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ON THE REACTION OF TRICHLOROACETYL ISOCYANATE (TAI) WITH FURAN AND PYRROLE NUCLEUS. A CAUTIONARY NOTE ON THE APPLICATION OF THE TAI-METHOD TO THE CLASSIFICATION OF ALCOHOLS BY PMR SPECTROSCOPY

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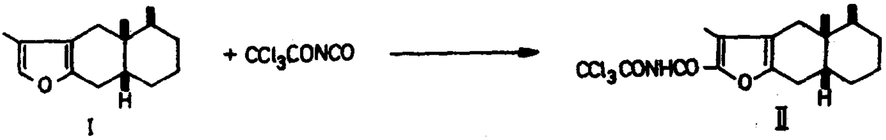
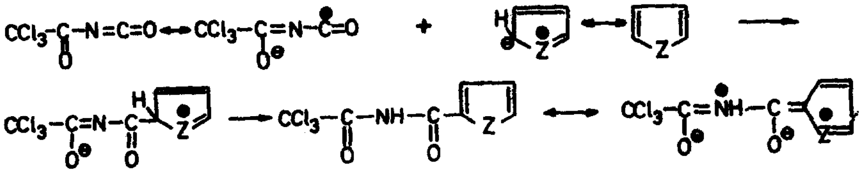
In the course of our structural studies of sesquiterpenes by PMR spectroscopy we recently started systematically to use in situ acylation of free hydroxy groups with trichloroacetyl isocyanate (CCl_3CONCO = TAI). Originally, this reaction was proposed for the classification of alcohols and for the determination of the number of free OH groups by PMR spectroscopy (TAI-method)[1,2]. Our experience indicated that the TAI-method is very useful especially in the study of natural substances where it can substitute the still used method of acetylation and where it allows to obtain various important structural information from PMR spectra even when only a small amount of substances is available[3].

However, when correlating the PMR spectra of the parent substances and of their trichloroacetylcarbamidyl derivatives (TAC-derivatives, TAC = $CCl_3CONHCO$) the fact must be kept in mind that the O-acylation with TAI is often accompanied by other reactions[3]. Recently we observed an especially interesting reaction when the TAI-method was applied to sesquiterpenic alcohols of furoeremophilane type. We found that after the addition of TAI to $CDCl_3$ solutions of these substances not only the OH protons were transformed to amidic protons but also the α-protons of the furan ring. We also immediately confirmed this reaction by a direct application of TAI-method to unsubstituted furoeremophilane (I). The reaction of I with TAI took place instantaneously and the analysis of the PMR spectrum showed unambiguously the formation of TAC-derivative II (NH: δ 9.63, bs; $CO\text{-}C(O){=}C(R)\text{-}CH_3$: δ 2.29, s). Substance II was also isolated by chromatography and its structure confirmed by mass spectroscopy.

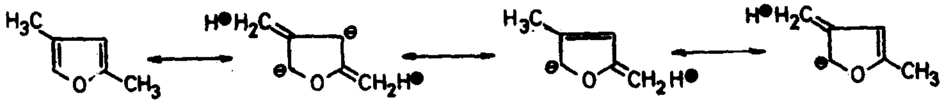


Preliminary experiments with unsubstituted parent five-membered heterocycles demonstrated that under conditions used ($CDCl_3$, 25°C) only pyrrole reacts with TAI instantaneously, affording mono-TAC-derivative (H_1: δ 10.27, bm; H_3: δ 6.89, ddd; H_4: δ 6.32, dt; H_5: δ 7.18, ddd; J_{13}=2.6, J_{14}=2.5, J_{34}=4.0, J_{35}=1.3, and J_{45}=2.6 Hz; CONHCO: δ 9.22), while thiophene and furan were resistant even after several days standing of the solution.

These results indicate that the reaction is related to electrophilic substitution with the usual sequence of reactivities according to ionisation potential of the heteroatom (N > O > S)[4] corresponding to the following scheme :



The different reactivity of the α-position of the unsubstituted furan and the substituted furan ring in the case of furoeremophilane derivatives may be explained, in principle, by the hyperconjugation effects of the alkyl groups. Experiments with various mono- and dimethylfurans demonstrated that one of the necessary conditions for a significant reactivity of the α-position of the furan ring is the presence of 2,4-dialkyl substitution (of all the mentioned isomers only 2,4-dimethylfuran reacted under conditions used; in the case of corresponding thiophene derivatives the reaction was in no case observed). This condition is, of course, fulfilled in the case of furoeremophilane derivatives. The role of the hyperconjugation effects may be demonstrated in the terms of VB-structures in the following manner:



An analogous activation of the α-position may be expected generally in the case of -I, +M substituents in position 2 and 4. When the -I, -M substituents are in α-position a polarisation in the sence of fulvenoid structure may be expected, such as are formulated for the case of the TAC-group in scheme 3, and hence also the deactivation of the second α-position for an electrophilic attack. In agreement with this only a mono-TAC derivative is formed in the case of pyrrole. For the same reason TAI does not react with 9-oxo-furoeremophilanes either.

The reaction of TAI with nucleophilic substrates is presently under study and the results will be published later. These experiments show that TAI is a relatively strong electrophile and that in some cases O-acylation may be simulated by C-acylation. This circumstance must be taken into consideration especially during a global determination of the number of the OH groups by the TAI-method.

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