*Tetrahedron* Vol. 34, pp. 2035–2037
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0040-4020/78/0701-2035/$02.00/0

# 2,5,5-TRIMETHYL-2-OXAZOLIN-4-ONE, ITS PERCHLORATE, AND α-ACETOXYISOBUTYRONITRILE BY ACETYLATION OF ACETONE CYANOHYDRIN

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(*Received in UK* 29 *November* 1977; *Accepted for publication* 22 *December* 1977)

**Abstract**—Acetone cyanohydrin (**1**) yields on acylation and ring closure with anhydrides and perchloric acid, 2-oxazolin-4-onium perchlorates **5a**, **5c** or **5d**. The same perchlorates (**5a**, **5b**) may be obtained under similar conditions from acyloxy-nitriles (**2**) or -amides (**4**). Perchlorates **5** may be deprotonated in pyridine to 2-oxazolin-4-ones (**6**), but in aqueous solution they undergo ring opening to acyloxy-amides **4a,c,d**, or to N-benzoyl-α-hydroxy-isobutyramide **7b**.

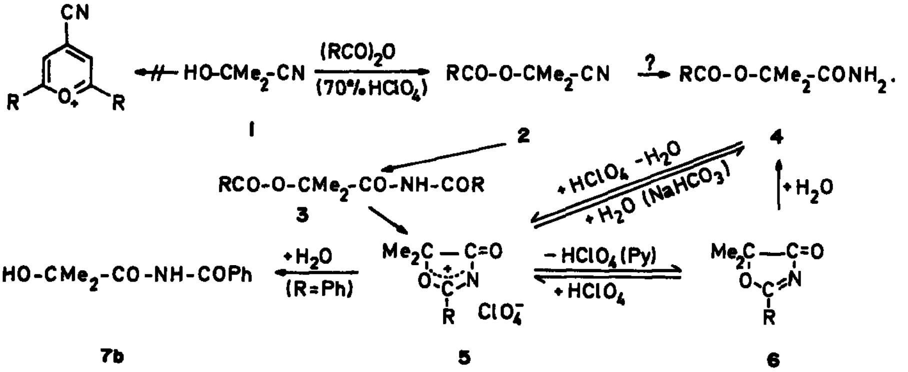
Treatment of tertiary carbinols, $RCMe_2OH$, with acylating agents affords pyrylium salts,[1] e.g. t-butanol yields trimethylpyrylium perchlorate on treatment with acetic anhydride and perchloric acid.[2] The reaction involves dehydration of the carbinol to a propene derivative, $H_3C{-}CR'{=}CH_2$, which is then diacylated to the 4-R′-substituted pyrylium salt. It is sometimes preferable to work with the carbinol instead of the olefin, for instance in the above case when the olefin, 2-methylpropene (isobutene), is gaseous at room temperature, or when the olefin polymerizes readily. In an earlier attempt to obtain 2,6-dimethyl-6-cyanopyrylium by diacetylation of methacrylonitrile (either with $Ac_2O + HClO_4$ or with $AcCl + AlCl_3$), only polymers were obtained.

## 2,5,5-*Trimethyl-2-oxazolin-4-onium perchlorate* (5a)

We therefore investigated the reaction of acetone cyanohydrin[3] (**1**) with acetic anhydride and 70% perchloric acid. A crystalline perchlorate m.p. 183° was obtained in high yield (92%). It was not, however, the expected 4-cyanopyrylium salt. It could be recrystallized from acetic acid, or from ethanol–ether, but not from water in which it dissolved instantly. The elemental analysis revealed that only one acetyl residue was incorporated, so that the formula of the product (**5a**) was $C_6H_{10}NO_2{}^+ClO_4{}^-$. In the IR spectrum (KBr pellet), a strong broad band at 1840 cm$^{-1}$ indicates the presence of a CO group adjacent to a positively-charged centre, while several broad bands between 2500 and 2700 cm$^{-1}$ indicate $\overset{+}{N}$H bonds. Two bands at 1590 and 1540 cm$^{-1}$ are assigned to the fragment $\overline{O{-}C{\overset{+}{-}}N}$. $^1$H NMR peaks appear in TFA at τ 8.09 (6H) and 6.95 (3H). The $^{13}$C NMR spectrum of **5a** in $D_3C$–CN evidences two types of methyls at δ 22.37 (2C) and 18.09 (1C), one quaternary carbon at δ 98.49, and two carbons at δ 175.73 and 193.43 which, by off-resonance experiments, were also shown to have no hydrogen attached; the same peaks appeared in $D_2CCl_2$ (20%) + $F_3CCOOH$ (80%) at δ 23.04 (2C), 18.14 (1C), 96.66 (1C), 175.13 (1C) and 194.22 (1C).

The reaction scheme assigns to **5a** the structure of 2,5,5-trimethyl-2-oxazolin-4-onium perchlorate, in agreement with recent data[4,5] on the formation of oxazolinonium salts by cycliacylation of amides with carboxylic anhydrides.

The reaction involves the intermediate formation of an α-acyloxy-nitrile (**2**). Indeed, α-benzoyloxy-isobutyronitrile (**2b**) cyclizes to **5b** under the action of anhydrous perchloric acid in acetic acid (or of 70% perchloric acid in the corresponding amount of acetic anhydride to react with the water); this can be considered as an indication that **2** is an intermediate in this reaction; the formation of the second intermediate, imide **3** or amide **4**, probably occurs via addition of acetic acid to the nitrile group in **2**



a, R = Me ; b, R = Ph ; c, R = Et ; d, R = n-Pr yielding RCO–O–CMe$_2$–C(OAc)=NH which then rearranges to **3** or reacts with one molecule of water from the medium.[6]

A similar reaction with propionic and butyric anhydrides converts **1** into perchlorates **5c** and **5d**, respectively (Table 1).

### *α-Acetoxy-isobutyramide* (4a)

Treatment of the perchlorate **5a** with H$_2$O or D$_2$O slowly causes a change in the NMR spectra; treatment of **5a** with a cold aqueous solution of an equimolar amount of sodium hydrogen carbonate followed by continuous extraction of the aqueous solution with ether yields, on concentrating the ethereal extract, a crystalline colourless product **4a**, m.p. 110°; the ethereal filtrate contains small amounts of **6a** (see below); compound **4a** is readily soluble in water or in most organic solvents, less in ether, and sparingly in carbon disulphide; it regenerates perchlorate **5a** on treatment with 70% perchloric acid in acetic anhydride. It may be purified by sublimation. The $^1$H NMR spectrum of **4a** in CDCl$_3$ presents two Me bands at $\tau$ 7.90 (3H) and $\tau$ 8.37 (6H) and a broad band at $\tau$ 3.59 (2H) which disappears on deuteration: the Me bands appear at $\tau$ 7.86 and $\tau$ 8.38 in D$_2$O (external TMS) and at $\tau$ 7.75 and $\tau$ 8.24 in F$_3$C–COOH. The $^{13}$C NMR spectrum of **4a** in CDCl$_3$ evidences Me groups at $\delta$ 21.72 (1C) and 24.49 (2C), one quaternary carbon at $\delta$ 80.79 and two CO carbons at $\delta$ 169.76 (acetoxy) and $\delta$ 176.19 (amide); the same peaks appear in D$_2$O at $\delta$ 20.93 (1C), 23.93 (2C), 80.11 (1C), 172.95 (1C) and 178.51 (1C). The IR spectrum of **4a** (KBr pellet) presents strong bands at 1710 and 1730 cm$^{-1}$ (CO bands) and 3385 cm$^{-1}$ (NH). The mass spectrum of **4a** (partly deuterated by evaporation from D$_2$O) evidences parent peaks at 145 (NH$_2$), 146 (NHD) and 147 (ND$_2$). One peak at *m/e* 128 corresponds to loss of (deuterated) water, confirmed by a metastable peak at 112.5. Two peaks at 103 (M–CH$_3$CO) and 101 (M–CONHD), three peaks at 58–60 (CH$_3$CO$_2$) and one peak at 41 (CH$_3$CO) are the most intense in the spectrum. Other peaks occur at *m/e* 87–90 (M–CH$_3$CO$_2$), 69 and 70 (M–H$_2$O–CH$_3$CO$_2$). It appears therefore that **4a** is the ring-opened amide-ester (*α*-acetoxy-isobutyramide).

### *2,5,5-Trimethyl-2-oxazolin-4-one* (6a)

To prevent ring opening, the perchlorate **5a** was treated in anhydrous ether with an equimolar amount of pyridine. The precipitated pyridinium perchlorate was filtered off; evaporation of the ethereal filtrate affords a liquid **6a** which may be distilled with partial decomposition to **4a** under reduced pressure; **6a** is miscible with water and most solvents but not with CS$_2$. The IR spectrum of **6a** (in CCl$_4$ solution) presents in the CO range a strong band at 1720 cm$^{-1}$.

The product **6a** can be isolated in low yield and less pure on treating perchlorate **5a** with aqueous sodium hydrogen carbonate and extracting the aqueous solution with ether (once). Most of the reaction product is, however, the ring-opened **4a** which is much more soluble and is obtained by continuous extraction. Like **4a**, product **6a** affords perchlorate **5a** on treatment with perchloric acid. The $^1$H NMR spectrum of **6a** in CDCl$_3$ presents two Me bands at $\tau$ 7.54 (3H) and $\tau$ 8.50 (6H).

On dissolving 2,5,5-trimethyl-2-oxazolin-4-one (**6a**) in water or in aqueous sodium hydrogen carbonate solution, and on continuous extraction with ether, the ethereal solution affords after concentration *α*-acetoxy-isobutyramide **4a**, identical in every respect to the product obtained from perchlorate **5a**.

Unlike **5a**, compound **5b** ring opens differently on hydrolysis yielding **7b** instead of **4b**.

## EXPERIMENTAL

*2,5,5-Trimethyl-2-oxazolin-4-onium perchlorate* (**5a**). To a mixture of **1**[3] (4.5 ml, 50 mmoles) and Ac$_2$O (30 ml, 300 mmoles), in a 3-necked flash with stirrer, reflux condenser and dropping funnel, 3 ml (50 mmoles) of 70% perchloric acid was added dropwise during 1 hr without cooling. After 3 hr stirring, when the temp had dropped from 80–90° to 25–30°, anhydrous ether was added until the white crystals precipitated completely (about an equal volume of ether is necessary). The crystals of **5a** were filtered off and washed with ether, yield: 5.2 g, 92%. Compound **5a** may be recrystallized from AcOH, or from EtOH–ether, m.p. 183°. Similar reactions with **1**, HClO$_4$ and propionic or butyric anhydrides afforded **5c**, and **5d**, respectively (Table 1).

On treating **2a** (1 g), prepared according to the literature,[7] in 5 ml AcOH, with 1 ml 70% HClO$_4$ in 3 ml Ac$_2$O, then refluxing the mixture for 15 min and adding ether after cooling, perchlorate **5a** was obtained in 80% yield.

Treatment of 1 mole of **4a** (see below) with Ac$_2$O (6 moles) and 70% perchloric acid (1 mole), also affords perchlorate **5a** in 90% yield.

*5,5-Dimethyl-2-phenyl-2-oxazolin-4-onium perchlorate* (**5b**) was prepared by treatment of 1.27 g **2b** (obtained according to literature[7]) in 5 ml AcOH with 1 ml 70% HClO$_4$ in 3 ml water, then refluxing gently for 15 min and adding ether; 2.02 g (70%) of **5b** was obtained, m.p. 209–210° (dec.), Table 1.

*α-Acetoxy-isobutyramide* (**4a**). A concentrated aqueous solution of **5a** (2.27 g in 10 ml water) was treated with an equimolar amount of solid NaHCO$_3$. After the evolution of CO$_2$ subsided, the aqueous mixture was extracted with ether twice in a separating funnel (these ethereal extracts contain a small amount, 0.2 g, of **6a**), then the aqueous solution was extracted for 10 hr in a continuous extractor. The ethereal extract crystallized on concentration and cooling, yielding white crystals (1.1 g) which were purified (after filtration and drying) by sublimation under reduced pressure, m.p. 110°. (Found: C, 49.75; H, 7.61; N, 9.43. C$_6$H$_{11}$NO$_3$ requires: C, 49.63; H, 7.64; N, 9.65%). The same product **4a** could be obtained by continuous (10 hr) extraction with ether of a concentrated aqueous solution of **6a** (see below) 2 g, 17 mmol in 10 ml water. On evaporating the ethereal extract, crystals of **4a** were obtained (0.8 g) together with 1.2 g unreacted liquid **6a**. If the aqueous solution in this latter procedure contained an equimolar amount of NaHCO$_3$, the amount of ring-opened product **4a** was 80%, leaving 20% unreacted **6a**.

N-*Benzoylamide-α-hydroxyisobutyric acid* (**7b**). To 1.45 g (50 mmol) perchlorate **5b**, 8 ml water was added. On standing, crystals of **7b** appeared. After filtration and drying, the product

Table 1. 5,5-Dimethyl-2-R-2-oxazolin-4-onium perchlorates (5)

| | | M.p. | | Found % | | | | Calc. % | | | | Yield |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Comp. | R | (°C) | Formula | C | H | Cl | N | C | H | Cl | N | (%) |
| **5a** | CH$_3$ | 183 | C$_6$H$_{10}$NO$_2^+$ClO$_4^-$ | 31.64 | 4.37 | 15.47 | 5.91 | 31.66 | 4.43 | 15.58 | 6.16 | 92 |
| **5c** | C$_2$H$_5$ | 197–8 | C$_7$H$_{12}$NO$_2^+$ClO$_4^-$ | 34.97 | 5.40 | 14.38 | 5.47 | 34.85 | 4.97 | 14.73 | 5.80 | 79 |
| **5d** | C$_3$H$_7$ | 162–3 | C$_8$H$_{12}$NO$_2^+$ClO$_4^-$ | 37.27 | 5.14 | 13.33 | 5.22 | 37.66 | 5.49 | 13.84 | 5.49 | 80 |
| **5b** | C$_6$H$_5$ | 209–10 | C$_{11}$H$_{12}$NO$_2^+$ClO$_4^-$ | 45.87 | 4.37 | 11.95 | 3.71 | 45.67 | 4.15 | 12.30 | 3.59 | 70 |

weighed 0.8 g, 80% yield, m.p. 79–80° (from aqueous EtOH). IR bands: 3420 (OH), 3290 (NH), 1745 and 1678 (CONHCO), 1609 and 1590 (arom), 1311 and 1420 cm$^{-1}$ (C–O–H). (Found: C, 64.02; H, 6.51. $C_{11}H_{13}NO_3$ requires: C, 63.76; H, 6.28%). $^1$H NMR spectrum in $CDCl_3$: $\tau$ 1.55 [6H, s, $(CH_3)_2$]; 4.25 (1H, s, OH), 7.45–8.45 (5H, m, $C_6H_5$), 9.05 ppm (1H, s, NH).

*2,5,5-Trimethyl-2-oxazolin-4-one* (**6a**). Perchlorate **5a** (2.3 g, 10 mmole) was dissolved in an equimolar amount (0.8 g) of anhydrous pyridine, then anhydrous ether was added, and the mixture was stirred for 30 min. The resulting pyridinium perchlorate was filtered off, and the ethereal filtrate was distilled under reduced pressure, yielding a colourless liquid product (**6a**), 1.3 g, in 90% yield. On treatment with perchloric acid, **6a** regenerated **5a**. The IR and $^1$H NMR spectra are described in the text.

*5,5-Dimethyl-2-phenyl-4-oxazolin-5-one* (**6b**). To 3.89 g (10 mmoles) of **5b** in 15 ml absolute benzene, 1.02 g (20 mmoles) anhydrous triethylamine was added. The mixture was left overnight. After filtration and evaporating of the benzene, **6b**, m.p. 52–53°, was obtained (1.7 g, 90% yield).

IR spectrum: 1751 (CO), 1609 and 1654 (arom.), 1541 (C=N) and 1170 cm$^{-1}$ (C–O–C). (Found: C, 70.15; H, 5.92; N, 7.27. $C_{11}H_{11}NO_2$ requires: C, 69.84; H, 5.82; N, 7.46%).

*Spectra*. IR spectra were recorded with Jena UR-10 instruments, $^1$H NMR spectra with Varian A-60A and Tesla BS 467 instruments at 60 MHz, and $^{13}$C NMR spectra with a Varian CFT-20 instrument. We express our gratitude to Dr. V. Wray for the latter spectra.

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