

Le Maux and G. Jaouen, unpublished results.
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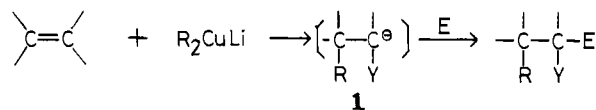
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Zinc-Promoted One-Step Joining Reaction of Alkyl Halides, Activated Olefins, and Carbonyl Compounds

Sir:

Conjugate addition of organocopper reagents has been accepted as a versatile tool to introduce an alkyl group into the



Y: electron-withdrawing group
 E: electrophile

β -position of α,β -conjugated olefinic systems.¹ The trapping of the anionic intermediate **1** with electrophiles² other than alkylating agents³ has also been shown in some syntheses. The organocopper reagents, however, are not necessarily simple in their preparation and operation.

We wish to report a novel zinc-promoted joining reaction^{4,5} of three components consisting of alkyl halides **2**, activated olefins **3**, and carbonyl compounds **4**. This one-step joining reaction is characterized by remarkable simplicity and high yield. The reaction may proceed through formation of an anionic species from **2** followed by addition of the anion to **3** and

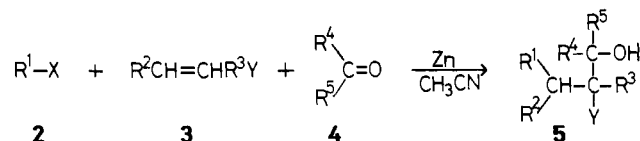



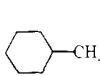


Table I. One-Step Joining Reaction of Three Components **2**, **3**, and **4** in Acetonitrile^a

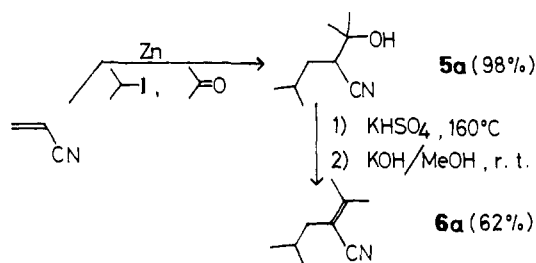
Halide 2 , R ¹ X	Activated Olefin 3			Carbonyl Compound 4		Product 5	Yield, ^b %
	R ²	R ³	Y	R ⁴	R ⁵		
(CH ₃) ₂ CHI	H	H	CN	CH ₃	CH ₃	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)C(CH ₃) ₂ (5a ^f)	98
(CH ₃) ₂ CHI	H	H	CN	C ₆ H ₅	H	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)CHC ₆ H ₅ (5b)	94
(CH ₃) ₂ CHI	H	H	CN	(CH ₂) ₅		(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)(CH ₂) ₅ (5c)	99
(CH ₃) ₂ CHI	H	H	CN	(CH ₂) ₄		(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)(CH ₂) ₄ (5d)	92
(CH ₃) ₂ CHI	H	H	CN	C ₂ H ₅	H	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)CH ₂ CH ₃ (5e)	65
	H	H	CN	CH ₃	CH ₃	 (5f)	95
CH ₃ CH ₂ CH ₂ I	H	H	CN	CH ₃	CH ₃	CH ₃ CH ₂ CH ₂ CH ₂ CH ₂ CH(OH)C(CH ₃) ₂ (5g)	63
CH ₃ I	H	H	CN	CH ₃	CH ₃	CH ₃ CH ₂ CH ₂ CH ₂ CH(OH)C(CH ₃) ₂ (5h ^d)	52
C ₆ H ₅ CH ₂ Br	H	H	CN	CH ₃	CH ₃	C ₆ H ₅ CH ₂ CH ₂ CH ₂ CH(OH)C(CH ₃) ₂ (5i)	46
(CH ₃) ₂ CHI	CH ₃	H	CN	C ₆ H ₅	H	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)CHC ₆ H ₅ (5j)	95
(CH ₃) ₂ CHI	H	CH ₃	CN	C ₆ H ₅	H	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)C(CH ₃)CHC ₆ H ₅ (5k)	73
(CH ₃) ₂ CHI	H	CH ₃	CN	CH ₃	CH ₃	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)C(CH ₃) ₂ (5l ^f)	72
(CH ₃) ₂ CHI	H	H	COOCH ₃	CH ₃	CH ₃	(CH ₃) ₂ CHCH ₂ CH ₂ CH(OH)C(CH ₃) ₂ (5m)	57
	H	H	COOCH ₃	CH ₃	CH ₃	 (5n)	52

^a The molar ratios of **2**, **4**, and zinc to **3** were 3.0, 3.0, and 5.0, respectively. ^b Isolated yields. ^c Substitution of isopropyl iodide with isopropyl bromide resulted in the decrease in the yield (31%) of **5a**. ^d The molar ratio of **2** to **3** was 5.0. ^e Acetone was used as solvent. An unexpected product, (CH₃)₂CHCH₂C(CN)(CH₃)COCH₃ was obtained in acetonitrile, the yield being 42%.⁸

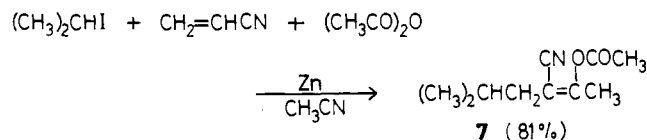
subsequent nucleophilic attack of the intermediate to **4**.

A typical procedure is as follows. Under an atmosphere of nitrogen, a mixture of 2.40 g (37 mmol) of zinc powder,⁶ 0.50 mL (7.6 mmol) of freshly distilled acrylonitrile, 1.70 mL (23 mmol) of acetone, and 14 mL of acetonitrile was refluxed with stirring, and 0.55 mL (5.5 mmol) of isopropyl iodide was added slowly to the mixture. After a short period, an exothermic reaction took place. After the vigorous reaction subsided, an additional 1.65 mL (16.5 mmol) of isopropyl iodide was added dropwise over 10 min, and the mixture was refluxed for 4–5 h. The usual workup gave the β -hydroxy nitrile **5a** in a 98% yield: bp 74–75 °C (1.0 mm); NMR (CCl₄) δ 0.98 (d, 3 H, >CHCH₃), 1.08 (d, 3 H, >CHCH₃), 1.32 (s, 3 H, >C(OH)-CH₃), 1.35 (s, 3 H, >C(OH)CH₃), 1.40–1.75 (m, 2 H, -CH₂-), 1.74–2.10 (m, 1 H, >CH-), 2.60 (d of d, 1 H, >CHCN), 3.00 (br s, 1 H, -OH); IR (neat) 3430–3390, 2240, 1385, 1365, 1140–1160 cm⁻¹. Anal. Calcd for C₉H₁₇ON: C, 69.63; H, 11.04; N, 9.02. Found: C, 69.90; H, 11.24, N, 8.96. In a similar manner, β -hydroxy nitriles **5a–l** and esters **5m,n** were obtained in satisfactory yields as shown in Table I.⁷

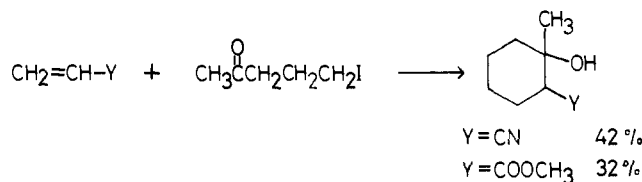
It is noteworthy that the reaction is feasible for a variety of compounds **2** or **4**. The dehydration of the product **5a** gave readily the activated olefin **6a**.⁷



Similar to ketones and aldehydes, acetic anhydride behaved as an electrophile yielding the expected cyanoenol acetate **7**⁷ in a good yield. Furthermore, the pattern of the joining reaction suggests the feasibility of some types of cycloaddition. Indeed,



the zinc-promoted reaction of 5-iodopentan-2-one with acrylonitrile or methyl acrylate gave the corresponding cycloaddition product⁷ in a reasonable yield.



In view of its simplicity and generality, this three-components joining reaction seems one of the promising methods for the synthesis of such selective aldol-type compounds as the conventional condensation between carbonyl compounds and esters or nitriles scarcely yields.⁹ The application of this novel joining reaction to synthesis is in progress.

References and Notes

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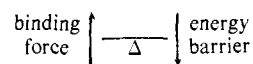
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On Binding to Transition States and Ground States: Remote Catalysis

Sir:

How binding forces increase reaction rates is a crucial question in catalysis, particularly enzymic catalysis. Many recent models use binding forces to reduce entropies of activation *before* a process occurs.¹ In this communication we demonstrate how binding forces may be used *as* a process occurs, with maximum binding at the transition state.² To ensure that binding and activation are simultaneous, we have constructed a molecular lever in which these forces are mechanically coupled.



The design of such a mechanism requires knowledge of transition-state geometry and the racemization of biphenyl derivatives is a process for which reasonable inferences regarding this geometry may be drawn.³ In cyclic systems, e.g., **1**, the transition state for racemization is reached when the two aromatic rings become coplanar. The reaction coordinate is θ , the dihedral angle defined by the aromatic ring planes, and the transition state occurs at $\theta = 0^\circ$. In **1** the process is most easily monitored by DNMR; racemization occurs with inversion of the cycloheptatriene ring and the environments of the *gem*-dimethyl groups are exchanged. Sutherland⁴ has reported that coalescence of the *gem*-dimethyl singlets of **1** occurs at 102 °C with $\Delta G^\ddagger = 18.8$ kcal/mol for the racemization process.

