Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 2359–2361

TETRAHEDRON LETTERS

Convenient synthesis of *t*-butyl *Z*-3-substituted glycidates under conditions of phase-transfer catalysis

Andrzej Jonczyk* and Tomasz Zomerfeld

Warsaw University of Technology, Faculty of Chemistry, Koszykowa 75, 00-662 Warsaw, Poland

Received 22 November 2002; revised 13 January 2003; accepted 24 January 2003

Abstract—Reactions of mixtures of *t*-butyl *E*- and *Z*-3-substituted glycidates **1a**–**h** with 50% aq. sodium hydroxide and a catalyst, benzyltriethylammonium chloride, TEBAC in dichloromethane (phase-transfer catalysis, PTC) led to preferential hydrolysis of the *E*-isomers to afford pure (90–98%) *t*-butyl *Z*-3-substituted glycidates **1a**–**i** in good yields; PTC cleavage of glycidates additionally substituted at C-2, **1g** or C-3, **1h**,**i** suggests that an aryl group in the *Z* isomers hampers attack of HO^- on the carbonyl carbon atom. As described in the literature, the diastereoselective PTC synthesis of *Z*-3-substituted glycidates and glycidonitriles consists of fast hydrolysis of *E* isomers present in mixtures with *Z* ones.

Esters of glycidic acid are usually prepared by base-promoted reaction of esters of α-halogeno acids with carbonyl compounds (Darzens condensation).[1] A variety of base–solvent systems have been applied for this purpose, including alkali metal hydroxides or carbonates in the presence of a quaternary ammonium salt or a crown ether as a catalyst[2] (phase-transfer catalysis, PTC[3]). Methyl or ethyl chloroacetate are cleaved by alkali metal hydroxides; therefore, Darzens condensations with these esters are carried out in the presence of powdered potassium carbonate and a phase-transfer catalyst[4] (solid–liquid variant of PTC). On the other hand, Darzens condensations with *t*-butyl chloroacetate can be performed with alkali metal hydroxides and a PT catalyst.[5] Irrespective of the PTC conditions, these processes are usually restricted to aromatic aldehydes and produce mixtures of *Z*- and *E*-3-arylglycidates. Recently, diastereoselective Darzens condensations of α-chloroesters, amides and nitriles with aromatic aldehydes, carried out in the presence of powdered potassium hydroxide and tetrahexylammonium bromide (THAB) as a catalyst in THF or diethyl ether, which led to formation of *Z*-glycidic acid derivatives, have been described.[6] We wish to report that, in fact, this process consists of the formation of mixtures of *E* and *Z* isomers of the products, the first of which hydrolyses at a relatively high rate.

When we carried out the condensation of *t*-butyl chloroacetate with benzaldehyde in the presence of 50% aq. sodium hydroxide and benzyltriethylammonium chloride (TEBAC) as a catalyst in dichloromethane at 10–15°C for 1 h, the formation of white solid product was noticed. This material was isolated and identified (^{1}H NMR, transformation into phenylacetaldehyde[7]) as the slightly impure sodium salt of *E*-3-phenylglycidic acid. The experiment described above indicates that *t*-butyl 3-phenylglycidate **1a** is prone to basic hydrolysis, to some extent. The organic products from the reaction were conventionally worked-up and distilled to afford *t*-butyl-3-phenylglycidate **1a**, *E*/*Z* ca. 0.25 (yield 65%).

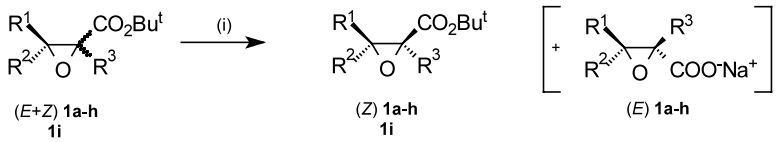
This observation prompted us to investigate hydrolysis of a mixture of *t*-butyl *E*- and *Z*-3-phenylglycidate **1a** under PTC conditions. Stirring such a mixture (*E*/*Z* ca. 0.25) with 50% aq. sodium hydroxide and TEBAC as a catalyst, in dichloromethane at 10–15°C, indicated that the *E* isomer is cleaved at a much higher rate than the *Z* isomer. After ca. 6 h, the crude mixture contained ≥97% of the *Z* isomer which, after isolation and distillation, was obtained in a yield of 84%[8,9] (with >0.5% of the *E* isomer and 2.5% of impurities determined by GC) (Table 1, entry 1). Without the catalyst, not less than ca. 80% of ester **1a** of practically the same *E*/*Z* ratio was recovered. To determine the scope of this reaction, mixtures of *Z* and *E* isomers of *t*-butyl glycidates substituted at C-3 with aryl **1b**–**d**, heteroaryl, **1e** or cyclohexyl, **1f** groups were hydrolysed under the same PTC conditions, to afford *Z* isomers **1b**–**f** of high purity and in good yield[9] (Table 1, entries 2–6). Simi-

Keywords: phase transfer; hydrolysis; esters.

* Corresponding author. Tel.: +48-22-621-4230; fax: +48-22-628-2741; e-mail: anjon@ch.pw.edu.pl

0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00234-X

Table 1. Hydrolysis of glycidates **1a–j** under conditions of PTC. *Reagents and conditions*: (i) 50% aq. NaOH, cat. TEBAC, CH_2Cl_2, 10–15°C, 5–6 h



Entry	**1**	R^1	R^2	R^3	E/Z in starting **1**[a]	*Z*-**1**	
						Yield (%)	Purity (%)[a]
1[b]	**a**	Ph	H	H	0.25	84	98
2	**b**	2-FC_6H_4	H	H	0.40	78	97
3	**c**	2-MeC_6H_4	H	H	0.21	75	97
4	**d**	4-ClC_6H_4	H	H	0.32	66	98
5	**e**	3-C_4H_3S	H	H	2.95	70	90[c]
6	**f**	*c*-C_6H_{11}	H	H	0.93	68	93[c]
7	**g**	Ph	H	Me	0.56	86	95
8	**h**	Ph	Me	H	0.40	60	95
9	**i**	Ph	Ph	H	–	50[d]	92[d]

[a] Determined by GC.
[b] *i*-Propyl 3-phenylglycidate (**1j**, $E/Z \approx 0.69$) gives after 0.5h *Z*-**1a** in yield of 51% (purity 95%).
[c] 5% of isomer *E*.
[d] Recovered ester **1g**.

larly, mixtures of *E*- and *Z*-3-phenylglycidates substituted with a methyl group at C-2, **1g** or C-3, **1h** gave *Z* isomers (Table 1, entries 7 and 8). In accordance with expectation, the *E* isomer of *i*-propyl 3-phenylglycidate **1j** was cleaved much faster than the analogous *t*-butyl ester **1a** (Table 1, entry 1). *t*-Butyl *Z*-3-arylglycidates can be prepared by this two-step procedure in higher yield than by previously described methodology.[6]

When we repeated the reaction of *t*-butyl chloroacetate with benzaldehyde under the conditions described,[6,10] samples taken after 2 h and analysed by GC showed the presence of both isomers of **1a** ($E/Z \approx 0.41$); the *E* isomer was removed when a second portion of powdered potassium hydroxide was added and the reaction was carried out for 22 h.

Reaction of chloroacetonitrile with benzaldehyde carried out under the same conditions,[6,10] gave after 8 h a mixture of *E*- and *Z*-3-phenylglycidonitrile ($E/Z \approx$ 1.32), but after 100 h only the *Z* isomer was detected by GC. So, the diastereoselective[6] Darzens condensations leading to esters and nitriles of *Z* glycidic acids are actually based on selective hydrolysis of the *E* isomers of *E*/*Z* mixtures.

The literature indicates that cleavage of esters carried out in a two-phase system can be accelerated by a PT catalyst. Thus dimethyl adipate hydrolyses exothermically in the presence of 50% aq. sodium hydroxide and a Q^+X^- catalyst while no reaction occurs without the catalyst. On the other hand, hydrolysis of methyl tetradecanoate is arrested after ca. 35% of reaction. In the latter case, the Q^+ ion associates with the long chain carboxylate anion rather than with HO^-, hampering extraction of Q^+OH^- into the organic phase, and the catalytic process is arrested.[11] Typical liquid–liquid PTC systems (conc. aq. sodium hydroxide and a catalyst, Aliquat 336) are not suitable for hydrolysis of alkyl mesitoates while they are efficiently cleaved by powdered potassium hydroxide with the same catalyst.[12] Thorough investigations indicate that PTC hydrolysis of esters carried out in the presence of 50% aq. sodium hydroxide depends on their structure, type of solvent and catalyst used.[13] Even *t*-butyl benzoate is cleaved by means of 60% aq. potassium hydroxide under conditions of triphase catalysis in high yield.[14]

Hydroxide anion associated with Q^+ is inefficiently transferred from water into an organic phase, particularly when more lipophilic anions like Cl^- or Br^- are present. This is the case in the reactions studied; chloride anion is introduced by the TEBAC catalyst. Furthermore, phenylglycidate anions produced during the reaction form ion pairs with Q^+ which also seem to be lipophilic. Thus, interfacial mechanisms of ester hydrolysis cannot be discarded though results obtained without the TEBAC catalyst are in favour of a reaction via Q^+OH^- extracted into the organic phase.

Our investigations open the question as to why *E* isomers of glycidates and glycidonitriles are more easily hydrolysed than *Z* ones. The results described above, as well as the rather slow rate of cleavage of 3,3-diphenyl substituted glycidate **1i** (Table 1, entry 9) suggest that the aryl groups in *Z* isomers hampers attack by hydroxide on the carbonyl carbon of the *t*-butoxycarbonyl or the cyano group.[15] Further work aimed at an explanation of the experimental data is in progress.

Nevertheless, our paper reports a simple and efficient method for preparation of *t*-butyl *Z*-3-arylglycidates which are useful substrates in organic synthesis.[16]

References

1. (a) Newman, M. S.; Magerlin, B. J. *Org. React.* **1949**, *5*, 413–440; (b) Ballester, M. *Chem. Rev.* **1955**, *55*, 283–300.
2. Keller, W. A. *Phase-Transfer Reactions*, *Fluka-Compendium*; Georg Thieme: Stuttgart, New York; 1986, Vol. 1, p. 329; 1987, Vol. 2, p. 806.
3. (a) Dehmlow, E. V.; Dehmlow, S. S. *Phase-Transfer Catalysis*; 3rd ed.; Verlag Chemie: Weinheim, 1993; (b) Starks, C. M.; Liotta, C. L.; Halpern, M. *Phase-Transfer Catalysis*; Chapman & Hall: New York, 1994; (c) Mąkosza, M.; Fedorynski, M. In *Handbook of Phase Transfer Catalysis*; Sasson, Y.; Newmann, R., Eds.; Blackie Academic & Professional: London, 1997; pp. 135–167.
4. (a) Fedorynski, M.; Wojciechowski, K.; Matacz, Z.; Mąkosza, M. *J. Org. Chem.* **1978**, *43*, 4682–4684; (b) Gladiali, S.; Soccolini, F. *Synth. Commun.* **1982**, *12*, 355–360; (c) Kimura, Ch.; Kashiwaya, K.; Murai., K.; Katada, H. *Ind. Eng. Chem. Prod. Res. Dev.* **1983**, *22*, 118–120; (d) Dehmlow, E. V.; Kinnius, J. *J. Prakt. Chem.* **1995**, *337*, 153–155.
5. (a) D'Incan, E.; Seyden-Penne, J. *Compt. Rend.* **1975**, *281*, 1031–1033; (b) Baldoli, C.; Del Buttero, P.; Licandro, E.; Maiorana, S.; Papagni, A. *J. Chem. Soc., Chem. Commun.* **1987**, 762–764.
6. Arai, S.; Suzuki, Y.; Tokumaru, K.; Shioiri, T. *Tetrahedron Lett.* **2002**, *43*, 833–836.
7. This reaction was carried out as described in Ref. 1 p. 428 for conversion of 3-phenylglycidic acid into hydratropaldehyde.
8. Jonczyk, A.; Zomerfeld, T. Polish Pat. Appl. No. T349124, 2001.
9. Procedure: *t*-butyl 3-phenylglycidates **1a**, *E*/*Z* ca. 0.25 (1.15 g, 5.2 mmol), 50% aq. sodium hydroxide (4 mL), TEBAC (0.05 g, 0.22 mmol) and CH_2Cl_2 (4 mL) were vigorously stirred at 10–15°C for 6 h. The mixture was diluted with water, the phases were separated, the aqueus phase was extracted with CH_2Cl_2 (2×10 mL), the combined organic extracts were washed with water, dried ($MgSO_4$), the solvent was evaporated, and the residue was distilled in a Kugelrohr apparatus (bath temperature 120°C/0.6 Torr) to give *t*-butyl *Z*-3-phenylglycidate **1a** (0.75 g, yield 84%, based on the amount of *Z* isomer in the substrate) of purity ≥97% (GC). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.26 (m, 5H, ArH), 4.22 (d, J=4.8 Hz, 1H, **H**CCO$_2$Bu-*t*), 3.71 (d, J=4.8 Hz, 1H, **H**CPh), 1.17 (s, 9H, *t*-Bu). Characterisation data for compounds **1b**–**g**: ^{1}H NMR spectra were measured at 400 MHz, ^{13}C NMR spectra at 100 MHz in $CDCl_3$ solution, chemical shifts (δ) are given in ppm relative to TMS and coupling constant (J) in Hz. All distillations were carried out in a Kugelrohr apparatus. *t*-Butyl *Z*-3-(2-fluoro)phenylglycidate **1b**: bp 89–94°C/0.4 Torr; ^{1}H NMR: 1.19 [s, 9H, C(C**H**$_3$)$_3$], 3.69 (d, J=4.7, 1H, C**H**CO$_2$Bu^t), 4.16 (d, J=4.7, 1H, C**H**Ph), 7.0–7.6 (m, 4H, Ar**H**); ^{13}C NMR: 27.42, 52.56, 55.05, 82.20, 114.46 (d, J=20.0), 120.78 (d, J=13.4), 123.39 (d, J=3.5), 128.76 (d, J=3.5), 129.63 (d, J=8.3), 161.00 (d, J=246), 165.37; anal. calcd for $C_{13}H_{16}O_3F$ C, 65.55, H, 6.30; found C, 65.11, H, 6.39%; *t*-butyl *Z*-3-(2-methyl)phenylglycidate **1c**: bp 109–110°C/0.8 Torr; ^{1}H NMR: 1.11 [s, 9H, C(C**H**$_3$)$_3$], 2.34 (s, 3H, C**H**$_3$), 3.77 (d, J=4.3, 1H, C**H**CO$_2$Bu^t), 4.20 (d, J=4.3, 1H, C**H**Ph), 7.0–7.5 (m, 4H, Ar**H**); *t*-butyl *Z*-3-(4-chloro)phenylglycidate **1d**: bp 130°C/0.6 Torr; mp 55–58°C (MeOH); ^{1}H NMR: 1.17 [s, 9H, C(C**H**$_3$)$_3$], 3.82 (d, J=4.6, 1H, C**H**CO$_2$Bu^t), 4.32 (d, J=4.6, 1H, C**H**Ph), 7.2–7.6 (m, 4H, Ar**H**); *t*-butyl *Z*-3-(3-thiophenyl)glycidate **1e**: column chromatography, hexane:AcOEt 50:1; ^{1}H NMR: 1.26 [s, 9H, C(C**H**$_3$)$_3$], 3.69 (d, J=4.4, 1H, C**H**CO$_2$Bu^t), 4.21 (dd, J=4.4, J=0.4, 1H, ArC**H**), 7.11 (dd, J=5.0, J=1.2, 1H, Ar**H**), 7.26 (dd, J=5.0, J=2.8, 1H, Ar**H**), 7.33 (m, 1H, Ar**H**);); *t*-butyl *Z*-3-cyclohexylglycidate **1f**: bp 140°C/10 Torr; ^{1}H NMR: 1.1–1.9 (m, 11H, *c*-hexyl), 1.45 [s, 9H, C(C**H**$_3$)$_3$], 2.79 (dd, J=9.2, J=4.6, 1H, *c*-hexyl-C**H**), 3.37 (d, J=4.6, 1H, C**H**CO$_2$Bu^t); ^{13}C NMR: 25.1, 27.9, 28.6, 30.4, 36.1, 53.1, 61.3, 82.1 167.3; *t*-butyl *Z*-2-methyl-3-phenylglycidate **1g**: bp 100–104°C/0.8 Torr; ^{1}H NMR: 1.12 [s, 9H, C(C**H**$_3$)$_3$], 1.68 (s, 3H, C**H**$_3$), 3.97 (s, 1H, C**H**Ph), 7.2–7.4 (m, 5H, Ar**H**); *t*-butyl *Z*-3-methyl-3-phenylglycidate **1h**: bp 130°C/0.6 Torr; ^{1}H NMR: 1.11 [s, 9H, C(C**H**$_3$)$_3$], 1.71 (s, 3H, C**H**$_3$), 3.55 (s, 1H, C**H**CO$_2$Bu^t), 7.24–7.42 (m, 5H, Ar**H**); *t*-butyl 3,3-diphenylglycidate **1i**: bp 140°C; mp 59–61°C (MeOH), ^{1}H NMR: 1.20 [s, 9H, C(C**H**$_3$)$_3$], 3.88 (s, 1H, C**H**CO$_2$Bu^t), 7.3–7.5 (m, 10H, Ar**H**); *i*-propyl *Z*-3-phenylglycidate **1j**, ^{1}H NMR 0.98 [d, J=6.8, 3H, CH(C**H**$_3$)(CH$_3$)], 0.99 [d, J=6.8, 3H, CH(CH$_3$)(C**H**$_3$)], 3.79 (d, J=4.6 Hz, 1H, **H**CPh), 4.25 (d, J=4.6 Hz, 1H, **H**CCO$_2$Pr-*i*), 4.85 [qq, 1H, J=6.8, J=6.8, C**H**(CH$_3$)$_2$], 7.2–7.5 (m, 5H, ArH).
10. Tetra-octylammonium bromide as a catalyst was used in this reaction.
11. Starks, C. M. *J. Am. Chem. Soc.* **1971**, *93*, 195–199.
12. Loupy, A.; Pedoussaut, A.; Sansoulet, J. *J. Org. Chem.* **1986**, *51*, 740–742.
13. Dehmlow, E. V.; Barahona-Naranjo, S. *J. Chem. Res. (S)* **1979**, 238–239.
14. Kimura, Y.; Regen, S. L. *Synth. Commun.* **1983**, *13*, 443–447.
15. Selective hydrolysis of the ethoxycarbonyl group in the *E* isomer of an (*E*+*Z*) mixture of ethyl 2-phenylcyclopropanecarboxylate (NaOH, EtOH, H_2O) has been described. See: Kaiser, C.; Weinstock, J.; Olmstead, M. P. *Org. Synth.* **1970**, *50*, 94–97.
16. Procedures for transfomation of *E* into *Z* glycidates, see: (a) Adger, B. M.; Barkley, J. V.; Bergeron, S.; Cappi, M. W.; Flowerdew, B. M.; Jackson, M. P.; McCague, R.; Nuget, T. C.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, *23*, 3501–3507; (b) Righi, R.; Rumboldt, G.; Bonini, C. *J. Org. Chem.* **1996**, *61*, 3557–3560.