversion, often with compromised overall yield.

On the other side, *O*-carbamoyl protected alcohols proved their directing capability in stereoselective lithiation chemistry.[3] Nevertheless, this chemistry has to be mediated by strong base such as BuLi, thus limited scope of substrates could be applied for this useful methodology. Besides, preparations of some *O*-carbamoyl protected alcohols often fail to give satisfying yields, largely due to the low reactivity and instability of carbamoyl chlorides. Efficient syntheses of *O*-carbamoyl protected alcohols with higher structure diversity are of particular interest.

Compared to carbamoyloxy substitution, sulfonyl or sulfinyl group is stronger activating factor for C–H bond upon metalation (deprotonation). It is reasonable to propose that *gem*-sulfonyl (or sulfinyl) carbamoyloxy bisubstitution will significantly increase the C–H acidity, thus broaden the scope of organometallic reagents used for *O*-carbamoyl directed metalation and the subsequent nucleophilic reactions. Structures containing *gem*-sulfonyl carbamoyloxy bisubstitutions were first prepared by Hoppe et al.[4] However, their behavior upon metalation, and the following nucleophilic reactions of the resulting carbanion were not systematically investigated. Hereby, we propose carbamoyloxymethyl sulfone or sulfoxide (**1**) as a new building block. It is hoped that this type of structure could be metalated under milder conditions. While maintaining the usefulness of carbamoyloxy substitution in the subsequent nucleophilic reactions, the additional sulfone or sulfoxide will open possibilities for further transformations. Also, as a surrogate of carbamoyl chloride, building block (**1**) could be used to append carbamoyloxy group to complex structures.

Encouraged by early works from Hoppe et al.,[4] we further envisioned a preliminary application of structure (**1**): metalated structure (**1**) will be added to carbonyl group, and the resulting oxy anion will abstract the *O*-carbamoyl protection with the driving force of subsequent elimination of the sulfonyl (or sulfinyl) group. The useful intermediate, *O*-carbamoyl protected α-hydroxyl aldehyde (**4**), should be readily reduced to 1,2-diol structures (**5**) with known methods (Scheme 1). In our lab, this proposal was realized by experiments with unexpected findings, which led to highly

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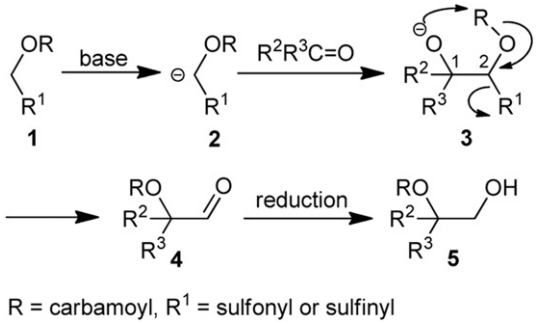
efficient one-pot preparation of three types of 1,2-diols, including both possible regioselectively *O*-carbamoyl protected and unprotected 1,2-diols, from readily available starting materials. This work provides a new solution for the problems described in the beginning, and it will be elaborated in the following.

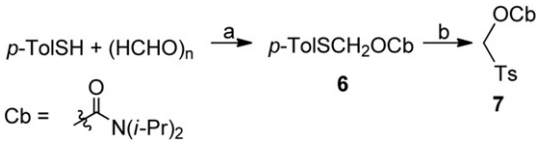


Scheme 1. Proposed 1,2-diol synthesis from general structure (**1**).

2. Results and discussion

Various compounds of structure **1** were screened against the deprotonation step. It was found, for example, that when R^1=sulfinyl, structure **1** is not particularly stable upon deprotonation, and did not give high yield of structure **3**. On the other hand, when R=2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl (Cby),[5] structure **1** was identified as a difficult synthetic target, hence not further pursued. Eventually we discovered that $TsCH_2OCb$ (**7**, Cb=*N*,*N*-diisopropylcarbamoyloxy) serves our purpose.

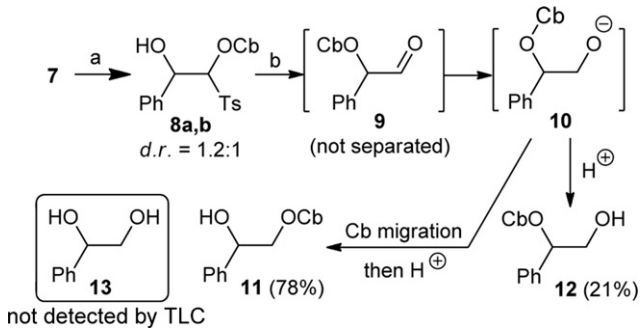
Similar to literature, compound **7** might be prepared by mixing lithiated MeOCb[6] and TsF.[4a,c,e] However lithiation of this simplest carbamate[7] may not be the best method for our purpose. Benneche et al. prepared $PhSCH_2OTMS$ from $PhSCH_2OH$ and TMSCl.[8] We found that *p*-$TolSCH_2OH$ was readily formed from *p*-TolSH and paraformaldehyde, however the reaction between *p*-$TolSCH_2OH$ and CbCl was rather sluggish. Bases play important role in this reaction, and they have to be carefully scrutinized to shift the reaction to compound **6**, but not decompose *p*-$TolSCH_2OH$ back to thiol and formaldehyde. *N*,*N*-Dimethylaniline was recognized particularly good for this aim. Subsequent oxidation of sulfide with *m*-CPBA readily gave the sulfone **7** with good yield. Thus, we are able to prepare compound **7** in large scale from inexpensive starting materials, avoiding using *s*-BuLi (Scheme 2).



Scheme 2. Preparation of the starting material **7**. (a) (i) Neat, 110 °C, 0.5 h; (ii) *N*,*N*-dimethylaniline, CbCl, DCM, reflux, overnight, 76%; (b) *m*-CPBA, DCM, 0 °C, 0.5 h, 60%.

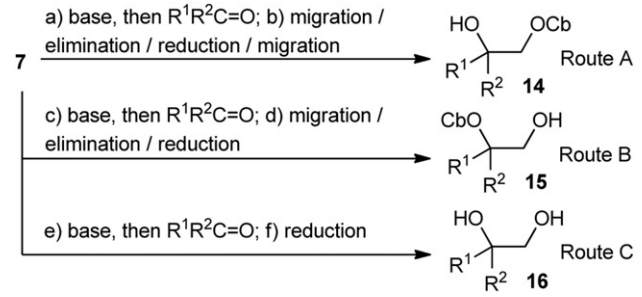
As expected, compound **7** was readily deprotonated with *n*-BuLi or Grignard reagents (preferably with *i*-PrMgCl). According to hydrogen/deuterium exchange experiments, NaHMDS and *t*-BuOK are capable to partially deprotonate compound **7**, too. To the best of our knowledge, this is the first time that *O*-carbamoyl protected alcohol is deprotontated with bases much weaker than BuLi. In the following works, both *n*-BuLi and *i*-PrMgCl were used to deprotonate compound **7**, and the results demonstrated their own advantages, respectively.

In realizing the plan in Scheme 1, preliminary experiments indicated that: with *n*-BuLi, the addition of deprotonated **7** to simple aldehydes generally gave slightly higher yield of structure **3** than with *i*-PrMgCl. To make the results comparable with previous reports,[4a,b,c,e] we kept *n*-BuLi as base in this part. According to early experiments,[4a,b,c,e] structure **3** (often bearing more substituents on C-2 than our compounds) should decompose to structure **4** in situ. However, it was found difficult to initiate the Cb migration and Ts elimination on our compounds of structure **3**: protonated **3** can always be separated in good yields. After screening numbers of conditions, it was eventually discovered that sodium containing base, such as NaHMDS, NaH or NaOMe, is crucial for the desired migration and elimination from structure **3**. We therefore reasoned that the early working examples are probably due to: (1) more substituents on C-2 of structure **3** facilitates migration and elimination for steric reasons and (2) Li metal used for preparing BuLi often contains variable amount of sodium,[9] which might accelerate the *O*-Cb migration. As illustrated in Scheme 3, compound **7** was deprotonated with *n*-BuLi, and then mixed with benzaldehyde to give diastereomers **8a** (53%) and **8b** (45%) after separation. Compounds **8a**,**b** (as a 1.2:1 diastereomeric mixture) were then treated with NaOMe (30% in methanol) to give an unstable aldehyde **9**, which was reduced immediately by addition of $NaBH_4$ in situ. Unexpectedly again, compound **11** was separated as a major product (78%), along with 21% of desired product **12**. The conversion from compound **9** to **11** should proceed through structure **10**: the steric repulsion on C-2 of structure **10**, coupled with the alcoholysis condition of methanolated NaOMe, repels the Cb group[10] from *O*-2 back to *O*-1.[11] Of particular note is the stability of the *O*-Cb protection: compound **13** was never observed under above reaction conditions (Scheme 3).



Scheme 3. Migration of Cb and elimination of Ts should give compound **12**, while the second migration of Cb leads to **11** as a major product instead. (a) *n*-BuLi, then PhCHO, THF, −78 °C, 50 min , 53% for **8a**, 45% for **8b**; (b) NaOMe in MeOH, then $NaBH_4$, THF, 0 °C to rt, 2 h.

Next, we turned our attention to one-pot reactions using compound **7** as starting material for the syntheses of regioselectively protected and unprotected 1,2-diols, due to the following reasons: (1) In view of the reaction conditions in Scheme 3, it is not only intriguing, but also possible to combine all steps for the conversion from **7** to **11** into one pot. (2) At this stage, however, we were still not able to produce compound **12** (as a major product) from separated compound **8**. It was felt that a one-pot reaction directly from compound **7** may yield compound **12** (or compounds of general structure **5**), analogously to the literature conditions.[4a,b,c,e] (3) On the other hand, previous experiments also demonstrated reduction of *gem*-carbamoyloxy-tosyl structure with DIBAH[12] to carbinol.[4e] After compound **8** (or compounds of general structure **3**) being formed from compound **7**, this reduction might also be carried out in situ to yield unprotected 1,2-diol. The ideas are combined and illustrated in Scheme 4.



Scheme 4. One-pot syntheses of regioselectively *O*-protected and unprotected 1,2-diols. Conditions for route A: (a) *n*-BuLi, then $R^1R^2C{=}O$, −78 °C, 50 min; (b) NaOMe in MeOH, $NaBH_4$, 0 °C to rt, 2 h. Conditions for route B: (c) *n*-BuLi, then $R^1R^2C{=}O$, −78 °C, 50 min; (d) $NaBH_4$, 0 °C to rt, 2 h. Conditions for route C: (e) *i*-PrMgCl, then $R^1R^2C{=}O$, 0 °C, 2 h; (f) DIBAH, −78 °C to rt, overnight.

For route A in Scheme 4, it was straightforward to combine two operation steps in Scheme 3. Initial deprotonation (Scheme 4, step a) was done preferably with *n*-BuLi than *i*-PrMgCl due to higher yields, and the later migration/elimination/reduction/migration sequence (Scheme 4, step b) was carried out in situ by simultaneous addition of $NaBH_4$ and methanolic NaOMe to give structure **14**. Sometimes structure **15** was isolated from this route as a minor product, too. Structure **16** was never observed from this route. For route B, the initial deprotonation (Scheme 4, step c) was done with *n*-BuLi as well. Treatment in situ with methanolic or absolute NaOMe along with $NaBH_4$ invariably gave structure **14** as a major product; changing the reducing reagent from $NaBH_4$ to $LiBH_4$ or several Selectrides seemed not affecting the reaction direction, too. We therefore used $NaBH_4$ as a base and a reducing reagent to create a strict aprotic condition, and structure **15** was then isolated as a major product, with excellent selectivity for most examples (Scheme 4, step d). Interestingly, to use this reduction condition for step d, the initial step c has to be done with *n*-BuLi. When *i*-PrMgCl was applied, the same $NaBH_4$ condition for step d failed to give either structure **15**, or structure **14**. We have not detected the formation of structure **16** from route B. For route C in Scheme 4, addition intermediate from step e with *n*-BuLi could not react with DIBAH in situ. However, when *i*-PrMgCl was used for deprotonation, DIBAH readily reduced the intermediate to desired product **16**, without any detectable formation of structures **14** and **15**.

It is obvious that the organometallic reagents used for every single step interfere with the subsequent conversions, and the reaction direction can therefore be tuned by matching reagents used for consecutive steps. Examples for Scheme 4 are showcased in Table 1.

As demonstrated in Table 1, route A (entries 1–10, Table 1) is compatible with common substituted benzaldehydes. The yields of desired products **11** and **14a**–**i** are moderate to good, and not significantly altered by the substitutions on the phenyl ring. Pyridine carboxaldehydes[13] gave complex products in the reaction sequence. The selectivities of route A to structure **14** are moderate to good. Minor product **15** was removed readily by chromatography, while structure **16** was never observed. However the purification of structure **14** was occasionally disturbed by the presence of benzyl alcohols from reduction of unreacted benzaldehydes. In such cases, stepwise alternative of route A is recommended. It is noteworthy that acetone gave the desired product as well with excellent selectivity. Although it is difficult to understand the selectivity pattern according to present data, products **11** and **14a**–**i** with 1-OCb group remain useful for synthesis, particularly with well-established Cb directed lithiation chemistry.[3]

Similar to route A, route B (entries 11–19, Table 1) is compatible with common substituted benzaldehydes, but not with pyridine carboxaldehydes.[13] Yields of structure **15** are consistently moderate to good, and selectivities to structure **15** are good to excellent. Structure

Table 1
Examples for one-pot syntheses described in Scheme 4

Entry (route)[a]	$R^1R^2C{=}O$		HO OCb R^1 R^2 **14**	CbO OH R^1 R^2 **15**	HO OH R^1 R^2 **16**
	R^1	R^2			
1 (A)	*n*-Pentyl	H	**14a**, 12%	**15a**, *n.d.*[b]	**16a**, *n.d.*
2 (A)	Ph	H	**11**, 67%	**12**, 26%	**13**, *n.d.*
3 (A)		H	**14b**, 59%	**15b**, 27%	**16b**, *n.d.*
4 (A)		H	**14c**, 80%	**15c**, 9%	**16c**, *n.d.*
5 (A)		H	**14d**, 54%	**15d**, 16%	**16d**, *n.d.*
6 (A)		H	**14e**, 56%	**15e**, 22%	**16e**, *n.d.*
7 (A)		H	**14f**, 71%	**15f**, *n.d.*	**16f**, *n.d.*
8 (A)		H	**14g**, 57%	**15g**, *n.d.*	**16g**, *n.d.*
9 (A)		H	**14h**, 60%	**15h**, 11%	**16h**, *n.d.*
10 (A)	Me	Me	**14i**, 64%	**15i**, *n.d.*	**16i**, *n.d.*
11 (B)	Ph	H	**11**, *n.d.*	**12**, 49%	**13**, *n.d.*
12 (B)		H	**14j**, *n.d.*	**15j**, 57%	**16j**, *n.d.*
13 (B)		H	**14b**, 6%	**15b**, 50%	**16b**,*n.d.*
14 (B)		H	**14c**, *n.d.*	**15c**, 51%	**16c**, *n.d.*
15 (B)		H	**14k**, *n.d.*	**15k**, 68%	**16k**, *n.d.*
16 (B)		H	**14l**, *n.d.*	**15l**, 68%	**16l**, *n.d.*
17 (B)		H	**14d**, 11%	**15d**, 49%	**16d**, *n.d.*
18 (B)		H	**14e**, *n.d.*	**15e**, 70%	**16e**, *n.d.*
19 (B)		H	**14g**, *n.d.*	**15g**, 49%	**16g**, *n.d.*
20 (C)	Ph	H	**11**, *n.d.*	**12**, *n.d.*	**13**, 57%
21 (C)		H	**14d**, *n.d.*	**15d**, *n.d.*	**16d**, 62%
22 (C)		H	**14e**, *n.d.*	**15e**, *n.d.*	**16e**, 62%
23 (C)		H	**14g**, *n.d.*	**15g**, *n.d.*	**16g**, 61%
24 (C)	Ph	Ph	**14m**, *n.d.*	**15m**, *n.d.*	**16m**, 57%

[a] Reaction routes are described in Scheme 4.
[b] *n.d.*: not detected by NMR. After workup, the reaction mixture was inspected by proton NMR to identify the presence of substance in question. Flash chromatography was then used to determine the yield.

14 was rarely (entries 14 and 18, Table 1), and structure **16** was never observed from this route. 2-*O*-Protected 1,2-diols **12**, **15b**–**e**, **15g**, and **15j**–**l** generally have to be prepared via multistep conversion according to established 1,2-diols synthesis and protective group chemistry. Moreover, installations of *O*-Cb protection on such secondary alcohols are often difficult. However, they could now be prepared in one pot, from readily available aldehydes and building block **7**.

Route C invariably gives moderate yields of the desired unprotected diols **13**, **16d**–**e**, **16g**, and **16m** (entries 21–24, Table 1) with excellent selectivity to structure **16**, even when very hindered diphenyl ketone was used (entry 24, Table 1). This route offers a quick access to many useful 1,2-diol target molecules.

3. Conclusion

In summary, we have proposed and efficiently synthesized a new building block **7**, which was found to be readily deprotonated with *n*-BuLi and Grignard reagents. Thanks to this finding, the following one-pot 1,2-diol syntheses became possible: By carefully choosing organometallic reagents for consecutive steps, from **7**, readily available carbonyl compounds, and inexpensive reagents, we developed highly telescoped one-pot syntheses for three types of 1,2-diols, including both possible regioselectively *O*-Cb protected and unprotected 1,2-diols, which generally require multistep synthesis according to known methods. Based on the importance of 1,2-diols and well-established carbamoyloxy-directed lithiation chemistry, it is possible for building block **7**, above described one-pot syntheses of 1,2-diols, and various Cb-protected alcohol products to find more applications in organic synthesis. Further use of building block **7** is under active exploration in our group.

4. Experimental section

4.1. General

All solvents were dried and purified prior to use: Toluene was distilled from sodium, Et_2O and THF were distilled from potassium, and CH_2Cl_2 was distilled from CaH_2. All other commercially available reagents were used as received. Reactions at −78 °C were performed in a dry ice/acetone bath. All moisture sensitive reactions were performed under N_2 (ca. +1.1 bar) in heating-gun (500–600 °C)/vacuum dried glassware sealed with rubber septa. Flash chromatography was performed on silica gel (300–400 mesh ASTM), and monitored by thin layer chromatography (TLC) on HSGF-254 (10–40 μm) TLC plates. NMR data were collected on a *Varian* Mercury-300 High Performance Digital FT-NMR, a *Varian* Mercury-400 High Performance Digital FT-NMR, or a *Bruker* Ultrashield 500 NMR. Spectra from solutions in $CDCl_3$ (δ_C=77.0 ppm) are calibrated relative to $SiMe_4$ (δ_H=0.00 ppm). HRMS were carried out on a *Thermo Finnigan* MAT-95 spectrometer (for EI), or on a *Waters*, Q-Tof Ultima Global spectrometer (for ESI). Melting points were measured on an uncorrected SGW X-4 micro melting point apparatus. HPLC analysis was performed on a Gilson HPLC system (306 pump, UV/vis-156 Detector, 215 liquid handle) with an YMC-ODS column (4.6×50 mm, 5 μm). HPLC conditions: solvent A=H_2O containing 0.1% (v/v) TEA, solvent B=MeCN containing 0.1% (v/v) TEA; flow rate=2.5 mL/min; gradient (B%): 0–5 min (4%–95%); peaks were identified at 254 nm and 214 nm. An Elementar Vario EL Cube analyzer was used for elemental analysis.

4.2. Preparation of substrates and initial explorations described in Schemes 2 and 3

*4.2.1. p-Tolyl-(N,N-diisopropylcarbamoyloxy)-methyl sulfide (**6**).* *p*-TolSH (11.4 g, 0.10 mol, 1 equiv), paraformaldehyde (3.0 g, 0.10 mol, 1 equiv), and methanolic NaOMe (30%, 0.03 mL, 0.0017 equiv) were mixed and heated at 110 °C for 30 min under nitrogen. The mixture was then cooled to rt to give crude *p*-TolSCH$_2$OH as a colorless oil, which was directly dissolved in DCM (150 mL), treated with CbCl (24.5 g, 150 mmol, 1.5 equiv) and *N*,*N*-dimethylaniline (13.3 g, 110 mmol, 1.1 equiv), and refluxed overnight. The resulting brown mixture was then cooled to rt, washed with 2 N aq HCl, satd aq $NaHCO_3$, and brine. The organic phase was then separated and concentrated to give an oil, which was purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give product **6** (light yellow oil, 21.4 g, 80 mmol, 76%). Compound **6**: R_f 0.39 (ethyl acetate/60–90 °C petroleum ether, 1:20); HPLC t_R 3.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.35 (m, 2H, Ar), 7.13–7.11 (m, 2H, Ar), 5.44 (s, 2H, CH_2OCb), 4.01 (br s, 1H, Cb), 3.78 (br s, 1H, Cb), 2.33 (s, 3H, Ar-CH_3), 1.19 (d, J=5.8 Hz, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4 (C=O), 137.2 (Ar_q), 131.5(Ar_q), 131.0 (2C, Ar), 129.7 (2C, Ar), 69.0 (SCH_2OCb), 46.5 (Cb), 45.5 (Cb), 21.3 (2C, Cb), 21.0 (Ar-CH_3), 20.6 (2C, Cb); HRMS (ESI$^+$) calcd for $C_{15}H_{23}NO_2SNa^+$ 304.1347, found 304.1336.

*4.2.2. (N,N-Diisopropylcarbamoyloxy)methyl p-tolyl sulfone (**7**).* Compound **6** (20.0 g, 71.07 mmol, 1 equiv) was dissolved in DCM (300 mL). To this solution at 0 °C, a solution of *m*-CPBA (75%, 49.1 g, 213.21 mmol, 3 equiv) in DCM (200 mL) was added dropwise. Monitored by TLC, the resulting slurry was stirred for further 30 min at 0 °C, and then treated with satd aq $Na_2S_2O_3$ and satd aq $NaHCO_3$. The organic phase was separated and the aqueous phase was washed with DCM. Combined organic phases were washed with brine, concentrated, and purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give product **7** (white solid, 13.4 g, 42.76 mmol, 60%). Compound **7**: R_f 0.43 (ethyl acetate/60–90 °C petroleum ether, 1:4); mp 68–69 °C; HPLC t_R 3.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.77 (m, 2H, Ar), 7.37–7.32 (m, 2H, Ar), 5.19 (s, 2H, TsCH_2OCb), 3.92 (br s, 1H, Cb), 3.71 (br s, 1H, Cb), 2.44 (s, 3H, Ar-CH_3), 1.16 (d, J=6.4 Hz, 6H, Cb), 1.09 (d, J=6.4 Hz, 6H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7 (C=O), 145.3 (Ar_q), 133.8 (Ar_q), 129.7 (2C, Ar), 129.0 (2C, Ar), 76.7 (TsCH_2OCb), 46.5 (Cb), 46.4 (Cb), 21.6 (Ar–CH_3), 21.0 (2C, Cb), 20.0 (2C, Cb); HRMS (ESI$^+$) calcd for $C_{15}H_{23}NO_4SNa^+$ 336.1245, found 336.1250. Anal. Calcd for $C_{15}H_{23}NO_4S$ (313.13): C, 57.48; H, 7.40; N, 4.47; S, 10.23. Found: C, 57.54; H, 7.50; N, 4.46; S, 10.29.

*4.2.3. 1-(N,N-Diisopropylcarbamoyloxy)-2-hydroxyl-2-phenylethyl p-tolyl sulfones (**8a**,**b**).* Compound **7** (300 mg, 0.96 mmol, 1 equiv) was dissolved in anhydrous Et_2O (9 mL), cooled to −78 °C, and treated with *n*-BuLi (1.6 M in hexanes, 0.8 mL, 1.25 mmol, 1.3 equiv). The mixture was stirred at this temperature for 45 min, treated with benzaldehyde (112 mg, 1.06 mmol, 1.1 equiv), and again stirred at −78 °C for 1 h. TLC indicated the reaction has been completed. The resulting clear solution was quenched by satd aq NH_4Cl. The organic layer was separated, and the aqueous phase was washed with ether for several times. Combined organic phases were washed with brine, concentrated, and purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give products **8a** (colorless oil, 215 mg, 0.51 mmol, 53%) and **8b** (colorless oil, 180 mg, 0.43 mmol, 45%). Compound **8a**: R_f 0.29 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.78 (m, 2H, Ar), 7.42–7.36 (m, 2H, Ar), 7.35–7.20 (m, 5H, Ar), 5.92 (d, J=1.4 Hz, 1H, C*H*OH), 5.76 (*pseudo*-s, 1H, CHOCb), 4.18–4.02 (m, 1H, Cb), 3.70 (d, J=1.4 Hz, 1H, OH), 3.46–3.31 (m, 1H, Cb), 2.41 (s, 3H, Ar–CH_3), 1.15 (d, J=6.9 Hz, 3H, Cb), 1.13 (d, J=6.9 Hz, 3H, Cb), 0.87 (d, J=6.9 Hz, 3H, Cb), 0.82 (d, J=6.9 Hz, 3H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2 (C=O), 145.2 (Ar_q), 137.5 (Ar_q), 132.5 (Ar_q), 129.2 (2C, Ar), 129.1 (2C, Ar), 127.8 (2C, Ar), 127.7 (Ar), 125.8 (2C, Ar), 86.1 (*C*HOCb), 69.6 (CHOH), 46.1 (Cb), 45.5 (Cb), 21.2 (CH_3), 20.5 (Cb), 20.3 (Cb), 19.3 (Cb), 19.2 (Cb); HRMS (ESI$^+$) calcd for $C_{22}H_{29}NO_5SNa^+$ 442.1664,

found 442.1663. Compound **8b**: R_f 0.19 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.79 (m, 2H, Ar), 7.42–7.36 (m, 2H, Ar), 7.35–7.23 (m, 5H, Ar), 6.02 (d, J=8.9 Hz, 1H, CHOCb), 5.34 (dd, J=8.9, 2.4 Hz, 1H, C*H*OH), 3.92–3.79 (m, 1H, Cb), 3.62 (d, J=2.4 Hz, 1H, OH), 3.31–3.15 (m, 1H, Cb), 2.42 (s, 3H, Ar–CH_3), 0.96–0.77 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.4 (C=O), 145.0 (Ar_q), 137.3 (Ar_q), 133.2 (Ar_q), 129.2 (2C, Ar), 128.9 (2C, Ar), 128.1 (Ar), 127.8 (2C, Ar), 127.2 (2C, Ar), 86.0 (*C*HOCb), 71.4 (CHOH), 46.1 (Cb), 45.0 (Cb), 21.2 (Ar-CH_3), 20.0 (Cb), 19.9 (Cb), 19.3 (2C, Cb); HRMS (ESI$^+$) calcd for $C_{22}H_{29}NO_5SNa^+$ 442.1664, found 442.1651.

*4.2.4. 1-Phenyl-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**11**) and 1-O-(N,N-diisopropylcarbamoyl)-1-phenyl-1,2-ethanediol (**12**).* Compounds **8a**,**b** (as 1.2:1 diastereomeric mixture, 100 mg, 0.24 mmol, 1 equiv) were dissolved in dry THF (3 mL) and cooled to 0 °C. To this solution, $NaBH_4$ (72 mg, 1.92 mmol, 8 equiv) and methanolic NaOMe (30% w/v, 0.17 mL, 0.96 mmol, 4 equiv) were added. The resulting suspension were stirred at this temperature for 30 min, slowly warmed to rt, and stirred at rt for 2 h with frequent TLC inspection. Upon completion (indicated by TLC), the reaction was quenched with satd aq NH_4Cl. The organic layer was separated, and the aqueous phase was washed with ether for several times. Combined organic phases were washed with brine, concentrated, and purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give products **11**[14] (colorless oil, 49 mg, 0.18 mmol, 78%) and **12** (colorless oil, 13 mg, 0.05 mmol, 21%). Compound **11**: R_f 0.35 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.4 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.01 (m, 5H, Ph), 4.97 (dt, J=7.0, 3.5 Hz, 1H, C*H*OH), 4.26 (d, J=3.7 Hz, 1H, CH_2OCb), 4.28 (d, J=7.0 Hz, 1H, CH_2OCb), 4.02 (br s, 1H, Cb), 3.81 (d, J=3.5 Hz, 1H, OH), 3.77 (br s, 1H, Cb), 1.19 (br s, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4 (C=O), 140.6 (Ph_q), 128.4 (2C, Ph), 127.8 (Ph), 126.2 (2C, Ph), 73.5 (CHOH), 70.4 (*C*H_2OCb), 46.6 (Cb), 45.7 (Cb), 21.2 (2C, Cb), 20.5 (2C, Cb); HRMS (ESI$^+$) calcd for $C_{15}H_{23}NO_3Na^+$ 288.1576, found 288.1587. Compound **12**: R_f 0.40 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.2 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.27 (m, 5H, Ph), 5.84 (dd, J=7.8, 3.6 Hz, 1H, CHOCb), 4.07 (s, 1H, Cb), 3.92–3.80 (m, 3H, Cb, C*H*$_2$OH), 3.08 (br s, 1H, OH), 1.22 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4 (C=O), 137.3 (Ph_q), 128.1 (2C, Ph), 127.7 (Ph), 126.2 (2C, Ph), 77.9 (*C*HOCb), 66.9 (CH_2OH), 46.3 (Cb), 45.2 (Cb), 21.0 (2C, Cb), 20.0 (2C, Cb); HRMS (ESI$^+$) calcd for $C_{15}H_{23}NO_3Na^+$ 288.1576, found 288.1589.

4.3. General procedure for route A

Compound **7** (100 mg, 0.32 mmol, 1 equiv) was dissolved in dry THF (2 mL), and cooled to −78 °C. To this solution, *n*-BuLi (1.6 M in hexanes, 0.26 mL, 0.42 mmol, 1.3 equiv) was added. The yellow solution was stirred at −78 °C for 45 min, treated with corresponding carbonyl compound (neat, 0.35 mmol, 1.1 equiv), stirred at −78 °C for further 50 min, and treated with $NaBH_4$ (121 mg, 3.2 mmol, 10 equiv) and methanolic NaOMe (30% w/v, 0.34 mL, 1.92 mmol, 6 equiv). The resulting mixture was gradually warmed to rt and stirred at rt until completion (ca. 2 h, indicated by TLC). The reaction was quenched with satd aq NH_4Cl. The organic layer was separated, and the aqueous phase was washed with ether for several times. Combined organic phases were washed with brine, concentrated, and purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give products **11** and **14a**–**i**.

4.4. General procedure for route B

Compound **7** (100 mg, 0.32 mmol, 1 equiv) was dissolved in dry THF (2 mL), and cooled to −78 °C. To this solution, *n*-BuLi (1.6 M in hexanes, 0.26 mL, 0.42 mmol, 1.3 equiv) was added. The yellow solution was stirred at −78 °C for 45 min, treated with corresponding carbonyl compound (neat, 0.35 mmol, 1.1 equiv), stirred at −78 °C for further 50 min, and treated with $NaBH_4$ (121 mg, 3.2 mmol, 10 equiv). The resulting suspension was gradually warmed to rt and stirred at rt until completion (ca. 2 h) indicated by TLC. The reaction was quenched with satd aq NH_4Cl. The organic layer was separated, and the aqueous phase was washed with ether for several times. Combined organic phases were washed with brine, concentrated, and purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give products **12**, **15b**–**e**, **15g**, and **15j**–**l**.

4.5. General procedure for route C

Compound **7** (100 mg, 0.32 mmol, 1 equiv) was dissolved in dry THF (2 mL), and cooled to 0 °C. To this solution, *i*-PrMgCl (2.0 M in THF, 0.22 mL, 0.44 mmol, 1.4 equiv) was added. The clear solution was stirred at 0 °C for 2 h, treated with corresponding carbonyl compound (neat, 0.38 mmol, 1.2 equiv), stirred at 0 °C for further 50 min, cooled to −78 °C, and treated with DIBAH (1.0 M in hexanes, 3.8 mL, 3.8 mmol, 12 equiv). The resulting mixture was gradually warmed to rt and stirred overnight. Upon completion (indicated by TLC), the reaction was quenched with satd aq NH_4Cl, and stirred with satd aq Rochelle salt. The organic layer was separated, and the aqueous phase was washed with ether for several times. Combined organic phases were washed with brine, concentrated, and purified with flash chromatography (on silica gel with 60–90 °C petroleum ether and EtOAc) to give products **13**, **16d**–**e**, **16g**, and **16m**.

4.6. Experiments described in Scheme 4 and Table 1

*4.6.1. 1-O-(N,N-Diisopropylcarbamoyl)-1,2-heptanediol (**14a**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compound **14a** (colorless oil, 10 mg, 0.04 mmol, 12%) was obtained. Compound **14a**: R_f 0.29 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (m, 1H, C*H*OH), 4.05 (br s, 1H, Cb),3.79 (br s, 1H, Cb), 3.74–3.62 (m, 2H, C*H*$_2$OCb), 3.18 (br s, 1H, OH), 1.70–1.48 (m, 2H, C*H*$_2$(CH$_2$)$_3$CH$_3$), 1.44–1.25 (m, 6H, CH$_2$(C*H*$_2$)$_3$CH$_3$), 1.22 (d, J=6.8 Hz, 12H, Cb), 0.88 (m, 3H, CH$_2$(CH$_2$)$_3$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7 (C=O), 77.2 (CHOH), 66.3 (*C*H$_2$OCb), 46.5 (Cb), 45.5 (Cb), 31.7 (CH$_2$), 31.1 (CH$_2$), 25.2 (CH$_2$), 22.5 (CH$_2$), 21.5 (2C, Cb), 20.6 (2C, Cb), 14.0 (CH$_2$(CH$_2$)$_3$*C*H$_3$); HRMS (ESI$^+$) calcd for $C_{14}H_{29}NO_3Na^+$ 282.2045, found 282.2050.

*4.6.2. 1-Phenyl-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**11**) and 1-O-(N,N-diisopropylcarbamoyl)-1-phenyl-1,2-ethanediol (**12**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compounds **11** (colorless oil, 57 mg, 0.21 mmol, 67%) and **12** (colorless oil, 22 mg, 0.08 mmol, 26%) were obtained. Their NMR data are identical with the products obtained from compound **8**.

*4.6.3. 1-(2,4-Dimethylphenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14b**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(2,4-dimethylphenyl)-1,2-ethanediol (**15b**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compounds **14b** (white solid, 55 mg, 0.19 mmol, 59%) and **15b** (colorless oil, 25 mg, 0.09 mmol, 27%) were obtained. Compound **14b**: R_f 0.43 (ethyl acetate/60–90 °C petroleum ether, 1:4); mp 109–110 °C; HPLC t_R 3.8 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J=7.9 Hz, 1H, Ar), 7.04 (d, J=7.9 Hz, 1H, Ar), 6.96 (s, 1H, Ar), 5.22–5.11 (m, 1H, C*H*OH), 4.28–4.13 (m, 2H, CH$_2$OCb), 4.01 (br s, 1H, Cb), 3.82 (br s, 1H, Cb), 3.47 (s, 1H, OH), 2.34 (s, 3H, Ar-CH$_3$), 2.30 (s, 3H, Ar-CH$_3$), 1.35–1.15 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3 (C=O), 137.2 (Ar_q), 135.3 (Ar_q), 134.5 (Ar_q), 131.1 (Ar), 126.8 (Ar), 126.0 (Ar), 70.2

(CHOH), 69.3 (CH_2OCb), 46.4 (Cb), 45.6 (Cb), 21.2 (2C, Cb), 21.0 (Ar–CH_3), 20.5 (2C, Cb), 19.0 (Ar–CH_3); HRMS (ESI^+) calcd for $C_{17}H_{27}NO_3Na^+$ 316.1889, found 316.1889. Compound **15b**: R_f 0.48 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.6 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J=7.8 Hz, 1H, Ar), 7.02 (d, J=7.8 Hz, 1H, Ar), 6.99 (s, 1H, Ar), 6.03 (dd, J=8.1, 3.2 Hz, 1H, CHOCb), 4.05 (br s, 1H, Cb), 3.95–3.61 (m, 3H, Cb, CH_2OH), 3.17 (br s, 1H, OH), 2.38 (s, 3H, Ar–CH_3), 2.29 (s, 3H, Ar–CH_3), 1.42–1.04 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6 (C=O), 137.0 (Ar_q), 134.6 (Ar_q), 132.6 (Ar_q), 130.9 (Ar), 126.3 (Ar), 125.7 (Ar), 74.7 (CHOCb), 66.2 (CH_2OH), 46.1 (Cb), 45.3 (Cb), 21.1 (2C, Cb), 20.5 (Ar-CH_3), 20.0 (2C, Cb), 18.7 (Ar–CH_3); HRMS (ESI^+) calcd for $C_{17}H_{27}NO_3Na^+$ 316.1889, found 316.1886.

*4.6.4. 1-(3-Chlorophenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14c**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(3-chlorophenyl)-1,2-ethanediol (**15c**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compounds **14c** (colorless oil, 77 mg, 0.26 mmol, 80%) and **15c** (colorless oil, 9 mg, 0.03 mmol, 9%) were obtained. Compound **14c**: R_f 0.39 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.7 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.38 (m, 1H, Ar), 7.30–7.22 (m, 3H, Ar), 4.94 (dt, J=6.6, 3.1 Hz, 1H, CHOH), 4.35–4.20 (m, 3H, CH_2OCb, OH), 4.00 (br s, 1H, Cb), 3.74 (br s, 1H, Cb), 1.19 (s, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4 (C=O), 142.9 (Ar_q), 134.3 (Ar_q), 129.6 (Ar), 127.8 (Ar), 126.4 (Ar), 124.3 (Ar), 72.8 (CHOH), 70.2 (CH_2OCb), 46.6 (Cb), 45.8 (Cb), 21.0 (2C, Cb), 20.4 (2C, Cb); HRMS (ESI^+) calcd for $C_{15}H_{22}NO_3ClNa^+$ 322.1186, found 322.1187. Compound **15c**: R_f 0.35 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.5 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.20 (m, 4H, Ar), 5.78 (dd, J=7.4, 3.8 Hz, 1H, CHOCb), 4.05 (br s, 1H, Cb), 3.95–3.75 (m, 3H, Cb, CH_2OH), 2.85 (br s, 1H, OH), 1.23 (s, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9 (C=O), 139.5 (Ar_q), 134.0 (Ar_q), 129.4 (Ar), 127.8 (Ar), 126.3 (Ar), 124.4 (Ar), 76.9 (CHOCb), 66.4 (CH_2OH), 46.3 (Cb), 45.2 (Cb), 21.1 (2C, Cb), 20.0 (2C, Cb); HRMS (ESI^+) calcd for $C_{15}H_{22}NO_3ClNa^+$ 322.1186, found 322.1179.

*4.6.5. 1-(4-Methoxyphenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14d**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(4-methoxyphenyl)-1,2-ethanediol (**15d**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compounds **14d** (colorless oil, 51 mg, 0.17 mmol, 54%) and **15d** (colorless oil, 15 mg, 0.05 mmol, 16%) were obtained. Compound **14d**: R_f 0.53 (ethyl acetate/60–90 °C petroleum ether, 1:2); HPLC t_R 3.3 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.28 (m, 2H, Ar), 6.97–6.81 (m, 2H, Ar), 4.92 (t, J=5.5 Hz, 1H, CHOH), 4.25 (d, J=0.6 Hz, 1H, CH_2OCb), 4.23 (s, 1H, CH_2OCb), 4.02 (br s, 1H, Cb), 3.80 (s, 3H, OCH_3), 3.78 (br s, 1H, Cb), 3.62 (br s, 1H, OH), 1.20 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2 (Ar_q), 156.3 (C=O), 132.7 (Ar_q), 127.4 (2C, Ar), 113.8 (2C, Ar), 72.9 (CHOH), 70.3 (CH_2OCb), 55.2 (OCH3), 46.5 (Cb), 45.7 (Cb), 21.1 (2C, Cb), 20.5 (2C, Cb); HRMS (ESI^+) calcd for $C_{16}H_{25}NO_4Na^+$ 318.1681, found 318.1664. Compound **15d**: R_f 0.25 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.2 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.27 (m, 2H, Ar), 7.06–6.65 (m, 2H, Ar), 5.78 (dd, J=7.9, 3.6 Hz, 1H, CHOCb), 4.09 (br s, 1H, Cb), 3.92–3.86 (m, 1H, CH_2OH), 3.81–3.76 (m, 5H, Cb, CH_2OH, OCH_3), 3.02 (m, 1H, OH), 1.20 (m, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4 (Ar_q), 156.0 (C=O), 129.9 (Ar_q), 128.1 (2C, Ar), 114.0 (2C, Ar), 78.0 (CHOCb), 67.3 (CH_2OH), 55.2 (OCH_3), 46.8 (Cb), 45.5 (Cb), 21.6 (2C, Cb), 20.5 (2C, Cb); HRMS (ESI^+) calcd for $C_{16}H_{25}NO_4Na^+$ 318.1681, found 318.1685.

*4.6.6. 1-(2,4-Dimethoxyphenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14e**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(2,4-dimethoxyphenyl)-1,2-ethanediol (**15e**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compounds **14e** (colorless oil, 58 mg, 0.18 mmol, 56%) and **15e** (colorless oil, 23 mg, 0.07 mmol, 22%) were obtained. Compound **14e**: R_f 0.47 (ethyl acetate/60–90 °C petroleum ether, 1:2); HPLC t_R 3.4 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J=8.4 Hz, 1H, Ar), 6.49 (dd, J=8.4, 2.4 Hz, 1H, Ar), 6.44 (d, J=2.4 Hz, 1H, Ar), 5.16–5.07 (m, 1H, CHOH), 4.30 (d, J=2.4 Hz, 1H, CH_2OCb), 4.29 (s, 1H, CH_2OCb), 4.13–3.91 (br s, 1H, Cb), 3.86–3.74 (m, 2H, Cb, OH),3.82 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 1.19 (m, 12H, Cb). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3 (Ar_q), 157.3 (Ar_q), 156.5 (C=O), 128.1 (Ar), 121.0 (Ar_q), 104.0 (Ar), 98.3 (Ar), 69.2 (CHOH), 68.9 (CH_2OCb), 55.3 (2C, OCH_3), 46.4 (Cb), 45.6 (Cb), 21.1 (2C, Cb), 20.5 (2C, Cb); HRMS (ESI^+) calcd for $C_{17}H_{27}NO_5Na^+$ 348.1787, found 348.1775. Compound **15e**: R_f 0.34 (ethyl acetate/60–90 °C petroleum ether, 1:2); HPLC t_R 3.3 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J=8.4 Hz, 1H, Ar), 6.49 (dd, J=8.4, 2.4 Hz, 1H, Ar), 6.45 (d, J=2.4 Hz, 1H, Ar), 6.15 (dd, J=6.6, 4.0 Hz, 1H, CHOCb), 4.15–4.00 (br s, 1H, Cb), 3.90–3.75 (m, 3H, Cb, CH_2OH), 3.81 (s, 3H, OCH_3), 3.80(s, 3H, OCH_3), 3.12 (br s, 1H, OH), 1.22 (m, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6 (Ar_q), 157.3 (Ar_q), 156.2 (C=O), 128.0 (Ar), 118.6 (Ar_q), 104.2 (Ar), 98.4 (Ar), 73.5 (CHOCb), 66.6 (CH_2OH), 55.4 (2C, OCH_3), 46.6 (Cb), 45.6 (Cb), 21.5 (2C, Cb), 20.5 (2C, Cb); HRMS (ESI^+) calcd for $C_{17}H_{27}NO_5Na^+$ 348.1787, found 348.1773.

*4.6.7. 1-(4-Fluorophenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14f**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compound **14f** (colorless oil, 64 mg, 0.23 mmol, 71%) was obtained. Compound **14f**: R_f 0.36 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.4 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.32 (m, 2H, Ar), 7.09–6.97 (m, 2H, Ar), 4.98–4.92 (m, 1H, CHOH), 4.32–4.18 (m, 2H, CH_2OCb), 4.00 (br s, 2H, OH, Cb), 3.76 (br s, 1H, Cb), 1.19 (br s, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (d, J=245.5 Hz, Ar_q), 156.3 (C=O), 136.4 (d, J=2.9 Hz, Ar_q), 127.9 (Ar), 127.8 (Ar), 115.3 (Ar), 115.1 (Ar), 72.8 (CHOH), 70.3 (CH_2OCb), 46.6 (Cb), 45.7 (Cb), 21.2 (2C, Cb), 20.4 (2C, Cb); HRMS (ESI^+) calcd for $C_{15}H_{22}NO_3FNa^+$ 306.1481, found 306.1485.

*4.6.8. 1-(3,4-Difluorophenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14g**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compound **14g** (colorless oil, 55 mg, 0.18 mmol, 57%) was obtained. Compound **14g**: R_f 0.27 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 3.5 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.20 (m, 1H, Ar), 7.19–7.06 (m, 2H, Ar), 4.93 (dt, J=6.5, 3.1 Hz, 1H, CHOH), 4.34–4.17 (m, 3H, CH_2OCb, OH), 4.00 (br s, 1H, Cb), 3.76 (br s, 1H, Cb), 1.18 (br s, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4 (C=O), 151.0 (dd, J=75.4, 12.7 Hz, Ar_q), 149.1 (dd, J=74.8, 12.7 Hz, Ar_q), 137.1–136.9 (m, Ar_q), 122.0 (dd, J=6.2, 3.6 Hz, Ar), 117.1 (d, J=17.3 Hz, Ar), 115.3 (d, J=17.9 Hz, Ar), 72.5 (CHOH), 70.2 (CH_2OCb), 46.7 (Cb), 45.8 (Cb), 21.1 (2C, Cb), 20.4 (2C, Cb); HRMS (ESI^+) calcd for $C_{15}H_{21}NO_3F_2Na^+$ 324.1387, found 324.1368.

*4.6.9. 1-(4-Trifluoromethylphenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14h**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(4-trifluoromethylphenyl)-1,2-ethanediol (**15h**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compounds **14h** (colorless oil, 64 mg, 0.19 mmol, 60%) and **15h** (colorless oil, 12 mg, 0.04 mmol, 11%) were obtained. Compound **14h**: R_f 0.33 (ethyl acetate/60–90 °C petroleum ether, 1:4); mp 53–54 °C; HPLC t_R 3.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J=8.2 Hz, 2H, Ar), 7.53 (d, J=8.2 Hz, 2H, Ar), 5.03 (dd, J=7.1, 2.5 Hz, 1H, CHOH), 4.37–4.24 (m, 3H, CH_2OCb, OH), 4.00 (br s, 1H, Cb), 3.74 (br s, 1H, Cb), 1.19 (br s, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4 (C=O), 144.7 (Ar_q), 129.9 (q, J=32.5 Hz, CF_3), 126.4 (2C, Ar), 125.2 (m, 2C, Ar), 122.7 (Ar_q), 73.0 (CHOH), 70.2 (CH_2OCb), 46.6 (Cb), 45.8 (Cb), 21.0 (2C, Cb), 20.4 (2C, Cb); HRMS (ESI^+) calcd for $C_{16}H_{22}NO_3F_3Na^+$ 356.1449, found 356.1467. Compound **15h**: R_f 0.30 (ethyl acetate:petroleum ether, 1:3); t_R 3.7 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J=8.1 Hz,

2H, Ar), 7.48 (d, J=8.1 Hz, 2H, Ar), 5.86 (dd, J=7.2, 3.8 Hz, 1H, CHOCb), 4.05 (br s, 1H, Cb), 3.96–3.79 (m, 3H, Cb, CH_2OH), 2.68 (br s, 1H, CH_2OH), 1.41–1.16 (m, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3 (C=O), 142.0 (Ar_q), 130.3 (q, J=32.6 Hz, CF_3), 127.0 (2C, Ar), 125.6 (m, 2C, Ar), 122.9 (Ar), 77.5 (*C*HOCb), 67.0 (CH_2OH), 46.9 (Cb), 45.8 (Cb), 21.6 (2C, Cb), 20.4 (2C, Cb); HRMS (ESI^+) calcd for $C_{16}H_{22}NO_3F_3Na^+$ 356.1449, found 356.1467.

*4.6.10. 1-Methyl-2-O-(N,N-diisopropylcarbamoyl)-1,2-propanediol (**14i**).* According to route A, from compound **7** (100 mg, 0.32 mmol), compound **14i** (colorless oil, 45 mg, 0.20 mmol, 64%) was obtained. Compound **14i**: R_f 0.23 (ethyl acetate/60–90 °C petroleum ether, 1:4); HPLC t_R 2.8 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (br s, 1H, Cb), 4.02 (s, 2H, CH_2OCb), 3.83 (br s, 1H, Cb), 2.79 (br s, 1H, OH), 1.23 (d, J=6.8 Hz, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2 (C=O), 73.0 ($C(CH_3)_2OH$), 70.2 (CH_2OCb), 46.6 (Cb), 45.6 (Cb), 26.5 (2C, $C(CH_3)_2OH$), 21.5 (2C, Cb), 20.5 (2C, Cb); HRMS (EI^+) calcd for $C_{11}H_{23}NO_3$ 217.1678, found 217.1679.

*4.6.11. 1-O-(N,N-Diisopropylcarbamoyl)-1-phenyl-1,2-ethanediol (**12**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compound **12** (colorless oil, 42 mg, 0.16 mmol, 49%) was obtained. Its NMR data are identical with the products obtained from compound **8**.

*4.6.12. 1-O-(N,N-Diisopropylcarbamoyl)-1-(naphthalen-2-yl)-1,2-ethanediol (**15j**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compound **15j** (colorless oil, 58 mg, 0.18 mmol, 57%) was obtained. Compound **15j**: R_f 0.40 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.6 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J=8.5 Hz, 1H, Ar), 7.90–7.79 (m, 2H, Ar), 7.63–7.45 (m, 4H, Ar), 6.64 (dd, J=7.2, 3.3 Hz, 1H, CHOCb), 4.16–3.83 (m, 4H, Cb, CH_2OH), 3.27 (br s, 1H, OH), 1.24 (m, 12H, Cb); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0 (C=O), 133.8 (Ar_q), 133.5 (Ar_q), 130.3 (Ar_q), 128.9 (Ar), 128.7 (Ar), 126.6 (Ar), 125.9 (Ar), 125.2 (Ar), 124.2 (Ar), 123.1 (Ar), 75.8 (*C*HOCb), 67.3 (CH_2OH), 46.7 (Cb), 46.0 (Cb), 21.4 (2C, Cb), 20.6 (2C, Cb); HRMS (ESI^+) calcd for $C_{19}H_{25}NO_3Na^+$ 338.1732, found 338.1732.

*4.6.13. 1-(2,4-Dimethylphenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14b**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(2,4-dimethylphenyl)-1,2-ethanediol (**15b**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compounds **14b** (white solid, 6 mg, 0.02 mmol, 6%) and **15b** (colorless oil, 47 mg, 0.16 mmol, 50%) were obtained. Their NMR data are identical with the products obtained via route A.

*4.6.14. 1-O-(N,N-Diisopropylcarbamoyl)-1-(3-chlorophenyl)-1,2-ethanediol (**15c**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compound **15c** (colorless oil, 49 mg, 0.16 mmol, 51%) was obtained. Its NMR data are identical with the products obtained via route A.

*4.6.15. 1-O-(N,N-Diisopropylcarbamoyl)-1-(4-bromophenyl)-1,2-ethanediol (**15k**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compound **15k** (colorless oil, 75 mg, 0.22 mmol, 68%) was obtained. Compound **15k**: R_f 0.37 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.6 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.47 (m, 2H, Ar), 7.27–7.22 (m, 2H, Ar), 5.76 (dd, J=7.5, 3.8 Hz, 1H, CHOCb), 4.06 (br s, 1H, Cb), 3.94–3.72 (m, 3H, Cb, CH_2OH), 2.91 (br s, 1H, OH), 1.21 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0 (C=O), 136.5 (Ar_q), 131.2 (2C, Ar), 127.9 (2C, Ar), 121.6 (Ar_q), 77.0 (*C*HOCb), 66.4 (CH_2OH), 46.3 (Cb), 45.2 (Cb), 21.1 (2C, Cb), 20.0 (2C, Cb); HRMS (ESI^+) calcd for $C_{15}H_{22}NO_3BrNa^+$ 366.0681, found 366.0689.

*4.6.16. 1-O-(N,N-Diisopropylcarbamoyl)-1-(2-methoxyphenyl)-1,2-ethanediol (**15l**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compound **15l** (white solid, 64 mg, 0.22 mmol, 68%) was obtained. Compound **15l**: R_f 0.34 (ethyl acetate/60–90 °C petroleum ether, 1:3); mp 83–84 °C; HPLC t_R 3.3 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, J=7.5, 1.7 Hz, 1H, Ar), 7.28 (ddd, J=8.2, 7.5, 1.7 Hz, 1H, Ar), 6.96 (td, J=7.5, 1.0 Hz, 1H, Ar), 6.88 (dd, J=8.2, 1.0 Hz, 1H, Ar), 6.24 (dd, J=6.7, 3.7 Hz, 1H, CHOCb), 4.05 (br s, 1H, Cb), 3.96–3.76 (m, 3H, Cb, CH_2OH), 3.84 (s, 3H, OCH_3), 3.06 (dd, J=6.7, 5.1 Hz, 1H, OH), 1.23 (m, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6 (C=O), 128.5 (Ar_q), 126.6 (2C, Ar), 125.6 (Ar_q), 120.0 (Ar), 110.0 (Ar), 73.0 (*C*HOCb), 66.0 (CH_2OH), 54.9 (OCH_3), 46.1 (Cb), 45.2 (Cb), 21.0 (2C, Cb), 20.0 (2C, Cb); HRMS (ESI^+) calcd for $C_{16}H_{25}NO_4Na^+$ 318.1681, found 318.1684.

*4.6.17. 1-(4-Methoxyphenyl)-2-O-(N,N-diisopropylcarbamoyl)-1,2-ethanediol (**14d**) and 1-O-(N,N-diisopropylcarbamoyl)-1-(4-methoxyphenyl)-1,2-ethanediol (**15d**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compounds **14d** (colorless oil, 10 mg, 0.04 mmol, 11%) and **15d** (colorless oil, 46 mg, 0.16 mmol, 49%) were obtained. Their NMR data are identical with the products obtained via route A.

*4.6.18. 1-O-(N,N-Diisopropylcarbamoyl)-1-(2,4-dimethoxyphenyl)-1,2-ethanediol (**15e**).* According to route B, from compound **7** (100 mg, 0.32 mmol), compound **15e** (colorless oil, 73 mg, 0.22 mmol, 70%) was obtained. Its NMR data are identical with the products obtained via route A.

*4.6.19. 1-O-(N,N-Diisopropylcarbamoyl)-1-(3,4-difluorophenyl)-1,2-ethanediol (**15g**).* According to route B, from compound **7** (200 mg, 0.64 mmol), product **15g** (colorless oil, 94 mg, 0.31 mmol, 49%) was obtained. Compound **15g**: R_f 0.29 (ethyl acetate/60–90 °C petroleum ether, 1:3); HPLC t_R 3.4 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.03 (m, 3H, Ar), 5.76 (dd, J=7.3, 4.0 Hz, 1H, C*H*OCb), 4.05 (br s, 1H, Cb), 3.94–3.75 (m, 3H, Cb, CH_2OH), 2.92 (br s, 1H, OH), 1.22 (br s, 12H, Cb); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7 (C=O), 150.9 (dd, J=26.9, 12.6 Hz, Ar_q), 148.4 (dd, J=26.9, 12.6 Hz, Ar_q), 134.7 (t, J=4.5 Hz, Ar_q), 122.4 (dd, J=6.3, 3.6 Hz, Ar), 116.9 (d, J=17.4 Hz, Ar), 115.3 (d, J=17.9 Hz, Ar), 76.2 (*C*HOCb), 66.1 (CH_2OH), 46.3 (Cb), 45.2 (Cb), 21.1 (2C, Cb), 19.9 (2C, Cb); HRMS (ESI^+) calcd for $C_{15}H_{21}NO_3F_2Na^+$ 324.1387, found 324.1375.

*4.6.20. 1-Phenyl-1,2-ethanediol (**13**).* According to route C, from compound **7** (100 mg, 0.32 mmol), compound **13** (white solid, 25 mg, 0.18 mmol, 57%) was obtained. Compound **13**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H, Ph), 4.77 (dd, J=8.2, 3.5 Hz, 1H, C*H*OH), 3.73–3.58 (m, 2H, CH_2OH), 3.49 (br s, 1H, OH), 3.13 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5 (Ph_q), 128.5 (2C, Ph), 128.0 (Ph), 126.1 (2C, Ph), 74.7 (CHOH), 68.0 (CH_2OH). NMR of data of compound **13** are consistent with the literature.[15]

*4.6.21. 1-(4-Methoxyphenyl)-1,2-ethanediol (**16d**).* According to route C, from compound **7** (100 mg, 0.32 mmol), compound **16d** (white solid, 33 mg, 0.20 mmol, 62%) was obtained. Compound **16d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J=8.7 Hz, 2H, Ar), 6.87 (d, J=8.7 Hz, 2H, Ar), 4.72 (dd, J=8.2, 3.5 Hz, 1H, C*H*OH), 3.79 (s, 3H, OCH_3), 3.68–3.58 (m, 2H, CH_2OH), 3.35 (br s, 1H, OH), 3.02 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3 (Ar_q), 132.6 (Ar_q), 127.4 (2C, Ar), 113.9 (2C, Ar), 74.3 (CHOH), 68.0 (CH_2OH), 55.3 (OCH_3). NMR of data of compound **16d** are consistent with the literature.[16]

*4.6.22. 1-(2,4-Dimethoxyphenyl)-1,2-ethanediol (**16e**).* According to route C, from compound **7** (100 mg, 0.32 mmol), compound **16e** (white solid, 39 mg, 0.20 mmol, 62%) was obtained. Compound **16e**: R_f 0.17 (ethyl acetate/60–90 °C petroleum ether, 1:1); mp 112–113 °C; HPLC t_R 2.0 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J=8.3 Hz, 1H, Ar), 6.49 (dd, J=8.3, 2.3 Hz, 1H, Ar), 6.45 (d, J=2.3 Hz, 1H, Ar), 4.97 (dd, J=8.0, 3.5 Hz, 1H, C*H*OH), 3.81 (s, 3H, OCH_3), 3.80

(s, 3H, OCH_3), 3.78–3.64 (m, 2H, CH_2OH), 2.98 (br s, 1H, OH), 2.38 (br s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5 (Ar_q), 157.6 (Ar_q), 128.0 (Ar), 120.9 (Ar_q), 104.2 (Ar), 98.6 (Ar), 71.0 (CHOH), 66.6 (CH_2OH), 55.4 (CH_3), 55.3 (CH_3); HRMS (EI^+) calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0887.

*4.6.23. 1-(3,4-Difluorophenyl)-1,2-ethanediol (**16g**).* According to route C, from compound **7** (100 mg, 0.32 mmol), compound **16g** (colorless oil, 34 mg, 0.20 mmol, 62%) was obtained. Compound **16g**: R_f 0.21 (ethyl acetate/60–90 °C petroleum ether, 1:1); HPLC t_R 2.1 min; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25–7.10 (m, 2H, Ar), 7.07 (m, 1H, Ar), 4.78 (dd, J=8.1, 3.1 Hz, 1H, C*H*OH), 3.78–3.54 (m, 2H, CH_2OH), 3.21 (br s, 1H, OH), 2.65 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8 (dd, J=38.9, 24.0 Hz, Ar_q), 148.2 (dd, J=75.8, 42.9 Hz, Ar_q), 138.3–135.2 (m, Ar_q), 121.5 (dd, J=6.3, 3.6 Hz, Ar), 116.8 (d, J=17.3 Hz, Ar), 114.6 (d, J=17.8 Hz, Ar), 73.0 (CHOH), 67.3 (CH_2OH); HRMS (EI^+) calcd for $C_8H_8F_2O_2$ 174.0492, found 174.0494.

*4.6.24. 1,1-Diphenyl-1,2-ethanediol (**16m**).* According to route C, from compound **7** (100 mg, 0.32 mmol), compound **16m** (white solid, 39 mg, 0.18 mmol, 57%) was obtained. Compound **16m**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.40 (m, 4H, Ph), 7.37–7.30 (m, 4H, Ph), 7.28–7.24 (m, 2H, Ph), 4.13 (d, J=6.4 Hz, 2H, CH_2OH), 3.27 (s, 1H, CHO*H*), 2.03 (t, J=6.4 Hz, 1H, CH_2OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8 (2C, Ph_q), 128.4 (4C, Ph), 127.5 (2C, Ph), 126.4 (4C, Ph), 78.6 (CHOH), 69.4 (CH_2OH). NMR of data of compound **16m** are consistent with the literature.[17]

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Supplementary data

Copies of the ^1H NMR and ^{13}C NMR spectra of new intermediates and products are provided. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.08.025.

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