1,3-Diethoxycarbonylallene: an Active Dienophile and Ethoxycarbonylketen Equivalent in the Synthesis of Antibiotic *C*-Nucleosides

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Summary The remarkable ease with which 1,3-diethoxycarbonylallene (**1**) undergoes cycloaddition with furans and pyrroles, and the ability of this reagent to serve as an ethoxycarbonylketen equivalent are described.

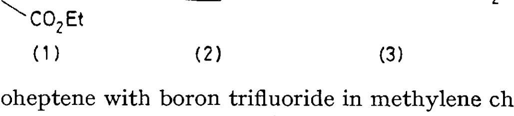
In our studies directed toward the total synthesis of the antibiotic *C*-nucleosides and their analogues, the preparation of a dienophile which would readily cycloadd to furan and its derivatives and, moreover, function as a alkoxycarbonyl keten equivalent was essential for future syntheses planning. These requirements led us to investigate further the reactivity of the readily available reagent, 1,3-diethoxycarbonylallene,[1] with a variety of diene substrates. Although the dienophilic character of allenes has been noted previously,[2] the facility with which the allene (**1**) enters into the [4 + 2] cycloaddition process encourages us to report our findings. The reactions of (**1**) with several homocyclic dienes are summarized in the Table. These reactions are all characterized by low reaction temperatures and good yields. Compounds (**2c**) and (**2d**) (Table) are particularly noteworthy, for they emphasize the reactivity of this reagent even toward pyrroles, a class of dienes which is known for its reluctance to undergo cycloaddition.

Table. Reaction of (**1**) with homocyclic dienes (**2a**—**f**).

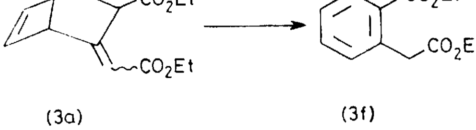
Diene	Reaction conditions[a] Temp./°C	Time/h	Yield/%[b]
(**2a**) Furan	40	24	87
(**2b**) 2,5-Dimethylfuran	40	48	64
(**2c**) *N*-Methoxycarbonylpyrrole	80	90	60
(**2d**) *N*-Methoxycarbonyl-2,5-dimethylpyrrole	80	72	66
(**2e**) Cyclopentadiene	80	36	80
(**2f**) 3-Hydroxy-2-pyrone[c]	80	72	68

[a] Benzene was employed as solvent in all reactions. The cycloadducts are mixtures of stereoisomers. [b] The reaction products were purified by chromatography (silica gel) or by bulb-to-bulb distillation. [c] This diene undergoes cycloaddition with loss of carbon dioxide and aromatization to afford diethyl 3-hydroxyhomophthalate.

The Diels–Alder reaction of 3-hydroxy-2-pyrone[3] (**2f**) with the allene (**1**) occurs with loss of carbon dioxide to furnish diethyl 3-hydroxyhomophthalate (**3f**) which is also obtained by the Lewis acid-catalysed rearrangement of the cycloadduct (**3a**).[4] Accordingly, treatment of this oxabicycloheptene with boron trifluoride in methylene chloride for 3 h at room temperature affords a single major product which is isolated in 51% yield after silica gel chromatography. The n.m.r. spectrum of this product is identical to that of the previously prepared compound (**3f**), thus confirming the direction of the oxygen bridge heterolysis. The overall process of cycloaddition–rearrangement provides a remarkably simple entry into this valuable class of compounds (**3f**).[5]

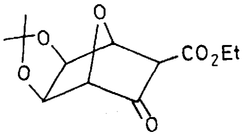


(1) (2) (3)



(3a) (3f)

Further chemical transformations of (**3a**), which are along the pathway to the *C*-nucleosides, confirmed the ability of the allene (**1**) to serve as a suitable substitute for ethoxycarbonyl keten in the Diels–Alder reaction. Hydroxylation of (**3a**), acetonide formation, and ozonolytic



(4)

cleavage, yielded (**4**), a key intermediate in our projected synthesis of this class of antibiotic agents.

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