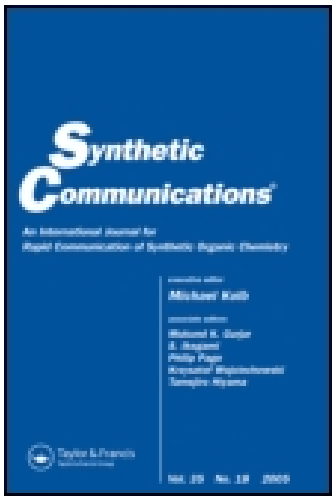

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A Convenient Synthesis of Esters of β-Phenylglutamic Acid Under Aqueous Conditions

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ABSTRACT

Several esters of β-phenylglutamic acid (**3**, **4**) are prepared by Michael reaction of glycine ester Schiff bases **1** and **2** under aqueous conditions.

β-Phenylglutamic acid has long been known[1] and procedures for its preparation are of current interest because of the important activities of glutamic acid derivatives on glutamic acid receptors in the central nervous system.[2–4] Among the various approaches to the preparation of β-phenylglutamic acid,[1,5–9] the conjugate addition of Schiff bases derived from glycine to cinnamic acid derivatives is the most direct one.[10–16] Thus, the Michael reaction of methyl cinnamate and

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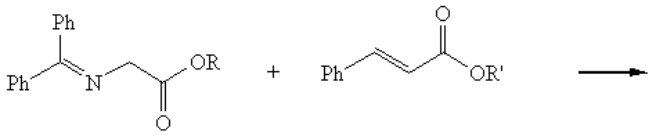
nickel (II) complex of chiral Schiff base of glycine,[10] respectively the reaction of lithium enolate of ethyl *N*-(diphenylmethylene)glycinate with alkoxyalkenylcarbene complexes of chromium,[11] afforded the corresponding Michael adducts with high diastereoselectivity,[10,11] and in some cases, enantioselectivity.[11] In recent years it has been reported that addition of methyl ester of *p*-nitrocinnamic acid and various Michael acceptors to the resin-bound benzophenone imine of glycine resulted in variety of glutamic acid derivatives in high yields and purity.[12]

The conjugate addition of glycine Schiff bases to α,β-unsaturated compounds under phase-transfer catalysis (PTC) has received little attention.[13,14] Methyl and *tert*-butyl *N*-[*bis*(methylthio)methylene] glycinates have been found to react with cinnamates under solid-liquid phase-transfer catalysis to give the corresponding glutamic acid derivatives.[15] β-Phenylglutamic acid derivatives have also been prepared in an aq. $NaOH/Bu_4NBr/CH_2Cl_2$ system.[16] However, the data given in the reported in Chemical Abstracts symposium document are scarce. Now we report a convenient procedure for the preparation of esters of β-phenylglutamic acid by reaction of methyl and ethyl *N*-(diphenylmethylene)glycinate (**1**, **2**) and several esters of cinnamic acid (**3**) under aqueous conditions (Sch. 1).

Preliminary experiments for optimization of the reactions of methyl cinnamate with both **1** and **2** revealed that better stereoselectivity and yield for the adducts **4a** and **5a** were obtained by performing the reactions in acetonitrile solution at 0°C, using 50% aqueous sodium hydroxide without any phase-transfer catalyst. The presence of TEBA did not effect any improvment of either yield or selectivity. Thus, HPLC monitoring of the reaction of **1** and **3a** under PTC conditions (50% NaOH, TEBA, 0°C, 30 min) showed diastereoisomeric ratio 89:11, and repeated recrystallization of the isolated crude product (86% yield) did not result in pure diastereoisomer. On the other hand, ratio 97.2:2.8 (HPLC), respectively 97:3 (^{1}H NMR) was observed for the crude **4a**, obtained in a yield of 85% from **1** and **3a** in the absence of TEBA. One fold recrystallization of this product produced **4a** in a yield of 76% as a single diastereoisomer.

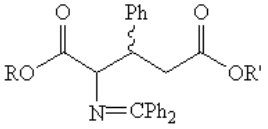
Under these conditions (50% NaOH, CH_3CN, 30 min at 0°C) the ester Schiff bases **1** and **2** were reacted with the cinnamates **3** to give the protected glutamic esters **4** and **5**. They were isolated as single diastereoisomers in moderate to good yields by recrystallization or column chromatography (**4c**, **5c**) of the crude products (Table 1).

The diphenylmethylene protection is known to be easily removed under acidic conditions.[17–19] For instance, refluxing of the ester **5a** with 6N HCl and subsequent ion-exchange chromatography afforded



1 R = CH_3 **3 a - e**

2 R = CH_2CH_3



4 R = CH_3 **5** R = CH_2CH_3

a R' = CH_3 **b** R' = CH_2CH_3 **c** R' = CH_2Ph **d** R' = $CH(CH_3)_2$

e R' = $C(CH_3)_3$

Scheme 1.

4a, 7 R = CH_3

5a, 8 R = CH_2 CH_3

Scheme 2.

β-phenylglutamic acid (**6**) in 63% yield, while cleavage of the azomethine bond only was observed by treatment of both **4a** and **5a** with hydroxylamine hydrochloride (Sch. 2).

Compounds **4a–e**, **5a–e**, **7**, and **8**, which are unknown to the best of our knowlege, were characterized by elemental analysis, IR and ^{1}H NMR spectra (Tables 1 and 2), TLC and HPLC.

Table 1. Compounds **4**, **5**, **7**, and **8** prepared.

Compound	Yield[a] (%)	M.p. (°C)	Molecule formula	Found/calculated (%) C	H	N
4a	76	119–121	$C_{26}H_{25}NO_4$	75.42	5.81	3.42
			(415.5)	75.16	6.06	3.37
4b	72	98–100	$C_{27}H_{27}NO_4$	75.55	6.63	3.37
			(429.5)	75.50	6.34	3.26
4c	63	Oil	$C_{32}H_{29}NO_4$	78.05	6.10	2.88
			(491.6)	78.19	5.95	2.85
4d	62	114–115	$C_{28}H_{29}NO_4$	75.93	6.56	3.28
			(443.5)	75.82	6.59	3.16
4e	47	117–119	$C_{29}H_{31}NO_4$	76.16	6.75	3.20
			(457.6)	76.12	6.83	3.06
5a	82	120–122	$C_{27}H_{27}NO_4$	75.74	6.10	3.20
			(429.5)	75.50	6.34	3.26
5b	78	99–101	$C_{28}H_{29}NO_4$	75.80	6.29	3.20
			(443.5)	75.82	6.59	3.16
5c	68	Oil	$C_{33}H_{31}NO_4$	78.14	6.44	2.56
			(505.6)	78.39	6.18	2.77
5d	48	84–86	$C_{29}H_{31}NO_4$	76.19	6.61	3.23
			(457.6)	76.12	6.83	3.06
5e	41	103–104	$C_{30}H_{33}NO_4$	76.44	7.37	3.29
			(471.6)	76.41	7.05	2.97
7	53	127–129	$C_{13}H_{18}ClNO_4$	54.31	5.44	4.76
			(287.7)	54.26	5.31	4.87
8	50	113–115	$C_{14}H_{20}ClNO_4$	56.09	6.21	4.79
			(301.8)	55.72	6.35	4.64

[a]Yield of pure diastereoisomer obtained after recrystallization (MeOH and EtOH (**5b**, **5d**, **5e**) or column chromatography (**4c**, **5c**).

In conclusion, this procedure represents a simple and efficient way for the preparation of glutamic esters **4** and **5** by Michael addition of the ready available glycine ester Schiff bases **1** and **2** to esters of cinnamic acid.

EXPERIMENTAL

Melting points were determined on a Boetius micro melting point apparatus and are uncorrected. The IR spectra were recorded on a Zeiss-Jena Specord 71. The ^{1}H NMR spectra were obtained on an AVANCE DRX- 250 (250 MHz) and BRUKER ARX 300 (300 MHz)

spectrometer using TMS as an internal standard. TLC analysis was performed on silica gel precoated plates "Silufol UV 254" using hexane and acetone (6:1) as eluent. Column chromatography was perfopmed by SiO_2 (0.063–0.200 mm) with the same solvents as eluent. The HPLC analyses were performed by a modular HPLC system, consisting of reciprocating pump Waters 510, injector (Waters) U6K, automated gradient controller Waters 680, UV-VIS Detector SHIMADZU SPD-10AV VP, Eurosphere C_{18} column (250×4 mm i.d.), 5 μm and isocratic elution with 57% CH_3CN, 43% H_2O (10 mM DBA + H_3PO_4, pH 6.5), flow rate 1.2 mL/min, temperature 33°C, detection- 245 and 280 nm. The ester Schiff bases **1** and **2**,[18] isopropyl cinnamate and *tert*-butyl cinnamate[21] were prepared according to literature procedures.

5-Alkyl-1-methyl-*N*-(diphenylmethylidene)-3-phenylglutamates (**4**) and 5-alkyl-1-ethyl-*N*-(diphenylmethylidene)-3-phenylglutamates (**5**)

General Procedure

To a cooled to 0°C (ice bath) stirred solution of methyl *N*-(diphenylmethylene)glycinate (**1**, 1.27 g, 5 mmol) or ethyl *N*-(diphenylmethylene)-glycinate (**2**, 1.34 g, 5 mmol), the corresponding alkyl cinnamate (**3**, 5 mmol) in CH_3CN (2.5 mL), was added aqueous sodium hydroxide (50%, 1.5 mL). The reaction mixture was stirred at 0°C until crystallization began, or 30 min (**4c**, **5c–e**). Water (100 mL) was added and the solid was collected, washed with water until neutral and recrystallyzed from methanol or ethanol (**5b**) to give **4** and **5** as white crystals. In the cases of compounds **4c**, **5c**, **5d–e**, the mixtures were extracted with methylene chloride (3×25 mL), and the residues obtained after removing of the solvent were treated with ethanol to give **5d** and **5e** as white crystals, or purified by column chromatography (hexane/acetone 18:1 (**4c**) and 25:1 (**5c**)) to give **4c** and **5c** as colorless oils (Tables 1 and 2).

β-Phenylglutamic Acid (6)

A mixture of 0.83 g (2 mmol) of **5a** and 6N hydrochloric acid (16 mL) was refluxed for 6 h. After cooling the separated benzophenone was removed with ether (3×10 mL), and then water was evaporated under reduced pressure until dryness. Distilled water (50 mL) was added to the residue and the mixture was stirred overnight with a strongly acidic cation exchange resin (Amberlite IR 120-H^+, 10 mL). The resin was collectedc on a Buchner funnel, washed with water until the filtrate

Table 2. IR and ^{1}H NMR spectra of compounds **4**, **5**, **7**, and **8** prepared.

Compound	IR[a] cm^{-1}	^{1}H NMR[b](δ, J)
4a	1730	3.01 (m, 2H, CH_2COOCH_3), 3.51 (s, 3H, $COOCH_3$-γ), 3.62 (s, 3H, $COOCH_3$-α), 4.01 (dt, 1H, J_1 =
	1620	5.3, J_2 = 7.6, PhCH), 4.22 (d, 1H, J = 5.3, $CHCOOCH_3$), 6.66–7.66 (m, 15H, arom.)
4b	1730	1.06 (t, 3H, J = 7.1, $COOCH_2CH_3$), 2.99 (m, 2H, $CH_2COOCH_2CH_3$), 3.62 (s, 3H, $COOCH_3$), 3.93–4.06
	1720	(m, 3H, PhCH + $COOCH_2CH_3$), 4.23 (d, 1H, J = 5.5, $CHCOOCH_3$), 6.69–7.82 (m, 15H, arom.)
	1615	
4c	1730	3.06 (m, 2H, CH_2COOCH_2Ph), 3.60 (s, 3H, $COOCH_3$), 3.99–4.07 (m, 1H, PhCH), 4.21(d, 1H, J =
	1720	5.4, $CHCOOCH_3$), 4.95 (s, 2H, $COOCH_2Ph$), 6.66–7.63 (m, 20H, arom.)
	1620	
4d	1730	1.00, 1.03 (2d, 6H, J = 6.3, $COOCH(CH_3)_2$), 2.94 (m, 2H, $CH_2COOCH(CH_3)_2$), 3.61 (s, 3H, $COOCH_3$),
	1720	3.94–4.01 (m, 1H, PhCH), 4.21 (d, 1H, J = 5.6, $CHCOOCH_3$), 4.81 (sept, 1H, J = 6.3, $COOCH(CH_3)_2$),
	1620	6.70–7.67 (m, 15H, arom.)
4e	1730	1.21 (s, 9H, $COOC(CH_3)_3$), 2.93 (m, 2H, $CH_2COOC(CH_3)_3$), 3.63 (s, 3H, $COOCH_3$), 3.94(dt, 1H, J_1 =
	1720	6.0, J_2 = 9.4, PhCH), 4.25 (d, 1H, J = 5.6, $CHCOOCH_3$), 6.68–7.70 (m, 15H, arom.)
	1620	
5a	1730	1.15 (t, 3H, J = 7.1, $COOCH_2CH_3$), 3.02 (m, 2H, CH_2COOCH_3), 3.51 (s, 3H, $COOCH_3$),4.00–4.10
	1620	(m, 3H, PhCH + $COOCH_2CH_3$), 4.19 (d, 1H, J = 5.5, $CHCOOCH_2CH_3$), 6.70–7.66(m, 15H, arom.)

5b	1730 1620	1.05 (t, 3H, $J=7.2$, $COOCH_2C\underline{H}_3$ -γ), 1.15 (t, 3H, $J=7.1$,$COOCH_2C\underline{H}_3$-α), 2.96 (m, 2H, $C\underline{H}_2COOCH_2CH_3$), 3.91–4.10 (m, 5H, $PhC\underline{H}$ + $COOC\underline{H}_2CH_3$-α+ $COOC\underline{H}_2CH_3$-γ), 4.18 (d, 1H, $J=5.8$, $C\underline{H}COOCH_2CH_3$-α), 6.71–7.68 (m, 15H, arom.)
5c	1730 1620	1.12 (t, 3H, $J=7.1$, $COOCH_2C\underline{H}_3$), 3.02 (m, 2H, $C\underline{H}_2COOCH_2Ph$), 3.99–4.09 (m, 3H, $PhC\underline{H}$ + $COOC\underline{H}_2CH_3$), 4.19 (d, 1H, $J=5.7$, $C\underline{H}COOCH_2CH_3$), 4.94 (s, 2H, $COOC\underline{H}_2Ph$), 6.69–7.66 (m, 20H, arom.)
5d	1730 1625	1.00, 1.03 (2d, 6H, $J=6.3$, $COOCH(C\underline{H}_3)_2$), 1.12 (t, 3H, $J=7.1$, $COOCH_2C\underline{H}_3$), 2.93 (m, 2H, $C\underline{H}_2COOCH(CH_3)_2$, 3.95–4.11 (m, 3H, $PhC\underline{H}$ + $COOC\underline{H}_2CH_3$), 4.19 (d, 1H, $J=5.9$, $C\underline{H}COOCH_2CH_3$), 4.77–4.85 (m, 1H, $COOC\underline{H}(CH_3)_2$), 6.73–7.83 (m, 15H, arom.)
5e	1730 1625	1.13 (t, 3H, $J=7.1$, $COOCH_2C\underline{H}_3$), 1.20 (s, 9H, $COOC(C\underline{H}_3)_3$), 2.85, 2.91 (A + B part of an ABX, $J_{AB}=15.4$, $J_{AX}=5.5$, $J_{BX}=10.5$, 2H, $C\underline{H}_2COOC(CH_3)_3$), 3.88–3.96 (m, 1H, $PhC\underline{H}$), 4.01–4.11 (m, 2H, $COOC\underline{H}_2CH_3$), 4.16 (d, 1H, $J=5.9$, $C\underline{H}COOCH_2CH_3$), 6.70–7.68 (m, 15H, arom.)
7	3400–2400 1720, 1590	3.00, 3.24 (2 dd, 2H, $J_1=8.8$, $J_2=16.8$, $J_3=6.4$, $C\underline{H}_2COOCH_3$), 3.52 (s, 3H, $COOC\underline{H}_3$-γ), 3.65 (s, 3H, $COOC\underline{H}_3$-α), 3.97–4.04 (m, 1H, $PhC\underline{H}$), 4.56 (d, 1H, $J=4.8$ $C\underline{H}COOCH_3$), 7.22–7.32 (m, 5H, arom.), 8.78 (brs, 3H, $N\underline{H}_3^+$)
8	3400–2400 1750, 1720 1570	1.18 (t, 3H, $J=7.1$, $COOCH_2C\underline{H}_3$), 3.03, 3.29 (2 dd, 2H, $J_1=8.5$, $J_2=16.8$, $J_3=6.6$), 3.58(s, 3H, $COOC\underline{H}_3$), 4.01–4.08 (m, 1H, $PhC\underline{H}$), 4.15 (q, 2H, $J=7.1$, $COOC\underline{H}_2CH_3$), 4.57 (brs, 1H, $C\underline{H}COOCH_3$), 7.27–7.36 (m, 5H, arom.), 8.80 (brs, 3H, $N\underline{H}_3^+$)

[a]Measured in $CHCl_3$.
[b]Determined in $CDCl_3$ (250 MHz, compounds **4a**, **4c**, **5a**, **5b**, **5c**, and **5e**; 300 MHz, **4b**, **4d**, **4e**, **5d**, **7**, and **8**).

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showed a negative test of chloride ion (silver nitrate) and stirred overnight with 6N ammonium hydroxide (75 mL). Then the resin was filtered and water was removed in vacuo to give 0.28 g (63%) of pure **6**. M.p. 228–231°C (dec.). Lit. M.p. 168–178°C dec.[7] 186–188°C dec.[20]

IR (nujol). 3300−2500, 1710, 1650, 1600, 1550 cm^{-1}.

^1H NMR (300 MHz, D_2O): 2.78, 2.82 (A + B part of an ABX system, 2H, $J_{AB} = 15.4$ Hz, $J_{AX} = 5.1$ Hz, $J_{BX} = 10.3$ Hz, $C\underline{H}_2COOH$), 3.55–3.62 (m, 1H, PhC<u>H</u>), 3.95 (d, 1 H, $J = 5.2$ Hz, C<u>H</u>COO^-), 7.29–7.39 (m, 5H, arom.)

Anal. calcd. for $C_{11}H_{13}NO_4$: C 59.19, H 5.87, N 6.27. Found C 60.28, H 6.67, N 6.79.

Dimethyl 3-Phenylglutamate Hydrochloride[7]

A mixture of 0.58 g (1.4 mmol) of **4a** and 0.10 g (1.4 mmol) hydroxylamine hydrochloride in anhydrous methanol (20 mL) was refluxed at 60°C for 3 h. After removing of 15 mL of methanol, anhydrous ether (15 mL) was added and the mixture was left to cool overnight in refrigerator. The separated crystal product was collected and recrystallized from a mixture of anhydrous methanol and anhydrous ether to give 0.21 g (53%) of **7** (Tables 1 and 2).

1-Ethyl-5-methyl-3-phenylglutamate Hydrochloride[8]

Following the above procedure, 0.20 g (50%) of **8** was prepared starting from 0.60 g (1.4 mmol) of **5a** and 0.10 g (1.4 mmol) hydroxylamine hydrochloride (Tables 1 and 2).

REFERENCES

1. Harington, C.R. Synthesis of 3,4,5-triiodophenylpyrrolidone-carboxylic acid, a possible isomer of thyroxin. J. Biol. Chem. **1925**, *64*, 29–39; Chem. Abstr. **1925**, *19*, 2203.
2. Patel, S.; Chapman, A.G.; Millan, M.H.; Meldrum, B.S. Epilepsy and excitatory amino acid antagonists. In *Excitatory Amino Acids in Health and Disease*; Lodge, D., Ed.; John Wiley and Sons: Inc.: New York, 1988; 353–378.

3. Lynch, M.A. In *Excitatory Amino Acids and Synaptic Transmission*; Wheal, H.W., Thomson, A.M., Eds.; Academic Press: London, 1991; 355–372.
4. Wermuth, C.G.; Mann, A.; Schoenfelder, A.; Wright, R.A.; Johnson, B.G.; Burnett, J.P.; Mayne, N.G.; Schoepp, D.D. (2S,4S)-2-Amino-4-(4,4-diphenylbut-1-yl)-pentane-1,5-dioic acid: a potent and selective antagonist for metabotropic glutamate receptors negatively linked to adenylate cyclase. J. Med. Chem. **1996**, *39* (4), 814–816.
5. Dornow, A.; Frese A. Über einige anlagerungs- und kondensationstreaktionen des nitroessigsäureäthylesters. Ann. **1952**, *578* (2), 122–136.
6. Sasaki, H.; Takahashi, F. A new synthesis of β-phenylglutamic acid. Nippon Kagaku Zasshi **1956**, *77*, 410–412; Chem. Abstr. **1958**, *52*, 9016.
7. Zymalkowski, F.; Pachaly P. Eine stereoselective synthese von *cis*- and *trans*-3-phenyl-2-carboxypyrrolidon(5). Chem. Ber. **1967**, *100* (4), 1137–1143.
8. Gershon, H; Parmegiani, R.; Giannasio, V.R.; Krull, I.S. Amino acid analogs III: new syntheses of monomethyl- and monophenylglutamic acids. J. Pharm. Sci. **1975**, *64* (11), 1855–1858.
9. Kobzareva, V.N.; Deiko, L.I.; Vasilieva, O.S.; Berestovitskaya, V. M.; Berkova, G.A. New method for the synthesis of 3-phenylglutamic acid. Russ. J. Org. Chem. **1997**, *33* (8), 1253–1254.
10. Belokon, Y.N.; Bulychev, A.G.; Ryzhov, M.G.; Vitt, S.V.; Batsanov, A.S.; Struchkov, Y.I.; Bakhmutov, V.I.; Belikov, V.M. Synthesis of enantio- and diastereoisomerically pure β- and γ-substituted glutamic acids via glycine condensation with activated olefins. J. Chem. Soc. Perkin Trans. 1 **1986**, (11), 1865–1872.
11. Ezquerra, J.; Pedregal, C.; Merino, I.; Flórez, J.; Barluenga, J.; Garcia-Granda, S.; Llorca, M.-A. Stereoselective michael addition of glycine anions to chiral fischer alkenylcarbene complexes. Asymmetric synthesis of β-substituted glutamic acids. J. Org. Chem. **1999**, *64* (18), 6554–6565.
12. Dominguez, E.; O'Donnell, M.J.; Scott, W.L. Solid-phase synthesis of substituted glutamic acid derivatives via michael addition reactions. Tetrahedron Lett. **1998**, *39* (15), 2167–2170.
13. Dehmlow, E.V.; Dehmlow, S.S. Practical applications of phase transfer catalysis, michael additions. In *Phase-Transfer Catalysis*, 3rd Ed.; VCH: Weiheim, 1993; 190–195.
14. Starks, Ch.M.; Liotta, Ch.L.; Halpern M.E. Phase-transfer catalysis reaction with strong bases, condensation reactions. In

Phase-Transfer Catalysis; Chapman and Hall: New York, 1994; 430–437.

15. Alvarez-Ibarra, C.; Csakÿ, A.G.; Marato, M.; Luz Quiroga, M. Diastereoselective synthesis of substituted glutamic acid derivatives via michael additions of *N*-[*bis*(methylthio)methylene]glycinates under solid-liquid phase transfer catalysis. J. Org. Chem. **1995**, *60* (21), 6700–6705.
16. Bryan, W.M.; Moore, M.L. Facile synthesis of β-substituted glutamic acids. In *Pept. Chem. Struct. Biol.*, Proceedings of the Am. Pept. Symp.,13th, 1993 (Pub. 1994), 173–174; Hodges, R.S., Smith, J.A. Eds.; ESCOM: Leiden, Neth.; Chem. Abstr. 1995, 122, 10509.
17. O'Donnell, M.J; Brudder, W.A.; Eckrich, Th.M.; Schullenberger, D.; Staten, G.S. Simple synthesis of the amino acids: 1-aminocyclopropane-1-capboxylic acid, cycloleucine and 2,6-diaminopimelic acid. Synthesis **1984**, (2), 127–128.
18. O'Donnell, M.J; Polt, R.L. A Mild and efficient route to schiff base derivatives of amino acids. J. Org. Chem. **1982**, *47* (13), 2663–2666.
19. Balsamini, C.; Diamantini, G.; Duranti, A.; Spadoni, G.; Tontini, A. A new synthesis of 2-substituted DL-tryptophan derivatives. Synthesis **1995**, (4), 370–372.
20. Pachaly, P. Die darstellung von *threo*- und *erythro*-3-aryl-glutaminssäuren. Arch. Pharm. (Weinheim) **1972**, *305* (3), 176–182.
21. Hauser C.R.; Hudson B.E.; Abramovitch B.; Schivers J.S. In *Org. Synth.*; Horning, E.C., Ed.; John Wiley and Sons Inc.: London, 1955; Coll. Vol. 3, 142–144.

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