Diethyl Acetylenedicarboxylate

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Introduction

Diethyl acetylenedicarboxylate (1) is a light yellow liquid which has a disagreeable smell. It is a cheap and readily available material in industry. The triple bond is a critical and useful functional group, and it has extensive applications in organic synthesis. It can react with amines, aldehydes, ketones, etc. Therefore it can be used to form various heterocycles. This article mainly reviews the major applications of diethyl acetylenedicarboxylate in the synthesis of heterocycles, as well as some improvements in reaction conditions. Diethyl acetylenedicarboxylate (1) can be prepared using different methods. For example, it can be prepared using a mixture of (Z)-diethyl-2,3-dibromomaleate and (E)-diethyl-2,3-dibromofumarate in the presence of 1,2-dimethylindazolium-3-carboxylate (2) in acetonitrile under reflux within 45 min.1 It can also be prepared using triphenylphosphonium ylides (Scheme 1)2.

Table 1 Use of Diethyl Acetylenedicarboxylate

(A) Self-condensation reaction:
A one-pot reaction of aldehydes, amines and 1 can be realized in the presence of acetic acid at room temperature. Good to excellent yields are achieved within short times. These product skeletons show a wide range of biological activities, such as antimicrobial, anti-inflammatory, anticancer, and anti-viral HIV-1.3

(B) Mannich reaction catalyzed by ammonium salt:
Sajadikhah and Hazeri reported that, with the help of [n-Bu₄N][HSO₄], the Mannich (one-pot) reaction of amines, 1 and formaldehyde can be achieved with excellent yield in methanol at ambient temperature. The isolation of the reaction product is possible without column chromatography.4

(C) Reaction with dicarbonyl compounds:
In 2012, Cao’s group found that DABCO is a convenient catalyst for the reaction between 1,3-dicarbonyl compounds and 1. DABCO showed high catalyst efficiency in the formation of C–C bond Michael addition.5

Scheme 1 Synthesis of diethyl acetylenedicarboxylate (1)
(D) Rhodium-catalyzed linear cross-trimerization: Kobayashi and Tanaka reported the cross-trimerization of an alkene, 1 and a different alkyn which is catalyzed by cationic rhodium(I)-biaryl bishphosphate complexes. The products turned out to be linear and were formed with excellent enantioselectivity.6

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\begin{align*}
\text{R}^1 & \quad \text{CO}_2\text{Et} \\
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{CH}_2\text{Cl}_2, \text{r.t.}, 24 \text{ h} & \quad \text{EtO}_2\text{C} \\
10 \text{ mol\% } \text{[Rh(cod)\text{BF}_4]} & \quad (\text{R})-\text{BINAP} \\
\Delta & \quad \text{EtO}_2\text{C} \\
68-95\% \text{ ee} & \quad 21-66\% \text{ yield}
\end{align*}
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References

(2) 2011, 1004, 284.