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DITHIOESTERS AS HETERO-DIENOPHILES IN DIELS-ALDER CYCLOADDITION - SYNTHESIS OF 6-ALKYLTHIO-5,6-DIHYDRO-2H-THIOPYRANS.

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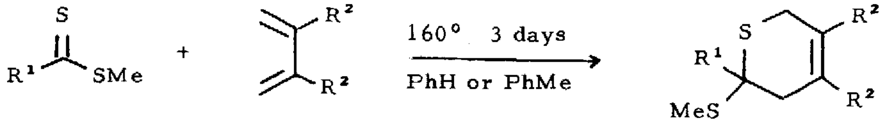
The Diels-Alder reaction of methyl alkanedithiocarboxylates with various dienes at 160°C affords 6-alkylthio-5,6-dihydro-2H-thiopyrans. The regioselectivity and the scope of the reaction were examined.

Dithioesters bearing a strong electron-withdrawing group, such as CF_3CS_2Et and $NC-CS_2Me$, are very reactive heterodienophiles.[1] The Diels-Alder reaction with butadienes proceeds respectively at 0° and -78°. In the literature,[2] there is no example of this cycloaddition involving dithioesters which do not bear an electron-withdrawing group. Our interest in thiocarbonyl chemistry led us to explore this reaction with the now easily available alkanedithiocarboxylates.[3] The expected dihydrothiopyrans could be versatile intermediates[4] in the synthesis of functionalyzed Z-olefins with high isomeric purity.

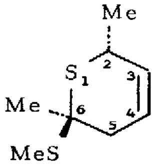
As substrates we selected methyl dithioacetate 1, dithiopropanoate 2, dithioisobutyrate 3 and dithiobenzoate 4. A solution of ca 10 mmol dithioester, 5 fold excess diene and a catalytic amount of hydroquinone in benzene or toluene was heated in a vacuum sealed tube for a standard period of 3 days at 160°. The cooled mixture is concentrated in vacuo, analyzed by NMR, purified by medium pressure liquid chromatography and bulb to bulb distillation.[5]

With symmetrical dienes (butadiene and 2,3-dimethylbutadiene) and dithioesters 1, 2, good yields of products 5, 6, 7 are obtained. Dithiobenzoate also reacts well in these conditions but attempts to isolate the product 9 led to substantial decomposition. In the case of dithioisobutyrate 3, a poor yield of 8 is obtained, probably in relation with its steric hindrance and its propensity towards enethiolization.



1	R^1 = Me	R^2 = H	5	60 %
		R^2 = Me	6	73 %
2	R^1 = Et	R^2 = H	7	50 %
3	R^1 = isoPr	R^2 = H	8	20 %
4	R^1 = Ph	R^2 = Me	9	(70 %)

We then focused our attention on the regioselectivity of the reaction of methyl dithioacetate 1 with unsymmetrical dienes : isoprene and 1,3-pentadiene. With isoprene, a 1 : 1 mixture (77 % yield) of two unseparated isomers 10 and 11 is obtained. Reaction with *trans*-1,3-pentadiene exhibits a slight regioselectivity 2 : 1 in favour of 2-substituted adducts. GC separation of the mixture (75 % yield) affords pure 2-Me isomers (ratio 12 : 34 % ; 13 : 29 %) and a 1 : 1 mixture of the 5-Me isomers (14 + 15 : 37 %).



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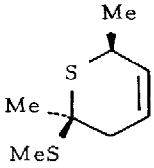

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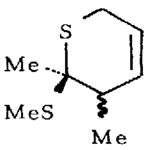
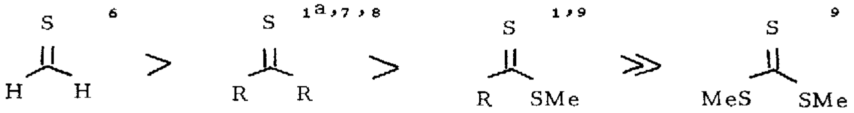


14 + 15

Thus, Diels-Alder addition of dithioesters, which do not possess an electro-withdrawing substituant at the thiocarbonyl site, with dienes is feasible and furnishes reasonable yields of 6-alkylthio-5,6-dihydro-2*H*-thiopyrans in the case of R= Me, Et.

In order to compare the reactivity of various thiocarbonyl compounds as hetero-dienophiles, we also treated methyl trithiocarbonate with butadiene under the same conditions and noted that the starting material was recovered. From these results and literature reports, the following reactivity order is suggested :



It is also noteworthy that the preceding reactions occur under much milder conditions than with oxygenated analogues.[10]

We are currently investigating the possibility of improving the regioselectivity via a catalytic effet, and the utilization of dihydrothiopyrans in the synthesis of natural Z-olefins.

References and notes

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