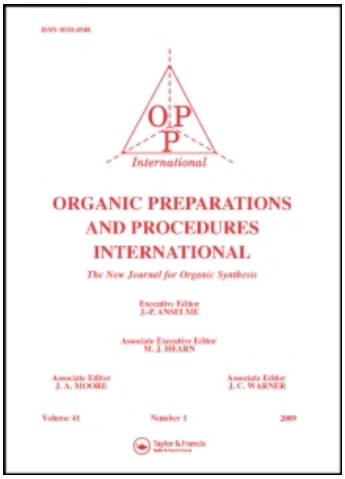


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF α-ARYL-β-KETOESTERS

John L. Wong[a]; Mohammad K. Ali[a]
[a] Department of Chemistry, University of Louisville, Louisville, Kentucky

To cite this Article Wong, John L. and Ali, Mohammad K.(1970) 'SYNTHESIS OF α-ARYL-β-KETOESTERS', Organic Preparations and Procedures International, 2: 3, 193 — 195
To link to this Article: DOI: 10.1080/00304947009458657
URL: http://dx.doi.org/10.1080/00304947009458657

ORGANIC PREPARATIONS AND PROCEDURES 2(3), 193-195 (1970)

SYNTHESIS OF α-ARYL-β-KETOESTERS

John L. Wong and Mohammad K. Ali
Department of Chemistry
University of Louisville, Louisville, Kentucky 40220

Ethyl α-phenylacetoacetate has been prepared by ethanolysis of α-phenylacetoacetonitrile followed by hydrolysis,[1] by mixed Claisen condensation of ethyl phenylacetate with phenyl acetate in the presence of sodium amide,[2] by boron trifluoride-catalyzed reaction of ethyl diazoacetate with acetophenone,[3] and by acetylation of the magnesium salt of ethyl hydrogen phenylmalonate.[4] Several of these procedures suffer from drawbacks such as erratic yields and difficultly separable side-products, and none of them is known to be a convenient, general synthesis of α-aryl-β-ketoesters. The direct arylation of the ethyl acetoacetate anion with activated aryl halides since restricted to the obtention of α-(2,4-dinitrophenyl)acetoacetate[5] and the like is limited in scope.

We wish to report a simple and general method for the preparation of α-aryl-β-ketoesters. The procedure involves the formation of the anion of a phenylacetone by the action of sodium hydride in tetrahydrofuran. The homogeneous solution of the carbanion is then allowed to react with ethyl chloroformate for carbethoxylation. The optimum yields were obtained

$$CH_3COCH_2Ar \xrightarrow[THF]{NaH} CH_3\bar{C}OCHAr\ Na^+ \xrightarrow{ClCO_2Et} CH_3COCHCO_2Et \quad (Ar)$$

Ar = Ph; o-, m-, p-ClPh; o-, p-OCH_3Ph

when a ratio of 2 moles of base for one mole each of the ketone and ester was used.[6] The yields are generally good and no side products other than

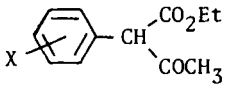
unreacted starting ketone were found. The β-ketoesters are readily purified by distillation at reduced pressure. The nuclear substituted phenylacetones were prepared according to known methods[7] from the corresponding aromatic aldehydes and nitroethane via the nitroalkenes.

$$ArCHO + C_2H_5NO_2 \longrightarrow ArCH = C(NO_2)CH_3 \longrightarrow ArCH_2COCH_3$$

EXPERIMENTAL

Ethyl α-phenylacetoacetate. -- To a stirred mixture of 4.8 g (0.2 mole) of sodium hydride[8] in 100 ml of tetrahydrofuran was added 13.4 g (0.1 mole) of freshly distilled phenylacetone. The evolution of hydrogen subsided after 30 min. and a homogeneous reddish-colored solution remained. The flask was cooled in an ice-bath, and 10.8 g (0.1 mole) of distilled ethyl chloroformate was added slowly. The solution was allowed

TABLE I

	Yield	Bp	Analyses,%			
			Calcd		Found	
	%	°C/mm	C	H	C	H
X = H	85	128-9/7	69.9	6.8	70.2	6.9
X = p-Cl	76	143-3/1	59.9	5.4	60.1	5.1
X = m-Cl	64	91-3/2	59.9	5.4	60.1	5.1
X = o-Cl	67	73-4/1	59.9	5.4	60.2	5.6
X = p-OCH_3	72	185-7/7	66.1	6.8	66.4	6.6
X = o-OCH_3	46	116-9/1	66.1	6.8	66.5	7.0

to stir for 2 hrs., neutralized with cold dilute aqueous hydrochloric acid, extracted with 3 x 50 ml-portions of ether, dried, concentrated and distilled under reduced pressure through a short spinning band column to give 17.5 g (0.085 mole, 85% yield) of ethyl α-phenylacetoacetate, nmr. (CCl_4,δ): 7.3 (m,5), 5.8 (s,1), 4.2 (q,2,J 7cps), 2.1 (s,3), 1.25 (t,3,J 7cps), entirely compatible with the assigned structure.

Other β-ketoesters were prepared following the same procedure, and the yields are shown in Table I.

ACKNOWLEDGEMENT

This work was supported by Grant No. T-469 from the American Cancer Society.

REFERENCES

1. R. H. Kimball, G. D. Jefferson, and A. B. Pike, Org. Syn. Coll. Vol. II, 284 (1943).

2. J. C. Shivers, M. L. Dillon, and C. R. Hauser, J. Am. Chem. Soc., 69, 119 (1947).

3. W. T. Tai and E. W. Warnhoff, Can. J. Chem., 42, 1333 (1964).

4. R. E. Ireland and J. A. Marshall, J. Am. Chem. Soc., 81, 2906 (1959).

5. G. E. Hall, D. Hughes, D. Rae, and A. P. Rhodes, Tetrahedron Letters, 241 (1967).

6. Sodium hydride is also consumed by the acidic β-ketoester produced, hence 2 moles of base are needed for the complete conversion of the phenylacetone to the carbanion form.

7. H. B. Hass, A. G. Susie, and R. L. Heider, J. Org. Chem., 15, 8 (1950).

8. The sodium hydride dispersion purchased from Ventron Metal Hydrides Division was washed with anhydrous hexane to remove oil before use.

(Received March 19, 1970)