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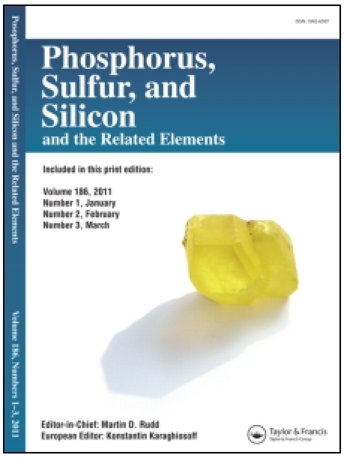

Phosphorus, Sulfur, and Silicon and the Related Elements

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To cite this Article Kiesewetter, René and Margaretha, Paul(1988) 'Photochemical Synthesis of 3, 4-Annulated Tetrahydrothiophenes', Phosphorus, Sulfur, and Silicon and the Related Elements, 39: 3, 263 — 265

To link to this Article: DOI: 10.1080/03086648808072884

URL: http://dx.doi.org/10.1080/03086648808072884

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Phosphorus and Sulfur, 1988, Vol. 39, pp. 263–265
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COMMUNICATION

Photochemical Synthesis of 3,4-Annulated Tetrahydrothiophenes

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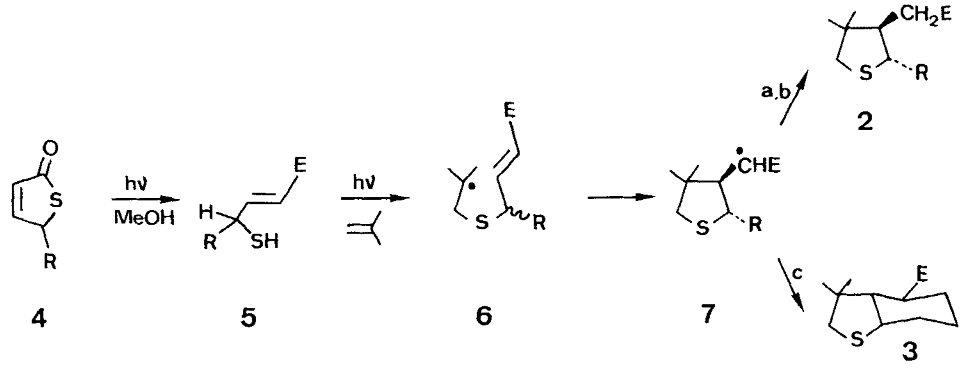
(Received April 24, 1988)

Irradiation of 2(5*H*)-thiophenones **4** in either methanol containing 1,4-pentadiene or in allyl alcohol affords as major products the *cis*-fused 3,4-annulated tetrahydrothiophenes **10** and **12**, respectively.

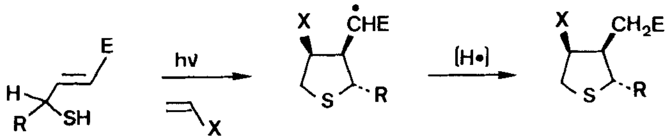
Key words: Tetrahydrothiophene; cyclopenta[c]thiophene; benzo[c]thiophene; 3H-thieno[3,4-c]pyran; photochemistry; radical cyclization.

Among important natural products biotin (**1**) is one of the very few ones containing a tetrahydrothiophene moiety.[1] For the synthesis of this and other 3,4-annulated thiolanes only long multistep procedures are known.[2,3] We have recently described a new synthetic approach to tetrahydrothiophene-3-acetates (e.g. **2**) and 2,3-annulated thiolanes (e.g. **3**) based on the photochemical conversion of 2(5*H*)-thiophenones **4** to γ-mercapto-α,β-unsaturated esters **5** and on the further photochemical transformation of **5** in the presence of alkenes (e.g. 2-methylpropene) to **2** or **3** *via* radical intermediates **6** and **7** (*Scheme 1*).[4-8]



a: R = H b: R = CH_3 c: R = CH_2CHCH_2 E = CO_2CH_3

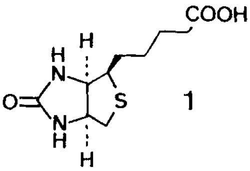
We now report on an expansion of this method to the *one-pot* synthesis of 3,4-annulated tetrahydrothiophenes which is based on the fact that 1-alkyl substituted 5-hexenyl radicals cyclize stereoselectively to *cis* 1,2-disubstituted cyclopentanes.[9,10] Therefore the photochemical conversion of **5** in the presence of a *monosubstituted* ethylene should give the 3,4-*cis* disubstituted thiolane **8** *via* the radical intermediate **9**. Two strategies for the second cyclization step were considered: *a*) addition of X to the radical center in **9** ($X = CH_2CH{=}CH_2$), and *b*) reaction of X with the ester group in **8** ($X = CH_2OH$) (*Scheme 2*).



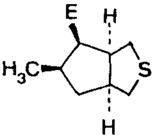
5 **9** **8**

Irradiation ($\lambda = 300$ nm) of **4a** in methanol containing a tenfold molar excess of 1,4-pentadiene affords a 4:2:1 mixture (GC) of **10a**, **10b** and **11**, whose mass spectra with M^+ at m/z = 200 indicate that they are isomers formed from one molecule **4a**, methanol and alkene, respectively. The 1*H*-cyclopenta[c]thiophene structure of **10a** (30% isolated yield) and **10b** (20% as a 1:1 mixture of **10a** and **10b**) result from the ^{1}H-NMR spectra, wherein the coupling constants for the thiolane protons are very similar to those found in biotin.[11] The all-*cis* configuration of the major component **10a** is indicated by the coupling constants $J_{H_{3a},H_4} = 9.2$ Hz and $J_{H_4,H_5} = 11.2$ Hz suggesting that these three hydrogens are all *cis*. The configuration of diastereomer **10b** is not known. The *trans*-fused benzo[c]thiophene structure of **11** (10% isolated yield) results from the ^{1}H-NMR spectrum ($J_{H_{3a},H_{7a}} = 11.2$ Hz) and from comparison of the ^{13}C-NMR chemical shifts with those reported for the parent *trans*-octahydrobenzo[c]thiophene.[12]

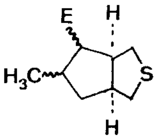
Similarly irradiation of **4b** (chosen in order to simplify the ^{1}H-NMR spectra) in allyl alcohol as solvent affords a 3:1 mixture (GC) of **12a** and **12b** whose mass spectra with M^+ at m/z = 172 and IR-spectra ($v' = 1750$ cm^{-1} in CCl_4) suggest the expected bicyclic lactone structure. Apparently the (thermal) lactone ring closure in **8** ($X = CH_2OH$, $E = CO_2CH_2CHCH_2$) occurs spontaneously, as no such



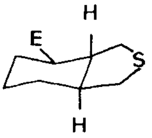
1



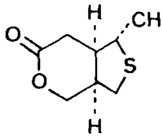
10a



10b



11



12a

compounds were detected by GC/MS. The major component **12a** was isolated in 27% yield, the *cis*-fusion of the two rings resulting from the ^{1}H-NMR spectrum ($J_{H_{3a},H_{7a}} = 9.0$ Hz). The minor component **12b** was not isolated, the ^{1}H-NMR spectrum indicating a *trans*-fusion between the rings ($J_{H_{3a},H_{7a}} = 12.0$ Hz).

The *one-pot* formation of the hexahydro-1*H*-cyclopenta[c]thiophene-4-carboxylates **10** and the 3a,4,7,7a-tetrahydro-1*H*,3*H*-thieno[3,4-c]pyran-6-one **12a** from acyclic precursors, i.e. **5** formed by photosolvolysis of **4**, thus represents an interesting new application of tandem cyclizations in the synthesis of otherwise hardly accessible or even unknown bicyclic thiolane derivatives.

EXPERIMENTAL

Irradiations were performed in a *Rayonet RPR-100* photoreactor using 300 nm lamps. Argon degassed 0.1 M solutions of **4** (2.10^{-3} mol) were irradiated for 7–10 h up to total conversion of starting material. Evaporation of the solvent and bulb to bulb distillation (150°/0.01 Torr) was followed by chromatography on SiO_2. For **10** and **11**: a mixture of pentane/ether 3:1 affords **10a** ($R_f = 0.43$), **10b** ($R_f = 0.40$) and **11** ($R_f = 0.20$); for **12a**: a mixture of pentane/ether 1:4 affords **12a** ($R_f = 0.25$). Compounds **10–12** were all obtained as colourless oils.

ACKNOWLEDGMENT

We are grateful to *Dr. V. Sinnwell* for recording the 2D ^{1}H-NMR spectra of the new compounds and to the *Deutsche Forschungsgemeinschaft* for financial support.

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