1,8-Diazabicyclo[5.4.0]undec-7-ene: A Remarkable Base in the Debromination of 4- or 5-Substituted *N*-Benzyl α-Bromo-α-*p*-toluenesulfonylglutarimide

Meng-Yang Chang[a] (張夢揚), John, Yi-Chung Lin[a] (林裕鈞),
Shui-Tein Chen*[a] (陳水田) and Nein-Chen Chang[b] (張彥誠)
[a]*Institute of Biological Chemistry, Academia Sinica, Nankang, Taipei 115, Taiwan, R.O.C.*
[b]*Department of Chemistry, National Sun Yat-Sen University, Kaohsiung 804, Taiwan, R.O.C.*

Debromination of *N*-benzyl 4- or 5-substituted α-bromo-α-*p*-toluenesulfonylglutarimides is achieved with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides. The DBU/THF system is applied to a new methodology for the synthesis of bicyclic glutarimide skeleton in moderate yields.

INTRODUCTION

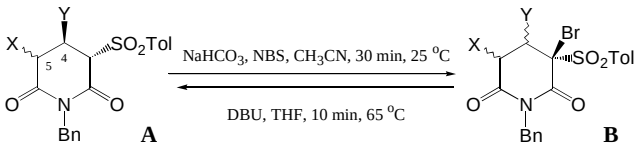
DBU is a bicyclic amidine that has become of particular interest as a reagent in synthetic organic chemistry. The extinction coefficient (ε) of this bicyclic amidine (DBU) is greater than for other bases.[1] It is widely used as an organic base in dehydrohalogenation to olefins.[1-3] Some important applications are esterification of carboxylic acid with alkyl halides,[4] alkylation and acylation of active methylene compounds,[5] epoxidation of α,β-unsaturated δ-lactones and other enones by *t*-butyl hydroperoxide,[6] ring-opening of epoxide by titanium (IV) chloride to give chlorohydrins,[7] synthesis of acylurea and carbamate from amide by Bu_4NBr_3-DBU reagent system,[8] and DBU-promoted addition of chloroform to carbonyl compounds.[9] In order to investigate the other applications of DBU, we find that DBU can abstract the bromide ion in the α-*p*-toluenesulfonylglutarimide.

RESULTS AND DISCUSSION

Bromination using NBS/$NaHCO_3$/CH_3CN system in the skeleton of *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides

First, *N*-benzyl α-*p*-toluenesulfonylacetamide was prepared from acylation and substitution of chloroacetyl chloride. The starting materials **A**[10-12] of the debromination reaction in turn were prepared by the formal [3+3] cycloaddition reactions of *N*-benzyl α-*p*-toluenesulfonylacetamide with various α,β-unsaturated esters. Then, bromination reaction is the next step. However, there have been few reports[13-15] on the halogenation of α-*p*-toluenesulfonylacetamide. The NBS/$NaHCO_3$/CH_3CN system is an efficient method for the bromination of α-*p*-toluenesulfonylglutarimides **A** as summarized in Scheme I and Table 1.

Scheme I



This is a facile, mild and high yield (82~97%) method for the bromination on α-*p*-toluenesulfonylpiperidine-2,6-dione. But, the bromination was unsuccessful on the α-*p*-toluenesulfonylpiperidine-2-one and pyrrolidine-2-one. The difference between α-*p*-toluenesulfonylpiperidine-2,6-dione and piperidine-2-one was not clear. We also attempted to use the Br_2/$CHCl_3$ reagent system, but the yield (40~71%) was less than for the NBS/$NaHCO_3$/CH_3CN system. All bromides **B** have the expected two isomers except No. 1 (R=H) in Table 1.

Debromination using DBU/THF system in the skeleton of *N*-benzyl 4- or 5-substituted α-bromo-α-*p*-toluenesulfonylglutarimides

With this result in hand, the next focus was to examine the elimination of these bromides from **B**. Bromides **B** when treated with DBU yielded debrominated products **A** as shown in Scheme I. The reactions yielded purified products in the range of 53~89%. Two isomers of bromides **B** were converted to compounds **A** by the DBU/THF system. The stereochemistry of compounds **A** at C-3 and C-4 retained its *trans* form (reactions No. 2~17)[10] and at the relatively positions of C-3 and C-5 (reactions 18~20)[11] maintained the mixed iso-

Table 1. Representative Examples of NBS Mediated Bromination of *N*-Benzyl 4- or 5-Substituted α-*p*-Toluenesulfonylglutarimides and DBU/THF Mediated Debromination of *N*-Benzyl 4- or 5-Substituted α-Bromo-α-*p*-toluenesulfonylglutarimides

Reaction No.	X, Y	Yield (%) **B** (bromination)	Yield (%) **A** (debromination)
1	H, H	92	81
2	H, $C_{10}H_{21}$	93	79
3	H, $CH(OCH_3)_2$	96	70
4	H, C_3H_6OH	90	89
5	H, C_4H_8OH	91	83
6	H, $C_5H_{10}OH$	90	88
7	H, C_3H_6Obn	95	79
8	H, C_4H_8Obn	97	76
9	H, $C_5H_{10}Obn$	95	80
10	H, $CH_2CH_2CH(OH)CH_3$	90	68
11	H, $CH_2CH_2CH(OTBS)CH_3$	89	72
12	H, $CH_2CH_2CH=CH_2$	94	66
13	H, C_6H_5	92	56
14	H, 4-F-C_6H_4	89	61
15	H, 4-NO_2-C_6H_4	84	53
16	H, 4-OMe-C_6H_4	84	59
17	H, 3,4-$(OMe)_2$-C_6H_3	85	64
18	Me, H	91	72
19	NHBoc, H	82	64
20	Phthalimido, H	85	58

mer forms.

How is the bromide removed from the compounds **B**? Our hypothesis is that DBU functions as a promoter for the debromination in the skeleton of *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides. This hypothesis has not usually been reported in the literature. The *p*-toluenesulfonyl group is the important factor in the debromination process (Fig. 1). Hydrogen bonding between the lone pair of electrons of *p*-toluenesulfonyl oxygen atom and the proton of the C-4 position fastens this proton into two rigid conformations of bromides **B**. The second factor is the 1,3-repulsion force between the nitrogen lone pair of electrons and bromide, and which may promote the release of the bromide group.

Furthermore, a reaction of bromides **B** in tetrahydrofuran without DBU at refluxed temperature did not cause

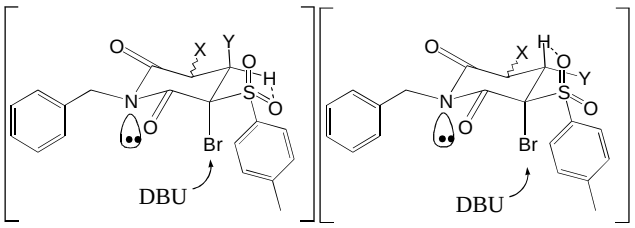


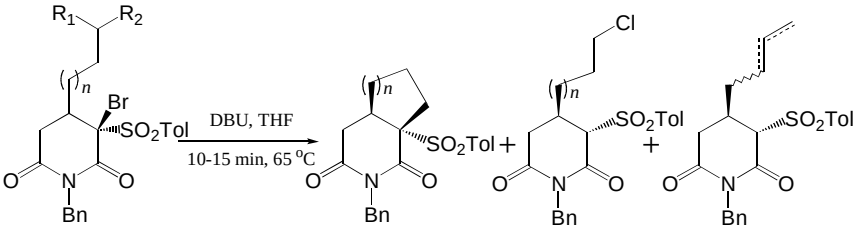
Fig. 1.

debromination. Therefore, the debromination process required DBU as an assistant. The quenched water supplied the proton in the intermediate state to give compounds **A**. The reaction must be heated to increase reaction rate. If the reaction was refluxed over 30 min, the desired product disappeared and a complex mixture resulted. Therefore, the best condition for debromination reaction is 65 ℃ within 10 min. DBU was recognized as an efficient promoter in these debrominations since other bases such as triethylamine and diisopropylethylamine were not useful to deliver the same products.

DBU promoted debromination process in the intramolecular cyclization and elimination of the skeleton of *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides

With these results in hand, the DBU/THF system was applied to synthesize the bicyclic glutarimide skeletons **C1**, **C2** from chloro-substituted glutarimides **B1**, **B2** (as shown in Scheme II). Chlorides **B1**, **B2**, **B3** were converted from alcohols (reaction No. 4~6) by chlorination of triphenylphosphine and carbon tetrachloride in 50~61% yield. When chlorides **B1** and **B2** were treated with DBU in tetrahydrofuran, the desired bicyclic glutarimides **C1** and **C2** were obtained. When the chloride **B3** was treated with DBU in tetrahydrofuran, only the debrominated compound **C3** was obtained.

Scheme II



B1 n = 1, R_1=H, R_2=Cl
B2 n = 2, R_1=H, R_2=Cl
B3 n = 3, R_1=H, R_2=Cl
B4 n = 1, R_1=Me, R_2=OMs

C1 n = 1 (57%)
C2 n = 2 (66%)

C3 n = 3 (52%)

C4 (51%)

This structure of **C3** was confirmed by X-ray analysis. 6,7-Fused bicyclic glutarimide was not easily formed, because the ring size was too large to cyclize. Mesylate **B4** was converted from alcohol (reaction No. 10) by mesylation of methanesulfonyl chloride and pyridine in 48% yield. The mesylate **B4** was treated with DBU in tetrahydrofuran to obtain the elimination compound **C4** as a mixture of *exo* and *endo* olefins. This reaction revealed that the secondary mesylate group was not attacked by the intramolecular anion intermediate, but it was easily eliminated by DBU. These results represented the interesting reaction types of different functional groups of 4- or 5-substituted α-*p*-toluenesulfonylglutarimides using DBU.

CONCLUSION

In summary, we demonstrate two methodologies: (1) bromination using NBS/$NaHCO_3$/CH_3CN system and (2) debromination using DBU/THF system in the skeleton of *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides. We propose that DBU is a promoter in the debromination process of the skeleton of *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides, and it also promotes the intramolecular cyclization and elimination.

EXPERIMENTAL

General

Tetrahydrofuran (THF) was distilled prior to use from a deep-blue solution of sodium-benzophenone ketyl. All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Organic layers were dried with anhydrous magnesium sulfate before concentration *in vacuo*. Crude products were purified using preparative TLC or column chromatography on silica gel. All reported melting points were uncorrected.

N-Benzyl-2-*p*-toluenesulfonylacetamide

Chloroacetyl chloride (5.99 g, 53.0 mmol) in tetrahydrofuran (40 mL) was added to a solution of benzylamine (5.35 g, 50.0 mmol) and triethylamine (5.57 g, 55.0 mmol) in tetrahydrofuran (100 mL) over a period of 1 h at 0 °C. Stirring continued at room temperature for 4 h. The mixture was concentrated under reduced pressure. Water (30 mL) was added to the residue and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (2 × 50 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. Without further purification, the crude product was refluxed with sodium salt of *p*-toluenesulfinic acid ($TolSO_2Na$-$2H_2O$, 16.05 g, 75.0 mmol) in dioxane (150 mL) and water (150 mL) for 10 h. Then the mixture was concentrated under reduced pressure, and the residue was extracted with ethyl acetate (3 × 150 mL). The combined organic layers were washed with brine (2 × 50 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. Recrystallization on hexane and ethyl acetate (100 mL and 50 mL) produced 12.88 g (85%, two steps) of α-*p*-toluenesulfonylacetamide: mp 157-159 °C; IR ($CHCl_3$) 2361, 1664, 1528, 1290, 1147 cm^{-1}; ESI-MS: $C_{16}H_{18}NO_3S$ *m/z* (%) = 91 (100), 154 (65), 304 (M^++1, 85); HRMS (EI, M^+) calcd for $C_{16}H_{17}NO_3S$ 303.0930, found 303.0925; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.2 Hz, 2H), 7.33-7.24 (m, 7H), 7.06 (br s, 1H), 4.42 (d, J = 5.9 Hz, 2H), 3.99 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.64, 145.58, 137.35, 135.12, 130.04, 128.74, 128.16 (4×), 127.97 (2×), 127.70, 62.01, 44.02, 21.70; Anal. Calcd for $C_{16}H_{17}NO_3S$ C, 63.34; H, 5.65.

Found C, 63.14; H, 5.44.

Preparation of various α,β-unsaturated ethyl esters

No. 2~17 in Table 1, Wittig reaction

A solution of aldehyde (3.0 mmol) in methylene chloride (10 mL) was added to a rapidly stirred solution of $Ph_3P{=}CHCO_2Et$ (3.1 mmol) in methylene chloride (20 mL), then stirred at room temperature for 2 h. The resulting mixture was concentrated under reduced pressure. Water (20 mL) was added to the residue and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with brine (2 × 20 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. Purification of the crude product by column chromatography on silica gel with hexane/ethyl acetate (20/1~15/1) produced various α,β-unsaturated ethyl esters.

No. 19 in Table 1, Jackson's method[11,16]

No. 20 in Table 1, Trost's method: 2-Phthalimidoacrylic acid methyl ester[17,18]

Formal [3+3] cycloaddition reaction of *N*-benzyl α-*p*-toluenesulfonylacetamide with various α,β-unsaturated ethyl esters

A solution of *N*-benzyl α-*p*-toluenesulfonylacetamide (1.0 mmol) in tetrahydrofuran (30 mL) was carefully added to a rapidly stirred suspension of sodium hydride (2.1 mmol, 60%) in tetrahydrofuran (30 mL). After the reaction mixture was stirred at room temperature for 15 min, a solution of ethyl ester (1.0 mmol) in tetrahydrofuran (30 mL) was added. The resulting mixture was heated at reflux for 30 min (for reaction No. 1, at room temperature for over 2 h), quenched with saturated ammonium chloride solution (2 mL) in an ice bath, and concentrated under reduced pressure. Water (20 mL) was added to the crude product and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with brine (2 × 20 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. Purification of the crude product by column chromatography on silica gel with hexane/ethyl acetate (4/1~2/1~1/1) produced starting materials **A** in 68~92% yield.

Bromination from *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides A to *N*-benzyl 4- or 5-substituted α-bromo-α-*p*-toluenesulfonylglutarimides B using NBS/$NaHCO_3$/CH_3CN system

The typical procedure is as follows: *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimide (1.0 mmol) was added to a solution of *N*-bromosuccinimide (NBS, 1.2 mmol) and sodium bicarbonate (4.0 mmol) in dry acetonitrile (10 mL). The mixture was stirred under nitrogen atmosphere at room temperature for 30 min, and the reaction was quenched with water (1 mL). Evaporation of solvent followed by purification of the crude product by column chromatography on silica gel with hexane/ethyl acetate (8/1~4/1) produced pure bromides **B** as an isomeric mixture (reaction, No. 1 is a pure compound).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)piperidine-2,6-dione

Gum; IR ($CHCl_3$) 1731, 1691 cm^{-1}; HRMS (EI, M^+) calcd for $C_{19}H_{18}BrNO_4S$ 435.0146, found 435.0138; ^1H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.7 Hz, 2H), 7.31-7.25 (m, 7H), 5.06 (d, *J* = 13.8 Hz, 1H), 4.87 (d, *J* = 13.8 Hz, 1H), 3.22-3.00 (m, 2H), 2.92-2.82 (m, 1H), 2.76-2.66 (m, 1H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.47, 164.25, 146.40, 135.70, 132.17 (2×), 131.09, 129.02 (2×), 128.47 (2×), 128.35 (2×), 127.58, 71.97, 44.19, 30.14, 27.87, 21.81.

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-*n*-decylpiperidine-2,6-dione

Gum; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41-7.14 (m, 9H), 5.24-5.17 (m, 1H), 4.83-4.73 (m, 1H), 3.65-2.77 (m, 2H), 2.40 (s, 3H), 2.15-1.80 (m, 1H), 1.25 (br s, 18H), 0.92-0.82 (m, 3H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-dimethoxymethylpiperidine-2,6-dione

Gum; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.3 Hz, 4/5H), 7.44-7.16 (m, 41/5H), 5.19-5.15 (m, 1H), 4.97-4.67 (m, 2H), 3.51-2.91 (m, 2H), 3.40 (s, 3H), 3.13 (s, 3H), 3.01-2.92 (m, 1H), 2.46 (s, 6/5H), 2.40 (s, 9/5H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(3-hydroxypropyl)piperidine-2,6-dione

Gum; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39-7.12 (m, 9H), 5.20 (d, *J* = 13.9 Hz, 1/2H), 5.19 (d, *J* = 13.8 Hz, 1/2H), 4.81 (d, *J* = 13.9 Hz, 1/2H), 4.74 (d, *J* = 13.8 Hz, 1/2H), 3.68 (t, *J* = 6.3 Hz, 3/2H), 3.63 (t, *J* = 6.1 Hz, 3/2H), 3.57 (ddd, *J* = 0.8, 5.3, 17.8 Hz, 1/2H), 3.35 (dd, *J* = 10.5, 18.4 Hz, 1/2H), 3.11 (*J* = 5.8, 18.3 Hz, 1/2H), 3.04-2.98 (m, 1/2H), 2.89-2.81 (m, 1H), 2.57-2.49 (m, 1/2H), 2.40 (s, 3/2H), 2.39 (3/2H), 2.30-2.22 (m, 1/2H), 2.01-1.22 (m, 3H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(4-hydroxybutyl)piperidine-2,6-dione

Gum; ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.13 (m,

9H), 5.20 (d, *J* = 13.8 Hz, 3/5H), 5.18 (d, *J* = 13.7 Hz, 2/5H), 4.82 (d, *J* = 13.8 Hz, 3/5H), 4.75 (d, *J* = 13.7 Hz, 2/5H), 3.65-3.57 (m, 2H), 3.41-2.75 (m, 2H), 2.40 (br s, 3H), 2.18-1.85 (m, 1H), 1.62-1.23 (m, 7H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(5-hydroxypentyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.13 (m, 9H), 5.22 (d, *J* = 13.8 Hz, 1/2H), 5.18 (d, *J* = 13.7 Hz, 1/2H), 4.82 (d, *J* = 13.8 Hz, 1/2H), 4.75 (d, *J* = 13.7 Hz, 1/2H), 3.65-3.58 (m, 2H), 3.30-2.74 (m, 2H), 2.41 (br s, 3H), 2.16-1.88 (m, 1H), 1.59-1.23 (m, 9H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(3-benzyloxypropyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.11 (m, 14H), 5.23 (d, *J* = 13.9 Hz, 1/2H), 5.21 (d, *J* = 13.8 Hz, 1/2H), 4.82 (d, *J* = 13.9 Hz, 1/2H), 4.74 (d, *J* = 13.8 Hz, 1/2H), 4.50 (s, 1H), 4.47 (s, 1H), 3.62 (dd, *J* = 5.5, 18.1 Hz, 1/2H), 3.52 (t, *J* = 6.2 Hz, 1H), 3.50 (t, *J* = 6.1 Hz, 1H), 3.38 (dd, *J* = 11.9, 18.4 Hz, 1/2H), 3.11 (dd, *J* = 5.8, 18.4 Hz, 1/2H), 3.08-3.00 (m, 1/2H), 2.90-2.81 (m, 1H), 2.60-2.50 (m, 1/2H), 2.41 (s, 3/2H), 2.39 (s, 3/2H), 2.30-2.20 (m, 1/2H), 2.05-1.92 (m ,1/2H), 1.88-1.69 (m, 1H), 1.68-1.51 (m, 1H), 1.43-1.32 (m, 1/2H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(4-benzyloxybutyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.12 (m, 14H), 5.22 (d, *J* = 13.8 Hz, 1/2H), 5.20 (d, *J* = 13.8 Hz, 1/2H), 4.80 (d, *J* = 13.8 Hz, 1/2H), 4.74 (d, *J* = 13.8 Hz, 1/2H), 4.49 (s, 1H), 4.47 (s, 1H), 3.60-3.32 (m, 3H), 3.11-2.84 (m, 2H), 2.40 (br s, 3H), 2.17-1.86 (m, 1H), 1.69-1.24 (m, 5H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(5-benzyloxypentyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.13 (m, 14H), 5.23 (d, *J* = 13.8 Hz, 1/2H), 5.20 (d, *J* = 13.8 Hz, 1/2H), 4.83 (d, *J* = 13.8 Hz, 1/2H), 4.76 (d, *J* = 13.8 Hz, 1/2H), 4.50 (s, 1H), 4.49 (s, 1H), 3.64-3.31 (m, 3H), 3.11-2.73 (m, 2H), 2.40 (br s, 3H), 2.19-1.80 (m, 1H), 1.65-1.25 (m, 7H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-phenylpiperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55-6.90 (m, 14H), 5.39 (d, *J* = 13.6 Hz, 2/7H), 5.21 (d, *J* = 13.6 Hz, 5/7H), 5.02 (d, *J* = 13.6 Hz, 2/7H), 4.90 (d, *J* = 13.6 Hz, 5/7H), 4.36 (dd, *J* = 1.5, 7.4 Hz, 2/7H), 4.11 (br t, *J* = 7.0 Hz, 5/7H), 3.96 (dd, *J* = 7.4, 18.5 Hz, 2/7H), 3.65 (dd, *J* = 7.0, 18.3 Hz, 5/7H), 3.40 (dd, *J* = 6.2, 18.3 Hz, 5/7H), 3.12 (dd, *J* = 1.5, 18.5 Hz, 2/7H), 2.41 (s, 6/7H), 2.39 (s, 15/7H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(4-fluorophenyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-6.80 (m, 13H), 5.35 (d, *J* = 13.5 Hz, 2/9H), 5.20 (d, *J* = 13.6 Hz, 7/9H), 5.02 (d, *J* = 13.5 Hz, 2/9H), 4.88 (d, *J* = 13.6 Hz, 7/9H), 4.35 (dd, *J* = 1.9, 7.2 Hz, 2/9H), 4.10 (dd, *J* = 6.1, 7.8 Hz, 7/9H), 3.93 (dd, *J* = 7.2, 18.5 Hz, 2/9H), 3.66 (dd, *J* = 7.8, 18.4 Hz, 7/9H), 3.37 (dd, *J* = 6.1, 18.4 Hz, 7/9H), 3.08 (dd, *J* = 1.9, 18.5 Hz, 2/9H), 2.41 (s, 2/3H), 2.39 (s, 7/3H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(4-nitrophenyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 8.8 Hz, 4/3H), 8.00 (d, *J* = 8.8 Hz, 2/3H), 7.52-7.11 (m, 11H), 5.34 (d, *J* = 13.5 Hz, 1/3H), 5.22 (d, *J* = 13.6 Hz, 2/3H), 5.05 (d, *J* = 13.5 Hz, 1/3H), 4.89 (d, *J* = 13.6 Hz, 2/3H), 4.51 (dd, *J* = 2.3, 7.1 Hz, 1/3H), 4.22 (dd, *J* = 6.2, 8.1 Hz, 2/3H), 3.93 (dd, *J* = 7.1, 18.5 Hz, 1/3H), 3.72 (dd, *J* = 8.1, 18.1 Hz, 2/3H), 3.38 (dd, *J* = 6.1, 18.1 Hz, 2/3H), 3.07 (dd, *J* = 2.3, 18.5 Hz, 1/3H), 2.45 (s, 1H), 2.40 (s, 2H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(4-methoxyphenyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.12 (m, 11H), 6.86-6.67 (m, 2H), 5.37 (d, *J* = 13.5 Hz, 1/4H), 5.20 (d, *J* = 13.6 Hz, 3/4H), 5.00 (d, *J* = 13.5 Hz, 1/4H), 4.89 (d, *J* = 13.6 Hz, 3/4H), 4.31-3.08 (m, 3H), 3.81 (s, 9/4H), 3.76 (s, 3/4H), 2.42 (br s, 3H).

1-Benzyl-3-bromo-3-(4-methylphenylsulfonyl)-4-(3,4-dimethoxyphenyl)piperidine-2,6-dione

Gum; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53-7.11 (m, 9H), 6.82-6.47 (m, 3H), 5.35 (d, *J* = 13.5 Hz, 1/4H), 5.18 (d, *J* = 13.6 Hz, 3/4H), 4.99 (d, *J* = 13.5 Hz, 1/4H), 4.87 (d, *J* = 13.6 Hz, 3/4H), 4.30-3.09 (m, 3H), 3.88 (s, 9/4H), 3.84 (s, 3/4H), 3.79 (s, 9/4H), 3.64 (s, 3/4H), 2.40 (br s, 3H).

Debromination from *N*-benzyl 4- or 5-substituted α-bromo-α-*p*-toluenesulfonylglutarimides B to *N*-benzyl 4- or 5-substituted α-*p*-toluenesulfonylglutarimides A using DBU/THF system

The typical experiment procedure is as follows: DBU (0.3 mmol) was added to a solution of *N*-benzyl 4- or 5-substituted α-bromo-α-sulfonylglutarimide (0.1 mmol) in tetra-

hydrofuran (5 mL). The mixture was stirred at refluxed temperature for 10 min, and the reaction was quenched with water (1 mL) at room temperature. Evaporation of solvent followed by purification of the crude product by column chromatography on silica gel with hexane/ethyl acetate produced pure compound **A**.

1-Benzyl-3-(4-methylphenylsulfonyl)piperidine-2,6-dione

Mp 66-69 ℃; IR ($CHCl_3$) 2936, 2858, 1728, 1677, 1382, 736 cm^{-1}; HRMS (EI, M^+) calcd for $C_{19}H_{19}NO_4S$ 357.1036, found 357.1032; ^1H NMR (300 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.1 Hz, 2H), 7.32-7.25 (m, 7H), 5.03 (d, *J* = 13.8 Hz, 1H), 4.86 (d, *J* = 13.8 Hz, 1H), 4.06 (br s, 1H), 3.38-3.20 (m, 1H), 2.82-2.68 (m, 2H), 2.43 (s, 3H), 2.40-2.20 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.66, 164.65, 145.59, 135.28, 134.36, 129.69 (2×), 128.94 (2×), 128.57 (2×), 128.24 (2×), 127.40, 65.62, 43.38, 29.15, 21.71, 17.62.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-*n*-decylpiperidine-2,6-dione

Mp 49-51 ℃; IR ($CHCl_3$) 2926, 2855, 1728, 1676, 1382, 754 cm^{-1}; HRMS (EI, M^+) calcd for $C_{29}H_{39}NO_4S$ 497.2602, found 497.2610; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.33-7.24 (m, 7H), 5.06 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.90 (br s, 1H), 3.47 (dd, *J* = 6.1, 18.1 Hz, 1H), 3.00-2.95 (m, 1H), 2.69 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.40-1.10 (m, 18H), 0.87 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.50, 164.39, 145.66, 136.43, 134.61, 129.80 (2×), 128.93 (2×), 128.64 (2×), 128.33 (2×), 127.48, 70.85, 43.31, 34.32, 34.02, 31.86, 29.49 (2x), 29.44, 29.24, 29.06, 28.76, 26.57, 22.65, 21.73, 14.09.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-dimethoxymethylpiperidine-2,6-dione

Mp 151-154 ℃; IR ($CHCl_3$) 2940, 2837, 1727, 1676, 1388, 765 cm^{-1}; HRMS (EI, M^+) calcd for $C_{22}H_{25}NO_6S$ 431.1404, found 431.1411; ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.3 Hz, 2H), 7.33-7.20 (m, 7H), 4.98 (d, *J* = 14.0 Hz, 1H), 4.84 (d, *J* = 14.0 Hz, 1H), 4.22 (br s, 1H), 4.17 (br s, 1H), 3.34-3.14 (m, 2H), 3.27 (s, 3H), 3.14 (s, 3H), 2.75 (d, *J* = 17.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.38, 164.43, 145.64, 136.65, 134.35, 129.78 (2×), 129.03 (2×), 128.96 (2×), 128.12 (2×), 127.26, 106.67, 65.79, 56.36, 55.94, 43.30, 32.00, 30.55, 21.75.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(3-hydroxypropyl)-piperidine-2,6-dione

Mp 97-100 ℃; IR ($CHCl_3$) 3390, 2941, 2868, 1727, 1679, 1383, 1148, 744 cm^{-1}; ESI-MS: $C_{22}H_{26}NO_5S$ *m/z* (%) = 91 (100), 137 (19), 154 (18), 260 (10), 416 (M^++1, 50); HRMS (ESI, M^++1) calcd for $C_{22}H_{26}NO_5S$ 416.1533, found 416.1536; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.37-7.15 (m, 7H), 5.06 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.94 (br s, 1H), 3.67 (t, *J* = 5.7 Hz, 2H), 3.49 (dd, *J* = 6.1, 18.1 Hz, 1H), 3.03-2.95 (m, 1H), 2.70 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.75-1.23 (m, 5H); Anal. Calcd for $C_{22}H_{25}NO_5S$ C, 63.59; H, 6.06. Found C, 63.16; H, 6.21.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(4-hydroxybutyl)-piperidine-2,6-dione

Mp 80-83 ℃; IR ($CHCl_3$) 3390, 2938, 2863, 1727, 1681, 1386, 753 cm^{-1}; ESI-MS: $C_{23}H_{28}NO_5S$ *m/z* (%) = 91 (100), 430 (M^++1, 22); HRMS (ESI, M^++1) calcd for $C_{23}H_{28}NO_5S$ 430.1689, found 430.1690; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.1 Hz, 2H), 7.35-7.23 (m, 7H), 5.05 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.92 (br s, 1H), 3.54 (t, *J* = 5.3 Hz, 2H), 3.47 (dd, *J* = 6.0, 18.1 Hz, 1H), 3.00-2.95 (m, 1H), 2.69 (d, *J* = 18.1 Hz, 1H), 2.41 (s, 3H), 1.75-1.23 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.47, 164.33, 145.74, 136.40, 134.50, 129.83 (2×), 128.94 (2×), 128.69 (2×), 128.34 (2×), 127.53, 70.70, 62.13, 43.34, 34.31, 33.80, 31.92, 28.80, 22.95, 21.74; Anal. Calcd for $C_{23}H_{27}NO_5S$ C, 64.31; H, 6.34. Found C, 64.21; H, 6.40.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(5-hydroxypentyl)-piperidine-2,6-dione

Mp 60-62 °C; IR ($CHCl_3$) 3391, 2935, 2860, 1727, 1679, 1383, 751 cm^{-1}; HRMS (EI, M^+) calcd for $C_{24}H_{29}NO_5S$ 443.1768, found 443.1761; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.2 Hz, 2H), 7.32-7.23 (m, 7H), 5.05 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.90 (br s, 1H), 3.55 (t, *J* = 6.4 Hz, 2H), 3.46 (dd, *J* = 6.1, 18.1 Hz, 1H), 2.99-2.95 (m, 1H), 2.68 (d, *J* = 18.1 Hz, 1H), 2.41 (s, 3H), 1.62-1.29 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.49, 164.37, 145.74, 136.42, 134.50, 129.83 (2×), 129.18 (2×), 128.94 (2×), 128.69 (2×), 127.53, 70.81, 62.47, 43.34, 34.30, 33.95, 32.18, 28.73, 26.33, 25.29, 21.75.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(3-benzyloxypropyl)-piperidine-2,6-dione

Mp 79-82 °C; IR ($CHCl_3$) 2938, 2860, 1727, 1680, 1382, 1148, 737 cm^{-1}; ESI-MS: $C_{29}H_{32}NO_5S$ *m/z* (%) = 91 (100), 181 (19), 398 (4), 506 (M^++1, 18); HRMS (ESI, M^++1) calcd for $C_{29}H_{32}NO_5S$ 506.2002, found 506.2001; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.35-7.23 (m, 12H), 5.06 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H),

4.43 (s, 2H), 3.94 (br s, 1H), 3.48 (dd, *J* = 6.0, 18.1 Hz, 1H), 3.46-3.37 (m, 2H), 3.02-2.98 (m, 1H), 2.70 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.55-1.35 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.39, 164.32, 145.68, 138.13, 136.42, 134.59, 129.81 (3×), 128.94 (4×), 128.63 (2×), 128.44 (2×), 128.35, 127.71, 127.48, 73.09, 70.75, 69.12, 43.36, 34.33, 30.99, 28.75, 26.94, 21.76; Anal. Calcd for $C_{29}H_{31}NO_5S$ C, 68.89; H, 6.18. Found C, 69.16; H, 6.03.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(4-benzyloxybutyl)-piperidine-2,6-dione

Mp 67-70 ℃; IR ($CHCl_3$) 2938, 2860, 1728, 1682, 1383, 750 cm^{-1}; ESI-MS: $C_{30}H_{34}NO_5S$ *m/z* (%) = 91 (100), 181 (11), 520 (M^++1, 5); HRMS (ESI, M^++1) calcd for $C_{30}H_{34}NO_5S$ 520.2159, found 520.2158; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.3 Hz, 2H), 7.34-7.23 (m, 12H), 5.06 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 4.44 (s, 2H), 3.90 (br s, 1H), 3.47 (dd, *J* = 6.1, 18.1 Hz, 1H), 3.39 (t, *J* = 5.9 Hz, 2H), 2.97-2.95 (m, 1H), 2.69 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.55-1.35 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.41, 164.32, 145.68, 138.39, 136.44, 134.58, 129.81 (3×), 128.94, 128.66 (3×), 128.40 (2×), 128.35, 127.67 (2×), 127.61, 127.50, 72.95, 70.73, 69.54, 43.32, 34.31, 33.80, 29.16, 28.80, 23.47, 21.74; Anal. Calcd for $C_{30}H_{33}NO_5S$ C, 69.34; H, 6.40. Found C, 69.39; H, 6.38.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(5-benzyloxypentyl)-piperidine-2,6-dione

Mp 51-53 ℃; IR ($CHCl_3$) 2936, 2858, 1727, 1681, 1382, 736 cm^{-1}; HRMS (EI, M^+) calcd for $C_{31}H_{35}NO_5S$ 533.2238, found 533.2239; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.33-7.23 (m, 12H), 5.06 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 4.46 (s, 2H), 3.88 (br s, 1H), 3.47 (dd, *J* = 6.1, 18.1 Hz, 1H), 3.40 (t, *J* = 6.4 Hz, 2H), 2.98-2.95 (m, 1H), 2.68 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.54-1.27 (m, 8H).

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(2-hydroxybutyl)-piperidine-2,6-dione

Viscous gum; IR ($CHCl_3$) 3353, 2944, 2354, 1715, 1681, 1381, 764 cm^{-1}; HRMS (EI, M^+) calcd for $C_{23}H_{27}NO_5S$ 429.1611, found 429.1613; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.2 Hz, 2H), 7.35-7.24 (m, 7H), 5.06 (dd, *J* = 2.2, 14.0 Hz, 1H), 4.85 (dd, *J* = 2.5, 14.0 Hz, 1H), 3.94-3.90 (m, 1H), 3.73-3.67 (m, 1H), 3.48 (dd, *J* = 6.1, 18.1 Hz, 1H), 3.02-2.90 (m, 1H), 2.70 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.65-1.34 (m, 5H), 1.18 (d, *J* = 6.2 Hz, 3H).

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(2-*t*-butyldimethyl-silyloxybutyl)piperidine-2,6-dione

Mp 58-60 °C; IR ($CHCl_3$) 2954, 2929, 1728, 1682, 1382, 775 cm^{-1}; HRMS (EI, M^+) calcd for $C_{29}H_{41}NO_5SSi$ 543.2476, found 543.2481; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.43 (m, 2H), 7.33-7.24 (m, 7H), 5.06 (dd, *J* = 4.6, 14.0 Hz, 1H), 4.84 (dd, *J* = 3.2, 14.0 Hz, 1H), 3.89 (br s, 1H), 3.73-3.69 (m, 1H), 3.50-3.44 (m, 1H), 3.02-2.94 (m, 1H), 2.69 (d, *J* = 18.1 Hz, 1H), 2.42 (s, 3H), 1.38-1.31 (m, 4H), 1.08-1.02 (m, 3H), 0.87-0.82 (m, 9H), 0.02-0.50 (m, 6H).

1-Benzyl-3-(4-methylphenylsulfonyl)-4-phenylpiperidine-2,6-dione

Mp 166-168 °C; IR ($CHCl_3$) 2977, 2361, 1724, 1678, 1382, 751 cm^{-1}; HRMS (EI, M^+) calcd for $C_{25}H_{23}NO_4S$ 433.1349, found 433.1359; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.3 Hz, 2H), 7.28-7.15 (m, 10H), 6.96-6.94 (m, 2H), 5.09 (d, *J* = 13.9 Hz, 1H), 4.91 (d, *J* = 13.9 Hz, 1H), 4.32 (d, *J* = 6.8 Hz, 1H), 4.20 (t, *J* = 1.5 Hz, 1H), 3.74 (dd, *J* = 6.9, 18.3 Hz, 1H), 3.05 (dt, *J* = 1.8, 18.3 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.34, 164.12, 145.89, 139.51, 136.05, 134.32, 129.88 (2×), 129.34 (3×), 129.04 (3×), 128.92, 128.28 (2×), 127.93, 127.55, 126.62, 71.66, 43.44, 34.95, 33.55, 21.76.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(4-fluorophenyl)-piperidine-2,6-dione

Mp 185-187 °C; IR ($CHCl_3$) 2976, 2362, 1721, 1676, 1380, 744 cm^{-1}; HRMS (EI, M^+) calcd for $C_{25}H_{22}NO_4SF$ 451.1255, found 451.1249; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.3 Hz, 2H), 7.30-7.24 (m, 7H), 6.92-6.82 (m, 4H), 5.08 (d, *J* = 13.8 Hz, 1H), 4.92 (d, *J* = 13.8 Hz, 1H), 4.31 (d, *J* = 6.7 Hz, 1H), 4.17 (br s, 1H), 3.74 (dd, *J* = 6.9, 18.2 Hz, 1H), 3.01 (d, *J* = 18.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.10, 164.00, 160.87, 146.00, 135.99, 135.31, 134.24, 129.92 (2×), 129.05 (3×), 129.04 (3×), 128.40, 128.32 (2×), 127.68, 127.68, 71.64, 43.45, 35.07, 33.02, 21.77.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(4-nitrophenyl)-piperidine-2,6-dione

IR ($CHCl_3$) 2930, 1724, 1680, 1380, 754 cm^{-1}; HRMS (EI, M^+) calcd for $C_{25}H_{22}N_2O_6S$ 478.1200, found 478.1203; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (dd, *J* = 1.9, 6.9 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.33-7.23 (m, 7H), 7.09 (dd, *J* = 1.9, 6.9 Hz, 2H), 5.08 (d, *J* = 13.7 Hz, 1H), 4.93 (d, *J* = 13.7 Hz, 1H), 4.43 (d, *J* = 6.8 Hz, 1H), 4.17 (t, *J* = 1.8 Hz, 1H), 3.79

(dd, *J* = 6.9, 18.3 Hz, 1H), 3.04 (dt, *J* = 1.8, 18.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.39, 163.58, 147.44, 146.48, 146.32, 135.82, 133.93, 130.02, 129.16, 129.11 (3×), 128.39 (3×), 127.92, 127.78 (3×), 124.46, 70.91, 43.55, 34.71, 33.71, 21.80.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(4-methoxyphenyl)-piperidine-2,6-dione

Mp 138-140 °C; IR ($CHCl_3$) 2958, 1727, 1678, 1382, 756 cm^{-1}; HRMS (EI, M^+) calcd for $C_{26}H_{25}NO_5S$ 463.1455, found 463.1461; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.2 Hz, 2H), 7.28-7.24 (m, 7H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.69 (d, *J* = 8.5 Hz, 2H), 5.09 (d, *J* = 13.9 Hz, 1H), 4.90 (d, *J* = 13.9 Hz, 1H), 4.27 (d, *J* = 6.6 Hz, 1H), 4.18 (br s, 1H), 3.77-3.69 (m, 1H), 3.72 (s, 3H), 3.02 (d, *J* = 18.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.48, 164.20, 159.10, 145.85, 136.12, 134.41, 131.39, 129.88 (3×), 129.03 (3×), 128.96 (3×), 128.29, 127.74 (2×), 127.54, 71.86, 55.29, 43.41, 35.15, 32.88, 21.76.

1-Benzyl-3-(4-methylphenylsulfonyl)-4-(3,4-dimethoxy-phenyl)piperidine-2,6-dione

Mp 170-172 °C; IR ($CHCl_3$) 2927, 2361, 1726, 1678, 1320, 754 cm^{-1}; HRMS (EI, M^+) calcd for $C_{27}H_{27}NO_6S$ 493.1560, found 493.1571; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.32-7.24 (m, 7H), 6.61 (d, *J* = 7.9 Hz, 1H), 6.45 (s, 1H), 6.43 (d, *J* = 7.9 Hz, 1H), 5.07 (d, *J* = 13.8 Hz, 1H), 4.90 (d, *J* = 13.8 Hz, 1H), 4.27 (d, *J* = 6.7 Hz, 1H), 4.21 (br s, 1H), 3.79 (s, 3H), 3.73 (dd, *J* = 6.9, 18.2 Hz, 1H), 3.59 (s, 3H), 3.04 (d, *J* = 18.2 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.47, 164.20, 149.53, 145.91, 136.09, 134.33, 131.99, 129.89 (3×), 129.07, 129.04 (2×), 128.31 (3×), 127.59, 118.54, 111.63, 109.84, 71.78, 55.92, 55.76, 43.48, 35.32, 33.20, 21.77.

1-Benzyl-3-(4-methylphenylsulfonyl)-5-methylpiperidine-2,6-dione

IR ($CHCl_3$) 3033, 1726, 1677, 1320, 755 cm^{-1}; HRMS (EI, M^+) calcd for $C_{20}H_{21}NO_4S$ 371.1192, found 371.1185; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.4 Hz, 1/2H), 7.54 (*J* = 8.1 Hz, 3/2H), 7.35-7.22 (m, 7H), 5.03 (d, *J* = 14.1 Hz, 3/4H), 4.90 (d, *J* = 14.1 Hz, 1H), 4.83 (d, *J* = 14.1 Hz, 1/4H), 4.23 (dd, *J* = 5.1, 12.3 Hz, 1/4H), 4.10 (dd, *J* = 2.1, 6.0 Hz, 3/4H), 3.42-3.18 (m, 1H), 2.95-2.87 (m, 1H), 2.44 (s, 3H), 2.13-2.00 (m, 1H), 1.36 (d, *J* = 6.6 Hz, 3H).

1-Benzyl-3-(4-methylphenylsulfonyl)-5-*t*-butoxycarbonyl-aminopiperidine-2,6-dione

Viscous gum; IR ($CHCl_3$) 2930, 2362, 1729, 1667, 1386, 756 cm^{-1}; HRMS (EI, M^+) calcd for $C_{24}H_{28}N_2O_6S$ 472.1670, found 472.1672; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.2 Hz, 4/5H), 7.51 (*J* = 8.1 Hz, 6/5H), 7.33-7.20 (m, 7H), 5.54-5.50 (m, 1H), 5.02 (d, *J* = 14.0 Hz, 1H), 4.91-4.77 (m, 2H), 4.39-4.32 (m, 3/5H), 4.13-4.11 (m, 2/5H), 3.07-2.92 (m, 1H), 2.41 (s, 3H), 2.28-2.18 (m, 1H), 1.44 (br s, 9H).

1-Benzyl-3-(4-methylphenylsulfonyl)-5-phthalimidopiperidine-2,6-dione

Mp 238-240 °C; IR ($CHCl_3$) 2927, 2360, 1720, 1686, 1390, 754 cm^{-1}; HRMS (EI, M^+) calcd for $C_{27}H_{22}N_2O_6S$ 502.1200, found 502.1211; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.74 (m, 14/3H), 7.50 (d, *J* = 8.2 Hz, 4/3H), 7.34-7.21 (m, 7H), 5.82 (dd, *J* = 6.4, 13.1 Hz, 2/3H), 5.05-4.97 (m, 1/3H), 5.05 (d, *J* = 14.1 Hz, 2/3H), 4.97 (d, *J* = 14.1 Hz, 2/3H), 4.95 (d, *J* = 14.1 Hz, 1/3H), 4.85 (d, *J* = 14.1 Hz, 1/3H), 4.33 (dd, *J* = 5.2, 13.7 Hz, 1/3H), 4.21 (dd, *J* = 1.3, 6.0 Hz, 2/3H), 3.25-2.74 (m, 2H), 2.44 (br s, 3H).

Chlorination from *N*-benzyl 4-hydroxy-substituted α-bromo-α-*p*-toluenesulfonylglutarimides B to *N*-benzyl 4-chloro-substituted α-bromo-α-*p*-toluenesulfonylglutarimide B1, B2 and B3 using PPh_3/CCl_4 system (entry 4, 5, 6 in Table 1)

Alcohol (1.0 mmol) was added to a solution of triphenylphosphine (1.5 mmol) and carbon tetrabromide (1.3 mmol) in methylene chloride (20 mL). The reaction mixture was stirred at room temperature for 4 h, then quenched with saturated aqueous ammonium chloride solution (5 mL) and concentrated. The residue was diluted with water (15 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (2 × 20 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. Purification of the crude product by column chromatography on silica gel with hexane/ethyl acetate produced **B1**, **B2** and **B3** in 50-61% yield.

Mesylation from *N*-benzyl 4-hydroxy-substituted α-bromo-α-*p*-toluenesulfonyl glutarimide B to *N*-benzyl 4-mesylate-substituted α-bromo-α-*p*-toluenesulfonyl glutarimide B4 (No. 10 in Table 1)

Methanesulfonyl chloride (1 mL) was added to a solution of secondary alcohol (1.0 mmol) in pyridine (5 mL) and stirred for 5 h at room temperature. The resulting mixture was poured into 0.1N hydrogen chloride (10 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried by magnesium sulfate, filtered and evaporated. Purification of the crude product by column chromatography

on silica gel with hexane/ethyl acetate produced **B4** in 48% yield.

Debromination (then cyclization or elimination) from *N*-benzyl 4-substituted α-bromo-α-*p*-toluenesulfonyl-glutarimides B1, B2, B3, B4 to *N*-benzyl bicyclic α-*p*-toluenesulfonylglutarimides C1, C2, C3, C4 using DBU/THF system

The procedure was the same as mentioned above for the procedure of debromination.

Spectral data of **C1**~**C4**:

C1: 1-Benzyl-7*a*-(4-methylphenylsulfonyl)hexahydro[2]-pyridine-1,3-dione

Yield 57%; viscous oil; IR ($CHCl_3$) 2960, 1725, 1681, 1315, 758 cm^{-1}; HRMS (EI, M^+) calcd for $C_{22}H_{23}NO_4S$ 397.1349, found 397.1348; ^1H NMR (400 MHz, $CDCl_3$): δ 7.35-7.24 (m, 7H), 7.18 (d, *J* = 8.3 Hz, 2H), 5.16 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.41 (dd, *J* = 6.4, 18.1 Hz, 1H), 3.24-3.21 (m, 1H), 2.81 (dd, *J* = 1.6, 18.1 Hz, 1H), 2.39 (s, 3H), 2.24-2.14 (m, 3H), 1.71-1.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.61, 168.02, 145.51, 136.67, 133.18, 130.09, 129.33 (2×), 128.63 (2×), 128.36 (2×), 127.45 (2×), 75.67, 43.93, 34.96, 34.76, 33.79, 31.77, 21.73, 21.03; Anal. Calcd for $C_{22}H_{23}NO_4S$: C, 66.48; H, 5.83. Found: C, 66.52; H, 5.88.

C2: 1-Benzyl-8*a*-(4-methylphenylsulfonyl)hexahydroiso-quinoline-1,3-dione

Yield 66%; mp 46-48 ℃; IR ($CHCl_3$) 2938, 1725, 1674, 1380, 1180, 756 cm^{-1}; HRMS (EI, M^+) calcd for $C_{23}H_{25}NO_4S$ 411.1506, found 411.1514; ^1H NMR (400 MHz, $CDCl_3$): δ 7.43-7.15 (m, 9H), 5.25 (d, *J* = 13.9 Hz, 1H), 4.86 (d, *J* = 13.9 Hz, 1H), 3.76 (dd, *J* = 6.0, 18.3 Hz, 1H), 2.80-2.77 (m, 1H), 2.56 (d, *J* = 18.3 Hz, 1H), 2.38 (s, 3H), 1.90-1.80 (m, 2H), 1.62-1.48 (m, 3H), 1.27-1.13 (m, 2H), 0.96-0.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.10, 166.99, 145.58, 136.70, 131.48, 130.56 (3×), 129.24 (2×), 129.06 (2×), 128.29, 127.44, 72.03, 43.89, 37.64, 31.99, 31.02, 30.49, 24.06, 22.28, 21.68.

C3: 1-Benzyl-3-(4-methylphenylsulfonyl)-4-(5-chloro-pentyl)piperidine-2,6-dione

Yield 52%; mp 116-118 ℃; IR ($CHCl_3$) 2938, 1728, 1682, 1323 cm^{-1}; HRMS (EI, M^+) calcd for $C_{24}H_{28}NO_4SCl$ 462.1507, found 462.1503; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.3 Hz, 2H), 7.34-7.24 (m, 7H), 5.05 (d, *J* = 14.0 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.89 (t, *J* = 1.5 Hz, 1H), 3.49 (dd, *J* = 6.1, 18.1 Hz, 1H), 3.45 (t, *J* = 6.3 Hz, 2H), 2.97-2.94 (m, 1H), 2.68 (dd, *J* = 1.5, 18.1 Hz, 1H), 2.42 (s, 3H), 1.70-1.20 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.36, 164.31, 145.76, 136.41, 134.55, 129.85 (2×), 128.96 (2×), 128.71 (2×), 128.37 (2×), 127.56, 70.79, 44.64, 43.35, 34.28, 33.87, 32.07, 28.72, 26.32, 25.87, 21.77. The structure of chloride **C3** was also determined by single-crystal X-ray analysis.

C4: 1-Benzyl-3-(4-methylphenylsulfonyl)-4-(*exo* 1- or *endo* 2-butenyl)piperidine-2,6-dione

Yield 51%; viscous oil; IR ($CHCl_3$) 1729, 1677 cm^{-1}; HRMS (EI, M^+) calcd for $C_{23}H_{25}NO_4S$ 411.1506, found 411.1510; ^1H NMR (400 MHz, $CDCl_3$): δ 7.46-7.43 (m, 2H), 7.33-7.24 (m, 7H), 5.07 (d, *J* = 14.1 Hz, 1H), 4.85 (d, *J* = 14.0 Hz, 1H), 3.92 (br s, 1H), 3.50-3.44 (m, 1H), 2.99-2.97 (m, 1H), 2.71-2.66 (m, 1H), 2.42 (br s, 3H), 2.03-1.98 (m, 2H), 1.63-1.55 (m, 3H), 1.45-1.35 (m, 2H).

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Key Words

1,8-Diazabicyclo[5.4.0]undec-7-ene; Debromination; *N*-Bromosuccinimide; Bromination; Glutarimide.

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