Synthesis of Ethyl Phenylpyruvate and Related Compounds using Chromium Tricarbonyl Complexes

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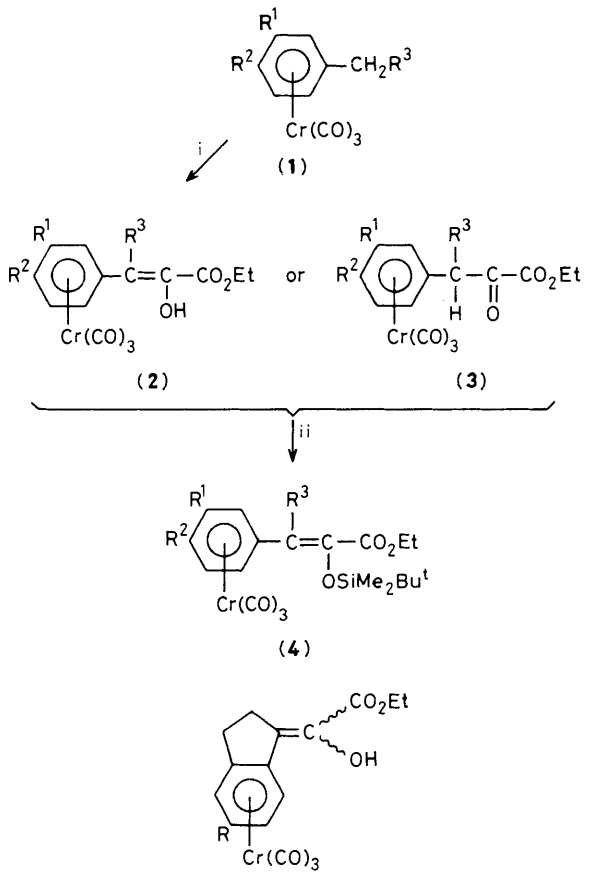
Phenylpyruvate derivatives can be readily obtained as stable enols *via* a new benzylic functionalization of arene $Cr(CO)_3$ complexes.

Despite a recent increase in interest, research into stabilized enols still remains relatively poorly documented.[1] The three principle ways to achieve stabilization of enolic forms involve (i) steric effects, (ii) electron-withdrawing groups, and (iii) conjugation.[2] Therefore, arene chromium tricarbonyl complexes would appear to be suitable substrates to form isolable enols since the bulky $Cr(CO)_3$ moiety is recognized to be an efficient electron-withdrawing unit while preserving aromatic conjugative effects.

We now report the synthesis, *via* chromium tricarbonyl complexation, of ethyl phenylpyruvate trapped in its enolic form, providing a new illustration of enhanced benzylic reactivity as a result of complexation with $Cr(CO)_3$.

The reaction of Bu^tOK with (toluene)$Cr(CO)_3$ (**1**; $R^1 = R^2 = R^3 = H$) in the presence of an equimolar amount of ethyl oxalate at 25 °C in dimethyl sulphoxide (DMSO) under N_2 gives rise, after hydrolysis, to the stable enol (**2**; $R^1 = R^2 = R^3 = H$) in good yield (78%) [m.p. 109 °C, i.r. (CCl_4) ν(OH) 3455 cm^{-1}] (Scheme 1). The base Bu^tOK in DMSO readily allows the formation of α-carbanionic species at $Cr(CO)_3$ benzylic sites.[3] The formation of isolable crystalline enols is not limited to the toluene complexes but can also be extended to alicyclic compounds (see Table 1).



Scheme 1. *Reagents:* i, $(CO_2Et)_2$ followed by Bu^tOK–DMSO; ii, $ClSiMe_2Bu^t$.

It is notable that difunctionalization does not occur with the starting materials (*m*-xylene)$Cr(CO)_3$ or (indan)$Cr(CO)_3$, in the presence of an excess of Bu^tOK and ethyl oxalate. Interestingly, by using (ethylbenzene)$Cr(CO)_3$ (**1**; $R^1 = R^2 = H$, $R^3 = Me$) as a substrate, only the ketonic form (**3**; $R^1 = R^2 = H$, $R^3 = Me$) [i.r. (oil) ν(CO) 1730 (s) and 1750 (sh.) cm^{-1}; ^1H n.m.r. ($CDCl_3$), δ(CH_3) 1.49 (d); δ(ring) 5.44 (m, 3H) and 5.28 (m, 2H); yield 62%] can be characterized. The bulky Me substituent, compared with H in the toluene complex, inhibits the conjugation in this molecule and favours the displacement of the equilibrium towards the ketone thus forming (**3**). It has been reported that steric hindrance usually favours enolic forms by destabilisation of ketonic species.[4] In the present example, clearly the reverse is seen. When (cumene)$Cr(CO)_3$ was used as a substrate, no functionalized product was isolated.

Finally, treatment of the reaction mixture with t-butyldimethylsilyl chloride leads to the isolation, even in the case of

Table 1. Formation of the enols (**2**) and (**5**).[a]

	Enol					
	R^1	R^2	R^3	% Yield	M.p./°C	^1H N.m.r., δ(OH)[c]
(**2**)	H	H	H	78	109	6.62
	H	Bu^t	H	90	110	6.72
	Me	H	H	65	110	6.80
(**5**)	R = H			40	192	6.26
	R = OMe			29 (44[b])	166	3.38

[a] Elemental analyses and mass spectra of all the compounds isolated are consistent with the proposed structures. The reactions are highly stereoselective, producing mainly the *Z*-isomer as shown by *X*-ray crystallography. Yields do not take account of the recovered starting material unless otherwise stated. [b] Recovered starting material taken into account. Ethyl oxalate was added to the previously generated carbanion of the indan complex. The reaction is stereospecific, only one isomer of (**5**) being detected. [c] In $CDCl_3$.

Table 2

	Bu^tMe_2Si derivative	
Starting material	M.p./°C	% Yield[a]
(**1**; $R^1 = R^2 = R^3 = H$)	76	38
(**1**; $R^1 = R^2 = H$, $R^3 = Me$)	82	34
(Indan)$Cr(CO)_3$	122	44
(3-Methoxyindan)$Cr(CO)_3$[b]	99	44

[a] The yields are based on the isolated derivative without taking into account the recovered starting materials. [b] Only one regioisomer was detected.

(**1**; $R^1 = R^2 = H$, $R^3 = Me$) of the corresponding enol ether (Table 2).

The involvement of phenylpyruvate derivatives in mechanistically puzzling enzymic liver reactions has not been lost on us.[5]

We thank Professors R. Sutherland and M. J. McGlinchey for helpful discussions.

Received, 2nd November 1983; Com. 1433

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