New Preparative Method for 2-Arylpropanoic Acids by Oxidative Aryl Migration in Aryl α-Seleno- and Aryl α-Telluro-ethyl Ketones

Sakae Uemura,*[a] Shin-ichi Fukuzawa,[a] Takayoshi Yamauchi,*[b] Kaneaki Hattori,[b] Shoichi Mizutaki,[b] and Kentaro Tamaki[b]

[a] *Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan*
[b] *Research & Development Laboratory, Sakai Plant, Kyowa Hakko Kogyo Co. Ltd., Sakai, Osaka 590, Japan*

Oxidation with *m*-chloroperbenzoic acid of the ethylene acetals of aryl α-phenylseleno- or aryl α-phenyltelluro-ethyl ketones prepared by treating the corresponding α-bromo compounds with diphenyl diselenide–sodium or diphenyl ditelluride–sodium, respectively, affords hydroxyethyl 2-arylpropanoates in moderate to good yields *via* aryl group migration.

It has recently been reported that oxidation of alkyl phenyl selenides[1] or tellurides[2] with *m*-chloroperbenzoic acid (MCPBA) in methanol gave dialkyl ethers. The reaction is accompanied by phenyl migration in selenides and tellurides having a phenyl group vicinal to the phenylselenium or phenyltellurium moieties. Using this reaction we have succeeded in developing a new method for the synthesis of 2-arylpropanoic acids which are pharmaceutically important compounds exhibiting anti-inflammatory and analgesic activities.[3]

Aryl ethyl ketone (**1**) was brominated at the α-position to give (**2**) which was then converted into acetal (**3**) with ethylene glycol in the presence of toluene-*p*-sulphonic acid [overall yield of (**3**) from (**1**) was 88—98%]. When (**3**) was added to a tetrahydrofuran–dimethylformamide solution of diphenyl diselenide or diphenyl ditelluride and sodium wire under a N_2

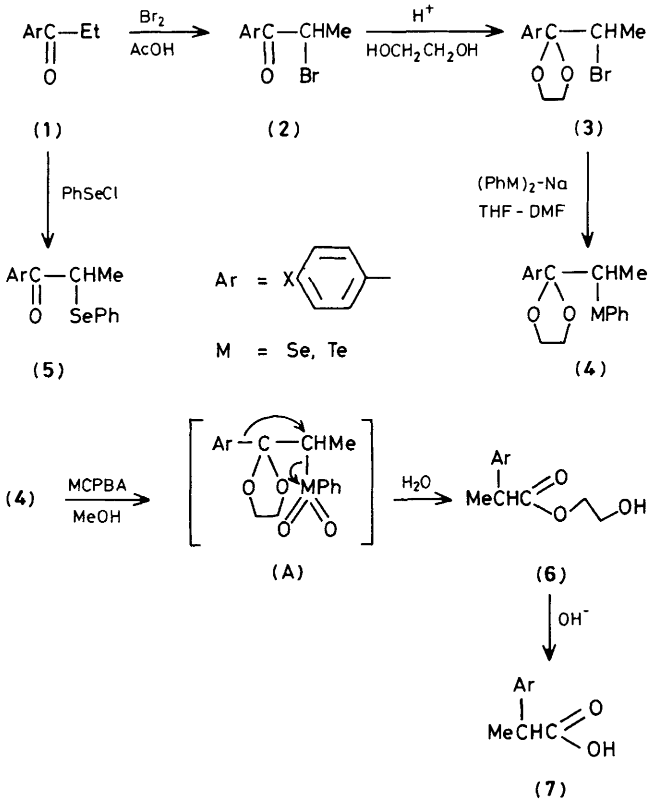

Table 1. 2-Arylpropanoic acids from aryl ethyl ketones (**1**).

M	X in Ar	Yield (%)	
		(**4**)[a]	(**6**)[b]
Se	H	75	80
Se	Me	83	86
Se	Bu^i	70	82
Se	Ph	81	56
Se	Br	74	85
Te	H	62	80
Te	Me	34	62
Te	Bu^i	50	85

[a] Isolated yield based on (**3**). [b] Isolated yield based on (**4**).

atmosphere and the resulting mixture was stirred under reflux for 6—20 h, the bromine atom was substituted by the PhSe or PhTe group to afford (**4**) in 50—80% (for M = Se) and in 35—60% (for M = Te) yield.†‡ This substitution did not proceed by using the $(PhM)_2$–$NaBH_4$–EtOH (M = Se, Te) system which is known as a source of PhM^- anion and the starting compound (**3**) was recovered. Attempts to prepare (**4**; M = Se) by acetalation of aryl α-phenylselenoethyl ketone (**5**), prepared by selenation of (**1**) with phenylselenenyl chloride, resulted in decomposition to (**1**) and diphenyl diselenide.

Compound (**4**) was then treated with 5 equiv. MCPBA in methanol at room temperature for 10 min to 1 h. After normal work-up (addition of aq. NaCl, washing with aq. $Na_2S_2O_3$ and aq. $NaHCO_3$, and diethyl ether extraction), evaporation of the solvent left an oily compound which was subjected to column chromatography [SiO_2, hexane–EtOAc (10/1 to 1/1) as eluent] to give the hydroxyethyl ester of 2-arylpropanoic acid (**6**).† The isolated yield of (**6**) was 55—58% based on (**4**). Alkaline hydrolysis of (**6**) readily afforded the corresponding acid (**7**). Typical results are summarized in Table 1. We assume that the reaction proceeds *via* a selenone or tellurone intermediate (A) in which aryl group migration occurs. Direct oxidation of (**5**) with MCPBA in methanol did not produce any of (**6**) or the analogous ester.

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References

1 S. Uemura and S. Fukuzawa, *Tetrahedron Lett.*, 1983, **24**, 4347.
2 S. Uemura, S. Fukuzawa, and A. Toshimitsu, *J. Chem. Soc., Chem. Commun.*, 1983, 1501.
3 For example, K. Fujii, K. Nakao, and T. Yamauchi, *Synthesis*, 1983, 444, and references therein.

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† All new compounds showed satisfactory combustion analytical and spectroscopic data (^{1}H and ^{13}C n.m.r. and i.r.).

‡ All compounds except (**4**; X = Me, M = Te) (pale yellow crystals, m.p. 105—106 °C) are yellow oily substances.