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New Preparation of Reactive Zinc Metal by Electrolysis and Its Use for A Facile Isoprenylation of Aldehydes and Ketones

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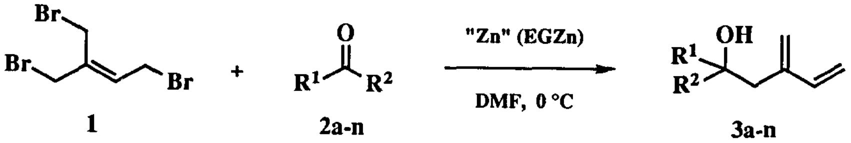
Abstract: Reactive zinc metal can be prepared by the electrolysis of a DMF solution containing Et_4NClO_4 with a platinum cathode and a zinc anode. The reaction of 2-bromomethyl-1,4-dibromo-2-butene (**1**) with aldehydes or ketones in the presence of the electrogenerated reactive zinc (EGZn) in DMF at 0 °C gave the corresponding isoprenylated alcohols (**3a-3n**) in good yields.

Various methods of zinc activation, such as the reduction of zinc halide with alkaline metal, itself, or alkali metal naphthalenide, have been reported.[1] They, however, require high temperatures and long reaction times. Perichon and colleagues recently reported that they prepared a small amount of active zinc by a cathodic reduction of zinc bromide in acetonitrile, and carried out the Blaise reaction in the presence of a catalytic amount of the active zinc under electrolytic or nonelectrolytic conditions.[2] Their report prompts us to report our results concerning a new preparation of activated zinc metal by electrolysis, and its use in the convenient isoprenylation of aldehydes and ketones.[3] Isoprenylated compounds are widely distributed in nature and are useful precursors for the Diels-Alder reaction.[4] These compounds have been prepared by a direct isoprenylation of various electrophiles with metalated isoprenes derived from unstable 2-halomethyl-1,3-butadiene[5] (prepared in low yield by a tedious procedure[5c, 5e, 5h, 6] and was difficult to purify). Our new isoprenylation of aldehydes and ketones uses a combination of 2-bromomethyl-1,4-dibromo-2-butene (**1**) as the source of the isoprene unit and electrogenerated reactive zinc (EGZn), as outlined in Scheme 1. Tribromide **1** can be readily prepared by the 1,4-addition of bromine to isoprene followed by allylic bromination,[5f] and is easily purified by distillation.



Scheme 1

Reactive zinc metal was readily prepared by the electrolysis of a DMF solution containing 0.1M Et_4NClO_4 in a one-compartment cell fitted with a platinum plate cathode (2x3 cm^2) and a zinc plate anode (2x3 cm^2).

Electrolysis was carried out at a constant current of 25 mA/cm^2 at 0 °C under a nitrogen atmosphere. The electrolysis resulted in an anodic dissolution of a zinc anode to give zinc ions, which were reduced at a platinum cathode to give a zero-valent reactive zinc. Electrogenerated reactive zinc (EGZn) was initially deposited on the platinum cathode and dispersed in a DMF solution at the end of the electrolysis. The metal thus obtained was so reactive that hydrogen gas was evolved when water was added to the solution. After the electrolysis, the zinc anode was removed from the electrochemical cell and a solution containing EGZn was immediately used for isoprenylation at 0 °C.

The isoprenylation of isovaleraldehyde (**2e**) with **1** in a cell containing EGZn under various conditions is summarized in Table 1. The reaction of **1** with 3 equiv. of **2e** in the presence of 2.6 equiv. of EGZn[7] at 0 °C gave a highest yield (85%) of the isoprenylated carbinol, ipsenol (**3e**) (run 3). The isoprenylation of various aldehydes (**2a-2i**) and ketones (**2j-2n**) under the same conditions as those of run 3 (Table 1) gave the corresponding isoprenylated carbinols (**3a-3n**)[8] in isolated yields of 23-99% (Table 2). A carbon-carbon double bond conjugated with a carbonyl in **2f**, **2g**, **2h**, **2k**, and **2m** was inert under the present reductive conditions and the corresponding isoprenylated carbinols were obtained in good yields. The isoprenylation of straight-chain aldehydes **2b**, **2c**, and **2d** gave **3b**, **3c**, and **3d** in 72-99% yield, although the reaction of these aldehydes with metalated isoprene has been reported to give the isoprenylated products in 20-38% yields, probably due to an aldol condensation of the aldehydes.[5c, 5h]

The isoprenylation of isovaleraldehyde (**2e**) with tribromide **1** in the presence of commercially available zinc powder under the same conditions as those of runs 3 and 5 (Table 1) or in THF containing ordinary zinc powder under reflux gave **3e** in lower yields (38-25%).

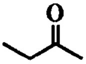
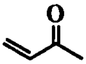
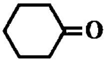
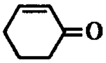
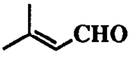
The present synthesis of isoprenylated products, ipsdienol (**3g**) and ipsenol (**3e**), which are the principal components of the aggregation pheromones of a bark beetle, *Ips paraconfusus* Lanier,[5e,9] is, to our knowledge, one of the simplest methods among a number of methods[5b-f,5h-j,10,11] including chiral synthesis of these pheromones.[12]

Table 1. Isoprenylation of Isovaleraldehyde (**2e**) with 2-Bromomethyl-1,4-dibromo-2-butene (**1**) in the presence of an Electrogenerated Reactive Zinc (EGZn) under Various Conditions[a]

run	EGZn (equiv.)[b]	Temp. (°C)	Time (h)	Yieldof **3c**[c] (%)
1	1.1	0	2	11
2	2.1	0	2	51 (36)[d]
3	2.6	0	2	85 (68)[d]
4	3.1	0	2	80
5	2.1	23	2	47 (37)[d]
6	2.1	23	8	67
7	2.6	23	2	46

a) A mixture of **1** (3 mmol) and **2e** (9 mmol) in DMF (30 ml) was stirred in the presence of EGZn.
b) Mol of EGZn per mol of **1**.[7]
c) NMR yield using an internal standard (dibenzosuberone).
d) Isolated yields.

Table 2. Isoprenylation of Aldehydes and Ketones with Tribromide **1** in the Presence of Electrogenerated Zinc (EGZn)[a]

$R^1R^2C=O$ (**2**)	Yield of **3** (%)[b]	$R^1R^2C=O$ (**2**)	Yield of **3** (%)[b]
$(HCHO)_n$ (**2a**)	34	 (**2h**)	62
 (**2b**)	72	**PhCHO** (**2i**)	72
 (**2c**)	75	 (**2j**)	23 (62)[c]
 (**2d**)	99	 (**2k**)	36
 (**2e**)	67 (85)[c]	 (**2l**)	83
 (**2f**)	71	 (**2m**)	57
 (**2g**)	58 (84)[c]	$PhCOCH_3$ (**2n**)	48 (95)[c]

a) A mixture of **1** (3 mmol), **2** (9 mmol), and EGZn (7.7 mmol) in 30 mL of DMF was stirred at 0 °C for 2 h

b) Isolated yields by TLC.

c) NMR yields using an internal standard (dibenzosuberone).

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7. Electrolysis of a DMF solution using a platinum cathode and a zinc anode with the passage of 1450 Coulombs resulted in a dissolution of 7.8 mmol of zinc anode. The amount of the dissoluted zinc metal corresponds to 2.6 equivalents of EGZn per mol of **1** to be used (3 mmol) if it is assumed that all of the dissoluted zinc metal was converted to zero-valent reactive zinc (EGZn).
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