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# 2-ACYLCYCLOBUTANONES FROM α-CYCLOPROPYLIDENE KETONES

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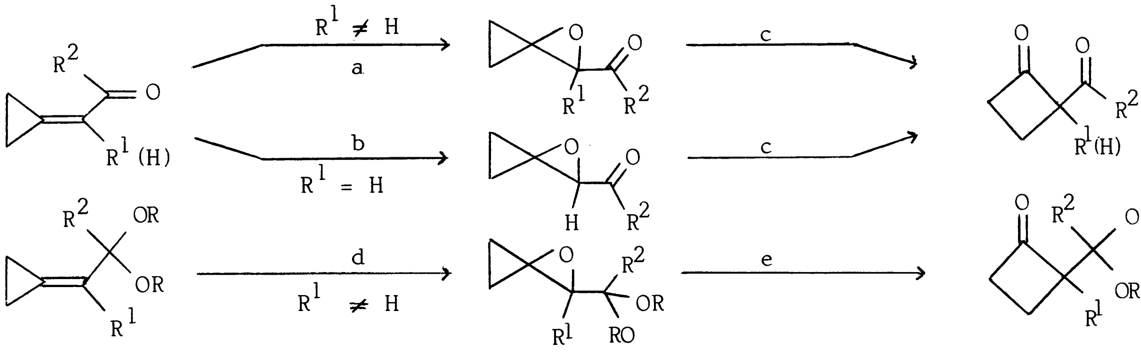
Oxaspiropentyl ketones and acetals prepared from α-cyclopropylidene ketones and acetals undergo, with lithium halides, isomerisation to 2-acylcyclobutanones and monoacetals.

Cyclobutanones bearing electron – withdrawing α-substituents such as alkenyl or alkynyl 1), ester 2), acid 2b) or nitrile 2b,3) are well known, but 2-acylcyclobutanones have never been described ; preceding attempts in our laboratory were unsuccessful, ring opening products or resinous compounds being formed.

The purpose of the present communication is to show that 2-acylcyclobutanones and their monoacetals can be obtained by epoxidation of α-cyclopropylidene ketones and acetals 4) leading to oxaspiropentyl ketones and their acetals followed by isomerisation with LiX (Scheme 1) (for the synthesis of cyclobutanone itself from methylene cyclopropane via oxaspiropentane, see ref. 5). The preparation of some oxaspiropentyl ketones is however better carried out by a three step synthesis (Scheme 1, exp. b, also see below).



a) m-Cl-$C_6H_4$-$CO_3H$ or p-nitro-$C_6H_4$-$CO_3H$, $Na_2HPO_4$, $CH_2Cl_2$, 30°C ; b) 1) $NaBH_4$, $CeCl_3$, MeOH ; 2) m-Cl-$C_6H_4$-$CO_3H$, $Na_2HPO_4$, $CH_2Cl_2$, 25°C ; 3) active $MnO_2$, $CH_2Cl_2$; c) LiBr, $CCl_4$; d) m-Cl-$C_6H_4$-$CO_3H$ - $NaHCO_3$, $CH_2Cl_2$, 25°C ; e) LiI, $CH_2Cl_2$ or spontaneously.

Scheme I. Preparation of 2-acylcyclobutanones and monoacetals from α-cyclopropylidene ketones and acetals.

The best results for the epoxidation of α-substitued α-cyclopropylidene ketones were obtained with m-Cl- or p-nitro-perbenzoïc acids in the presence of $Na_2HPO_4$ in order to limit the Baeyer Villiger reaction. Thus the oxaspiropentyl ketones 2a,b (Scheme 2) were

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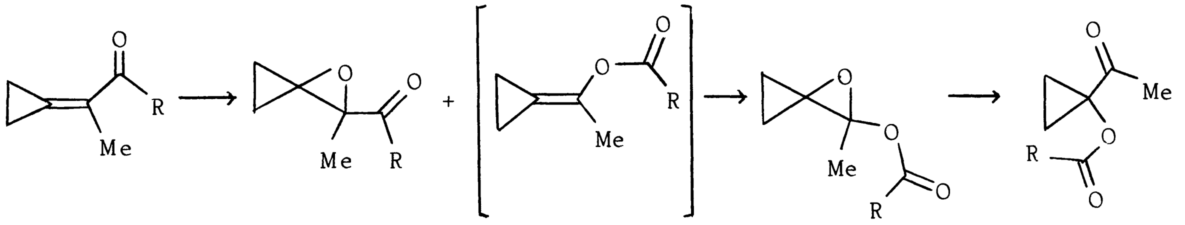
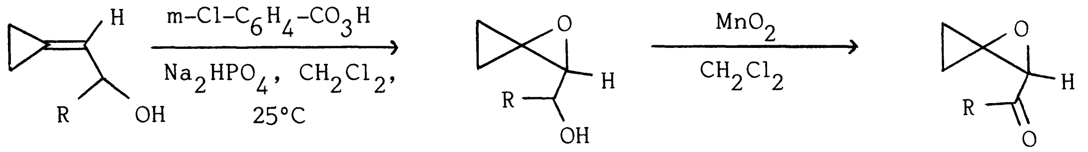
obtained from the corresponding α-cyclopropylidene ketones 1 4) (63 and 48% yield for isolated 2a and 2b, respectively), the by-products being mainly esters 3' and 3'' formed from the Baeyer Villiger oxidation product 3 6) The reaction of α-cyclopropylidenepropionaldehyde 1c with m-Cl-$C_6H_4$-$CO_3H$ only yields the ketoester 3''c and not the oxaspiropentylaldehyde. Formation of the postulated intermediate 3c (Scheme 2) can be detected by $^1$H-NMR.



| | | | | |
|---|---|---|---|---|
| 1a R = Me | 2a | 3a | | 3''a |
| b Ph | b | b | 3'b | |
| c H | | c | | c |

Scheme 2. Oxidation products from α-cyclopropylidene ketones and aldehydes.

Epoxidation of α-cyclopropylidene ketones unsubstituted in the α-position leads to a complex mixture which includes the conjugate addition product of carboxylic acid derived from the peracid. To prepare oxaspiropentyl ketones such as 6, α-cyclopropylidene ketones were reduced with $NaBH_4$, $CeCl_3$ in MeOH, 4) α-cyclopropylidene alcohols 4 were treated with m-Cl-$C_6H_4$-$CO_3H$ to yield oxaspiropentyl carbinols 5 and these were oxidized by active $MnO_2$. 7) Examples :



| | | |
|---|---|---|
| 4a R = Me | 5a 70%$^a$ | 6a 30%$^b$ |
| b Ph | b 92%$^a$ | b 56%$^a$ |

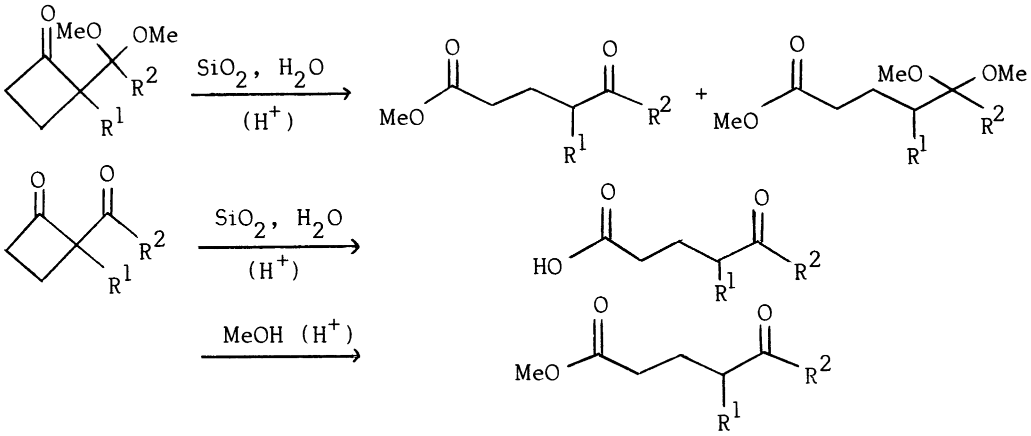
a) Yield of isolated product ; b) Yield from $^1$H-NMR

While epoxidation of unsubstituted α-cyclopropylidene acetals also leads to intractable mixtures, oxaspiropentyl derivatives are easily obtained from α-substituted α-cyclopropylidene acetals : thus oxaspiropentyl acetals 7a and 7b (Table 1) are obtained in 66 and 75% isolated yield, respectively.

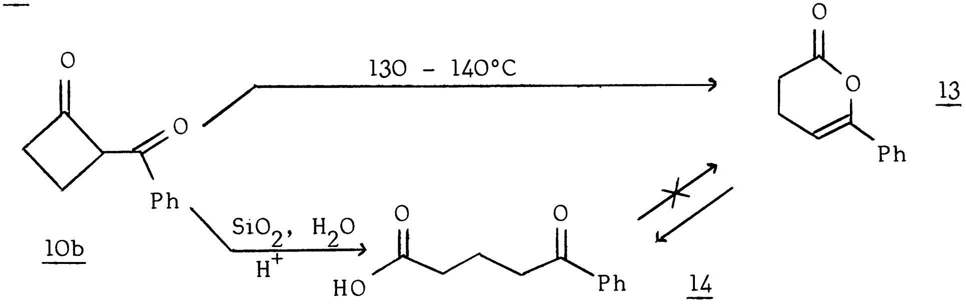
Isomerisation of all oxaspiropentyl ketones 2a,b, 6a,b and acetals 7a,b in the presence of LiBr or LiI leads to the hitherto unknown 2-acylcyclobutanones 9a,b, 10a,b and monoacetals 11a,b (Table 1). It should be noted that the oxaspiropentyl acetals 8a,b are not isolable ; they isomerize spontaneously to the cyclobutanone acetals 12a,b (similar effects of phenyl or cyclopropyl groups in analogous rearrangements were already observed. 8)

The β-diones 9a,b, 10a,b are not stable enough to be isolated: practically pure solutions in dry $CCl_4$ were obtained. In the IR spectra of such solutions two $\nu C{=}O$ bands are present : one at 1775-1785 $cm^{-1}$ (cyclobutanone) and the other at 1705 (10a), 1710 (9a), 1665 (9b) or 1670 $cm^{-1}$ (10b). In the IR spectra of the unsubstituted diones 10a,b bands due to keto-enol tautomers could not be detected ; the $^1H$-NMR spectra also confirm the postulated dione structure (multiplet at $\delta$ = 4.30 and 5.05 ppm for the proton in the 2 position of 10a and 10b respectively). The apparent absence of keto-enol tautomerism in 2-acylcyclobutanones is a distinctive feature of these diones and differenciates them from analogous diones with a larger ring.

All of these new β-diones and β-ketoacetals very easily undergo ring opening by hydrolysis or methanolysis in neutral or slightly acidic medium : this may explain our failure to deacetalise the monoacetals 11a,b, 12a,b even by mild hydrolytic methods such as $SiO_2$, $H_2O$ (9a), $SiMe_3I$ (9b) or $C_5H_5NH^+OTs^-$ . 9c)

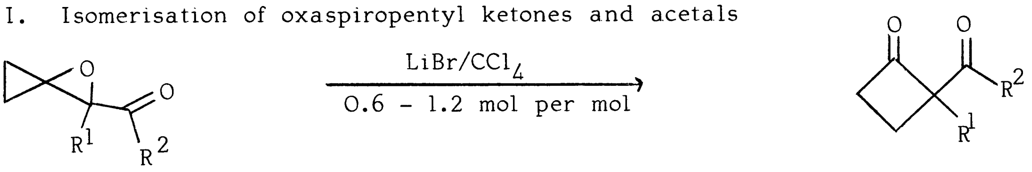


An unexpected thermal reaction of the β-dione 10b appears worth mentioning : upon distillation (bp 130-140°/0.085 torr) 10b is entirely converted into 3,4-dihydro-6-phenyl 2-pyrone 13.

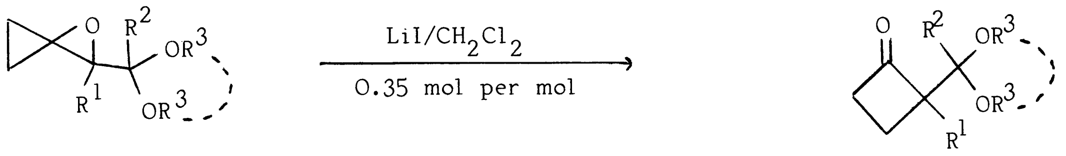


The keto-acid 14 is probably not an intermediate in the reaction : 10b ⟶ 13 as we were unable to convert this acid 14 to the lactone 13 by heating ; on the other hand the hydrolysis of 13 gives 14.

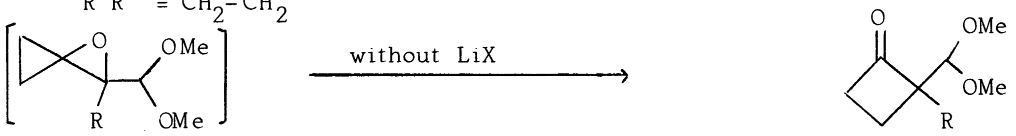
Table I. Isomerisation of oxaspiropentyl ketones and acetals



| | | | |
|---|---|---|---|
| 2a $R^1$ = Me $R^2$ = Me | 27 h | 60°C | 9a 100%$^a$ |
| b — Me — Ph | 45 h | 60°C | b 100%$^a$ |
| 6a $R^1$ = H $R^2$ = Me | 30 min | 30°C | 10a 60%$^a$ |
| b — H — Ph | 75 min | 45°C | b 78%$^a$ |



| | | | |
|---|---|---|---|
| 7a $R^1$ = $R^3$ = Me $R^2$ = H | 2 h | 25°C | 11a 60%$^b$ |
| b $R^1$ = n-Bu $R^2$ = Me<br>$R^3R^3$ = $CH_2$-$CH_2$ | 3.5 h | 40°C | b 50%$^b$ |



| | | |
|---|---|---|
| 8a R = Ph | complete after 12 h at 40°C | 12a 65%$^c$ |
| b cyclopropyl | spontaneously | b 85%$^c$ |

a) Yield from $^1$H-NMR ; b) Yield of isolated products ; c) Yield from 2-cyclopropylidene-2-phenyl-1,1-dimethoxyethane and 2-cyclopropylidene-2-cyclopropyl-1,1-dimethoxyethane for isolated 12a and 12b.

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