Study on the Reaction of Electron-deficient Cyclopropane Derivatives with Amines

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Reaction of electron deficient cyclopropane derivatives *cis*-1-methoxycarbonyl-2-aryl-6, 6-dimethyl-5, 7-dioxa-spiro-[2, 5]-4,8-octadiones (1a—d) (X = CH_3, H, Cl, NO_2) with anilines (2a—e) (Y = *p*-CH_3, H, *p*-Br, *p*-NO_2, *o*-CH_3) at room temperature gives *N*-aryl-*trans*, *trans*-α-carboxyl-β-methoxycarbonyl-γ-aryl-γ-butyrolactams (3a—p) in high yields with high stereoselectivity. For example, 1a (X = CH_3) reacts with ammonia 4 or benzyl amine 5 at room temperature to give inner ammonium salt 6 or 7 in the yield of 83% or 97% respectively. The reaction mechanisms for formation of the products are proposed.

Keywords γ-Butyrolactam, inner ammonium salt, high stereoselective synthesis

Introduction

Many chemists are interested in the synthesis of γ-butyrolactam derivatives or amino acid as these structural frameworks are often found in natural products and synthetic pharmaceutical molecules.[1,2]

Although many synthetic methods have been developed,[3-9] a simple approach to the highly stereoselective synthesis of polysubstituted γ-butyrolactam derivatives or amino acid is scarcely reported. The present paper describes the reaction of polysubstituted electron-deficient cyclopropane derivatives *cis*-1-methoxycarbonyl-2-aryl-6, 6-dimethyl-5, 7-dioxa-spiro-[2, 5]-4, 8-octadiones (**1a—d**) with anilines (**2a—e**) to afford *N*-aryl-*trans*, *trans*-α-carboxyl-β-methoxycarbonyl-γ-aryl-γ-butyrolactams (**3a—p**) in high yields with high stereoselectivity. Electron-deficient cyclopropane derivative **1a** reacts with ammonia **4** or benzyl amine **5** at room temperature to give inner ammonium salt **6** or **7** respectively in high yields.

Results and discussion

cis-1-Methoxycarbonyl-2-aryl-6,6-dimethyl-5,7-dioxa-spiro-[2,5]-4,8-octadiones (**1a—d**) (X = CH_3, H, Cl, NO_2) react with anilines (**2a—e**) (Y = *p*-CH_3, H, *p*-Br, *p*-NO_2, *o*-CH_3) in dimethylethylene glycol at room temperature generally giving rise to *N*-aryl-*trans*, *trans*-α-carboxyl-β-methoxycarbonyl-γ-aryl-γ-butyrolactams (**3a—p**) in good to excellent yields with high stereoselectivity (Scheme 1 and Table 1). When the substituent on aniline molecule is a weak electron-donating group with steric hindrance (**2e**), the yields of **3** (**3n**, **3o**, **3p**) are slightly lowered to 83—86%. If compound **1** contains a strong electron-withdrawing substituent (X = NO_2 in **1d**) or compound **1** (X = CH_3 in **1a**) reacts with *p*-NO_2-substituented aniline **2d**, the yields of **3** are lowered to 68—74% (**3d**, **3h**, **3l**) and 42% (**3m**) respectively. The reaction will be totally inhibited in the case of $-NO_2$ substituents in both reaction

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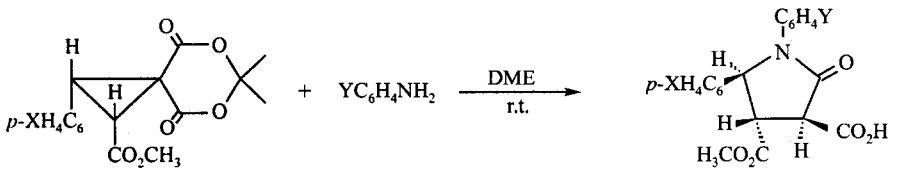
materials (**1d** and **2d**).

Electron-deficient cyclopropane derivative **1a** (X = CH_3) reacts with ammonia **4** or benzyl amine **5** at room temperature to give inner ammonium salt **6** or **7** (Scheme 2 and Table 2).

The structures of products **3**, **6**, **7** were confirmed by MS, IR, ^1H and ^{13}C NMR and elemental analyses and the configuration of product **3c** was assigned via its 2D Proton NOESY spectrum.

The reaction mechanism shown in Scheme 3 would account for the high stereoselectivity. The 1,2-*cis*-cyclopropane derivative **1** is attacked nucleophilically by a molecule of amine at C_a from the less hindered side of the cyclopropane ring. Cleavage of C_a—C_c bond of compound **1** yields the intermediate **A**, which undergoes proton-shift into intermediate **B** (R = Y-C_6H_4) and inner ammonium salt **6** or **7** (R = H; R = $CH_2C_6H_5$). Intermediate **B** transforms into intermediate **C** after the rotation of C_a—C_b bond. Then α,β,γ-*trans*, *trans*-γ-butyrolactams **3** is formed through intramolecular attacking of the amino group in intermediate **C** to break the Medlrum's acid ring with the elimination of a molecule of acetone.

Scheme 1



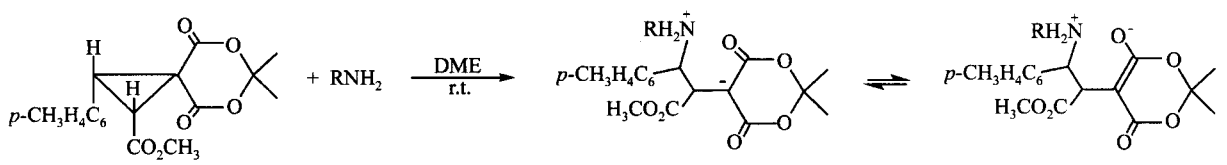
1a—d **2a—e** **3a—p**

1: **a** X=CH_3, **b** X=H, **c** X=Cl, **d** X=NO_2 **2**: **a** Y=*p*-CH_3, **b** Y=H, **c** Y=*p*-Br, **d** Y=*p*-NO_2, **e** Y=*o*-CH_3

Table 1 Physical data of compound **3**

Compd.	X	Y	Mp (℃)	Yield (%)	Compd.	X	Y	Mp (℃)	Yield (%)
3a	CH_3	*p*-CH_3	178—180	92	**3i**	CH_3	*p*-Br	168—170	95
3b	H	*p*-CH_3	164—166	97	**3j**	H	*p*-Br	160—162	98
3c	Cl	*p*-CH_3	163—165	96	**3k**	Cl	*p*-Br	165—167	97
3d	NO_2	*p*-CH_3	170—172	74	**3l**	NO_2	*p*-Br	164—166	68
3e	CH_3	H	160—162	97	**3m**	CH_3	*p*-NO_2	177—179	42
3f	H	H	161—163	98	**3n**	CH_3	*o*-CH_3	168—170	83
3g	Cl	H	164—165	97	**3o**	H	*o*-CH_3	162—164	84
3h	NO_2	H	168—170	70	**3p**	Cl	*o*-CH_3	163—165	86

Scheme 2



1a **4** or **5** **6** or **7**

4,**6**: R=H **5**,**7**: R=$CH_2C_6H_5$

Scheme 3

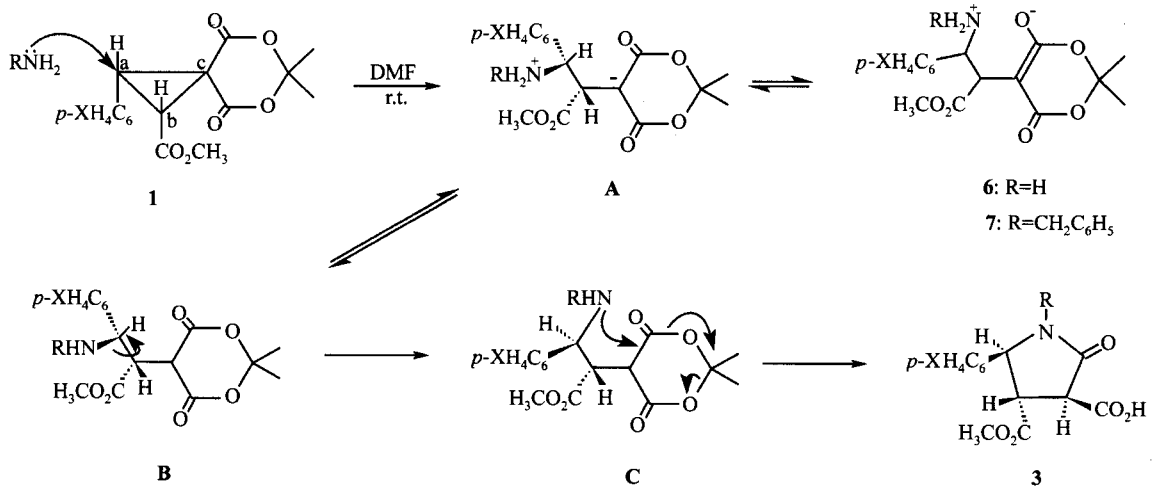


Table 2 Physical data of compound **6** or **7**

Compd.	X	R	Mp (℃)	Yield (%)
6	CH_3	H	150—152	83
7	CH_3	$CH_2C_6H_5$	130—132	97

In summary, a facile and highly stereoselective synthesis of *N*-aryl-*trans*, *trans*-α-carboxyl-β-methoxycarbonyl-γ-aryl-γ-butyrolactams and inner ammonium salt has been developed based on the reaction of *cis*-1-methoxycarbonyl-2-aryl-6, 6-dimethyl-5, 7-dioxa-spiro-[2,5]-4,8-octadiones with amines at room temperature. The simplicity of the procedure, the excellent yield and the high stereoselectivity of the products should offer a novel promising access to the synthesis of γ-butyrolactam and amino acid derivatives.

Experimental

Melting points were recorded on a WRS-1 melting point apparatus and uncorrected. IR spectra (KBr discs) measured on a 7400 spectrometer (Shanghai Analytical Instrument Factory, China). NMR spectra were taken on an AC-100SC spectrometer, using solutions in $CDCl_3$ with tetramethylsilane and $CDCl_3$ as internal standard. Coupling constants were given in hertz (Hz). Mass spectra were run on an HP 5989A spectrometer. Elemental data were obtained on a Foss Heraeus CHN-O-RAPID element analysis instrument.

Preparation of N-aryl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-aryl-γ-butyrolactams (**3**)

To a solution of *cis*-1-methoxycarbonyl-2-aryl-6,6-dimethyl-5,7-dioxa-spiro-[2,5]-4,8-octadione[10] (**1**) (0.5 mmol) in dimethyl ethylene glycol (5 mL) was added aniline (**2**) (0.75 mmol). The mixture was stirred at room temperature (monitored by TLC). The solvent was evaporated under reduced pressure and the product was purified by recrystallization from methylene chloride-light petroleum to give *N*-aryl-*trans*, *trans*-α-carboxyl-β-methoxycarbonyl-γ-aryl-γ-butyrolactam (**3**). The results are summarized in Table 1.

N-p-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-methylphenyl-γ-butyrolactam (**3a**) Yeild: 92%; m.p. 178—180℃; ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 2.26 (s, 3H, $NC_6H_4CH_3$), 2.29 (s, 3H, $C_6H_4CH_3$), 3.40 (s, 3H, OCH_3), 4.04 (dd, J = 11.1, 9.3 Hz, 1H, α-H), 4.36 (d, J = 11.1 Hz, 1H, α-H), 5.42 (d, J = 9.3 Hz, 1H, γ-H), 7.02—7.26 (m, 8H, ArH); IR (KBr) ν: 3451, 1733, 1656, 1608, 1165 cm^{-1}; MS *m/z* (%): 367 (M^+, 8), 323 (100), 264 (42), 210 (70), 209 (68), 208 (80), 91 (73); Anal. calcd for $C_{21}H_{21}NO_5$: C 68.65, H 5.76, N 3.81; found: C 68.52, H 5.66, N 3.71.

N-p-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-phenyl-γ-butyrolactam (**3b**) Yield: 97%; m.p. 164—166℃; ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 2.27 (s, 3H, $NC_6H_4CH_3$), 3.48 (s, 3H, OCH_3), 4.09 (dd, J = 11.1, 9.4 Hz, 1H, γ-H), 4.39 (d, J = 11.1 Hz, 1H, γ-H), 5.47 (d, J = 9.4

Hz, 1H, α-H), 7.03—7.23 (m, 4H, ArH), 7.22—7.43 (m, 5H, ArH); IR (KBr) ν: 3448, 1732, 1655, 1582, 1164 cm^{-1}; MS *m/z* (%): 353 (M^+, 8), 309 (100), 250 (36), 196 (96), 195 (76), 194 (68), 91 (68); Anal. calcd for $C_{20}H_{19}NO_5$: C 67.98, H 5.42, N 3.96; found: C 67.89, H 5.42, N 3.85.

N-p-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-chlorophenyl-γ-butyrolactam (**3c**) Yield: 96%; m.p. 163—165℃; ^1H NMR ($CDCl_3$, 100 MHz) δ: 2.28 (s, 3H, $NC_6H_4CH_3$), 3.43 (s, 3H, OCH_3), 4.10 (dd, *J* = 10.8, 9.3 Hz, 1H, β-H), 4.36 (d, *J* = 10.8 Hz, 1H, α-H), 5.46 (d, *J* = 9.3 Hz, 1H, γ-H), 7.10—7.29 (m, 8H, ArH); IR (KBr) ν: 3446, 1732, 1654, 1584, 1167 cm^{-1}; MS *m/z* (%): 387 (M^+, 5), 389 (2), 343 (83), 284 (31), 232 (33), 230 (100), 229 (70), 228 (57), 91 (67); Anal. calcd for $C_{20}H_{18}ClNO_5$: C 61.83, H 4.56, N 3.60; found: C 61.89, H 4.67, N 3.61.

N-p-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-nitrophenyl-γ-butyrolactam (**3d**) Yield: 74%; m.p. 170—172℃; ^1H NMR ($CDCl_3$, 100 MHz) δ: 2.27 (s, 3H, $NC_6H_4CH_3$), 3.42 (s, 3H, OCH_3), 4.21 (dd, *J* = 10.9, 9.6 Hz, 1H, β-H), 4.36 (d, *J* = 10.9 Hz, 1H, α-H), 5.47 (d, *J* = 9.6 Hz, 1H, α-H), 7.10—8.19 (m, 8H, ArH); IR (KBr) ν: 3436, 1734, 1687, 1606, 1176 cm^{-1}; MS *m/z* (%): 354 (M − 44$^+$, 89), 295 (14), 241 (100), 240 (72), 91 (29); Anal. calcd for $C_{20}H_{18}N_2O_7$: C 60.38, H 4.55, N 7.03; found: C 60.18, H 4.55, N 6.95.

N-Phenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-methylphenyl-γ-butyrolactam (**3e**) Yield: 97%; m.p. 160—162℃; ^1H NMR ($CDCl_3$, 100 MHz) δ: 2.30 (s, 3H, $C_6H_4CH_3$), 3.42 (s, 3H, OCH_3), 4.06 (dd, *J* = 11.2, 9.3 Hz, 1H, β-H), 4.38 (d, *J* = 11.2 Hz, 1H, α-H), 5.47 (d, *J* = 9.3 Hz, 1H, α-H), 7.04—7.41 (m, 9H, ArH); IR (KBr) ν: 3442, 1734, 1654, 1593, 1167 cm^{-1}; MS *m/z* (%): 353 (M^+, 5), 309 (90), 250 (38), 196 (74), 195 (81), 194 (100), 77 (96); Anal. calcd for $C_{20}H_{19}NO_5$: C 67.98, H 5.42, N 3.96; found: C 67.82, H 5.30, N 3.88.

N-Phenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-phenyl-γ-butyrolactam (**3f**) Yield: 98%; m.p. 161—163℃, ^1H NMR ($CDCl_3$, 100 MHz) δ: 3.40 (s, 3H, OCH_3), 4.11 (dd, *J* = 11.0, 9.3 Hz, 1H, β-H), 4.40 (d, *J* = 11.0 Hz, 1H, α-H), 5.51 (d, *J* = 9.3 Hz, 1H, γ-H), 7.19—7.41 (m, 10H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 6.3, 49.6, 51.7, 61.8, 122.5, 125.4, 127.0, 128.3, 128.5, 128.7, 135.9, 137.3, 167.5, 169.1; IR (KBr) ν: 3447, 1731, 1655, 1590, 1166 cm^{-1}; MS *m/z* (%): 339 (M^+, 6), 295 (81), 236 (38), 182 (70), 181 (77), 180 (85), 77 (88); Anal. calcd for $C_{19}H_{17}NO_5$: C 67.24, H 5.05, N 4.12; found: C 67.41, H 5.09, N 4.15.

N-Phenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-chlorophenyl-γ-butyrolactam (**3g**) Yield: 97%; m.p. 164—165℃; ^1H NMR ($CDCl_3$, 100 MHz) δ: 3.43 (s, 3H, OCH_3), 4.10 (dd, *J* = 10.7, 9.3 Hz, 1H, β-H), 4.36 (d, *J* = 10.7 Hz, 1H, α-H), 5.49 (d, *J* = 9.3 Hz, 1H, γ-H), 7.10—7.34 (m, 9H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 46.2, 49.6, 51.8, 61.1, 122.6, 125.6, 128.5, 128.8, 129.1, 133.1, 135.1, 137.1, 167.5, 169.0, 169.1; IR (KBr) ν: 3448, 1730, 1652, 1589, 1164 cm^{-1}; MS *m/z* (%): 373 (M^+, 3), 375 (1), 329 (66), 270 (30), 218 (34), 216 (100), 215 (67), 214 (59), 77 (86). Anal. calcd for $C_{19}H_{16}ClNO_5$: C 61.05, H 4.28, N 3.74; found: C 60.86, H 4.31, N 4.03.

N-Phenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-nitrophenyl-γ-butyrolactam (**3h**) Yield: 70%; m.p. 168—170℃; ^1H NMR ($CDCl_3$, 100 MHz) δ: 3.45 (s, 3H, OCH_3), 4.22 (dd, *J* = 10.8, 9.0 Hz, 1H, β-H), 4.34 (d, *J* = 10.8 Hz, 1H, β-H), 5.66 (d, *J* = 9.0 Hz, 1H, γ-H), 7.18—8.20 (m, 9H, ArH); IR (KBr) ν: 3446, 1732, 1653, 1584, 1167 cm^{-1}; MS *m/z* (%): 340 (M − 44$^+$, 51), 281 (38), 227 (100), 226 (81), 225 (36), 77 (50); Anal. calcd for $C_{19}H_{16}N_2O_7$: C 59.37, H 4.20, N 7.29; found: C 59.20, H 4.05, N 7.12.

N-p-Bromophenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-methylphenyl-γ-butyrolactam (**3i**) Yield: 95%; m.p. 168—170℃; ^1H NMR ($CDCl_3$, 100 MHz) δ: 2.31 (s, 3H, $C_6H_4CH_3$), 3.43 (s, 3H, OCH_3), 4.07 (dd, *J* = 11.1, 9.3 Hz, 1H, α-H), 4.31 (d, *J* = 11.1 Hz, 1H, α-H), 5.43 (d, *J* = 9.3 Hz, 1H, β-H), 7.07—7.37 (m, 8H, ArH); IR (KBr) ν: 3431, 1734, 1648, 1587, 1166 cm^{-1}; MS *m/z* (%): 431 (M^+, 3), 387 (67), 389 (71), 328 (25), 275 (58), 274 (100), 273 (56), 272 (80); Anal. calcd for $C_{20}H_{18}BrNO_5$: C 55.57, H 4.20, N 3.24; found: C 55.41, H 4.06, N 3.19.

N-p-Bromophenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-phenyl-γ-butyrolactam (**3j**) Yield: 98%; m.p. 160—162℃; ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 3.31 (s, 3H, OCH_3), 4.02 (dd, J = 11.1, 9.3 Hz, 1H, β-H), 4.30 (d, J = 11.1 Hz, 1H, β-H), 5.39 (d, J = 9.3 Hz, 1H, β-H), 7.06—7.32 (m, 9H, ArH); IR (KBr) ν: 3442, 1734, 1654, 1593, 1167 cm^{-1}; MS *m/z* (%): 417 (M^+, 2), 373 (61), 375 (62), 314 (16), 262 (66), 261 (59), 260 (100), 259 (54); Anal. calcd for $C_{19}H_{16}BrNO_5$: C 54.52, H 3.85, N 3.35; found: C 54.64, H 4.01, N 3.27.

N-p-Bromophenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-chlorophenyl-γ-butyrolactam (**3k**) Yield: 97%; m.p. 165—167℃; ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 3.44 (s, 3H, OCH_3), 4.13 (dd, J = 11.0, 9.3 Hz, 1H, β-H), 4.36 (d, J = 11.0 Hz, 1H, β-H), 5.48 (d, J = 9.3 Hz, 1H, γ-H), 7.09—7.41 (m, 8H, ArH); IR (KBr) ν: 3440, 1734, 1655, 1586, 1164 cm^{-1}; MS *m/z* (%): 453 (M^+, 3), 407 (79), 350 (38), 297 (18), 296 (92), 295 (73), 294 (100), 293 (55), 292 (37); Anal. calcd for C_{19}-H_{15} $BrClNO_5$: C 50.31, H 3.33, N 3.09; found: C 49.97, H 3.62, N 2.93.

N-p-Bromophenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-nitrophenyl-γ-butyrolactam (**3l**) Yield: 68%; m.p. 164—166℃, ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 3.36 (s, 3H, OCH_3), 4.13 (dd, J = 11.2, 9.3 Hz, 1H, α-H), 4.28 (d, J = 11.2 Hz, 1H, α-H), 5.54 (d, J = 9.3 Hz, 1H, α-H), 7.20—8.13 (m, 8H, ArH); IR (KBr) ν: 3432, 1734, 1718, 1588, 1187 cm^{-1}; MS *m/z* (%): 418 (M − 44$^+$, 100), 420 (49), 359 (5), 307 (68), 306 (50), 305 (86); 27 (100), 226 (81), 225 (36), 77 (50); Anal. calcd for $C_{19}H_{15}BrN_2O_7$: C 49.26, H 3.26, N 6.05; found: C 49.19, H 3.41, N 5.96.

N-p-Nitrophenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-methylphenyl-γ-butyrolactam (**3m**) Yield: 42%; m.p. 177—179℃, ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 2.32 (s, 3H, $C_6H_4CH_3$), 3.47 (s, 3H, OCH_3), 4.13 (dd, J = 11.3, 9.2 Hz, 1H, α-H), 4.42 (d, J = 11.3 Hz, 1H, α-H), 5.57 (d, J = 9.2 Hz, 1H, α-H), 7.04—8.15 (m, 8H, ArH); IR (KBr) ν: 3462, 1734, 1654, 1593 1156 cm^{-1}; *m/z* (%): 354 (M − 44$^+$, 100), 295 (26), 241 (99), 240 (86), 239 (66); Anal. calcd for $C_{20}H_{18}N_2O_7$: C 60.30, H 4.55, N 7.03; found: C 60.12, H 4.73, N 6.93.

N-o-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-methylphenyl-γ-butyrolactam (**3n**) Yield: 83%; m.p. 168—170℃, ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 2.22 (s, 3H, $NC_6H_4CH_3$), 2.32 (s, 3H, $C_6H_4CH_3$), 3.35 (s, 3H, OCH_3), 4.18 (dd, J = 11.0, 9.6 Hz, 1H, β-H), 4.48 (d, J = 11.0 Hz, 1H, α-H), 5.14 (d, J = 9.6 Hz, 1H, α-H), 6.85—7.24 (m, 8H, ArH); IR (KBr) ν: 3436, 1734, 1664, 1579, 1156 cm^{-1}; MS *m/z* (%): 367 (M^+, 12), 323 (84), 264 (100), 210 (61), 209 (55), 208 (90), 91 (93); Anal. calcd for $C_{21}H_{21}NO_5$: C 68.65, H 5.76, N 3.81; found: C 68.98, H 5.87, N 3.70.

N-o-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-phenyl-γ-butyrolactam (**3o**) Yield: 84%; m. p. 162—164℃; ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 2.21 (s, 3H, $NC_6H_4CH_3$), 3.31 (s, 3H, OCH_3), 4.20 (dd, J = 11.0, 9.6 Hz, 1H, β-H), 4.48 (d, J = 11.0 Hz, 1H, γ-H), 5.16 (d, J = 9.6 Hz, 1H, γ-H), 6.84—7.32 (m, 9H, ArH); IR (KBr) ν: 3458, 1734, 1665, 1579, 1156 cm^{-1}; MS *m/z* (%): 353 (M^+, 3), 309 (53), 250 (83), 196 (45), 195 (44), 194 (78), 91 (100); Anal. calcd for $C_{20}H_{19}NO_5$: C 67.98, H 5.42, N 3.96; found: C 67.90, H 5.30, N 3.85.

N-o-Methylphenyl-trans, trans-α-carboxyl-β-methoxycarbonyl-γ-p-chlorophenyl-γ-butyrolactam (**3p**) Yield: 86%; m.p. 163—165℃, ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 2.22 (s, 3H, $NC_6H_4CH_3$), 3.39 (s, 3H, OCH_3), 4.22 (dd, J = 10.7, 9.6 Hz, 1H, β-H), 4.47 (d, J = 10.7 Hz, 1H, γ-H), 5.18 (d, J = 9.6 Hz, 1H, γ-H), 6.83—7.33 (m, 8H, ArH); IR (KBr) ν: 3423, 1737, 1661, 1580, 1163 cm^{-1}; MS *m/z* (%): 343 (M − 44$^+$, 94), 345 (42), 284 (100), 230 (86), 229 (57), 228 (65), 91 (81).

Inner ammonium salt (**6**) Yield: 83%; m.p. 150—152℃; ^{1}H NMR (D_2O, 100 MHz) δ: 1.17 (s, 6H, CH_3), 2.35 (s, 3H, $C_6H_4CH_3$), 3.42 (s, 3H, CH_3), 3.60—3.72 (m, 2H, $CHCO_2CH_3$, $CHAr$-NH_3^+), 3.78—3.86 (m, 3H, NH_3), 7.30 (s, 4H, ArH); IR (KBr) ν: 2994, 1699, 1666, 1554, 1148 cm^{-1}.

Inner ammonium salt (**7**) Yield: 97%; m.p. 130—132℃; ^{1}H NMR ($CDCl_3$, 100 MHz) δ: 1.57 (s, 6H, CH_3), 2.38 (s, 3H, $C_6H_4CH_3$), 3.25—3.35 (m, 1H, $CHCO_2CH_3$), 3.60—3.68 (m, 1H,

CHArNH$_2$), 3.66 (s, 3H, OCH$_3$), 3.87—3.95 (m, 2H, PhCH$_2$), 4.48—4.54 (m, 2H, NH$_2$), 6.97—7.39 (m, 9H, ArH); IR (KBr) ν: 2984, 1702, 1679, 1577, 1169 cm^{-1}.

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