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Oxidative rearrangements of arylalkenes with [hydroxy(tosyloxy)iodo]benzene in 95% methanol: a general, regiospecific synthesis of α-aryl ketones

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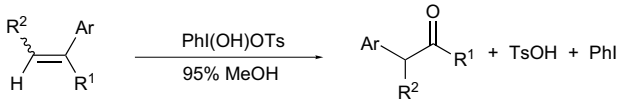
Abstract—The treatment of arylalkenes with [hydroxy(tosyloxy)iodo]benzene in 95% methanol affords the corresponding α-aryl ketones. This oxidative rearrangement is general for acyclic and cyclic arylalkenes and permits regioselective syntheses of isomeric α-phenyl ketone pairs.

Although the conversion of 1,1-diphenylethylene (**1**) to deoxybenzoin (**2**) with [hydroxy(tosyloxy)iodobenzene] (**3**, HTIB) in CH_2Cl_2 was first reported in 1981,[1,2] the use of HTIB for oxidative rearrangements of arylalkenes has received only limited attention. Documented reactions of this type include rearrangements of phenyl-substituted allenes **4** to α,β-unsaturated aldehydes or ketones **5** with HTIB in CH_2Cl_2,[3] and of chalcones **6** to β-ketoaldehyde acetals **7**, either with HTIB in MeOH or with iodosylbenzene (PhI=O) in MeOH under acidic conditions (i.e., FSO_3H, $MeSO_3H$, or $BF_3{\cdot}Et_2O$).[4,5] Rearrangements of styrene to acetal **8a** and of α-methylstyrene to ketal **8b** with HTIB in MeOH have also been reported, but published yields of **8a** and **8b** refer to the iodosylbenzene-fluorosulfonic acid–MeOH system.[4] The influence of methanol on reactions of styrene and chalcone with HTIB is indicated by the reported production of vicinal-ditosylates **9** when CH_2Cl_2 is the solvent.[1,2] In the absence of solvent, styrene gives the geminal-ditosylate **10** with HTIB[1,2] (Fig. 1).

We now report that the treatment of arylalkenes with HTIB in 95% methanol (i.e., 5% H_2O by volume) provides a versatile and convenient synthesis of α-aryl ketones; Eq. 1 and Tables 1–3. Such oxidative rearrangements proceed readily under ambient conditions and can be tested for completion with aqueous potassium iodide. For purposes of this study, reactions were conducted with 10 mmol of HTIB in conjunction with a slight excess of arylalkene. Arylalkenes were selected to explore variations in the nature of the aryl and alkyl groups; ring-size in 1-phenylcycloalkenes; and regiospecificity of α-aryl ketone production.



(1)

Except for three commercially available substrates (i.e., α-methylstyrene, 1,1-diphenylethene, and 1-phenylcyclohexene), the 1-phenylcycloalkenes listed in Table 2 were prepared from cycloalkanones by a Grignard-addition/alcohol dehydration sequence, while the acylic arylalkenes listed in Tables 1, 2 and 3 were prepared by Wittig olefination of the corresponding 1-arylalkanones. A modified procedure based on the potassium *tert*-butoxide method of Fitjer and Quabeck, was employed for the Wittig olefinations.[6] Experimental procedures for the preparation and oxidative rearrangement of 2-phenyl-1-pentene are representative and given below.

2-Phenyl-1-pentene: Potassium *tert*-butoxide (4.48 g, 40.0 mmol) was added under argon to a mechanically stirred mixture of methyltriphenylphosphonium iodide (16.16 g, 40.0 mmol) and dry Et_2O (80 mL). The canary

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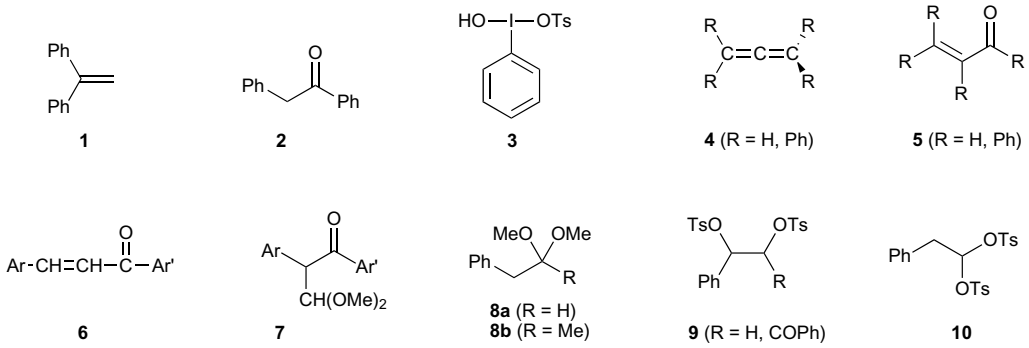
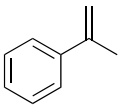
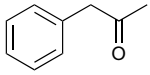
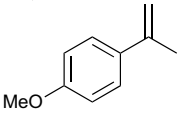
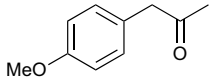
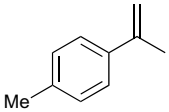
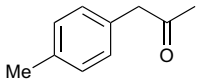
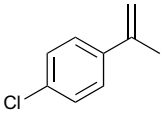
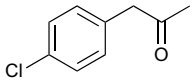
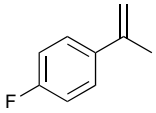
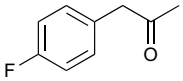
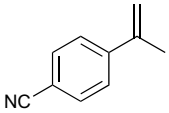
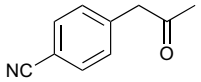
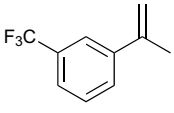
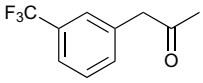
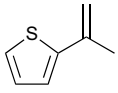
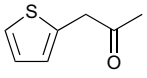
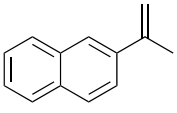
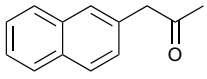
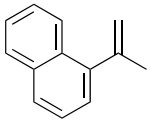
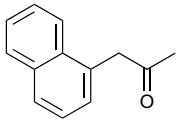


Figure 1.

Table 1. Products of reactions of 2-arylpropenes with HTIB in aqueous methanol

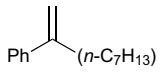
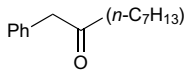
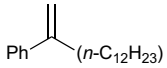
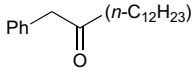
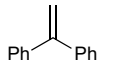
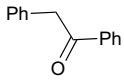
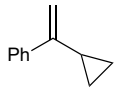
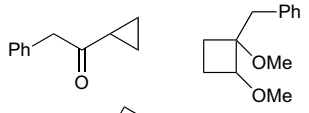
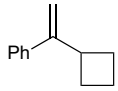
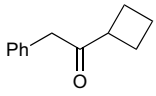
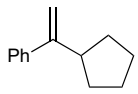
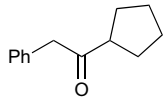
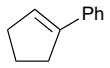
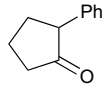
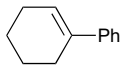
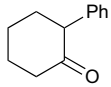
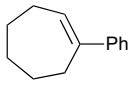
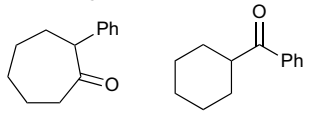
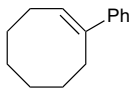
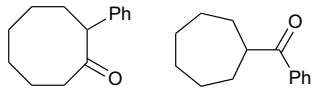
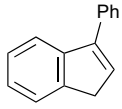
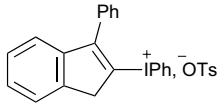
Substituted propene	Product[a]	Time[b]	Yield (%)
		20 min	84
		20 min	92
		20 min	89
		60 min	80
		20 min	73
		16 h	82
		6 h	59
		20 min	80
		20 min	90
		20 min	86

[a] Products were characterized by ^{1}H and ^{13}C NMR, FT-IR and in most cases comparison of melting points of compounds or their derivatives with literature values.

[b] Approximate reaction times; that is, times after which the reaction mixtures gave a negative KI test.

yellow mixture was stirred vigorously for 30 min. A solution of butyrophenone (5.19 g, 35.0 mmol) in Et_2O was then introduced (5 min), and stirring was continued for 4 h at room temperature, during which time the color

Table 2. Products of reactions of phenylalkenes with HTIB in aqueous methanol

Substituted propene	Product[a]	Time[b]	Yield(s) [%]
		20 min	87
		6 h	92
		20 min	72
		20 min	41, 21
		20 min	74
		20 min	85
		20 min	43
		20 min	84
		1 h	53, 27
		8 h	30, 22
		4 h	80

[a] Products were characterized by ^{1}H and ^{13}C NMR, FT-IR and in some cases comparison of melting points of compounds or their derivatives with literature values.

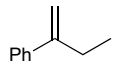
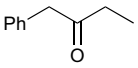
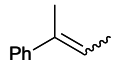
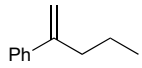
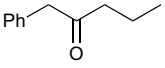
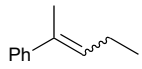
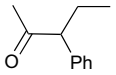
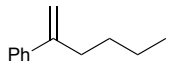
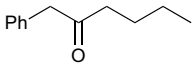
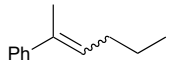
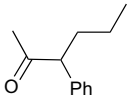
[b] Approximate reaction times; that is, times after which the reaction mixtures gave a negative KI test.

was discharged. The grayish-white mixture was then filtered through Celite (10 g) and the filtrate concentrated to a light-yellow oil. Elution of the oil with hexanes through a pad of silica gel (30 g, sintered glass funnel) under aspirator vacuum and concentration of the eluent gave 2-phenyl-1-pentene as a colorless oil; yield, 4.04 g (79%); ^{1}H NMR ($CDCl_3$): δ 0.98 (t, 3H), 1.54 (sextet, 2H), 2.54 (t, 2H), 5.11 (s, 1H), 5.33 (s, 1H), 7.28–7.40 (m, 3H), 7.46 (d, 2H); ^{13}C NMR ($CDCl_3$): δ 13.75, 21.32, 37.42, 112.11, 126.11, 127.21, 128.19, 141.70, 148.48; IR(neat) 1627 cm^{-1} (C=C).

1-Phenyl-2-pentanone: Crystalline HTIB (3.92 g, 10 mmol) was added to a magnetically stirred solution of 2-phenyl-1-pentene (1.60 g, 10.9 mmol) in 95% methanol (45 mL). The HTIB dissolved rapidly (~15 s) with mild heat evolution (41 °C) to give a colorless solution. After 20 min at room temperature, the solution was concentrated under aspirator vacuum, and the oily mixture that remained was partitioned between CH_2Cl_2 (40 mL) and H_2O (40 mL). The organic layer was washed with H_2O (2×40 mL) and brine (35 mL), dried over $MgSO_4$, and concentrated to a colorless oil (2.66 g). Flash column chromatography of the oil on silica gel with 10% EtOAc/hexanes gave 1-phenyl-2-pentanone as a colorless oil; 1.43 g (88%); R_f = 0.65 (10% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$): δ 0.87 (t, 3H), 1.58 (sextet, 2H), 2.42 (t, 2H), 3.68 (s, 2H), 7.20–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 13.43, 16.97, 43.74, 50.02, 126.94, 128.69, 129.41, 134.42, 208.56; IR(neat) 1713 cm^{-1}; semicarbazone, mp 175–176 °C [lit.[7] mp 177 °C].

Some indication of the scope of α-aryl ketone synthesis by HTIB-oxidative rearrangement method is provided by the entries in Table 1. The 2-arylpropenes surveyed in this study include representatives with α-thienyl, α- and

Table 3. Regiospecific syntheses of isomeric 1- and 3-phenyl-2-alkanones

Substituted propene	Product[a]	Time[b]	Yield (%)
		20 min	86
		2 h	80
		20 min	88
		2 h	75
		20 min	88
		6 h	70

[a] Products were characterized by ^{1}H and ^{13}C NMR, FT-IR and in most cases comparison of melting points of compounds or their derivatives with literature values.

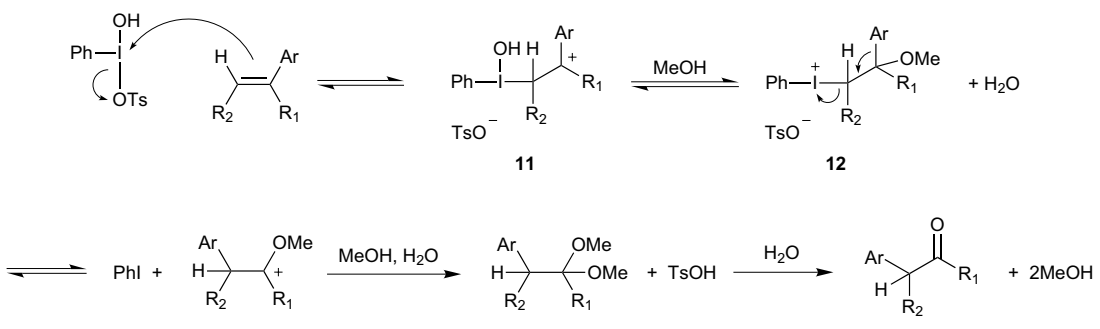
[b] Approximate reaction times; that is, times after which the reaction mixtures gave a negative KI test.

β-naphthyl, and variously substituted phenyl groups. Hammet sigma constants of substituents in the phenyl series range from −0.268 (4-OMe) to +0.660 (4-CN), and although longer reaction times (i.e., hours vs minutes) were required when electron withdrawing groups were present, aryl acetones were obtained in all cases. Except for the 3-$CF_3C_6H_4$ analog (59% yield), isolated yields of aryl acetones for the entire arylpropene series ranged from 73% to 92%.

HTIB-induced rearrangements of various 1-alkyl-1-phenylethylenes, including congeners with long alkyl chains and cycloalkyl groups (Table 2), typically resulted in high isolated yields (72–92%) of 1-phenyl-2-alkanones. The relatively low yield (41%) of benzyl cyclopropyl ketone from 1-cyclopropyl-1-phenylethylene is due, at least in part, to the competing formation of 1-benzyl-1,2-dimethoxycyclobutane, presumably via a cyclopropylcarbinyl–cyclobutyl rearrangement or a bicyclobutonium intermediate.

Among the 1-phenylcycloalkenes that were tested with HTIB in 95% methanol (Table 2) 1-phenylcyclohexene appears to be the optimum substrate for phenyl migration and gave 2-phenylcyclohexanone in 84% isolated yield. This may be contrasted with the thallium(III) nitrate-induced rearrangement of 1-phenylcyclohexene in methanol[8] and the semipinacol rearrangement of 2-amino-1-phenylcyclohexanol,[9] both of which afford cyclopentyl phenyl ketone.

With the seven- and eight-membered 1-phenylcycloalkenes ring contraction was competitive with aryl migration in the HTIB-95% methanol system. For example, 1-phenylcycloheptene gave a mixture of cyclohexyl phenyl ketone (27% yield) and 2-phenylcycloheptanone (53% yield), easily separated by column chromatography on silica gel with EtOAc/hexanes. The reaction of 1-phenylcyclopentene with HTIB in 95% methanol stopped at the dimethylketal stage and was unique in this regard. However hydrolysis of the ketal allowed isolation of 2-phenylcyclopentanone in 43% yield. Finally, 1-phenylindene did not undergo an HTIB-induced oxidative rearrangement in 95% methanol, but was instead converted to 1-phenyl-2-indenyl(phenyl)iodonium tosylate (80% yield).



Scheme 1.

Oxidative rearrangements of the 2-phenyl-2-alkenes shown in Table 3 proceeded more slowly than those of their 2-phenyl-1-alkene isomers. However after 1, or 6 h, 3-phenyl-2-alkanones were isolated in yields of 70–80%. Hence, by appropriate selection of phenylalkene pairs, regiospecific syntheses of isomeric 1-phenyl- and 3-phenyl-2-alkanones were accomplished. For example, 2-phenyl-1-pentene afforded 1-phenyl-2-pentanone (88% yield) with HTIB in 95% methanol, while 2-phenyl-2-pentene gave 3-phenyl-2-pentanone (75% yield), neither ketone being contaminated with the other isomer.

A general mechanism for the production of α-aryl ketones from arylalkenes with HTIB in 95% methanol, similar to that proposed by Moriarty and co-workers for the chalcone and styrene rearrangements discussed earlier is illustrated in Scheme 1. The intermediate existence of phenyl(hydroxy)iodanyl carbocations, **11**, and phenyl(β-methoxyalkyl)iodonium tosylates, **12**, in such reactions, coupled with the high nucleofugacity of iodobenzene, provides a comprehensive rationale for aryl migration, ring contractions of the higher phenylcycloalkenes, ring expansion of 1-cyclopropyl-1-phenylethylene, vinyliodonium salt formation from 1-phenylindene, and qualitative observations on reaction time.

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