Synthesis of *O*-Heterocycles *via* Intramolecular Reductive Deoxygenation of *o*-Aroyloxyacetophenones: One-step Synthesis of Benzofurans

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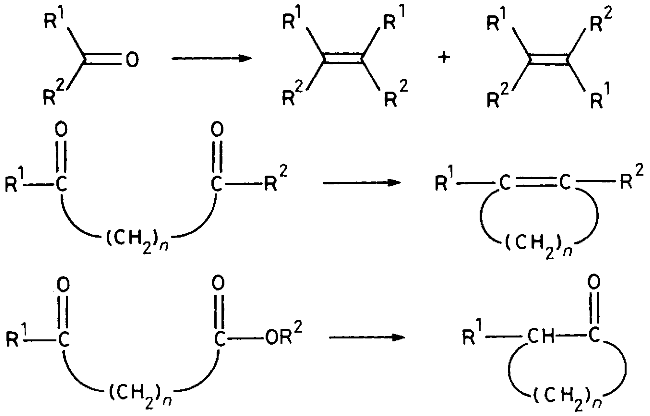
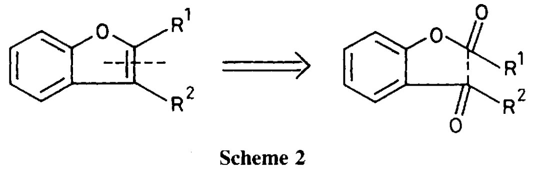
A one-step synthesis of benzofurans *via* intramolecular reductive coupling of *o*-aroyloxyacetophenones using titanium(IV) chloride and zinc is described.

Reactions involving carbon–carbon bond formations are of great importance and continue to draw the attention of synthetic organic chemists. Titanium compounds in different valence states have been used in the formation of carbon–carbon bonds, *e.g.*, reductive dimerization of aldehydes and ketones to pinacols, reductive deoxygenation of aldehydes, ketones, and keto aldehydes to alkenes, aldol condensation, *etc.*[1] Activated titanium metal has been employed for reductive coupling of mono-carbonyl compounds to symmetrical alkenes.[2] Similarly, cycloalkenes have been prepared by the intramolecular coupling of dicarbonyl compounds.[2] Recently McMurry *et al.*[3] have reported the synthesis of cyclic ketones from keto esters (Scheme 1). In this communication, we report for the first time the use of titanium(II) for C–C bond formation by intramolecular reductive coupling between carbonyl groups of ketones and esters resulting in the formation of oxygen heterocycles. Application of this reaction has been exemplified by the preparation of benzofurans from *o*-aroyloxyacetophenones.

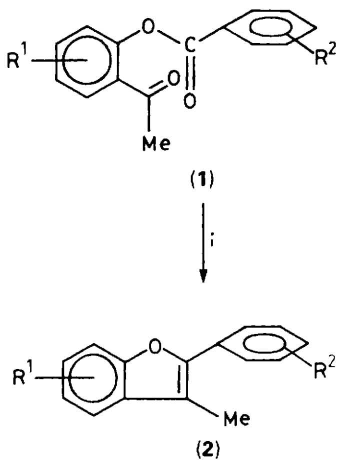
Benzofuran ring systems are present in many natural and synthetic products which show pharmacodynamic properties.[4] From a retrosynthetic perspective (Scheme 2), *o*-aroyloxyacetophenones could be appropriate substrates for the benzofuran synthesis. Mukaiyama's reagent ($TiCl_4$–Zn) which is known to give satisfactory yields for coupling reactions involving aromatic carbonyl compounds[5] was selected in the present study. A typical reaction is described below. To a well stirred cooled solution (5 °C) of 2-(3-methoxybenzoyloxy)-acetophenone (**1b**) (2.7 g, 10 mmol) in dry dioxane (100 ml), $TiCl_4$ (3.3 ml, 30 mmol) was added dropwise under argon atmosphere. After stirring the mixture for 0.5 h, Zn powder (3.93 g, 60 mmol) was added in small lots and then the mixture was refluxed for 6 h. The reaction mixture was worked up in the usual manner using aqueous NH_4Cl. Compound (**2b**) was isolated as a thick liquid (1.43 g, 60%) by column chromatography (silica gel). IR (film) $\nu_{max.}$: 1600, 1575, 1455, 745 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.5 (3H, s, Me), 3.92 (3H, s, OMe), 6.83—7.67 (8H, m, ArH); *m/z* 238 (M^+). The scope of this reaction was explored by using a variety of *o*-aroyloxyacetophenones (**1b**—**f**) as substrates when corresponding benzofurans (**2b**—**f**) were obtained in good yields (Table 1, Scheme 3). It has been proposed that Ti^{II} species (formed by the



Scheme 1



Scheme 2



Scheme 3. *Reagents and conditions*: i, $TiCl_4$/Zn, dioxane/Δ.

Table 1. Benzofurans (**2**) formed by reductive coupling of *o*-aroyloxyacetophenone (**1**) using $TiCl_4$–Zn.

	(**1**)		(**2**)	% Yield of (**2**)[a] (ref.)
a;	$R^1 = R^2 = H$	**a**;	$R^1 = R^2 = H$	55(6)
b;	$R^1 = H, R^2 = 3'$-OMe	**b**;	$R^1 = H, R^2 = 3'$-OMe	60[b]
c;	$R^1 = 4$-OMe, $R^2 = H$	**c**;	$R^1 = 6$-OMe, $R^2 = H$	45(7)
d;	$R^1 = 5$-OMe, $R^2 = H$	**d**;	$R^1 = 5$-OMe, $R^2 = H$	56(8)
e;	$R^1 = 6$-OMe, $R^2 = H$	**e**;	$R^1 = 4$-OMe, $R^2 = H$	58[b]
f;	$R^1 = 4,5$-$(OMe)_2$, $R^2 = H$	**f**;	$R^1 = 5,6$-$(OMe)_2$, $R^2 = H$	24(9)

[a] All compounds were fully characterised by ^{1}H NMR, IR, UV spectroscopies and mass spectral analysis. Yields are based on the product purified by preparative thin layer or column chromatography.
[b] Satisfactory spectroscopic and analytical data were obtained for the new compounds (**2b**) and (**2e**). *Selected spectroscopic data* for (**2e**): m.p. 50—51 °C; IR (KBr) $\nu_{max.}$: 1620, 1600, 1500, 1250, 1100, 740, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.66 (3H, s, Me), 3.97 (3H, s, OMe), 6.60—7.93 (8H, m, ArH); *m/z* 238 (M^+).

reduction of Ti^{IV} chloride with Zn) releases one electron each to the carbonyl functions resulting in pinacolate formation which undergoes subsequent deoxygenation to form the C=C bond.

Although many methods are described in the literature for the synthesis of benzofurans, this route is conceptually different and has not been explored so far. Mild reaction conditions and ready accessibility of the required starting materials are the main features of this synthesis. Application of this method towards the synthesis of naturally occurring benzofuranoid neolignans and other heterocycles will be reported elsewhere.

Received, 16th August 1989; Comm. 9/03515J

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