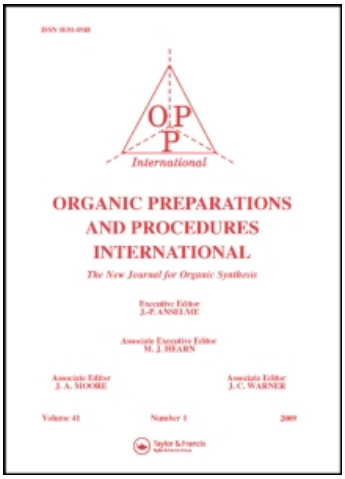


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

CONVENIENT SYNTHESIS OF 2,3,5-TRIARYL-5-OXOPENTANOIC ACIDS AND OF THEIR *t*-BUTYL ESTERS

V. Dryanska[a]; A. Popovich[a]
[a] Department of Chemistry, University of Sofia, Sofia, BULGARIA

To cite this Article Dryanska, V. and Popovich, A.(1994) 'CONVENIENT SYNTHESIS OF 2,3,5-TRIARYL-5-OXOPENTANOIC ACIDS AND OF THEIR *t*-BUTYL ESTERS', Organic Preparations and Procedures International, 26: 2, 237 — 241
To link to this Article: DOI: 10.1080/00304949409458027
URL: http://dx.doi.org/10.1080/00304949409458027

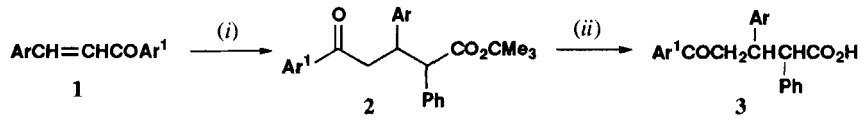
ORGANIC PREPARATIONS AND PROCEDURES INT., 26 (2), 237-241 (1994)

CONVENIENT SYNTHESIS OF 2,3,5-TRIARYL-5-OXOPENTANOIC ACIDS AND OF THEIR *t*-BUTYL ESTERS†

V. Dryanska* and A. Popovich

Department of Chemistry
University of Sofia
1126 Sofia, BULGARIA

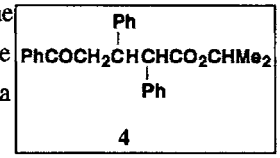
2,3,5-Triaryl-5-oxopentanoic acids and derivatives are useful intermediates in organic synthesis. In addition, 2,3,5-triphenyl-5-oxopentanoic acid and its sodium salt, in particular the (R,S)-(+)-enantiomer, exhibit highly selective herbicidal activity.[1] Several methods have been developed for their preparation;[2,6] most of these routes involve conjugate addition of derivatives of arylacetic acids (sodium phenylacetate,[2] methyl and ethyl phenylacetate[3,4] or phenylacetonitrile[3,5]) to 1,3-diarylpropenones, and subsequent hydrolysis of the resulting addition product. Another approach is the Friedel-Crafts reaction of 2,3-diphenylglutaric acid anhydride with aromatic hydrocarbons,[6] which requires anhydrous conditions like the Michael reactions mentioned earlier. Numerous Michael additions have been performed in recent years using phase-transfer catalysis (PTC)[7,8] This offers simple reaction procedure under mild conditions and the use of inexpensive and safe reagents and solvents; however, in reactions involving methyl and ethyl arylacetates, competing hydrolysis processes usually interfere. Recently, we reported that under PTC conditions *tert*-butyl phenylacetate undergoes facile reaction with compounds possessing activated double bonds.[9] This paper describes an efficient procedure for the preparation of 2,3,5-triaryl-5-oxopentanoic acids from *tert*-butyl phenylacetate and the enones **1** under aqueous conditions. Only a few *tert*-butyl 5-oxoalkanoates have been reported. *tert*-Butyl 3,4-diphenyl-5-oxohexanoate was prepared earlier by Michael addition of phenylpropanone to *tert*-butyl-3-phenylpropenoate in DMSO/aq.NaOH,[10] and quite recently Duhamel and co-workers[11] reported the



i) $PhCH_2CO_2CMe_3$ *ii*) Trifluoracetic acid

a) Ar = Ar^1 = C_6H_5 b) Ar = 4-ClC_6H_4, Ar^1 = C_6H_5 c) Ar = C_6H_5, Ar^1 = 4-ClC_6H_4
d) Ar = 4-$CH_3C_6H_4$, Ar^1 = C_6H_5 e) Ar = C_6H_5, Ar^1 = 4-$CH_3C_6H_4$
f) Ar = 4-$CH_3OC_6H_4$, Ar^1 = C_6H_5 h) Ar = C_6H_5, Ar^1 = 4-$CH_3OC_6H_4$

synthesis of mono- and disubstituted *tert*-butyl 5-oxo esters by conjugate addition of β-lithiated enamines to enoates. Treatment of *tert*-butyl phenylacetate with the arylideneacetophenones **1** at room temperature in the presence of aqueous sodium hydroxide and benzyltriethylammonium chloride (TEBA), using acetonitrile as solvent, gave the corresponding *tert*-butyl 5-oxopentanoates **2** as a mixture of diastereomers. The ^{1}H NMR spectra of the crude **2** exhibited signals from the *tert*-butyl group at δ 1.08-1.11 for the major diastereomer and at δ 1.37-1.41 for the minor diastereomers, respectively, their ratio varying from 77:23 to 91:9. Recrystallization afforded the major diastereoisomer in moderate to good yields (Table 1). Under the same conditions, **1a** reacted with isopropyl phenylacetate to give compound **4** as a single diastereoisomer in 60% yield after recrystallization.



4

TABLE 1. Yields, mps and Elemental Analyses of Compounds **2** and **3**

Cmpds	yield[a] (%)	mp. (°C)	Elemental Analyses (Found) C	H
2a	70	170-171	80.97 (80.91)	7.05 (6.90)
2b	62	158-160	74.56 (74.53)	6.26 (6.46)
2c	52	179-181	74.56 (74.31)	6.26 (6.47)
2d	54	147-149	81.13 (80.99)	7.29 (7.13)
2e	58	156-157	81.13 (80.98)	7.29 (7.21)
2f	49	130-130.5	78.11 (77.96)	7.02 (7.00)
2g	72	147-148	78.11 (78.14)	7.02 (7.12)
3a	85	256-258 (260-261)[2]	80.21 (80.47)	5.85 (6.09)
3b	88	246-248 (252-254)[13]	72.92 (72.98)	5.05 (5.11)
3c	79	237-239 (152)[6]	72.92 (73.19)	5.05 (5.22)
3d	85	249-251	80.42 (80.75)	6.19 (6.16)
3e	81	251-253 (177)[6]	80.42 (80.35)	6.19 (5.96)
3f	80	232-234 (235-237)[13]	76.99 (76.88)	5.92 (6.02)
3g	93	252-254	76.99 (77.10)	5.92 (5.64)

a) Yield of pure diastereomer obtained after recrystallization.

TABLE 2. Spectral Data of Compounds **2** and **3**

Cmpds	IR[a] (cm^{-1})	^1H NMR[b] (δ, Hz)
2a	1690, 1725	1,08 (s, 9H), 2.88 (dd, 1H, J = 16.5 and 3.0), 3.20 (dd, 1H, J = 16.5 and 10.5), 3.85 (d, 1H, J = 12,3), 4.21 (m, 1H), 7.08-7.72 (m, 15H)
2b	1690, 1725	1.11 (s, 9H), 2.89 (dd, 1H, J = 16.7 and 3.0), 3.16 (dd, 1H, J = 17.0 and 10.5), 3.81 (d, 1H, J = 12.0), 4.05 (m, 1H), 7.10-7.64 (m, 14H)
2c	1690, 1725	1.08 (s, 9H), 2.86 (dd, 1H, J = 16.4 and 3.1), ,3.14 (dd, 1H, J = 16.4 and 3.84 (d, 1H, J = 11.9), 4.02 (m, 1H), 7.08-7.67 (m, 14H)
2d	1690, 1725	1.09 (s, 9H), 2.26 (s, 3H) 2.87 (dd, 1H, J = 16.5 and 3.1), 3.17 (dd, 1H, J = 16.5 and 10.5), 3.83 (d, 1H, J = 11.9), 4.00 (m, 1H), 7.03-7.70 (m, 14H)
2e	1685, 1725	1.08 (s, 9H), 2.33 (s, 3H), 2.85 (dd, 1H, J = 16.4 and 3.1), 3.18 (dd, 1H, J = 16.4 and 10.5), ,3.85 (d, 1H, J = 11.9), 4.05 (m, 1H), 7.08-7.85 (m, 14H)
2f	1690, 1725	1.11 (s, 9H), 2.78 (dd, 1H, J = 16.0 and 3.0), 3.08 (dd, 1H, J = 16.0 and 10.0), 3.64 (s, 3H), 3.71 (d, 1H, J = 12.0), 3.91 (m, 1H), 6.73-7.69 (m, 14H)
2g	1680, 1725	1.08 (s, 9H), 2.83 (dd, 1H, J = 16.2 and 3.1), 3.16 (dd, 1H, J = 16.3 and 10.5), 3.80 (s, 3H), 4.02 (m, 1H), 3.81 (d, J = 12.0), 6.47-7.67 (m, 14H)
3a	1685, 1700, 2200-3400	2.38-2.70 (m, 2H),[c] 3.89 (m, 1H), 4.02(d, 1H, J = 11.75), 7.05-7.74 (m, 15H), 12,17 (br s, 1H)
3b	1680, 1700, 2300-3400	2.50-2.61 (m, 2H),[c] 3,92 (m, 1H), 4.01 (d, 1H, J = 11.7), 7.29-7.75 (m, 14H), 12.22 (br s, 1H)
3c	1685, 1700, 2200-3300	2.39-2.70 (m, 2H),[c] 3.89 (m, 1H), 4.00 (d, 1H, J = 11.6), 7.09-7.67 (m, 14H), 12,14 (br s, 1H)
3d	1685, 1700, 2300-3400	2.21 (s, 3H), 2.38-2,64 (m, 2H),[c] 3.87 (m, 1H), 3.98 (d, 1H, J = 11.7), 7.00-7.49 (m, 14H), 12.10 (br s, 1H)
3e	1680, 1710, 2300-3500	2.29 (s, 3H), 2.35-2.66 (m, 2H),[c] 3.87(m, 1H.), 4.00 (d, 1H, J = 11.8), 7.06-7.51 (m, 14H), 12.09 (br s, 1H)
3f	1680, 1700, 1740, 2300-3400	2.35-2.69 (m, 2H),[c] 3.68 (s, 3H), 3.85 (m, 1H), 3.96 (d, 1H, J = 11,8), 6.78 (d, 2H), 7.26-7.67 (m, 12H), 12.09 (br s, 1H)
3g	1680, 1700, 2200-3200	2.40-2.67 (m, 2H),[c] 3.77 (s, 3H), 3.91(m, 1H), 4.00 (d, 1H, J = 11.8), 6.89 (d, 2H), 7.08-7.67 (m, 12H), 12.12 (br s, 1H)

a) Recorded in $CHCl_3$ (**2**) or as Nujol mulls (**3**). b) Determined in $CDCl_3$ (**2**) and in DMSO-d_6 (**3**). c) Overlapped with DMSO signal.

Compounds **2** were readily converted in high yields (79-93%) to the acids **3** by treatment with trifluoroacetic acid (TFA) at room temperature. Attempts to develop a one-pot procedure for **3**, including the reaction of **1** with *tert*-butyl phenyl acetate under the same conditions, followed by treatment of crude **2** with TFA, without isolation and recrystallization, gave lower yields. Configurational

assignments were made on the basis of chemical correlations and ^{1}H NMR spectroscopy. The *erythro* configuration was assigned to the esters **2a**, **2b**, and **2d** based on the chemical correlation with the reported *erythro* acids **3a**, **3b**, and **3d**.[12,13] The configurations of **2c** and **2e-g** followed by comparison with **2a**, **2b**, and **2d** on the basis of similar ^{1}H NMR chemical shift patterns. The reported melting points of **3c** and **3f**,[6] obtained by Friedel-Crafts acylation by the anhydride of 2,3-diphenylglutaric acid are considerably lower than those observed and probably refer to the *threo* diastereomers. The reaction of *tert*-butyl phenylacetate with **1** was also successful when methylene chloride or benzene was used as solvent. However, better results with respect to yields and stereoselectivity, were obtained in acetonitrile, Attempts to react *tert*-butyl phenylacetate with **1a** under solid-liquid PTC conditions using potassium carbonate as a base failed.

In conclusion, the phase-transfer catalyzed reaction of *tert*-butyl phenylacetate with 1,3-diarylpropenones offers a convenient and efficient route for the preparation of 2,3,5-triaryl-5-oxopentanoic acids and their *tert*-butyl esters with good stereoselectivity.

EXPERIMENTAL SECTION

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 Bruker WH-250 spectrometer (250 MHz) using TMS as an internal standard. *tert*-Butyl phenylacetate[14] and the arylideneacetophenones **1** were prepared according to literature procedures.[15] Acetonitrile and TEBA were purchased from Fluka and used without further purification.

***tert*-Butyl 2,3,5-Triaryl-5-oxopentanoates (2). General Procedure.**- To a stirred solution of *tert*-butyl phenylacetate (1.92 g, 10 mmol), **1** (10 mmol) and TEBA (0.12 g, 0.5 mmol) in 5 mL of acetonitrile (10 mL in the case of **2f**), was added an aqueous solution of sodium hydroxide (50%, 3 mL). The reaction mixture was stirred magnetically at room temperature until crystallization began (3-20 min) and then it was allowed to stand overnight. Water (100 mL) was added and the solid was collected. washed with water until neutral, and recrystallized from ethanol (**2d-g**) or ethanol-ethyl acetate (1:1, **2a-c**), to give **2** as white crystals (Tables 1 and 2).

2,3,5-Triaryl-5-oxopentanoic Acids 3. General Procedure.- A solution of **2** (3 mmol) in TFA (5 mL) was allowed to stand at room temperature for 1 hr and then water (100 mL) was added. The precipitate was collected, washed until neutral, and recrystallized from DMF to afford **3** as white crystals.

Isopropyl-2,3,5-Triphenyl-5-oxopentanoate (4).- Aqueous sodium hydroxide (50% solution, 3 mL) was added to a magnetically stirred solution of isopropyl phenylacetate (1.78 g, 10 mmol), **1a** (2.08 g, 10 mmol) and TEBA (0.12 g, 0.5 mmol) in acetonitrile (5 mL). The mixture was stirred for 10 min and was allowed to stand at room temperature overnight. Water (100 mL) was added and the precipitate was collected, washed until neutral, and recrystallized from ethanol to give 2.30 g (60%) of **4**, mp. 158-160°. IR ($CHCl_3$): 1690, 1725 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 0.78 (d, 3H), 0.91 (d, 3H), 2.91 (dd, 1H, J = 16.6 and 3.1 Hz), 3.23 (dd, 1H, J = 16.6 and 10.3 Hz), 3.89 (d, 1H, J = 12.0 Hz), 4.13 (m, 1H),

4.67 (m, 1H), 7.10-7.66 (m, 15H).

Anal. Calcd. for $C_{26}H_{26}O_3$: C, 80.80; H, 6.78. Found: C, 80.90; H, 6.78.

REFERENCES

† Part XI of *Phase-Transfer Catalyzed Additions*; for part X, see V. Dryanska, *God. Sofii Univ., Khim. Fac.*, **86**, 55 (1993).

1. K. G. R. Sundelin and G. A. Bozarth, *US Pat. 4,466,823 (1984)*; *Chem. Abstr.*, **101**, 186154 (1984).

2. a) C. R. Hauser and M. T. Tetenbaum, *J. Org. Chem.*, **23**, 1146 (1958); b) D. Ivanov and G. Vasilev, *Compt. Rend. Acad. Bulg. Sci.*, **10**, 121 (1957); *Chem. Abstr.*, **52**, 5353 (1958).

3. a) H. Meerwein, *J. prakt. Chem.*, **97**, 275 (1918); b) S. Avery and G. G. Lorgensen, *J. Am. Chem. Soc.*, **52**, 3628 (1930).

4. a) W. Borsche, *Ber.*, **42**, 4496 (1909); b) R. Connors and D. B. Andrews, *J. Am. Chem. Soc.*, **56**, 2713 (1934).

5. E. P. Kohler and C. F. H. Allen, *ibid.*, **46**, 1522 (1924).

6. V. K. Chhatwal, R. K. Gautam and G. S. Saharia, *J. Indian Chem. Soc.*, **55**, 158 (1978).

7. E. V. Dehmlow and S. S. Dehmlow, "*Phase-Transfer Catalysis*", 2nd ed., Verlag Chemie, Weinheim, 1983.

8. W. E. Keller, "*Phase-Transfer Reactions*", Fluka Compendium, Thieme, Stuttgart; Vol. 1, 1986; Vol. 2, 1987.

9. V. Dryanska, *Synth. Commun.*, **15**, 899 (1985).

10. V. Dryanska, C. Ivanov and D. Demirov, *ibid.*, **14**, 843 (1984).

11. L. Duhamel, P. Duhamel, D. Enders, W. Karl, F. Leger, J. M. Poirier and G. Raabe, *Synthesis*, 649 (**1991**).

12. R. B. Meyer and C. R. Hauser, *J. Org. Chem.*, **27**, 1067 (1962).

13. L. Fisnerova, B. Kakac, E. Kraus and O. Nemecek, *Coll. Czech. Chem. Commun.*, **41**, 623 (1976).

14. C. R. Hauser, B. E. Hudson, B. Abramovitch and J. C. Shivers, *Org. Syn., Coll. Vol. III*, 142 (**1955**).

15. E. P. Kohler and H. M. Chadwell, *ibid., Coll. Vol. I*, 78 (**1941**).

(Received June 14, 1993; in revised form October 13, 1993)