

Alkenylation and Allylation of Aldehydes by Using an Ni/Cr/TDAE Redox System

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Cross-coupling of aldehydes with alkenyl and/or allyl bromides was promoted with tetrakis(dimethylamino)ethylene (TDAE) and a catalytic amount of NiBr₂ and CrCl₃ to afford the corresponding allyl and homoallyl alcohols, respectively, in good to excellent yields.

1. INTRODUCTION

An electron source and a catalytic amount of redox-active compounds constitutes electron-transfer systems exhibiting unique reactivity. Transition metals, having many oxidation stages, are redox active, and a combination of reductant and high-valent transition metal reagents provides a very active low-valent transition metal species. Under proper conditions, the redox cycle of the transition metal behaves as an electron-transfer catalysts. Moreover, reactivity and product selectivity are highly dependent on the component of the systems. Among them, we have focused our attention on combinations of aluminium and a metal salt catalyst because aluminium is 1) a potent reductant, 2) cheap, and 3) easy to handle. A combination of Al and metal salt catalyst, such as AlCl₃, AlBr₃, PbBr₂, and PbBr₂-NiCl₂(bpy), could be used successfully in construction of cephem derivatives.¹ In this system, Al was oxidized to generate Al³⁺, and the dissolved Al³⁺ acts as a Lewis acid, which sometimes accelerates the reactions and/or causes undesired side reactions. The system is heterogeneous, and electron transfer from Al is not always efficient.

Tetrakis(dimethylamino)ethylene (TDAE) has a reducing power close to zinc.² Standard redox potential of TDAE was measured in DMF to be -0.62 V vs SCE (a two-electron reversible peak). Therefore, we attempted to use TDAE as an electron source for new electron-transfer system involving transition metal catalysts (M1, M2) (Fig. 1).

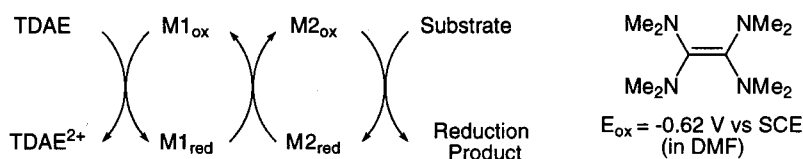


Fig. 1. Electron-Transfer System Using TDAE as an Electron Source.

The Cr-Ni promoted alkenylation and allylation of carbonyl compounds proceed in a highly chemoselective manner under very mild conditions,³ and have been used in the synthesis of complex natural products.⁴ The drawback of this system, however, is that large excess (400 mol%) of CrCl₂ is usually needed, which may cause serious environmental problems. If Cr(III) generated during the course of the

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reaction can be reduced *in situ* efficiently, only a catalytic amount of Cr reagent is sufficient to complete this reaction. Reduction of Cr with Mn^{5a} and Al,^{5b} and by electroreduction^{5c, 5d} were recently reported. We report herein that TDAE can be used as an electron source for this Cr-catalyzed coupling reaction (Fig. 2). Since CrCl₂ is highly sensitive to moisture and O₂, stable CrCl₃ was chosen as a Cr source.

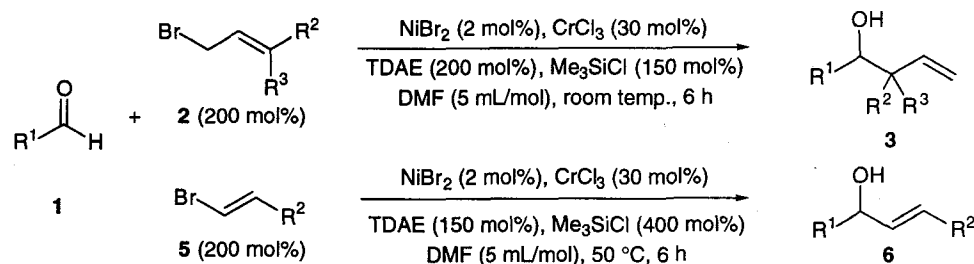


Fig. 2. TDAE/Ni/Cr Promoted Cross-Coupling Reaction of Aldehydes R'CHO with Allyl and/or Alkenyl Halides

2. RESULTS AND DISCUSSION

2-1. Allylation of Aldehydes

A typical procedure for allylation is as follows: To a mixture of *p*-anisaldehyde **1a** (1.5 mmol), allyl bromide **2** (3.0 mmol), CrCl₃ (30 mol%, Katayama Chemical Co.), NiBr₂ (2 mol%, Katayama Chemical Co.), and Me₃SiCl (150 mol%) was added TDAE (200 mol%) at room temperature. The mixture was stirred for 6 h at room temperature. After usual work-up, homoallyl alcohol **3a** was obtained in 94% yield (Table 1, Entry 1). The undesired methylated product **4a** was obtained in low yield when the reaction was performed with more excess of Me₃SiCl (450 mol%, Entry 2) and/or at higher temperature (50 °C, Entry 3). The yield of the desired product decreased when the reaction was carried out in THF (Entries 4, 5).

Table 1. Allylation of Aldehydes. Optimization of the Reaction Conditions

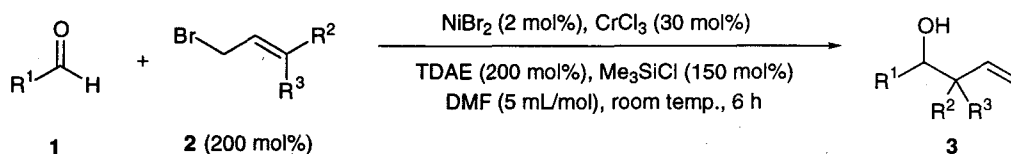
Entry	Solv	TDAE /mol%	Me ₃ SiCl /mol%	Temp /°C	Yield/% ^a	
					3a	4a
1	DMF	200	150	room temp	94	- ^b
2	DMF	400	450	room temp	57	8
3	DMF	400	450	50	76	1
4	THF	400	450	room temp	29	6
5	THF	400	450	50	44	5

^aIsolated yield. ^bNot detected.

Representative results of allylation of aldehydes **1** in the TDAE/CrCl₂/NiBr₂/DMF system are shown in Table 2. The allylation proceeded with both aromatic (Entries 1-5, 7) and aliphatic (Entry 6) aldehydes. Aromatic aldehydes bearing electron-donating substituents gave the corresponding allyl alcohol derivatives in good yields, whereas electron-poor aromatic aldehydes such as *p*-cyanobenzaldehyde gave poor results,

affording the corresponding pinacol derivatives predominantly. The cross-coupling reaction of *p*-anisaldehyde and prenyl bromide proceeded at γ -position of prenyl bromide to give 1-(4-methoxyphenyl)-2,2-dimethyl-3-buten-1-ol (**3g**) in 48% yield.

Table 2. TDAE/Ni/Cr Promoted Allylation of Aldehydes



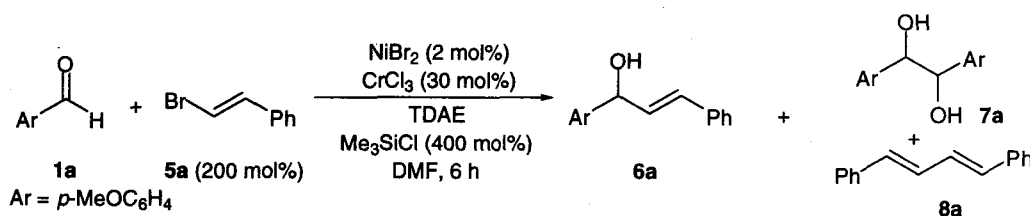
Entry	R ¹	R ²	R ³	reaction time/h	Yield of 3 /%
1	Ph	H	H	3.5	3a 70
2	4-MeOC ₆ H ₄	H	H	24	3b 94
3	2,3-(OCH ₂ O)C ₆ H ₃	H	H	1.5	3c 89
4	4-MeC ₆ H ₄	H	H	4	3d 75
5	4-ClC ₆ H ₄	H	H	3	3e 86
6	PhCH ₂ CH ₂	H	H	2	3f 72
7	4-MeOC ₆ H ₄	Me	Me	24	3g 48

^aIsolated yield.

2-2. Alkenylation of Aldehydes

Alkenylation of aldehydes using TDAE/Cr/Ni system was also investigated. A typical procedure for alkenylation is as follows: To a mixture of *p*-anisaldehyde **1a** (1.5 mmol), β -bromostyrene **5a** (3.0 mmol), CrCl₃ (30 mol%, Katayama Chemical Co.), NiBr₂ (2 mol%, Katayama Chemical Co.), and Me₃SiCl (400 mol%) was added TDAE (150 mol%). The mixture was stirred at 50 °C for 6 h. After usual work-up, allyl alcohol **6a** was obtained in 83% yield (Table 3. Entry 4). In contrast to allylation, alkenylation hardly proceeded at room temperature (Entry 1). When large excess of TDAE was used, the desired allyl alcohol derivatives **6a** was obtained in high yield (800 mol%, 77%; 400 mol, 91%) along with diene **8a** (~ 5%) as a side product (Entries 2, 3). The yield of **6a** decreased in 51% when 100 mol% of TDAE was used (Entry 5).

Table 3. Cross-Coupling of *p*-Anisaldehyde with β -Bromostyrene

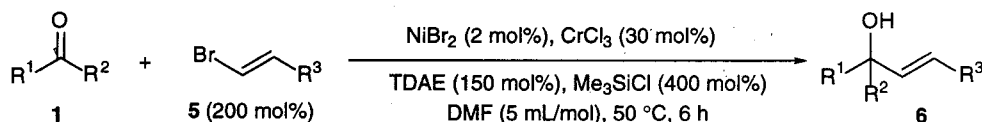


Entry	TDAE /mol%	Temp /°C	Yield/% ^a			
			6a	7a	8a	1a
1	800	room temp	8	- ^b	- ^b	51
2	800	50	77	- ^b	6	15
3	400	50	91	- ^b	4	- ^b
4	150	50	83	- ^b	- ^b	- ^b
5	100	50	51	5	- ^b	23

^aIsolated yield. ^bNot detected.

Representative results of alkenylation of aldehydes **1** in the TDAE/CrCl₂/NiBr₂/DMF system are summarized in Table 4. The alkenylation proceeded with aromatic aldehydes. Aromatic aldehydes bearing electron-donating substituents gave allyl alcohol derivatives (Entries 1-4, 6) in good yields, whereas electron-poor aromatic aldehydes such as *p*-cyanobenzaldehyde gave poor results (Entry 5), affording the corresponding pinacol derivatives predominantly. No pinacol product, 1,2-bis(4-chlorophenyl)-1,2-ethanediol, was obtained from *p*-chlorobenzaldehyde. On the other hand, when Al was used as an electron source in place of TDAE, cross-coupling of *p*-chlorobenzaldehyde and vinyl bromide gave 1-(4-chlorophenyl)-2-propen-1-ol in only 25% yield, and a considerable amount of the pinacol product was formed.^{5b} The chemoselectivity of this reaction was high: No reaction occurred when either 3-phenylpropanal (Entry 7, aliphatic aldehyde) or acetophenone (Entry 8, ketone) was used as a substrate.

Table 4. Alkenylation of Aldehydes by Using TDAE/Ni/Cr System



Entry	R ¹	R ²	R ³	Yield of 6 ^a
1	Ph	H	Ph	6a 75
2	4-MeOC ₆ H ₄	H	Ph	6b 96
3	2,3-(OCH ₂ O)C ₆ H ₃	H	Ph	6c 73
4	4-ClC ₆ H ₄	H	Ph	6d 66
5	4-NCC ₆ H ₄	H	Ph	6e 5
6	4-MeOC ₆ H ₄	H	H	6f 62
7	PhCH ₂ CH ₂	H	Ph	6g 0
8	Ph	Me	Ph	6h 0

^aIsolated yield.

2-3. Dimerization of Alkenyl Halide

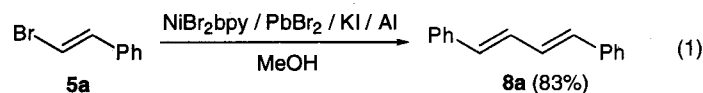
A combination of TDAE and a catalytic amount of NiBr₂ promoted dimerization of β-bromostyrene **5a** to give 1,4-diphenyl-1,3-butadiene **8a** in good yield (Table 5). When a mixture of **5a**, TDAE, and a catalytic amount of NiBr₂ in DMF was heated to 50 °C for 6 h, the homo-coupling product **8a** was obtained in 90% yield.

Table 5. Homo-Coupling of β-Bromostyrene Using TDAE/Ni System

Entry	Reagents / mmol					Time / h	Yield of 8a ^a / %
	NiCl ₂ bpy	NiBr ₂	KI	PbBr ₂	TDAE		
1	0.1	0	0.1	1.5	2.0	24	97
2	0	0.1	0	0	2.0	24	98
3	0	0.1	0	0	2.0	12	93
4	0	0.1	0	0	2.0	6	90

^aIsolated yield.

The similar reaction occurred with Al as an electron source in the presence of NiBr₂•bpy, PbBr₂, and KI (eq. 1, Entry 1 of Table 5).⁶ TDAE/Ni system presented much simpler way.



Synthesis of dienes *via* homo-coupling of alkenyl halides was listed in Fig. 3. Stereochemistry of the starting alkenyl halides was retained during the reaction: *E,E*-Dienes **8a-8d** were obtained from *E*-alkenyl bromides **5a-5d**, whereas *Z,Z*-diene **8e** was afforded from the corresponding *Z*-alkenyl iodide **5e**.

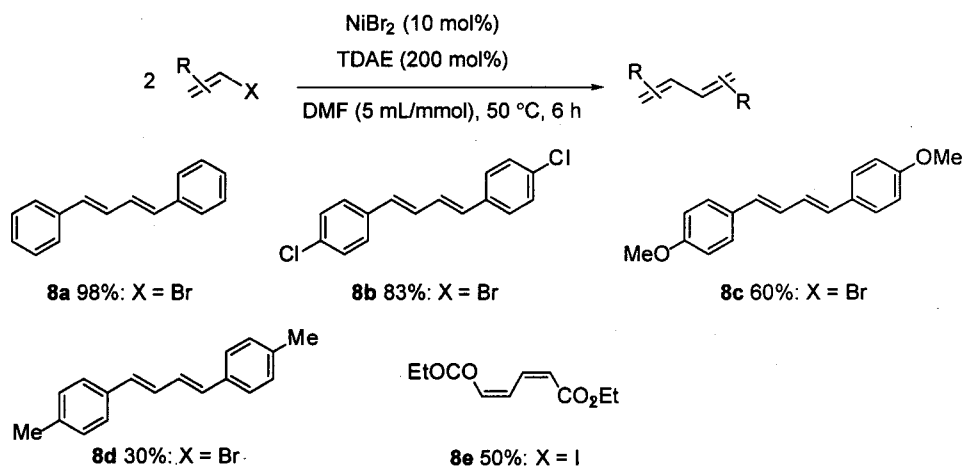
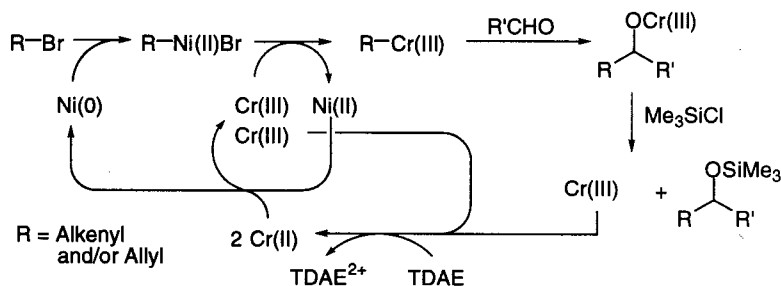


Fig. 3. Homo-Coupling of Alkenyl Halides Using TDAE/Ni System

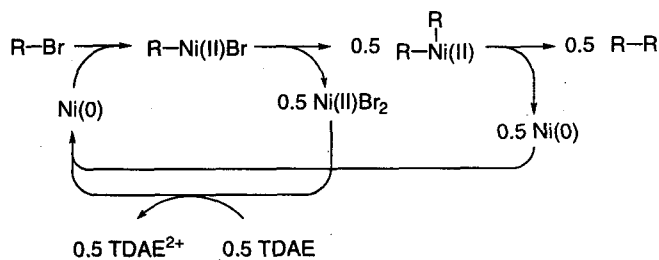
2-4. A Plausible Mechanism of Cross-Coupling

According to the literature,³ the mechanism of the cross-coupling of aldehydes and allyl and/or alkenyl halides was considered as follows (Fig. 4): On addition of TDAE, purple Cr(III) salt turned into green Cr(II). Therefore, Cr(III) was reduced to Cr(II) with TDAE. Reduction of Ni(II) with thus generated Cr(II) and/or TDAE would generate Ni(0) species, which may react with allyl and/or alkenyl bromide to afford the corresponding organonickel species. Transmetalation of the organonickel compound with Cr(III) species might afford the corresponding organochromium species, which would react with aldehydes to give the corresponding cross-coupling products, Cr-alkoxide. Chlorotrimethylsilane would liberate the Cr(III) species from thus generated Cr-alkoxide.



Scheme 1. A Plausible Mechanism of TDAE/Ni/Cr Promoted Cross-Coupling of Aldehydes and Alkenyl and Allyl Halides

In the absence of Cr salt, TDAE may reduce Ni(II) to Ni(0), which would react with organohalide to give the corresponding organonickel species. Disproportionation of the organonickel halide might give diorganonickel and nickel(II) bromide. Reductive elimination of the former, R-Ni(II)-R, would give the homo-coupling product, R-R, together with Ni(0) species.



Scheme 2. A Plausible Mechanism of Ni/TDAE Promoted Homo-Coupling of Alkenyl Halide

3. CONCLUSIONS

TDAE can act as a potent electron source, and electron-transfer system consisted with TDAE and Cr-Ni works smoothly to promote allylation and alkenylation of aldehydes.

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