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COMPLEXES OF NONCYCLIC CROWN-TYPE POLYETHERS WITH THIOUREA AND UREA

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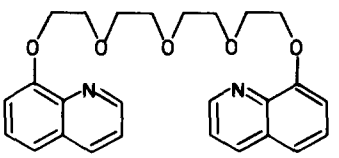
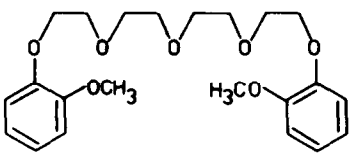
Except for a series of inclusion [1-4] and charge transfer compounds [5], little is known about complexes between neutral molecules. Systematic approaches to host molecules tailored to fit neutral guest particles are lacking above all. It is important to gain new knowledge in this field owing to the significance of such interactions between, e.g. proteins (enzymes) and nucleic acids [6] and again because of our poor understanding of the hydrophobic attractive forces [5,7] between pharmacons and receptors.

Pedersen [8] first reported on complexes of cyclic crown ethers with neutral molecules like thiourea. However, no adducts of such kind could be isolated with open chain glyme compounds possessing the same number of donor atoms [8]. Meanwhile, additional complexes of cyclic crown ethers with dimethyl acetylene dicarboxylate [9] as well as with CH-acidic compounds like acetonitrile [10], malodinitrile [11] etc. have been reported.

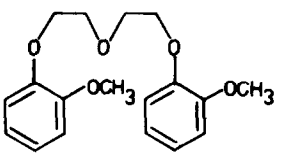
We chose noncyclic neutral ligands [12-14] as model substances for the systematic investigations of the interactions between neutral guest and host molecules and found that ligands such as I-III are quite capable of forming stable, crystalline 1:1 adducts with neutral guest molecules:



I



II



III

When solutions of thiourea (mp 180-182°C) and the noncyclic crown ether I [12a] (mp 73-75°C) in methanol are mixed, a colorless, crystalline adduct of mp 142°C,

unchanged on recrystallization from acetone, is obtained. Elemental analyses confirm an exactly 1:1 stoichiometry (table 1), even when the components are mixed in different stoichiometric ratios. The adducts as a rule give good elemental analysis values after only one recrystallization [15]. The appearance of numerous sharp bands in the IR spectrum of the $I \cdot SC(NH_2)_2$ adduct which are not present in the starting substances [11], is in accord with the formation of a definite complex. With urea, analogous complexes can be isolated (table 1).

Table 1. Data of the synthesized complexes of noncyclic crown-type polyethers with thiourea and urea

Host molecule mp [°C]	Guest molecule mp [°C]	Complex [a] stoichiometry host:guest (mp [°C])	Analyses (Calcd. / Found) C	H	N	S	^{1}H-NMR [b] $XC(NH_2)_2$	IR (in KBr) ν (cm^{-1}) [c]
I [d]	thiourea	1:1	61.81	6.15	10.68	6.11	7.05	3393,3290,
(73-75)	(182)	(142)	61.61	6.15	10.76	6.19		3168,1648
II	thiourea	1:1	57.31	7.10	5.80	6.64	7.02	3426,3325,
(oil)	(182)	(97-98)	57.14	7.03	5.66	6.68		3218,1614
III	urea	1:1	60.34	6.92	7.41	-	5.40	3480,3370,
(78)	(133-135)	(133-134)	60.33	6.92	7.41	-		1666,1623
IV	thiourea	1:3	47.23	5.23	-	15.13	7.03	3383,3280,
(162)	(182)	(153)	47.58	5.15	-	14.79		3180
V	thiourea	3:4	55.78	5.75	14.00	7.54	7.07	3375,3270,
(83-84)	(182)	(88-90)	55.61	5.70	14.27	7.35		3175
VI	thiourea	1:2	62.03	6.94	14.47	11.04	7.02	- [e]
(97-99)	(182)	(165-167)	62.25	7.00	14.24	10.59		

[a] *All adducts were recrystallized from acetone or acetone/methanol (1:1 - 4:1).*

[b] *In DMSO-d_6, δ-values, $TMS_{int.}$, 90 MHz. The chemical shifts of the NH_2 protons in the same solvent for urea and thiourea alone are δ=5.69 and 7.13 ppm respectively.*

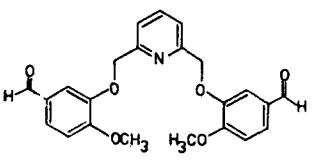
[c] *Only new bands, which appear, are mentioned.*

[d] *While I also forms a crystalline complex of mp 152°C with urea, no such adduct could be obtained with II.*

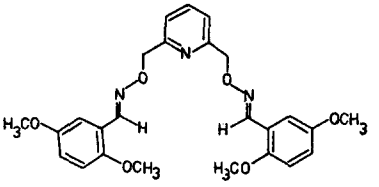
[e] *No significant change.*

Prevailing facts about neutral complexes allow us to draw up the following conclusions regarding the structures of the adducts:
Because of the 1:1 stoichiometry, it is most unlikely that the endgroup carrying systems I-V are incorporated in thiourea channels to form inclusion compounds. As a rule, stoichiometries of the order 5:1 or 6:1 (thiourea or urea : guest molecule like paraffin etc.) are usually observed for such channel adducts [1b].

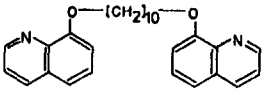
A different structure was assigned to the 1:1 adducts of quinoline, quinaldine and other hetero arenes with thiourea and urea [16]. In these adducts one aromatic system corresponds to one thiourea resp. urea molecule, whereas in our ligands the ratio is two aromatic systems per thiourea molecule.
Thus it seems that in the present case there may be a third possibility of adduct formation with interaction analogous to that of the cyclic crown ethers; in other words, 1:1 molecular inclusion compounds with thiourea as guest molecule may be present; also, a sandwich type or helical overlap of the quinoline rings with inclusion of a thiourea molecule is conceivable [17].
Participation of the ethylene glycol ether oxygen atoms in such a 1:1 formation is suggested by the fact that for the diether VI with a $(CH_2)_{10}$ chain, a crystalline thiourea adduct is similarly formed, but with a different stoichiometry, however, namely 2 thiourea molecules : 1 molecule of VI.



IV



V



VI

Further investigations concerning the relationship between host-ligand shape and complex structures, particularly the role of the ether oxygen atoms of crown ethers are under way.

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15) As expected, in the mass spectra there is no peak for the whole complex, but M^+-peaks of both components.

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17) X-ray analyses of the thiourea complexes of I and II are under way, for which we would like to thank Prof. Dr. *W.Saenger*, Max-Planck-Institut für Experimentelle Medizin, Abt. Chemie, Göttingen.