Diethyl Acetylenedicarboxylate

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Rui-Xia Yang was born in Yunnan, China, in 1991. She received her B.Sc. in applied chemistry in 2014 from Yunnan University. Under the supervision of Prof. Jun Lin and Prof. Sheng-Jiao Yan, she is currently working towards her M.Sc. at the same university. Her research interests focus on the synthesis of heterocyclic compounds and their applications.

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

<table>
<thead>
<tr>
<th>Method</th>
<th>Reaction Product</th>
<th>Conditions</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Self-condensation reaction:</td>
<td></td>
<td>Ni catalyst, PhMe, 23 or 80 °C</td>
<td>96% yield</td>
</tr>
<tr>
<td>(B) Mannich reaction catalyzed by ammonium salt:</td>
<td></td>
<td>[n-Bu₄N][HSO₄] (10 mol%) MeOH, r.t.</td>
<td>79–81% yield</td>
</tr>
<tr>
<td>(C) Reaction with dicarbonyl compounds:</td>
<td></td>
<td>DABCO DMF, 80 °C, 1 h</td>
<td>80–88% yield</td>
</tr>
</tbody>
</table>

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 alkene which is catalyzed by cationic rhodium(1)-
biaryl bishosphine complexes. The products turned out to be linear
and were formed with excellent enantioselectivity.9

(Rhcod)2BF4 / (R)-BINAP

10 mol% 1
CH2Cl2, r.t., 24 h

68–95% ee

21–66% yield

(85–92% yield

[bmim]BF4

(O86–96% yield

88–91% yield

H2O–EtOH

(51x246)References

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(E) Synthesis of 1-phenyl-1H-azepines:
Ramesh et al. showed a new method to synthesize N-substituted azepines. In the presence of β-cyclodextrin, aromatic amine, 1, and
2,5-dimethoxytetrahydrofuran react well and with very good yield
in water under neutral conditions. Besides, β-cyclodextrin can be
recycled and reused, and shows high catalysis efficiency.7

β-H2O

50–60 °C

R1, R2 = H, Ph, Me, Ph, etc.

80–92% yield

82–91% yield

(F) Synthesis of spiro-pyranopyrazoles:
Pore et al. utilized a green path to synthesize a wide range of novel
spiro-pyranopyrazole derivatives without catalyst. The one-pot
reaction of 1, hydrazine hydrate, malononitrile and iscan can be
conducted at room temperature in a mixed green solvent (H2O–
EtOH = 80:20) and leads to the product in very good yield.8

(G) Synthesis of pyroles:
Siddiqui et al. found that ionic liquid [bmim]BF4 is an ideal reaction
medium for the synthesis of multiple pyrrole derivatives. The reaction
can achieve excellent yield quickly at room temperature with-
out any catalyst. Moreover, [bmim]BF4 is easily available and can be
recycled.9

H2O-EtOH

80:20 [V/V]

β-CD
