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Preliminary communication

IRON-CATALYZED ALLYLIC ALKYLATION

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Summary

Diiron nonacarbonyl has been found to promote the catalytic coupling of allylic acetates with malonate ion in good yields. Preliminary results on the regioselectivity of these reactions argue against a mechanism involving direct nucleophilic attack on either $(\eta^3\text{-allyl})Fe(CO)_4^+$ or $(\eta^2\text{-allyl acetate})Fe(CO)_4$ complexes.

Among the various carbon—carbon bond-forming reactions promoted by transition metals, allylic alkylation has been one of the most aggressively sought after. Accordingly, numerous studies have appeared dealing with the chemo-, regio-, and stereo-selectivity of coupling between activated allyl substrates (e.g. acetates, carbonates) and nucleophiles and the applications of such reactions in synthesis [1a—1e]. Nonetheless, significant new opportunities for improved and/or different regio- and stereo-selectivities still exist [1c,d].

Encouraged by the early reports of Whitesides [2] and Pearson [3] on the regio- and stereo-selective attack on $(\eta^3\text{-allyl})Fe(CO)_4$ cations by amines, phosphines, stabilized enolates and organocadmium reagents and our own observations with activated aromatics [4], we have sought to effect iron-mediated couplings catalytically employing commercially available, cheap, iron carbonyls [5]. We report herein preliminary results of that successful effort.

Having shown earlier the formation of $(\eta^2\text{-allyl acetate})Fe(CO)_4$ (I) from the reaction of $Fe_2(CO)_9$ with allyl acetate [6], we next sought to establish enhanced reactivity of the coordinated substrate by examining the reaction of I with sodium diethylmalonate (NaDEM), our test nucleophile. Indeed, whereas allyl acetate itself is unreactive towards NaDEM in refluxing THF (2 h), its $Fe(CO)_4$ complex I reacts with the same reagent in minutes at room temperature cleanly to produce allyl diethylmalonate (eq. 1).

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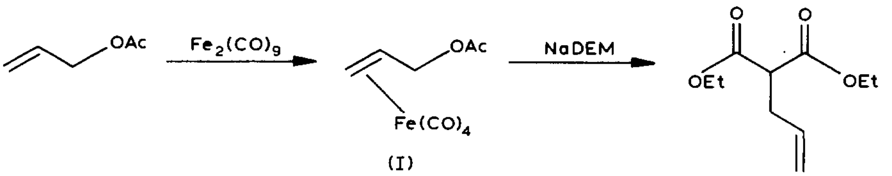
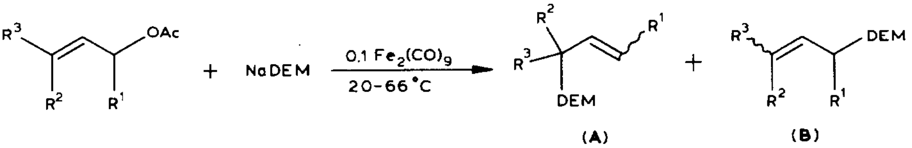


(1)

After demonstrating the viability of the substrate activation and nucleophilic coupling steps, it only remained to be seen if the activating $Fe(CO)_4$ group could be recycled to secure a catalytic process. When allyl acetate and NaDEM (2.0 equiv.*, from NaH and DEM) were stirred at 20°C with 0.1 equiv. $Fe_2(CO)_9$ in THF, GC analysis revealed the gradual appearance of the desired allyldiethyl malonate (74%, 1—3 days). Diethyl ether and toluene proved less satisfactory as reaction solvents, leading to lower rates with poorer catalyst lifetime. The efficacy of THF as a solvent may be due to its ability to stabilize the $Fe(CO)_4$ moiety by coordination** yet to have sufficient lability so as to be displaced by allyl acetate, thus recycling the Fe.

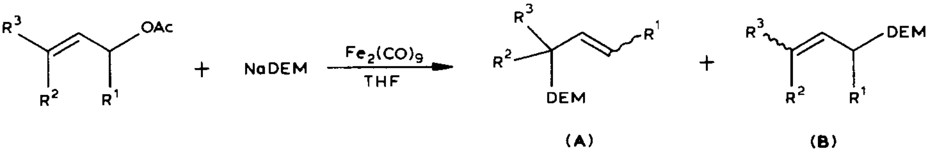
In order to test the generality and regio- and stereo-selectivity of the iron-promoted reaction, we conducted several experiments with the isomeric butenyl acetates (eq. 2, Table 1). Examination of the results in Table 1 reveal the following important features: (1) the reactions proceed under mild conditions in good isolated yield; (2) regioselectivity is modest and temperature depen-



(2)

TABLE 1

ALLYLIC ALKYLATION CATALYZED BY $Fe_2(CO)_9$



Entry	Substrate	*T* (°C)	Time	Yield (%)	% A[b]	% B[b]
1	$R^1 = R^2 = R^3 = H$	20	3—5 day	61(74)	—	—
2	$R^1 = R^2 = H$; $R^3 = Me$	66	24 h	62	64	36(*E*)[c]
3		20	48 h	—	58	42(*E*)[c]
4	$R^1 = R^3 = H$; $R^2 = Me$	66	24 h	84	41	59(*E*)[c]
5		20	4 day	(78)	69	31(*Z*)[d]
6	$R^1 = Me$; $R^2 = R^3 = H$	66	24 h	83	37[e]	63

[a] Isolated yield after aqueous workup followed by flash chromatography over silica gel; GC yields in parenthesis. [b] Determined by GC on OV 101 column; structures assigned on the basis of IR, ^1H and ^{13}C NMR of products isolated by preparative GC; predominant stereoisomer in parenthesis. [c] >95% *E*; no *Z* isomer detectable by ^1H or ^{13}C NMR. [d] >90% *Z*. [e] Undetermined mixture of *E*,*Z* isomers.

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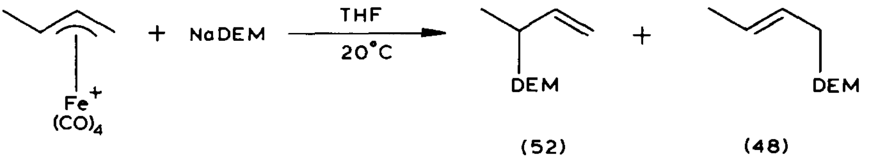
*Used to minimize dialkylation.

**The deep red reaction solutions in THF are characteristic of $Fe_2(CO)_9$/THF [7], believed to contain $(THF)Fe(CO)_4$.

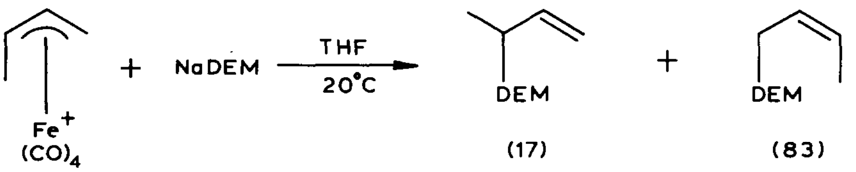
dent; and (3) stereoselective substitution with retention of olefin geometry can be achieved, but requires low reaction temperature in the case of *cis*-butenyl acetate (entry 5).

While the observed regioselectivities are not high, they are comparable to those obtained from DEM (or DMM) + *trans*-dialkyl substituted substrates with most other catalysts (e.g. W [1d]: A/B 76/24; Pd [1a] 65/35; Co [1e] 39/61). The regio- and stereo-selectivities of transition metal mediated allylic alkylations are well known to be very substrate-, nucleophile-, catalyst- and solvent-dependent and the present substrate/nucleophile pair appears to be one of the less selective combinations. Preferential attack of DEM at the more substituted carbon was surprising, nevertheless, since reactions of nucleophiles with $(\eta^3\text{-allyl})Fe(CO)_4^+$ complexes, seemingly likely intermediates, generally result in preferred attack at the less substituted position [2—4]. When the *syn*- and *anti*-methallyl complexes II and III were treated with NaDEM (eq. 3, 4), markedly different regiochemical results were obtained compared to the corresponding iron-catalyzed reactions (cf. entries 3 and 5 in Table 1).



(3)

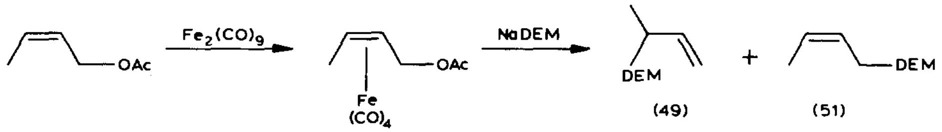
(II)



(4)

(III)

Furthermore, when preformed *cis*-(2-butenyl acetate)$Fe(CO)_4$ was treated with NaDEM at 20°C (eq. 5), the regioisomeric ratio (ca. 1/1) was distinctly different from that obtained in the corresponding catalytic reaction (entry 5).



We are thus forced to conclude that the catalytic reactions do not proceed primarily via direct nucleophilic attack on either $(\eta^3\text{-allyl})Fe(CO)_4^+$ or $(\eta^2\text{-allyl acetate})Fe(CO)_4$ species. It is interesting that allylic alkylations promoted by the isoelectronic $NaFe(CO)_3NO$ apparently do proceed via η^3-allyl complexes [1e].

The capability of achieving stereoselective retention of geometry about the double bond of the substrate (at 20°C) could prove synthetically valuable since both *E*- and *Z*-substrates typically afford *E*-products in the corresponding Pd catalyzed reactions [1a]. Control experiments revealed that whereas *cis*-crotyl acetate was stable under catalytic conditions (refluxing THF, 0.1 equiv. $Fe_2(CO)_9$, DEM^-), under the same conditions isomerization of the products occurred, accounting for the observed temperature dependent regio- and stereo-selectivity (entries 4, 5).

Efforts are underway to establish the scope and generality of allylic alkylations catalyzed by $Fe_2(CO)_9$, to probe further their mechanisms, and to demonstrate their utility in synthesis.

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