還元反応を抑制する *α*-ケトアミドの *O*-アルキル化反応の開発

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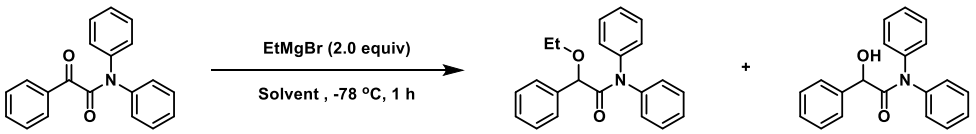
O-Alkylation of *α*-Ketoamides Suppressing the Hydride Reduction (*Graduate School of Engineering, Mie University*) ○Maika Yasue, Ayaki Yamamoto, Isao Mizota

Ether (R-O-R') is one of the most fundamental class of organic compounds widely existing around us. Among them, α-alkoxy carbonyl compounds are very important skeletons in that they are found in natural products and biologically active compounds, and are also synthetic intermediates of such compounds. In particular, α-alkoxy amides are known as compounds having fungicidal and PDE10A inhibitory (antipsychotic) effects, and many synthetic methods have been reported so far. We have already developed umpolung reactions of α-imino esters (*N*-alkylation) and integrated reactions utilizing *N*-alkylation. In this study, we examined the umpolung reaction (*O*-alkylation) of α-ketoamides suppressing the hydride reduction from Grignard reagents.
Keywords : α-Ketoamide; Umpolung Reaction; O-Alkylation; α-Alkoxy Carbonyl Compound; Hydride Reduction

当研究室では *α*-イミノエステルに対する *N*-アルキル化反応が円滑に進行することを見出し、多くの反応集積化に成功している。[1,2]今回 *α*-ケトアミドに対する極性転換反応（*O*-アルキル化）において副生成物である還元体を抑制し選択的に *O*-アルキル化が進行する条件を検討したので報告する。

α-ケトアミド **1** に対しエチル Grignard 反応剤を 2.0 当量、また様々な種類の溶媒や添加剤を用いて、-78 ℃で 1 時間反応させ、副生成物 **3** である還元体とともに目的の *O*-エチル化体 **2** を得た。



1 2 3

Entry	Solvent	Yield (%) 2	3	Entry	Solvent	Yield (%) 2	3
1	DCM	40	51	4	Xylene	44	42
2	Benzene	31	16	5	Mesitylene	50	23
3	Toluene	33	21	6	Pyridine	23	17

1) I. Mizota, M. Shimizu, *Chem. Rec.* **2016**, *16*, 688.
2) I. Mizota, Y. Nakamura, S. Mizutani, N. Mizukoshi, S. Terasawa, M. Shimizu, *Org. Lett.* **2021**, *23*, 4168.