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THALLIUM(III) NITRATE (TTN) OXIDATION OF 2,8-DIOXO-1,7-CYCLOERYTHRINANS: A NEW SKELETAL REARRANGEMENT [1)]

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Abstract ---- Oxidation of 2,8-dioxo-1,7-cycloerythrinans (1a,b) with excess TTN in MeOH gave rearrangement products (2a, b), whose structures were elucidated mainly on the basis of spectral evidence. The intermediate to 2 from the ketone (1) was found to be the dimethylketal.

Oxidation of cyclic ketones with TTN in MeOH sometimes causes α-methoxylation[2)] and often skeletal rearrangement[2,3)]: all the products by the latter process are the compounds due to a 1,2-shift of a C-C bond from the formally created intermediate oxocarbonium ions. Here we report a new skeletal rearrangement reaction by TTN oxidation, to which a nitrogen atom in the molecule is concerned.
Treatment of a 2,8-dioxo-1,7-cycloerythrinan (1a)[4)] with an excess of TTN in MeOH (r.t., 1 h ⟶ reflux, 3 h) yielded a product (A_1), $C_{21}H_{27}NO_6$, mp 252-253°C, in 57% yield. The ^{1}H-NMR of A_1 indicated that three methoxyl groups (δ 3.33, 3.27, 2.78) had been introduced into the molecule; two of them are easily removed by acid hydrolysis (1% HCl-acetone, 50°C, 15 min) to afford a ketone (B_1) (δ 3.00, OMe; ν_{max} 1725 cm^{-1}), $C_{19}H_{21}NO_5$, mp 258-260°C, proving that the compound A_1 is a methoxy-dimethylketal.
The 6-ethoxycarbonyl derivative (1b)[5)] similarly gave a methoxy-dimethylketal (A_2), $C_{24}H_{31}NO_8$, mp 238-240°C, on TTN oxidation in MeOH (r.t., 1h ⟶ reflux, 8h; 36%), and then a methoxy-ketone (B_2), $C_{22}H_{25}NO_7$, mp 168-170°C, on acid hydrolysis. Although the formulae of the compounds (B_1,B_2) corresponded to the α-methoxylation products (4a and 4b), their ^{13}C-NMR spectra (Table 1) revealed that they were not the expected products (4a and 4b), but were the rearrangement products (3a and 3b), respectively.

Table 1. ^{13}C-NMR spectra of cycloerythrinans (1a and 1b) and the oxidation products (3a, 3b, 8a, and 8b) in chloroform-d.

carbon No	1a	3a (J_{C-H}, Hz)	8a (J_{C-H}, Hz)	1b	3b (J_{C-H}, Hz)	8b (J_{C-H}, Hz)
1	30.3 d	30.0 d(179)	30.1 d(178)	35.1 d	34.2 d(178)	34.4 d(178)
2	203.3 s	198.0 s	197.6 s	200.7 s	195.9 s	195.7 s
3	34.7 t	59.3 d(150)	59.5 d(155)	34.9 t	58.9 d(148)	59.4 d(158)
4	27.5 t	42.2 t(129)	42.7 t(132)	28.7 t	43.3 t(138)	44.0 t(130)
5	59.1 s	78.8 s	79.1 s	61.9 s	80.6 s	81.0 s
6	28.8 d	42.2 d(172)	42.7 d(171)	46.5 s	52.0 s	52.5 s
7	33.6 d	29.0 d(178)	29.7 d(178)	33.6 d	33.3 d(178)	33.5 d(178)
8	168.8 s	168.2 s	167.9 s	167.1 s	165.7 s	165.6 s
10	36.2 t	46.2 t(139)	50.8 t(138)	36.9 t	46.6 t(140)	51.1 t(138)
11	33.6 t	36.1 t(128)	78.6 d(152)	35.2 t	36.5 t(127)	78.6 d(147)
12	129.8 s	133.1 s	132.5 s	127.5 s	131.8 s	131.2 s
13	125.3 s	128.5 s	130.0 s	126.5 s	129.0 s	130.4 s
14	107.3 d	111.7 d(156)	111.6 d(154)	108.9 d	114.0 d(156)	107.1 d(156)
15	148.0 s	148.7 s	148.9 s	147.6 s	148.1 s	148.4 s
16	148.2 s	148.7 s	149.3 s	148.5 s	148.8 s	149.4 s
17	112.0 d	115.1 d(156)	117.6 d(154)	112.3 d	114.7 d(157)	114.0 d(157)
OMe	55.7 q 56.0 q	55.7 q 55.8 q 50.5 q	55.7 q 55.9 q 50.5 q 58.5 q	55.9 q 56.0 q	55.5 q 55.8 q 55.5 q	55.6 q 55.9 q 51.0 q 58.5 q
CO_2Et				167.1 s 61.9 t 13.6 q	167.3 s 62.0 t 13.9 q	167.2 s 62.2 t 14.0 q

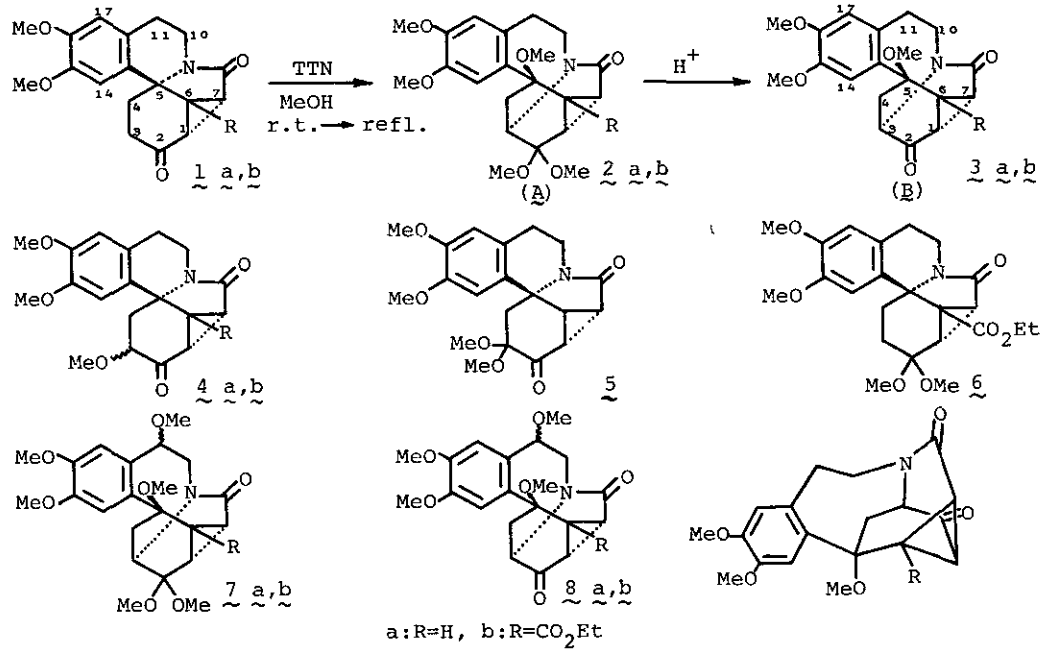

Chart 1

The C-5 in 1a resonates at δ_C 59.1, but the corresponding singlet in 3a appears at δ_C 78.8 implying the presence of $-\overset{|}{\underset{|}{C}}-O-$ system. Among the four non-aromatic >CH- signals, three ones (δ_C 42.2, 30.0, 29.0) are attributed to the carbons of a cyclopropane ring, since they have a large J_{C-H} (170-180 Hz) *suggesting that the* cyclopropane ring remains intact. The other >CH- signal at δ_C 59.3 resonates at too high field to assign as $-CO-\overset{|}{C}H-O-$, instead implies the presence of $CO-\overset{|}{C}H-N<$. The above spectral pattern is remarkably contrasted to that of a 3,3-dimethoxy-2,8-dioxo-1,7-cycloerythrinan (5)$^{5)}$ which showed an expected pattern. The same can also be said for 3b, except that it has only two >CH- (δ_C 34.2, 33.3) on the cyclopropane ring.

In addition, in the ^{1}*H-NMR of* 3b, *the* $COOCH_2\underline{CH_3}$ *signal* (δ_H 1.30) did not show any high field shift characteristic of 6-ethoxycarbonyl-erythrinans and the corresponding 1,7-cycloerythrinans. All of these evidence suggest the structures 3a and 3b for the compound B, and hence 2a and 2b for the compound A .

The assigned structures were supported by the following findings on the reaction pathway. The compound 1b, when treated with TTN (1.5 eq) in MeOH at room temperature for 24 h, only produced the dimethylketal (6)$^{6)}$ (identified with the compound prepared by an alternative synthesis using $CH(OMe)_3$ and p-TsOH). Further treatment of 6 with TTN in hot MeOH rapidly produced 2b indicating that the reactive species in the above oxidation is not the ketone (1b) but the dimethylketal (6) (and may be an enol ether 6'). We therefore consider the following mechanism for the above rearrangement reaction (Chart 2).

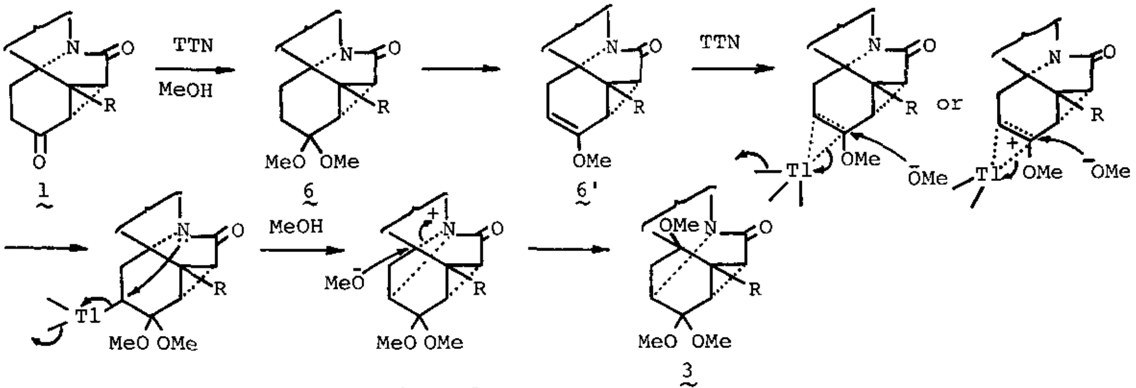

Chart 2

Further treatment of **2a** with TTN in hot MeOH introduced an additional methoxyl group producing a dimethoxy-dimethylketal (**7a**), $C_{22}H_{29}NO_7$, mp 231-233°C, which gave a dimethoxy-ketone (**8a**), $C_{20}H_{23}NO_6$, mp 262-264°C, on acid hydrolysis. Treatment of **1a** with excess TTN in hot MeOH (without pre-treatment at room temperature) directly produced **7a** in 62% yield. The 6-ethoxycarbonyl derivative (**1b**) also gave an analogous product (**8b**), on treatment with excess TTN in hot MeOH followed by acid hydrolysis, but in poor yield (7%). Their structures were tentatively elucidated as above (C_{11}-OMe) mainly by spectral evidence (see Table 1). The position of a newly introduced methoxyl group was assigned from the fact that C_{17}- signal of **8a** appears as clean doublet, while the corresponding peaks of **3a** showed a long-range coupling with 6 Hz (non-decoupling experiment).

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