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THIENO[3,4-c]ISOTHIAZOLE. SYNTHESIS OF A NEW NONCLASSICAL THIOPHENE AND ITS CYCLOADDITION TO ALKYNES AND ALKENES

Hans Gotthardt* and Friedemann Reiter

Institut für Organische Chemie der Universität München

Karlstrasse 23, D-8000 München 2, BRD

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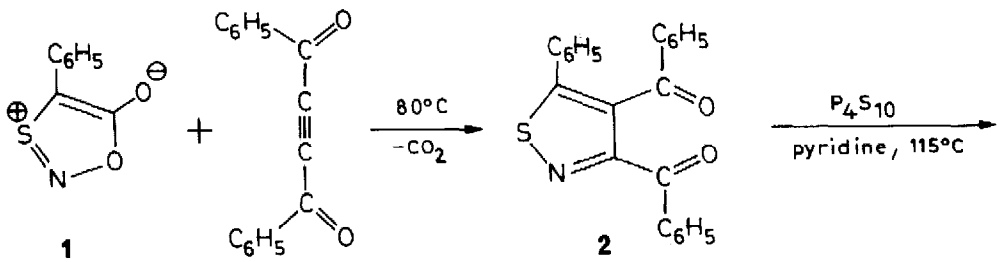
Recently, several nonclassical condensed thiophenes containing 10π electrons and two masked 1,3-dipoles have been prepared and subjected to cycloaddition reactions[1-6]. Examples are: tetraphenylthieno[3,4-c]thiophene[2,3], tetraphenylthieno[3,4-c]furan[4], substituted thieno[3,4-c]pyrroles[3,4], thieno[3,4-c]pyrazoles[5], and thieno[3,4-c]thiadiazole[6]. Our continuing interest in 1,3-dipolar cycloaddition reactions prompted us to synthesize the new thieno[3,4-c]isothiazole of type 3 and to study its cycloaddition to alkynes and alkenes.



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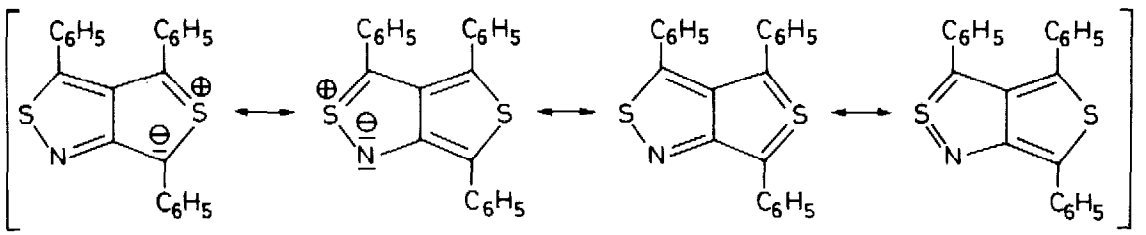
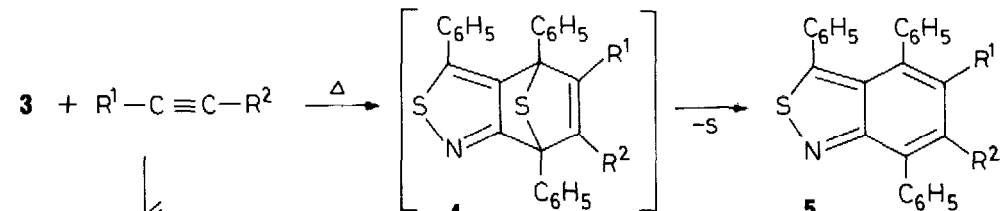


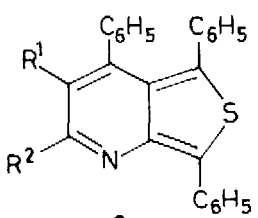
3a 3b 3c 3d

When a toluene solution of 4-phenyl-1,3,2-oxathiazolylium-5-olate (1)[7] and dibenzoylacetylene is warmed at 80°, carbon dioxide is evolved and 3,4-dibenzoyl-5-phenylisothiazole (2) is formed in 18% yield (mp 140-141.5°). Treat-

ment of 2 according to the method described by Potts et al.[3] with phosphorus pentasulfide in refluxing pyridine, affords triphenylthieno[3,4-c]isothiazole (3) in 80-93% yield as glistening, deep violet needles (3: mp > 120° dec.; uv (CH_2Cl_2) λ_{max} = 529 nm (lg ε = 4.13), 280 (4.34), 242 (4.23); ms (70 eV), m/e = 369 (100%, M^+), 184.5 (7%, M^{2+})). 3 is stable in the solid state, but solutions of it are readily bleached in the presence of air and light.

This novel 10π-electron heterobicycle 3 exhibits in the resonance formula 3a the 1,3-dipolar system of a thiocarbonyl ylide and in formula 3b that of a thiocarbonyl imine. It was of interest to us to examine which of the halves of the molecule will react with dipolarophiles.





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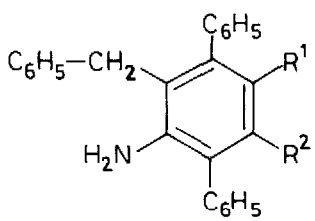
5,7	R^1	R^2
a	CO_2CH_3	CO_2CH_3
b	CO_2CH_3	H
c	H	CO_2CH_3



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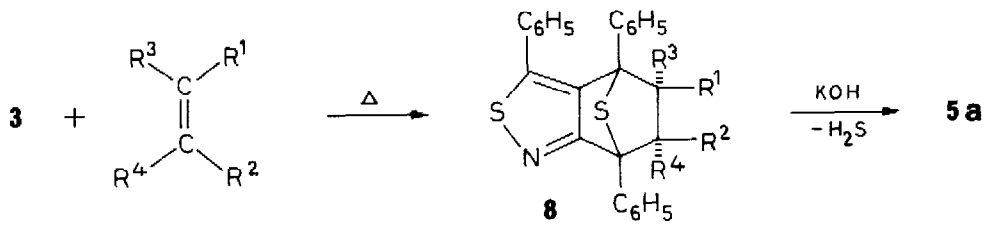
Refluxing a xylene solution of 3 in presence of dimethyl acetylenedicarboxylate under an atmosphere of dry nitrogen in the dark, proceeds with formation of the benzo[c]isothiazole derivative 5a in a 86% yield, after thin layer chromatography (5a: mp 190-190.5°; ir, 1723, 1710 cm^{-1} (C=O); nmr (60 MHz, $CDCl_3$), τ = 6.53, 6.43 (2s, 2 OCH_3), 3.14-2.22 (m, 3 C_6H_5); ms, m/e = 479 (100%, M^+)). The structure of 5a is established by the result of reductive desulfurization. Treatment of 5a with Raney nickel in benzene at 60° leads to formation of the aminoterphenyl derivative 7a (67%) which subsequently is transformed with acetylchloride into the N,N-bisacetyl derivative

of 7a (7a:mp 170-171°; ir, 3490, 3470, 3400, 3380 cm^{-1} (N-H), 1730, 1720 (C=O), 1621 (vinylogous amide); nmr, τ = 6.60, 6.53 (2s, 2 OCH_3), 6.17 (broad s, CH_2, NH_2), 3.03-2.43 (m, 3 C_6H_5)).

These results show clearly that the cycloaddition has occurred at the thiocarbonyl ylide system of 3 and not at the thiocarbonyl imine. The latter alternative pathway should have led to the thienopyridine 6. During the reaction course, the non-isolable primary cycloaddition product 4 has readily eliminated sulfur as a result of a cheletropic reaction. Of course, considering the resonance contributors to 3, the primary addition step can be interpreted as [3+2] or [4+2] cycloaddition.

Similarly, the reaction of 3 with methyl propiolate at 110° yields a mixture of the isomers 5b and 5c (5b:37%; mp 192-192.5°; ir, 1710 cm^{-1} (C=O); ms, m/e = 421 (100%, M^+); 5c:50%; mp 224-225°; ir, 1715 cm^{-1} (C=O)). Raney nickel desulfurization of 5b or 5c proceeds with formation of 7b (1712 cm^{-1} (C=O)) or 7c (1727 cm^{-1}), respectively. 7b exhibits the vinylogous amide band at 1615 cm^{-1}.

In contrast, the reactions of 3 with alkenes proceed without cheletropic elimination of sulfur; in these cases, the primary adducts remain stable under the reaction conditions.



Thus, heating a solution of 3 in dimethyl maleate at 115-120° until the deep violet color of 3 has completely disappeared, yields a 85:15 mixture of the two isomers 8a and 8b (8a: uv (CH_2Cl_2), λ_{max} = 262.5 nm (lg ε = 4.06); nmr, τ = 6.66, 6.59 (2s, 2 OCH_3), 5.77 (s, 2H), 3.38-2.08 (m, 3 C_6H_5); ms, m/e = 513 (24%, M^+), 369 (100, 3$^+$); 8b: uv (CH_2Cl_2), λ_{max} = 274 nm (lg ε = 4.18); nmr, τ = 6.50, 6.35 (2s, 2 OCH_3), 5.00 (s, 2H), 3.12-1.85 (m, 3 C_6H_5))

On the other hand, 3 reacts in the presence of dimethyl fumarate with

8	R^1	R^2	R^3	R^4	% isolated yield	mp (dec.)
a	CO_2CH_3	CO_2CH_3	H	H	74	222.5-223.5°
b	H	H	CO_2CH_3	CO_2CH_3	8	205.5-206°
c	CO_2CH_3	H	H	CO_2CH_3	47	163 -164°
d	H	CO_2CH_3	CO_2CH_3	H	38	205.5-206.5°

formation of the other stereoisomers 8c and 8d, indicating that the cycloaddition reactions proceed stereospecifically (8c: nmr, τ = 6.60, 6.47 (2s, 2 OCH_3), 5.84, 5.47 (2d, J = 4.5 Hz, 2H), 3.33-1.77 (m, 3 C_6H_5); 8d: nmr, τ = 6.70, 6.37 (2s, 2 OCH_3), 6.05, 4.93 (2d, J = 5.0 Hz, 2H), 3.05-2.37 (m, 3 C_6H_5)). Treatment of 8a-d with potassium hydroxide in methanol/acetonitrile (65°) afford 5a almost quantitatively.

Furthermore, similar adducts are obtained from 3 and fumaronitrile or N-phenylmaleimide.

All new compounds described showed satisfactory analytical data.

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