An Unexpected Addition Product of Nitrosobenzene with Pyran-2-thione†

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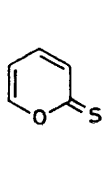
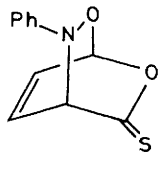
Pyran-2-thione reacts with stocheiometric amounts of nitrosobenzene, leading in quantitative yield to an unusual adduct whose structure is unambiguously determined by n.m.r. spectroscopy and *X*-ray data.

We previously described a new and facile three-step synthesis of an amino-sugar,[1] in which the first step was a regiospecific Diels–Alder cycloaddition of nitrosobenzene with 1-methoxycarbonyl-1,2-dihydropyridine. We then turned our attention to a similar model, starting with 2*H*-pyran derivatives as diene components in cycloadditions with nitroso-dienophiles. 2*H*-Pyran itself has never been described and should not be stable at room temperature. In most cases 2*H*-pyrans can only be obtained which bear two substituents at the C-6 sp^3 carbon atom and one substituent at the C-2 sp^2 carbon atom,[2] although a few examples have been described in which there is only one,[3] or even no, substituent at C-6.[4] Another possible candidate for Dields–Alder reactions with nitroso-derivatives was α-pyrone; this cyclic diene is known to react with nitrosobenzene but loses CO_2 rapidly in the second step.[5]

An alternative approach was the reaction of pyran-2-thione (**1**) as diene-component in Diels–Alder reactions with nitroso-derivatives. We surmised that (**1**) would react with nitrosobenzene, regiospecifically and without loss of the COS fragment, leading to the dioxa-azabicyclo[2.2.2]octane derivative (**2**). *cis*-Hydroxylation of (**2**), followed by hydrogenolysis of the N–O and C=S bonds ,was expected to lead to the desired amino-sugar (**3**).



(1)



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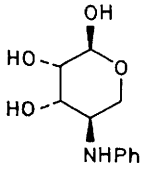

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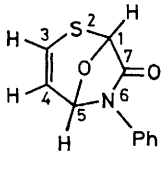

(4)

Pyran-2-thione did indeed react with stoicheiometric amounts of nitrosobenzene (methylene dichloride, room

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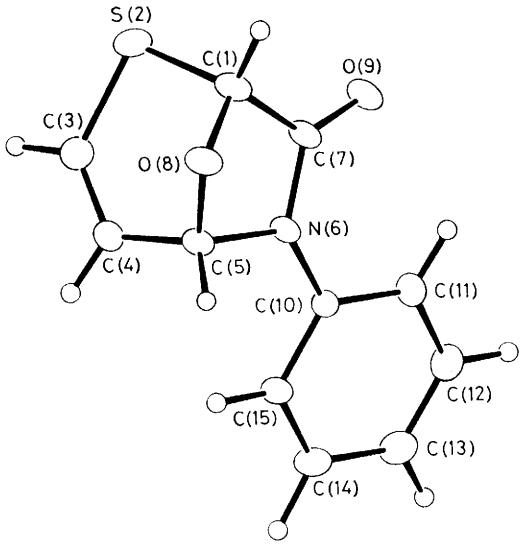

Figure 1. ORTEP view of the structure of the adduct (**4**).

temp., 3 days) and led, in quantitative yield, to a colourless addition product, m.p. 114—115 °C, whose elemental analyses were consistent with the Diels–Alder adduct (**2**). Although the high-field ^{1}H n.m.r. spectrum was compatible with structure (**2**),‡ the i.r. and ^{13}C n.m.r. spectra were not; thiocarbonyl signals were absent, and instead a carbonyl group was present [ν_{max} 1710 cm^{-1} (KBr); δ 165.86 p.p.m. ($CDCl_3$)], which rules out structure (**2**) or its regioisomer. Detailed ^{13}C and ^{1}H n.m.r. measurements allowed the unambiguous assignment of structure (**4**) for the adduct, on the basis of the following reasoning. (i) 1-H is coupled to C-5 with a coupling constant of 5.5 Hz, the size of which shows that it is a three-bond coupling, and there is a similar coupling constant between 5-H and C-1. The ^{13}C n.m.r. results indicate a partial structure with C-1–H separated from the other C–H groups by two heteroatoms.(ii) That 1-H is spatially removed from the other protons was also shown by a ^{1}H n.m.r. inversion recovery experiment; the time for passage through zero magnetization is about 40 s for 1-H, roughly ten times larger than for the other protons in the molecule. (iii) Irradiation of the aromatic *ortho*-protons led to a substantial nuclear Overhauser enhancement for 5-H, proving that this proton must be spatially close to the *N*-phenyl group. (iv) ^{13}C–^{13}C

‡ ^{1}H N.m.r. spectrum of (**4**) measured in $CDCl_3$ with a Bruker HX-360 spectrometer; δ 5.62 (1H, dd, $J_{1,3}$ 2.5, $J_{1,4}$ 0.5 Hz, 1-H), 5.79 (1H, dd, $J_{4,5}$ 4.0, $J_{3,5}$ 1.0 Hz, 5-H), 6.26 (1H, ddd, $J_{3,4}$ 10.0, $J_{4,5}$ 4.0, $J_{1,4}$ 0.5 Hz, 4-H), and 6.42 (1H, ddd, $J_{3,4}$ 10.0, $J_{3,5}$ 1.0, $J_{1,3}$ 2.5 Hz, 3-H), and aromatic signals.

Table 1. ^1J (^{13}C—^{13}C) Coupling constants and values for the ^{12}C—^{13}C isotope effects on the chemical shifts (in Hz at 90.5 MHz).

$(i–j)$[a]	$J(i,j)$ Hz	$j\Delta(i)$ Hz	$i\Delta(j)$ Hz
3–4	73.1	−2.4	−2.5
4–5	49.3	−0.7	−0.7
1–7	57.6	−0.5	−0.1
10–11	64.1	−1.4	−1.4
11–12	57.6	−1.6	−1.5
12–13	55.4	−1.9	−1.8

[a]For the numbering scheme see Figure 1.

Coupling constant parameters were obtained from the satellites observed in the broad-band-decoupled ^{13}C n.m.r. spectra of a concentrated solution in $CDCl_3$. Table 1 gives the values of the one-bond coupling constants and of the ^{12}C–^{13}C isotope effects on the chemical shifts, and these are consistent with structure (**4**).

Structure (**4**) is unexpected and would not have been predicted as the adduct of pyran-2-thione (**1**) with nitrosobenzene. Its formation necessitates a rather severe rearrangement after the assumed initial Diels–Alder cycloaddition step. In fact, when the reaction was monitored by 360 MHz ^{1}H n.m.r. spectroscopy during 72 h, the adduct (**4**) was formed in practically 100% yield. *No signals due to intermediates were observed.* As a tentative and partial mechanistic hypothesis, one may assume that the first step is a slow Diels–Alder cycloaddition, and that the subsequent steps leading to the final adduct (**4**), are fast.

A subsequent *X*-ray investigation confirmed the n.m.r. interpretations (Figure 1).§

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§ *Crystal data:* $C_{11}H_9NO_2S$, triclinic, space group $P\bar{1}$, $Z = 2$, $a = 6.574$, $b = 9.299$, $c = 9.532$ Å; $\alpha = 116.9$, $\beta = 102.7$, $\gamma = 78.7°$; 1981 reflections, final *R*-factor 0.048. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.