

2-ETHOXY-5,6-DIHYDRO-1,3-OXAZINES FROM
TRIETHYL AZOMETHINETRICARBOXYLATE

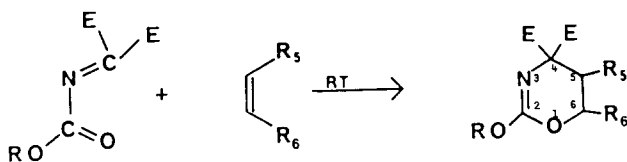
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Abstract: Inverse demand Diels-Alder reactions of triethyl azomethinetricarboxylate with electron-rich olefins lead to 2-ethoxy-5,6-dihydro-1,3-oxazines using the C=N-C=O moiety as the diene only.

The formation of 6-alkoxy-3,4-dihydropyrans from reactions of electron-rich olefins with substituted unsaturated esters was recently reported.^{1,2} The analogous 6-alkoxy-dihydrooxadiazine compound was found in a reaction of diethyl azodicarboxylate and 1,2-dimethoxyethene.³ The reactions are believed to proceed through a Diels-Alder reaction with inverse electron demand using a carbonyl group adjacent to the double bond as part of the diene. J. Hall and coworkers have reported the formation of dihydrooxadiazines from reactions of electron-rich olefins with azodiones or azodicarboxylates, either through a polar intermediate or by a concerted Diels-Alder reaction.⁴ In an attempt to investigate an intermediate class of compounds, imines, we looked at the reactions of triethyl azomethinetricarboxylate (TEI) with electron-rich olefins. Earlier, this compound was found to react as a dienophile in a normal Diels-Alder reaction with other diene systems under stringent conditions.⁵

We present here results showing that 2-ethoxy-5,6-dihydro-1,3-oxazine derivatives are formed and isolated in the reactions of TEI with electron-rich olefins ($R_5=H$ or CH_3 , $R_6=OEt$ or Aryl), at room temperature. In a typical experiment, a mixture of 0.36g (1.47 mmol) TEI and 0.2 mL (2 mmol) ethyl vinyl ether in 1 mL $CDCl_3$ was left at room temperature for 3 hours. The solvent was removed by vacuum and the residue was flash distilled in a Kugelrohr apparatus. Recrystallization from a chloroform/ether mixture yielded pure diethyl



2,6-diethoxy-5,6-dihydro-4H-1,3-oxazine-4,4-dicarboxylate (m.p. 34-36°). Products are characterized by IR and ¹H and ¹³C NMR (Table 1).

Stereochemistry and the overall conformation can be assigned based on the coupling constants obtained for H-5 and H-6. The Karplus equation dictates large coupling constants for diaxial vicinal hydrogens.⁶ These are observed for the aryl-substituted adducts (4-5). The small coupling constants in the vinyl ether adducts (1-3), indicate that the ethoxy group is in the axial position, due to the anomeric effect.⁷ Derivative 2 is observed and isolated as only one isomer in which the cis propenyl ethyl ether stereochemistry is retained, suggesting a concerted mechanism.

In the TEI molecule, two possible diene systems can be employed in the cycloaddition reaction, C=N-C=O or O=C-C=N. The ¹³C NMR data indicates only the former diene is involved in the inverse Diels-Alder reaction. The quaternary carbons, C-2 and C-4, are found at dramatically different chemical shifts. C-2, found in the 152-154 ppm range, is greatly influenced by the adjacent heteroatoms and the double bond, while C-4 is influenced only by one heteroatom and is found in the 65-68 ppm range. In 1 and 2, C-6 corresponds to a dioxygenated carbon of an acetal and is expected in the 88-112 ppm range,⁶ whereas in 4, C-6 is found further upfield (75 ppm) due to the aromatic ring.

These reactions are not entirely without precedent.^{8,9,10,11} Akiyama reports the first case of an anhydrochloralurethane functioning as a diene in a cycloaddition reaction with ketene acetals.¹² The reaction is believed to proceed via a Diels-Alder reaction with inverse electron demand, first forming the unstable 1,3-oxazine derivative and then hydrolyzing to form a carbamate derivative. N-(2,2,2-trichloroethylidene)acetamide has been found to undergo both normal and inverse Diels-Alder reaction with 2,3-dimethylbutadiene.¹³

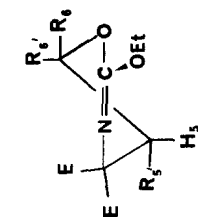
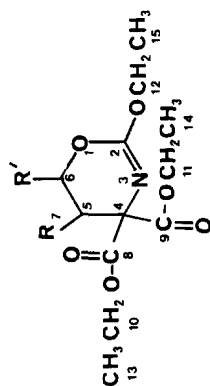


Table I



Compound No	Substituents	Chemical Shift δ (ppm)	Coupling Constants Hz	IR	Yield ^b %	Characteristic ¹³ C NMR Data ^c (CDCl ₃)
	R ₅ '	H ₅ /H ₅ '	H ₆ H ₅	C=N	%	Chemical Shift, δ (ppm)
	R ₆	H ₆	H ₆ H ₅ , H ₆ H ₅ '	cm ⁻¹		carbon number
1	H	2.4(dd)	4	1675	97	2 (s) ^d 4 (s) 6 (d)
2	CH ₃	2.77(dd)	3	1660	98	152.7 65.84 98.2
3	-CH ₂ CH ₂ O-	2.77(m)	4	--	(61)	151.8 68.68 100.3
			H ₆ 'H ₅ H ₆ 'H ₅ ' H ₅ 'H ₅			-- -- --
4	H ϕ -p-OCH ₃	2.67(dd) 2.00(dd)	12	1650	(83)	154.4 66.05 75.39
5	H ϕ -p-CH ₃	2.71(dd) 1.95(dd)	10	1660	--	-- -- --

^aSpectra determined on a Varian T-60 spectrometer.

^bYields reported between brackets are calculated by ¹H NMR, based on TEI as the limiting reagent.

Reactions of TEI and vinyl ethers proceed at room temperature over a 4-6 hour time period, whereas the styrene derivatives react very slowly at room temperature (2-4 weeks, > 50% yield).

^c Spectra determined on a Bruker WM-90 MHz spectrometer.

^doff resonance data.

In summary, TEI acts as a regioselective diene (C=N-C=O) with electron-rich olefins, in a Diels-Alder type reaction with inverse electron demand.

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