(125 mg) which was recrystallized from ethanol to afford pyran ester **3**, mp and mmp 37–39°.

A clean piece of sodium (350 mg) was dissolved in D_2O (5 ml). The carboxylic acid (226 mg) was dissolved in the solution and was refluxed for 3 hr under nitrogen atmosphere. Acetic anhydride was added dropwise until pH ~6. The precipitate was recrystallized from ethanol three times to afford the carboxylic acid, mp 205–206°. The infrared and mass spectra of this sample were completely indistinguishable from those of an authentic sample of carboxylic acid **4**.

Decarboxylation of the Carboxylic Acid.—A solution of the carboxylic acid (870 mg) in redistilled quinoline (20 ml) was refluxed for 1 hr. Upon a usual working up, the unreacted carboxylic acid (370 mg) and a neutral oil (310 mg) were obtained. The oil was recrystallized from ethanol–water (5:1) three times to give pyran **5**; mp 32.7–33.5° (sealed tube); $[\alpha]_D$ +63.9 (in EtOH); λ_{max} 221 mμ (ε 4600), 230 (2770), 275 (157), 286 (142), 303 (36), and 318 (21) in cyclohexane. The crystalline compound of **5** sublimed quickly on exposure to the air and gave red color with tetranitromethane in CCl_4. Pyran **5** shows their absorptions at 1715, 1678, and 812 cm^{-1}; nmr τ 9.03 (d, J = 4 Hz, 3 H), 8.96 (s, 6 H), 8.32 (d, 1 Hz, 3 H), 5.82 (q, J = 1 Hz, 1 H); plain positive ORD curve φ (mμ) 32 (550), 41 (500), 50 (450), 70 (400), 95 (350) and 160 (300) in ethanol and 70 (550), 95 (500), 119 (450), 155 (400), 234 (350) and 415 (300) in isooctane.

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.32; H, 10.48.

On treatment with Brady's reagent, pyran **5** gave a yellow precipitate which was recrystallized from ethanol–ethyl acetate three times to afford bishydrazone **11**: mp 184–186°; λ_{max} 229 mμ (ε 23,300), 260 (15,700), and 361 (30,100). The molecular weight determination by Rast method was 601.

Anal. Calcd for $C_{25}H_{30}N_8O_8$: C, 52.65; H, 5.35; N, 19.67. Found: C, 52.46; H, 5.30; N, 19.47.

Reaction of Pyran Ester 3 with $LiAlH_4$.—Pyran **3** was recovered unchanged on treatment with potassium borohydride in aqueous methanol solution overnight. A solution of **3** (850 mg) and lithium aluminum hydride (700 mg) in dry ether (100 ml) were refluxed for 5 hr. The reaction mixture was decomposed with ethyl acetate and was further treated with 20% ammonium hydroxide solution. The product was extracted with light petroleum in the usual manner to give a residue which was recrystallized from light petroleum several times to afford alcohol **6** (425 mg): mp 80–82.5°; $[\alpha]_D$ +62.5 (EtOH); λ_{max} 235 mμ (ε 2660), 285 (20), and 300 (10). Alcohol **6** exhibits the ir absorption (CCl_4) at 3640, 3520, 1710, 1665, and 1195 cm^{-1}; nmr signals at τ 5.82 (s, 2 H), 4.8 (broad, 1 H), 8.09 (s, 3 H), 8.85 (s, 6 H) and 9.02 (d, J = 5 Hz, 3 H); and a plain positive ORD curve of φ (mμ) 102 (550), 130 (500), 165 (450), 222 (400), 335 (350), 585 (300) and 850 (280) in ethanol and 105 (550), 130 (500), 170 (450), 225 (400), 340 (350), 655 (300), and 940 (280) in isooctane.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97; active H, 0.45. Found: C, 75.60; H, 9.76; active H, 0.40.

Although alcohol **6** was recovered unchanged on treatment in hot 1 *N* ethanolic sodium hydroxide solution, it decomposed on storage or on treatment in ethanol solution containing a trace of hydrochlorice acid. Amorphous precipitates were obtained on attempts to prepare 2,4-DNPH, semicarbazone, and thiosemicarbazone.

The acetate of alcohol **5** was formed (acetic anhydride–pridine) as an oil which showed the infrared absorption at 1740, 1715, 1670, 1235, and 1220 cm^{-1} and the nmr signals at τ 5.40 (s, 2 H), 8.02 (s, 3 H), 8.17 (s, 3 H), and 8.9 (s, 6 H).

Oxidation of Alcohol 6.—A solution of the alcohol (1 g) in pyridine (30 ml) was oxidized with a chromic oxide (900 mg) solution in pyridine (5 ml) overnight at 0–5°. After the usual working up, an oil (780 mg) was obtained as the neutral fraction but no material could be obtained from sodium hydroxide (2 *N*) extraction. This oil showed their peaks at 2750, 1712, and 1615 cm^{-1} and was oxidized with a slow stream of air in ethanol (100 ml) for several days. The solvent was evaporated and the remaining residue was triturated with light petroleum to give a crystalline precipitate (145 mg). The crystals were recrystallized from ethanol to give the carboxylic acid **4**. The oil remained from the isolation of the carboxylic acid was oxidized with air in the similar manner to give additional amounts of carboxylic acid **4**.

Hydrogenation of Pyran Ester 3.—A preliminary experiment showed that pyran ester **3** did not absorb hydrogen in ethanol in the presence of palladized carbon (10%) over 48-hr period. Pyran ester **3** (80 mg) platinum oxide (30 mg) in glacial acetic acid (10 ml) were hydrogenated at atmospheric pressure for 20 hr at room temperature. The product was isolated in the usual manner to give an oil. This oil was taken up in light petroleum and percolated through an alumina column to give a colorless oil which was distilled from bulb to bulb under 10 mm pressure. The distillate showed the infrared absorption at 1735 and 1715 cm^{-1} (medium) and, in the nmr region, complex multiplet at τ 5.85–6.75 and many singlets at 9.1–8.7. The mass spectrum showed the intense M^+ peak at 268.

Ozonolysis of Pyran Ester 3.—A solution of **3** (789 mg) in chloroform (30 ml) was ozonized at 0° for 15 min followed by a zinc dust decomposition.

The neutral fraction was taken up in chloroform and was chromatographed on a silicic acid column (10 g). The major component was eluted as the second fraction (125 mg) with chloroform and was distilled from bulb to bulb. This oil showed single spot on a tlc plate (alumina) with chloroform or 2% methanol in chloroform as eluents. Oil **8** possesses their absorption at 1750, 1715, 1180, and 1070 cm^{-1}, the mass spectral peaks at m/e 296 (M^+, 12%), 281 (10), 251 (13), 237 (12), 223 (35), 198 (32) and 171 (100); λ_{max} 207.5 mμ (ε 3600); nmr signals at τ 8.98 (d, J = 6 Hz, 3 H), 8.70 (s, 3 H), 8.82 (s, 3 H), 8.67 (t, J = 7 Hz, 3 H), 8.06 (s, 3 H), and 5.80 (q, J = 7 Hz, 2 H). At the ionization voltage of 15 eV the intensity of the mass peaks at 296, 281, and 237 are enhanced.

From a tlc analysis the acidic fraction was shown to be a mixture of at least six components and was not investigated further.

Registry No.—Pulegone, 89-82-7; ethyl acetoacetate, 141-97-9; **3**, 18600-02-7; **4**, 19614-44-9; **5**, 19614-45-0; **6**, 19614-46-1; **8**, 19640-43-8; **10**, 18588-73-3; **11**, 19614-47-2.

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The Hydroxylamine Route to 3-Unsubstituted Isoxazolium Salts

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The importance of 3-unsubstituted isoxazolium salts in the synthesis of peptides[2] has spurred the improvement of preparative methods for the heterocyclic cations[3] and the development of routes to new types of the salts. Recently those with bulky groups on nitrogen have been made available by the SN1 alkylation of isoxazoles with alcohols and perchloric acid,[4,5] while the first N-aryl compounds **1** were obtained by a new pathway to the heterocyclic ring.[4] Our study of the latter route has now provided a one-step synthesis of 3-unsubstituted isoxazolium perchlorates directly from α-formyl derivatives of carbonyl compounds and N-substituted hydroxylamines.

(1) National Science Foundation Graduate Trainee, 1966–1969.
(2) R. B. Woodward and D. J. Woodman, *J. Amer. Chem. Soc.*, **90**, 1371 (1968).
(3) B. D. Wilson and D. M. Burness, *J. Org. Chem.*, **31**, 1565 (1966).
(4) R. B. Woodward and D. J. Woodman, *ibid.*, **31**, 2039 (1966).
(5) D. J. Woodman, *ibid.*, **33**, 2397 (1968).

In the previous work[4] N-arylhydroxylamines were condensed with hydroxymethyleneacetophenone to give 3-(N-hydroxyanilino)acrylophenones, **2**. Although treatment with aqueous acid was known to lead to simple hydrolysis of compounds of type **2**,[6] it was found that dehydrative cyclization to **1** took place in concentrated sulfuric acid.

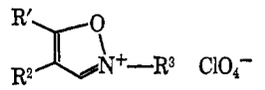
Our further examination of this approach with phenylmalonaldehyde, **3**, and N-benzylhydroxylamine, **4**, revealed that cyclization can also be achieved under mildly acidic conditions in nonaqueous media. Moreover, the condensation and cyclization steps can both be carried out simply by adding 70% perchloric acid to a solution of **3** and **4** in ether, from which the insoluble product 2-benzyl-4-phenylisoxazolium perchlorate, **5**, precipitates. The scope of the new method is demonstrated by the preparation of 2-benzyl-4-methyl-5-phenylisoxazolium perchlorate, **6**, from the more hindered dicarbonyl compound 2-benzoylpropanal, **7**, and of 2,5-diphenyl-4-methylisoxazolium perchlorate, **8**, from **7** and N-phenylhydroxylamine, **9** (Scheme I).

SCHEME I

$R'COCHR^2CHO + R^3NHOH + HClO_4 \longrightarrow$

3, $R' = H$; $R^2 = Ph$ **4**, $R^3 = PhCH_2$

7, $R' = Ph$; $R^2 = Me$ **9**, $R^3 = Ph$



5, $R' = H$; $R^2 = Ph$; $R^3 = CH_2Ph$

6, $R' = Ph$; $R^2 = Me$; $R^3 = CH_2Ph$

8, $R' = R^3 = Ph$; $R^2 = Me$

Experimental Section

Melting points were determined with a Mel-temp apparatus and are uncorrected. The nmr spectra were run on a Varian A-60 spectrometer, and the uv spectra were recorded with a Cary 14 spectrophotometer. Elemental analyses were performed by A. Bernhardt, Mikroanalytisches Laboratorium, West Germany.

2-Benzyl-4-phenylisoxazolium Perchlorate (5).—A mixture of 0.6 g (4.1 mmol) of phenylmalonaldehyde, **3**, and 0.5 g (4.1 mmol) of N-benzylhydroxylamine, **4**, in 50 ml of dry ether was stirred while 0.4 ml of 70% $HClO_4$[7] was added dropwise. After 24 hr the ether was decanted, leaving an orange oil. Several precipitations of the oil from MeCN (10-ml portions) with ether (75-ml portions) gave 0.85 g (62%) of white crystals: mp 125–125.5°; nmr (MeCN) δ 5.93 (s, 2), 7.4–7.82 (unresolved, 10), 9.37 (s, 1), 9.77 (s, 1).

Anal. Calcd for $C_{16}H_{14}ClNO_5$: C, 57.24; H, 4.20; N, 4.18. Found: C, 57.06; H, 4.24; N, 4.03.

2-Benzyl-4-methyl-5-phenylisoxazolium Perchlorate (6).—A solution of 4.0 g (24.7 mmol) of 2-benzoylpropanal, **7**, and 3.0 g (24.7 mmol) of **4** in 1 l. of ether was stirred vigorously at 0° while 2.6 ml of 70% $HClO_4$ was added dropwise. After 24 hr the crystals of **6**, 7.2 g (84%), were filtered and washed with ether. Precipitation of the product from 50 ml of MeCN with 800 ml of ether gave white crystals: mp 138–140°; uv max (CH_2Cl_2) 300 mμ (ϵ 19,000); nmr (98% H_2SO_4, positions upfield relative to H_2SO_4) δ 2.62 (s, 1), 3.7 (broad, 10), 5.5 (s, 1), 8.72 (s, 3).

Anal. Calcd for $C_{17}H_{16}ClNO_5$: C, 58.38; H, 4.61; Cl, 10.14; N, 4.00; O, 22.87. Found: C, 58.42; H, 4.65; Cl, 10.07; N, 4.18; O, 22.95.

(6) J. Thesing, A. Müller, and G. Michel, *Chem. Ber.*, **88**, 1027 (1955).

(7) In view of the explosion hazard associated with the use of perchloric acid, all reactions were carried out behind a sturdy safety shield. Although no detonations were encountered in the present work, it should be noted that some isoxazolium perchlorates have been found to be impact-sensitive explosives.[3]

2,5-Diphenyl-4-methylisoxazolium Perchlorate (8).—A solution of 4.5 g (27.8 mmol) of **7** and 3.0 g (28 mmol) of N-phenylhydroxylamine, **9**, in 1 l. of ether was stirred vigorously with protection from the light while 3 ml of 70% $HClO_4$ was added dropwise. After 3 hr a grey precipitate, 7 g (75%), was filtered, washed with ether, and dried. Precipitation of the product from MeCN with ether gave off-white, light-sensitive crystals: mp 166–167° dec; uv max (CH_2Cl_2) 332 mμ (15,900); nmr (98% H_2SO_4, positions upfield relative to H_2SO_4) δ 3.18–3.62 (m, 10), 2.05 (s, 1), 8.6 (s, 3).

Anal. Calcd for $C_{16}H_{14}NO_5Cl$: C, 57.24: H, 4.20; N, 4.18; Cl, 10.55; O, 23.82. Found: C, 57.30; H, 4.23; N, 4.28; Cl, 10.59; O, 23.79.

Registry No.—**5**, 19614-31-4; **6**, 19614-32-5; **8**, 19614-33-6.

Reaction of 2-Trichloroacetamido-5-chlorobenzhydrol with Potassium Hydroxide to Give 4-Phenyl-6-chloro-1,4-dihydro-2H-3,1-benzoxazin-2-one

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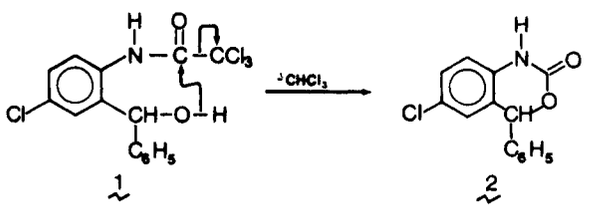
Several examples have been recently reported of cyclizations of 2-chloroacetamidobenzhydrols under basic conditions to give 1,5-dihydro-5-phenyl-4,1-benzoxazepin-2(3H)-ones.[1-4]

In the present study we investigated the reaction of 2-trichloroacetamido-5-chlorobenzhydrol (**1**) with alcoholic base. A crystalline compound $C_{14}H_{10}ClNO_2$ was the only product obtained; ir bands at 1705 and 3210 cm^{-1} suggested the presence of a RNHCOOR group,[5] and the nmr results established the oxazine structure **2**.[6] The formation of **2** might be considered as an intramolecular displacement of chloroform by the neighboring benzhydrilic function (Scheme I).

SCHEME I



An alternative mechanism, involving formation and cyclization of the intermediate isocyanate, could also be considered. To clarify this matter, we planned the synthesis of 2-(N-methyltrichloroacetamido)-5-chlorobenzhydrol, which cannot lead to an isocyanate. Unexpectedly, the reaction of 2-methylamino-5-chlorobenzhydrol with trichloroacetyl chloride in the presence

(1) E. Testa, L. Fontanella, and M. Bovara, *Farmaco, Ed. Sci.*, **18**, 815 (1963).

(2) G. I. Poos, U. S. Patent 3,122,554 (1964); *Chem. Abstr.*, **60**, 12036 (1964).

(3) Lepetit S.p.A., French Patent 1,405,271 (1965); *Chem. Abstr.*, **63**, 13298 (1965).

(4) E. Testa and L. Fontanella, *Farmaco, Ed. Sci.*, **20**, 323 (1965).

(5) L. J. Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen & Co. Ltd., London, 1962, pp 221–222.

(6) E. Testa and L. Fontanella, *Farmaco, Ed. Sci.*, **21**, 549 (1966).