A Convenient Way for the Conversion of Carboxylic Esters into 2-Substituted Allyl Halides

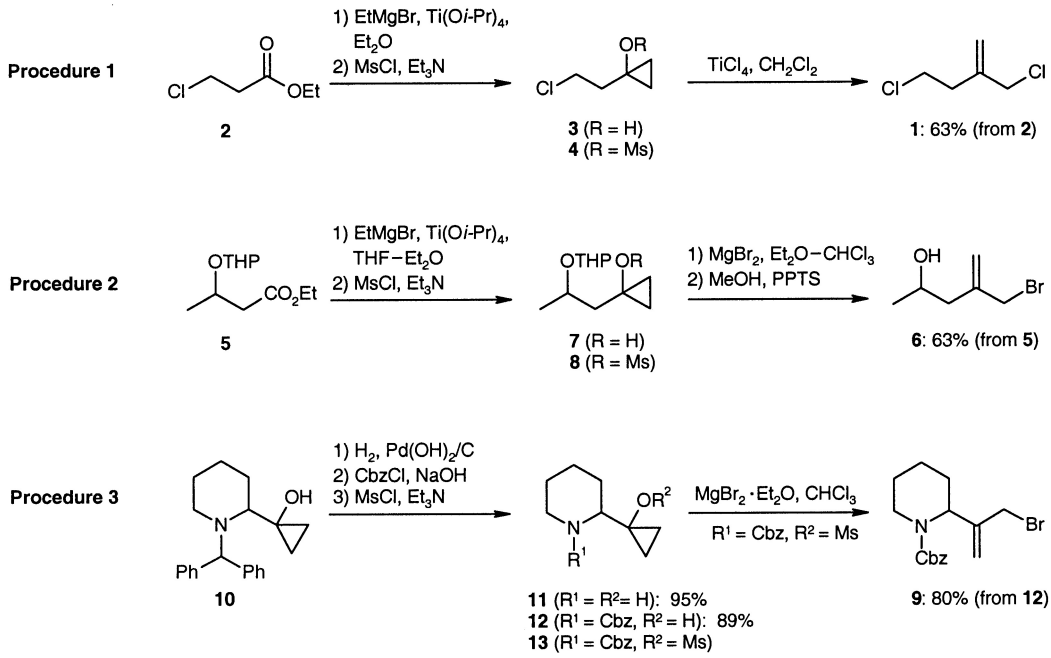
Oleg G. Kulinkovich,* Yurii Y. Kozyrkov, Andrei V. Bekish, Evgenii A. Matiushenkov, Ivan L. Lysenko

Department of Organic Chemistry, Belarusian State University, Skoriny av. 4, 220050 Minsk, Belarus
Fax +375(172)265609; E-mail: kulinkovich@bsu.by

Received 1 June 2004; revised 9 August 2004

Abstract: The preparation of functionalized 2-substituted allyl bromides and chlorides from carboxylic esters is reported. The carboxylic esters were transformed first to 1-substituted cyclopropanols by treating with ethylmagnesium bromide in the presence of titanium alkoxide. Mesylation of the cyclopropanols followed by halide displacement of the sulfonate group to halogen, accompanied by cyclopropyl-allyl rearrangement, affords the required allyl bromides and chlorides.

Key words: cyclopropanation, titanium alkoxides, cyclopropanols, cyclopropyl-allyl rearrangement, allyl halides



Scheme 1

Introduction

Transformation of the carbonyl group of carboxylic esters into other functionalities serves as the basis for various important methods of general preparative organic synthesis. Most of these methods are based on intermolecular carbon–carbon bond formation under the action of carbanionic reagents and are used mainly for the preparation of alcohols, ketones, enol esters as well as some bifunctional compounds.[1] For example, some years ago we have found that carboxylic esters are smoothly converted into 1-substituted cyclopropanols upon treatment with ethylmagnesium bromide in diethyl ether in the presence of catalytic amounts of titanium(IV) isopropoxide.[2] The oxygen atom attached to a cyclopropane ring facilitates several regioselective ring-opening or ring expansion reactions of substituted cyclopropanols.[3] This allows the cyclopropanation reaction to be used as an intermediate step in the conversion of an ester group into other functionalities masked in a cyclopropanol fragment.

The present paper describes the full experimental procedures for the transformation of carboxylic esters into 2-substituted allyl halides bearing halogen, oxygen or nitrogen containing functional groups via the cationic cyclo-

SYNTHESIS 2005, No. 10, pp 1713–1717
Advanced online publication: 03.11.2004
DOI: 10.1055/s-2004-834869; Art ID: Z11204SS

propyl-allyl isomerization of cyclopropyl sulfonates (Scheme 1).[4] Taking into account the fundamental importance of allyl halides as electrophilic synthetic intermediates and as precursors for allylic organometallic reagents, the development of the efficient methods for the preparation of substituted allyl halides, contributes to further progress in various concomitant fields of organic synthesis.[5]

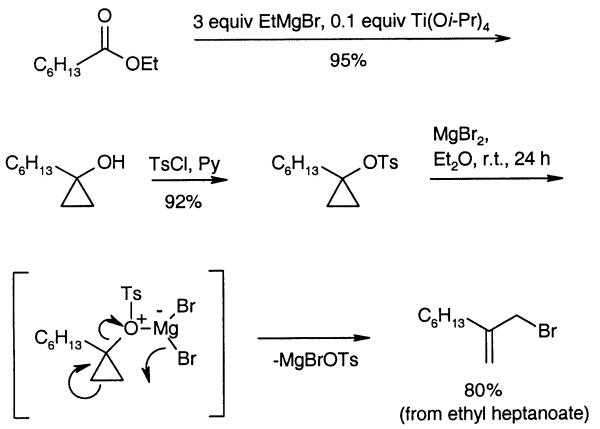
Scope and Limitations

It was supposed that cyclopropanation of carboxylic esters with ethylmagnesium bromide in the presence of titanium(IV) isopropoxide is initiated by diisopropoxytitanacyclopropane species formed by disproportionation of the corresponding diethyltitanium precursors.[2] They act in situ as 1,2-dicarbanionic equivalents in the reactions with esters leading to the corresponding cyclopropane derivatives. This reaction can be realized in a catalytic version.[2c] Carboxylic esters bearing halogen atoms, as well as alkoxy, acetal, dialkylamine, trialkylsilyl and some other insensitive to Grignard reagents groups usually smoothly undergo cyclopropanation under the action of dialkoxytitanacyclopropane reagents in diethyl ether.[2d] The cyclopropanation of the carboxylic esters having complex-forming substituents in such conditions could be complicated with precipitation of magnesium and titanium alkoxides, leading to decrease in the cyclopropanol yields. In some cases these difficulties can be overcome by the use of solvents possessing better solvating properties, such as tetrahydrofuran.[6]

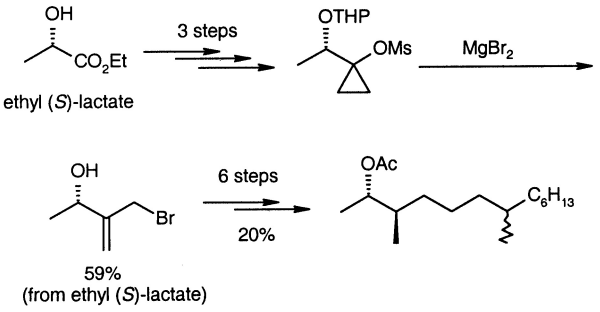
Recently, we have found convenient procedures for the conversion of the sulfonates of the tertiary cyclopropanols into 2-substituted allyl halides under the action of magnesium bromide, titanium tetrachloride, or some other metal halides in diethyl ether.[4] This reaction is induced by the metal halide-assisted heterolytic cleavage of the carbon–oxygen bond in cyclopropyl sulfonates which is accompanied by a C-2–C-3 cyclopropane ring cleavage (cationic cyclopropyl-allyl rearrangement).[7] For example, 2-(bromomethyl)oct-1-ene was obtained in a 80% overall yield starting from ethyl heptanoate using the cyclopropanation of the latter with ethylmagnesium bromide in the presence of titanium(IV) isopropoxide and treatment of tosylate of 1-hexylcyclopropanol with magnesium bromide (Scheme 2).[4]

Mesylate of (*S*)-1-tetrahydropyranyloxyethyl-1-cyclopropanol derived from ethyl (*S*)-lactate was successfully used as a key intermediate in the synthesis of (2*S*,3*R*,7*R*/*S*)-3,7-dimethyltridec-2-yl acetate and propionate, sex attractants of pine sawfly *Diprion pini* (Scheme 3).[5f]

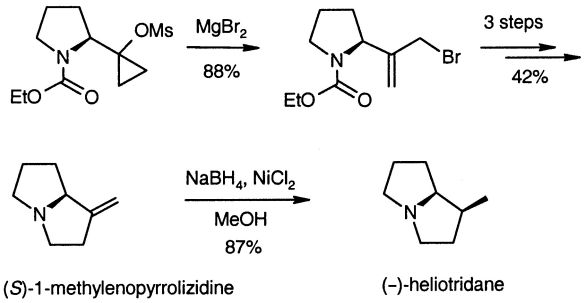
The alkaloids (*S*)-1-methylenopyrrolyzidine and (–)-heliotridane were synthesized starting from (*S*)-proline via a mesylate of the corresponding cyclopropanol in a similar way (Scheme 4).[8]



Scheme 2



Scheme 3



Scheme 4

In summary, cyclopropanation of carboxylic esters with ethylmagnesium bromide in the presence of titanium(IV) isopropoxide, followed by transformation of obtained tertiary cyclopropanols into the corresponding sulfonates and treatment of the latter with metal halides, allows 2-substituted allyl halides to be prepared in high overall yields. The flexibility of this approach is demonstrated by the syntheses of functionally substituted allyl halides, which are not readily available by the preparation with use of the conventional methods, such as allylic halogenation of isopropenyl group,[9] displacement of hydroxyl group in the corresponding 2-substituted allyl alcohols,[10] or coupling of the Grignard reagents with 2-(bromomethyl)allyl halides.[11]

We describe below three typical procedures which demonstrate the different experimental techniques allowing to obtain a high preparative yields of the 2-substituted allyl halides bearing various functional substituents (Scheme 1). In **Procedure 1**, we describe the preparation of 4-chloro-2-(chloromethyl)but-1-ene (**1**) starting from ethyl 3-chloropropanoate (**2**). 1-(2-Chloroethyl)cyclopropanol (**3**)[12] and mesylate **4**[4] are obtained in high yields using the previously described standard experimental procedures. Mesylate **4** easily reacts with magnesium bromide in ether at room temperature to afford the corresponding allyl bromide in 70% isolated yield.[4] However, the reaction with magnesium chloride or titanium(IV) chloride in a similar conditions proceeds slowly and its completion requires prolonged time (24 h or more). The interaction of mesylate **4** with titanium(IV) chloride in dichloromethane leads to full consumption of the substrate after 3 h to afford allyl chloride **1** in 73% yield. In the next procedure (**Procedure 2**) THP-protected ethyl 3-hydroxybutyrate **5** is converted to 4-hydroxy-2-(bromomethyl)pent-1-ene (**6**). The cyclopropanation of starting ester **5** under treatment with ethylmagnesium bromide in the presence of catalytic amount of titanium(IV) isopropoxide in diethyl ether is accompanied with formation of abundant precipitates. As a result, the cyclopropanol **7** is formed at this reaction conditions in only 27% yield and near 32% of starting compound **5** is recovered. The use of ether and tetrahydrofuran mixture as a solvent let to carry out the cyclopropanation in homogenous conditions and to improve up to 88% the yield of the cyclopropanol **7**. The latter was converted without further purification to the corresponding mesylate **8**, which is not enough reactive towards the action of magnesium bromide in diethyl ether, while under reflux in a mixture of the ether and chloroform at reflux is smoothly transformed to the corresponding allyl bromide **6** in 63% overall yield after deprotection. In the last procedure (**Procedure 3**) nitrogen containing allyl bromide **9** is prepared from cyclopropanol **10**.[13] Its mesylate does not react with magnesium bromide in diethyl ether, probably due to good complexing properties of nitrogen atom, and leads to the formation of resinous products in chloroform. This problem is solved by replacement of *N*-protecting benzhydryl group with benzyloxycarbonyl (Cbz) group via *N*-deprotected cyclopropanol **11**. Mesylation of carbamate **12** and subsequent treatment of mesylate **13** with the solid magnesium bromide etherate in refluxing chloroform resulted in 2-substituted allyl bromide **9** in 80% yield while the conversion of the mesylate **13** in Et_2O or Et_2O–$CHCl_3$ mixture was poor.

1-(2-Chloroethyl)cyclopropanol (3)[12]

A 1000 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with ethyl 3-chloropropanoate (**2**; 20.49 g, 150 mmol), Ti(OPr-*i*)$_4$ (4.33 g, 15 mmol) and anhyd Et_2O (100 mL), and cooled to 0 °C. A solution of EtMgBr prepared from Mg turnings (9.00 g, 375 mmol) and EtBr (41.42 g, 380 mmol) in anhyd Et_2O (260 mL) was then added dropwise for a 1.5 h to the stirred solution. After 30 min, the reaction mixture was quenched with 10% aq H_2SO_4 (400 mL). The organic layer was washed with H_2O (100 mL), aq sat. $NaHCO_3$ solution (100 mL), brine (100 mL), dried (Na_2SO_4) and concentrated in vacuo. The cyclopropanol **3** (16.80 g, more than 90% purity on NMR data) was obtained as a pale yellow oil and was used in the next step without further purification.

IR (CCl_4): 3590, 3455 (br), 3080, 1135, 1010, 655 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (t, *J* = 7.0 Hz, 2 H), 2.66 (s, 1 H), 1.99 (t, *J* = 7.0 Hz, 2 H), 0.75–0.79 (m, 2 H), 0.49–0.53 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 53.9, 41.9, 41.0, 13.3.

1-(2-Chloroethyl)cyclopropyl Methanesulfonate (4)[4]

A 500 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with **3** (16.80 g), Et_3N (20.24 g, 200 mmol) and anhyd CH_2Cl_2 (200 mL), and cooled to 0 °C. $MeSO_2Cl$ (18.33 g, 160 mmol) was then added dropwise over 30 min to the stirred solution. After 30 min, the reaction mixture was quenched with H_2O (200 mL). The organic layer was washed with H_2O (100 mL), 10% aq H_2SO_4 (100 mL), aq sat. $NaHCO_3$ solution (100 mL), brine (100 mL), dried ($MgSO_4$) and concentrated in vacuo. The methanesulfonate **4** (26.04 g, more than 90% purity on NMR data) was obtained as a yellow oil and used in the next step without further purification.

IR (CCl_4): 3110, 1345, 1175, 1025, 660 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (t, *J* = 7.0 Hz, 2 H), 2.98 (s, 3 H), 2.28 (t, *J* = 7.0 Hz, 2 H), 1.28–1.32 (m, 2 H), 0.79–0.83 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 63.9, 40.6, 39.6, 39.1, 11.6.

4-Chloro-2-(chloromethyl)but-1-ene (1)[14]

A 500 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with **4** (18.30 g) and anhyd CH_2Cl_2 (200 mL). $TiCl_4$ (26.70 g, 140 mmol) was then added dropwise for a 20 min to the stirred solution at r.t. After 3 h, the reaction mixture was quenched with H_2O (200 mL). The organic layer was washed with H_2O (2 × 100 mL), aq sat. $NaHCO_3$ solution (50 mL), brine (100 mL), dried ($CaCl_2$) and concentrated in vacuo. The crude product was distilled in vacuo yielding allyl chloride **1** as a colorless liquid (9.20 g, 63% from **2**); bp 51–54 °C/11 mm Hg.

IR (CCl_4): 1645, 675 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.26 (s, 1 H), 5.08 (s, 1 H), 4.07 (s, 2 H), 3.67 (t, *J* = 7.0 Hz, 2 H), 2.66 (t, *J* = 7.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.3, 117.2, 47.7, 42.1, 35.9.

Anal. Calcd for $C_5H_8Cl_2$: C, 43.20; H, 5.80; Cl, 51.00. Found: C, 43.35; H, 5.66; Cl, 50.79.

1-[2-(Tetrahydro-2*H*-pyran-2-yloxy)propyl]cyclopropanol (7)

A 250 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with THP-protected ethyl 3-hydroxybutyrate (**5**; 5.00 g, 23.1 mmol), Ti(O*i*-Pr)$_4$ (1.64 g, 5.8 mmol) and anhyd THF (40 mL) and cooled to 10 °C. The solution of EtMgBr prepared from Mg turnings (1.70 g, 70 mmol) and EtBr (7.63 g, 70 mmol) in a mixture of anhyd Et_2O (30 mL), THF (30 mL) and benzene (3 mL) was then added dropwise for a 4 h to the stirred solution. After 30 min, a solvent was removed under reduced pressure and the residue was diluted with CH_2Cl_2 (100 mL). The obtained solution was quenched with aq sat. NH_4Cl solution (20 mL). The reaction mixture was filtered and the inorganic precipitate was additionally washed with CH_2Cl_2 (4 × 20 mL). The filtrate was washed with aq sat. $NaHCO_3$ solution (20 mL), dried (Na_2SO_4) and concentrated in vacuo. The cyclopropanol **7** (4.49 g) was obtained as a pale yellow oil and was used in the next step without further purification. A portion of crude product (1.00 g) was purified by column chromatography (cyclohexane–EtOAc, 20 g Merck silica gel) yielding cyclopropanol **7** as a mixture of diastereomers (0.91 g, 88%).

IR (CCl_4): 3600, 3520, 3090 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.76–4.80 (m, 0.5 H), 4.64–4.67 (m, 0.5 H), 4.31 (br s, 1 H), 4.04–4.22 (m, 1 H), 3.88–3.97 (m, 1 H), 3.46–3.55 (m, 1 H), 1.66–1.90 (m, 3 H), 1.45–1.62 (m, 5 H), 1.31 (d, *J* = 6.1 Hz, 1.5 H), 1.16 (d, *J* = 6.2 Hz, 1.5 H), 0.62–0.81 (m, 2 H), 0.41–0.50 (m, 1 H), 0.32–0.40 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 99.4, 97.2, 75.2, 71.7, 63.8, 62.8, 54.5, 54.1, 44.6, 43.9, 31.2, 31.2, 25.3, 25.2, 22.0, 20.5, 19.9, 19.8, 14.3, 13.7, 12.0, 11.9.

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07; O, 23.97. Found: C, 66.14; H, 10.23; O, 23.63.

1-[2-(Tetrahydro-2*H*-pyran-2-yloxy)propyl]cyclopropyl Methanesulfonate (8)

A 250 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with cyclopropanol **7** (4.49 g), Et_3N (6.98 g, 69 mmol) and Et_2O (100 mL) and cooled to 0 °C. $MeSO_2Cl$ (4.00 g, 35 mmol) was then added dropwise over 30 min to the stirred solution. After 30 min, the reaction mixture was quenched with H_2O (100 mL) and extracted with Et_2O (2 × 20 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated in vacuo. The methanesulfonate **8** (6.18 g) was obtained as a yellow liquid and used in the next step without further purification. A portion of crude product (1.00 g) was purified by column chromatography (cyclohexane–EtOAc, 20 g Merck silica gel) affording methanesulfonate **8** as a mixture of diastereomers (0.91 g, 87% from ester **5**).

IR (CCl_4): 3090 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.75–4.79 (m, 0.5 H), 4.69–4.73 (m, 0.5 H), 4.06–4.22 (m, 1 H), 3.85–3.95 (m, 1 H), 3.44–3.53 (m, 1 H), 2.99 (s, 1.5 H), 2.98 (s, 1.5 H), 1.99–2.08 (m, 1 H), 1.65–1.92 (m, 3 H), 1.45–1.60 (m, 4 H), 1.15–1.32 (m, 2 H), 1.30 (d, *J* = 6.6 Hz, 1.5 H), 1.20 (d, *J* = 6.1 Hz, 1.5 H), 0.66–0.89 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 99.2, 94.9, 71.5, 67.9, 64.3, 64.2, 62.7, 61.9, 43.2, 43.0, 39.8, 31.1, 30.9, 25.5, 25.4, 22.3, 19.9, 19.3, 19.2, 12.1, 11.9, 11.6, 11.4.

4-(Bromomethyl)pent-4-en-2-ol (6)

A 500 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with methanesulfonate **8** (6.18 g) and anhyd $CHCl_3$ (120 mL). A solution of $MgBr_2$ prepared from Mg turnings (1.41 g, 58 mmol) and 1,2-dibromoethane (11.46 g, 61 mmol) in Et_2O (60 mL), was then added in one portion to the stirred solution at r.t. The reaction mixture was refluxed under argon for 1.5 h, then cooled to r.t., quenched with H_2O (100 mL) and extracted with Et_2O (4 × 20 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated in vacuo. The residue was diluted with MeOH (40 mL). Pyridinium *p*-toluenesulfonate (PPTS, 0.10 g) was then added to the solution and the mixture was refluxed under argon for 10 min and then concentrated in vacuo. The residue was diluted with CH_2Cl_2 (50 mL), washed with aq sat. $NaHCO_3$ solution (20 mL), and the aqueous layer was back-extracted with CH_2Cl_2 (4 × 5 mL). The combined organic fractions were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (cyclohexane–EtOAc, 15:1, 60 g Merck silica gel) yielding allyl bromide **6** as a pale yellow oil (2.61 g, 63% from **5**).

IR (CCl_4): 3610, 3480, 3080, 1630 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.30 (br s, 1 H), 5.07–5.08 (m, 1 H), 3.98–4.07 (m, 3 H), 2.45 (ddd, *J* = 14.5, 4.0, 1.1 Hz, 1 H), 2.27 (ddd, *J* = 14.5, 8.8, 0.8 Hz, 1 H), 1.60 (br s, 1 H), 1.25 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.6, 117.9, 65.7, 43.4, 36.5, 23.2.

Anal. Calcd for $C_6H_{11}BrO$: C, 40.25; H, 6.19. Found: C, 40.38; H, 6.08.

1-(Piperidin-2-yl)cyclopropanol (11)

A 100 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with 1-(1-benzhydrylpiperidin-2-yl)cyclopropanol[13] (**10**; 6.15 g, 20 mmol), 20% $Pd(OH)_2$ on charcoal (0.50 g) and MeOH (50 mL). The reaction mixture was stirred until the calculated amount of H_2 gas was absorbed. The catalyst was removed by filtration and the filtrate was concentrated in vacuo. The residue was diluted with hexane–Et_2O mixture (1:1, 10 mL) and cooled to –10 °C. The colorless crystals formed were filtered and washed with the same solvent (2 mL) giving cyclopropanol **11** (2.68 g, 95%); mp 81–82 °C (Et_2O).

IR ($CHCl_3$): 3420 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.4 (br s, 2 H), 3.35–3.50 (m, 1 H), 2.97 (td, *J* = 11.5, 3.0 Hz, 1 H), 2.32 (dd, *J* = 10.0, 4.0 Hz, 1 H), 2.13–2.26 (m, 1 H), 1.55–2.1 (m, 5 H), 0.95–1.20 (m, 2 H), 0.72–0.90 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 64.0, 56.9, 47.0, 27.8, 25.6, 24.5, 12.6, 11.2.

Anal. Calcd for $C_8H_{15}NO$: C, 68.04; H, 10.71. Found: C, 68.15; H, 10.69.

Benzyl 2-(1-Hydroxycyclopropyl)piperidine-1-carboxylate (12)

A 100 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with **11** (1.41 g, 10 mmol), benzyl chloroformate (2.05 g, 12 mmol) and CH_2Cl_2 (20 mL) and cooled to –10 °C. A 50% aq solution of NaOH (4 mL) was added dropwise to the stirred mixture. The reaction mixture was then stirred at r.t. for 6 h, the organic layer was separated, dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (benzene, then benzene–Et_2O, 1:1, 30 g Merck silica gel) yielding **12** as a pale yellow oil (2.45 g, 89%).

IR (CCl_4): 3605, 3405, 3060, 3000, 2920, 1685, 1420, 1320, 1160, 1025, 695 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.42 (m, 5 H), 5.16 (s, 2 H), 3.9 (br s, 1 H), 3.42–3.75 (m, 2 H), 3.2–3.35 (m, 1 H), 1.70–2.00 (m, 3 H), 1.42–1.64 (m, 3 H), 0.70–0.84 (m, 3 H), 0.48–0.60 (m, 1 H).

Anal. Calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69. Found: C, 69.96; H, 7.55.

Benzyl 2-[1-(Bromomethyl)vinyl]piperidine-1-carboxylate (9)

A 100 mL round-bottom flask, equipped with a magnetic stirring bar, was charged with cyclopropanol **12** (2.20 g, 8 mmol), Et_3N (2.43 g, 24 mmol) and Et_2O (30 mL) and cooled to –10 °C. $MeSO_2Cl$ (1.37 g, 12 mmol) was then added dropwise for a 10 min to the stirred solution. After stirring for 2 h at r.t., the reaction mixture was quenched with H_2O (10 mL). The organic layer was washed with aq 2 N HCl solution (5 mL), aq sat. $NaHCO_3$ solution (5 mL), then dried (Na_2SO_4) and concentrated in vacuo yielding mesylate **13** as a colorless oil (2.82 g). The latter was diluted with $CHCl_3$ (16 mL) and added to $MgBr_2{\cdot}OEt_2$ prepared from Mg turnings (0.58 g, 24 mmol) and 1,2-dibromoethane (4.51 g, 24 mmol) in Et_2O (30 mL) followed by removal of Et_2O in vacuo. The stirred reaction mixture was refluxed for 1.5 h, then cooled to 0 °C and quenched with H_2O (15 mL). The organic fraction was dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (cyclohexane, then benzene–Et_2O, 1:1, 25 g Merck silica gel) yielding **9** as a pale yellow oil (2.16 g, 80%).

IR (CCl_4): 2935, 1690, 1420, 1255, 1170, 700 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.39 (m, 5 H), 5.46 (d, *J* = 1.5 Hz, 1 H), 5.16 (s, 2 H), 5.08–5.15 (m, 2 H), 4.03–4.12 (m, 1 H), 3.90–3.98 (m, 2 H), 2.75–2.85 (m, 1 H), 2.0–2.08 (m, 1 H), 1.57–1.77 (m, 3 H), 1.40–1.56 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 142.7, 136.8, 128.4, 127.9, 127.8, 117.8, 67.2, 52.6, 40.6, 33.9, 26.2, 25.4, 19.7.

Anal. Calcd for $C_{16}H_{20}BrNO_2$: C, 56.82; H, 5.96. Found: C, 57.14; H, 5.69.

References

(1) (a) *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W., Eds.; Elsevier: Oxford, **1995**. (b) Satchell, D. P. N.; Satchell, R. S. In *The Chemistry of Carboxylic Acids and Esters*; Patai, S., Ed.; Wiley: New York, **1969**, 375. (c) Dieter, R. K. *Tetrahedron* **1999**, *55*, 4177.

(2) (a) Kulinkovich, O. G.; Sviridov, S. V.; Vasilevskii, D. A.; Prityts kaya, T. S. *Zh. Org. Khim.* **1989**, *25*, 2244; *J. Org. Chem. USSR (Engl. Transl.)* **1989**, *25*, 2027. (b) Kulinkovich, O. G.; Sviridov, S. V.; Vasilevskii, D. A.; Savchenko, A. I.; Prityts kaya, T. S. *Zh. Org. Khim.* **1991**, *27*, 294; *J. Org. Chem. USSR (Engl. Transl.)* **1991**, *27*, 250. (c) Kulinkovich, O. G.; Sviridov, S. V.; Vasilevskii, D. A. *Synthesis* **1991**, 234. (d) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789.

(3) (a) Kulinkovich, O. G. *Chem. Rev.* **2003**, *103*, 2597. (b) Gibson, D. H.; De Puy, C. H. *Chem. Rev.* **1974**, *74*, 605.

(4) Kozyrkov, Y. Y.; Kulinkovich, O. G. *Synlett* **2002**, 443.

(5) For recent applications of 2-substituted allyl halides in the syntheses of biologically active natural products, see: (a) Harada, T.; Takahashi, T.; Takahashi, S. *Tetrahedron Lett.* **1992**, *33*, 369. (b) Wovkulich, P. M.; Shankaran, K.; Kiegiel, J.; Uskoković, M. R. *J. Org. Chem.* **1993**, *58*, 832. (c) Fürstner, A.; Weintritt, H. *J. Am. Chem. Soc.* **1997**, *119*, 2944. (d) Wiliams, D. R.; Clark, M. P.; Berliner, M. A. *Tetrahedron Lett.* **1999**, *40*, 2287. (e) Hughes, R. S.; Dvorak, C. A.; Meyers, A. I. *J. Org. Chem.* **2001**, *66*, 6936. (f) Bekish, A. V.; Prokhorevich, K. N.; Kulinkovich, O. G. *Tetrahedron Lett.* **2004**, *45*, 5253.

(6) Raiman, M. V.; Il'ina, N. A.; Kulinkovich, O. G. *Synlett* **1999**, 1053.

(7) (a) De Puy, C. H.; Schnack, L. G.; Hausser, J. W. *J. Am. Chem. Soc.* **1966**, *88*, 3343. (b) Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 588; *Angew. Chem.* **1968**, *80*, 601. (c) Friedrich, E. C. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: Chichester, **1987**, 633. (d) Boche, G.; Walborsky, H. M. *Cyclopropane Derived Reactive Intermediates*; Patai, S.; Rappoport, Z., Eds.; Wiley: Chichester, **1990**, 117. (e) Jendralla, H. In *Houben-Weyl*, 4th ed., Vol. E17; de Meijere, A., Ed.; Thieme: Stuttgart, **1996**, 2313.

(8) Lysenko, I. L.; Kulinkovich, O. G. *Zh. Org. Khim.* **2004**, in press.

(9) (a) Xiong, Z. M.; Yang, J.; Li, Y. L. *Tetrahedron: Asymmetry* **1966**, *9*, 2607. (b) Bulliard, M.; Balme, G.; Gore, J. *Tetrahedron Lett.* **1989**, *30*, 5767. (c) Arora, S.; Binger, P.; Köster, R. *Synthesis* **1973**, 146. (d) Yamanaka, M.; Nishida, A.; Nakagawa, M. *Tetrahedron Lett.* **2002**, *43*, 2403. (e) Moreno-Dorado, F. J.; Guerra, F. M.; Manzano, F. L.; Aladro, F. J.; Jorge, Z. D.; Massanet, G. M. *Tetrahedron Lett.* **2003**, *44*, 6691; and references cited herein.

(10) (a) Hawthorne, M. F. *J. Am. Chem. Soc.* **1960**, *82*, 1886. (b) Marshall, J. A.; Andersen, N. H.; Hochstetler, A. R. *J. Org. Chem.* **1967**, *32*, 113. (c) Corey, J. P.; Helquist, P. *Tetrahedron Lett.* **1975**, 4167. (d) Baker, R.; Winton, P. M. *Tetrahedron Lett.* **1980**, *21*, 1175. (e) Trost, B.; Curran, D. *Tetrahedron Lett.* **1981**, *22*, 5023. (f) Rastetter, W. H.; Adams, J. *Tetrahedron Lett.* **1982**, *23*, 1319. (g) Overman, L. E.; Lesuisse, D. *Tetrahedron Lett.* **1985**, *26*, 4167.

(11) Stoller, A.; Moiskowski, C.; Sepulchre, C.; Belamy, F. *Tetrahedron Lett.* **1990**, *31*, 361.

(12) Sviridov, S. V.; Vasilevskii, D. A.; Kulinkovich, O. G. *Zh. Org. Khim.* **1991**, *27*, 1431; *J. Org. Chem. USSR (Engl. Transl.)* **1991**, *27*, 1251.

(13) Lysenko, I. L.; Bekish, A. V.; Kulinkovich, O. G. *Zh. Org. Khim.* **2002**, *38*, 918; *Russ. J. Org. Chem. (Engl. Transl.)* **2002**, *38*, 875.

(14) For other methods of preparation of compound **1**, see: (a) Applequist, D. E.; Fanta, G. F.; Henrikson, B. W. *J. Am. Chem. Soc.* **1960**, *82*, 2368. (b) See also: Fuchs, J.; Szeimies, G. *Chem. Ber.* **1992**, *125*, 2517.