In a similar manner, the reaction of diazonitrone (VI) with PhCOOH gave 4-benzoyloxymethyl-2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl (VIII) as an oil in 45% yield. Infrared spectrum ($CHCl_3$, ν, cm^{-1}): 1730 (C=O), 1610, 1590. Ultraviolet spectrum (λ_{max}, nm): 236 (log ε 4.29). EPR spectrum: triplet with $a_N = 14.0$ Oe. Found: N 9.79%. $C_{15}H_{19}N_2O_4$. Calculated: N 9.62%.

CONCLUSIONS

1. The oxidation of the 4-formyl- and 4-acetyl-1-hydroxy-2,2,5,5-tetramethyl-3-imidazoline hydraxones with either MnO_2 or NiO_2 gives the 4,4,6,6-tetramethyl- and 3,4,4,6,6-pentamethyl-4,5,6,6a-tetrahydroimidazo[1,5-c][1,2,3]triazole-5-oxyls.

2. The oxidation of 1-hydroxy-2,2,5,5-tetramethyl-3-imidazoline-3-oxide hydrazone leads to 4-diazomethyl-2,2,5,5-tetramethyl-3-imidazoline-3-oxide-1-oxyl, which is capable of alkylating carboxylic acids.

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SYNTHESES OF 2-OXO-2,3-DIHYDRO-1H-THIENO-[3,4-d]IMIDAZOLE DERIVATIVES

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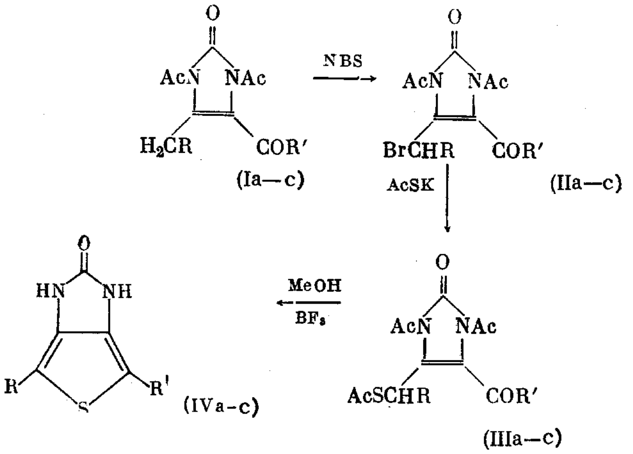
Previously the bromination of the ethyl ester of 1,3-diacetyl-4-methyl-5-(α-keto-ε-carbethoxyamyl)imidazolin-2-one (Ia) [1] with N-bromosuccinimide (NBS) in CCl_4, and subsequent reaction of the intermediate bromide (IIa) with AcSK, gave thioacetate (IIIa), which under the influence of MeOH and BF_3 etherate underwent deacetylation, cyclization, and transesterification to give 2-oxo-2,3-dihydro-4-(δ-carbomethoxybutyl)-1H-thieno[3,4-d]imidazole (IVa) [2]. In order to ascertain the applicability limits of a new method for the synthesis of the dihydrothienoimidazole (DTI) system in the present paper, starting with the corres-



(Ia—c) — (IIIa—c) and (IVb): R = H, R' = $(CH_2)_4COOEt$ (a); R = H, R' = Me (b); R = Me, R' = $(CH_2)_4COOEt$ (c)
(IVa, c): R = H, R' = $(CH_2)_4COOMe$ (a); R = Me, R' = $(CH_2)_4COOMe$ (c)

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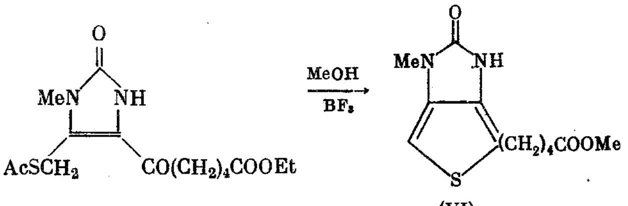
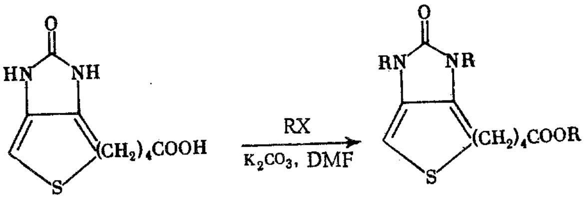
ponding imidazolin-2-ones, we studied the synthesis of DTI derivatives with substituents in the 1,3,4 and 6 positions. The bromination of 1,3,5-triacetyl-4-methylimidazolin-2-one (Ib) and 1,3-diacetyl-4-ethyl-5-(α-keto-ε-carbethoxyamyl)imidazolin-2-one (Ic) using NBS gave bromides (IIb, c), which react with AcSK in acetone to give thioacetates (IIIb, c). The reaction of the latter with MeOH and BF_3 etherate respectively gave the 4-methyl- and 4-methl-6-(δ-carbomethoxybutyl)-2-oxo-2,3-dihydro-1H-thieno[3,4-d]imidazoles (IVb, c).

To insert a substituent in the 1 position of the DTI system we used the previously synthesized 1-methyl-4-(α-keto-ε-carbethoxyamyl)-5-(acetylmercaptomethyl)imidazolin-2-one (V) [3]. As the result of deacetylation, transesterification, and cyclization, the reaction of (V) with MeOH and BF_3 etherate gave 2-oxo-2,3-dihydro-3-methyl-6-(δ-carbomethoxybutyl)-1H-thieno[3,4-d]imidazole (VI).



(V) (VI)

The above-described method proved to be unsuitable for the synthesis of 1,3-dialkyl-substituted DTI due to the unavailability of the corresponding 4-acylimidazolin-2-one derivatives. The insertion of alkyl substituents in the 1 and 3 positions of the DTI system could be accomplished by the direct alkylation of 2-oxo-2,3-dihydro-4-(δ-carboxybutyl)-1H-thieno[3,4-d]imidazole (VII) [3]. Exhaustive alkylation occurred when (VII) was treated with either excess MeI or $PhCH_2Cl$ in DMF, in the presence of K_2CO_3, to give the corresponding esters (VIII) and (IX).



(VII)

X = Cl, I; R = Me (VIII); R = CH_2Ph (IX)

The insertion of three substituents into (VII) follows from the elemental analysis and PMR spectra, while the location of two of the substituents on the N atoms is in agreement with the IR spectral data, where strong bands of ureido carbonyl are present at 1710 cm^{-1}.

EXPERIMENTAL

The UV spectra (λ_{max}) were taken in alcohol solution on a Specord UV-VIS instrument, the IR spectra were taken as KBr pellets on a UR-20 spectrometer, the PMR spectra were taken in C_5D_5N solution on a DA-60-IL instrument (internal standard = HMDS), and the TLC was run on Silufol UV-254 (ethyl acetate (EA), detection of the spots with I_2 vapors and in UV light).

1,3,5-Triacetyl-4-methylimidazolin-2-one (Ib). A mixture of 1 g of 4-methyl-5-acetylimidazolin-2-one [4] in 10 ml of Ac_2O was refluxed for 2 h, evaporated in vacuo, the residue was treated with 5 ml of Ac_2O, the mixture was refluxed for another 2 h, evaporated again in vacuo, the residue was treated with alcohol, and the precipitate was washed with alcohol and dried in the air to give 1.12 g (73%) of (Ib), mp 68-69°C (from alcohol), R_f 0.46. Ultraviolet spectrum: 273 nm. Found: C 53.60; H 5.46; N 12.48%. $C_{10}H_{12}N_2O_4$. Calculated: C 53.60; H 5.36; N 12.50%.

1,3,5-Triacetyl-4-(bromomethyl)imidazolin-2-one (IIb). A mixture of 2 g (0.0089 mole) of (Ib) and 1.59 g (0.0089 mole) of NBS in 10 ml of CCl_4 was heated for 2 h at 95° (bath temperature), cooled to ∿20°, the filtrate was evaporated in vacuo, and the residual bromide (IIb) (2.5 g, oil, R_f 0.86) was used as such in the next step.

1,3,5-Triacetyl-4-(acetylmercaptomethyl)imidazolin-2-one (IIIb). With stirring, to 2.26 g (0.0075 mole) of (IIb) in 5 ml of acetone was gradually added a solution of AcSK (from 0.63 g (0.011 mole) of KOH and 1.09 g (0.016 mole) of AcSH in 2 ml of water), the mixture was stirred for another hour at ∿20°, and then it was evaporated in vacuo. The residue was treated with water, and the precipitate was washed with water and dried in the air to give 1.42 g (66%) of (IIIb), mp 110-112° (from alcohol), R_f 0.80. Ultraviolet spectrum: 271 nm. PMR spectrum (δ, ppm): 2.08 s (CH_3COS), 2.28 s ($CH_3COC{=}C$); 2.50 s and 2.52 s ($2CH_3CON$), 4.02 s (CH_2S). Found: C 48.34; H 4.66; S 10.62%. $C_{12}H_{14}N_2O_5S$. Calculated: C 48.50; H 4.70; S 10.62%.

2-Oxo-2,3-dihydro-4-methyl-1H-thieno[3,4-d]imidazole (IVb). A mixture of 1 g of (IIIb) and 3 ml of BF_3 etherate in 6 ml of MeOH was kept for 100 h at ∿20°, evaporated in vacuo, and the residue was treated with excess aqueous Na_2CO_3 solution and extracted with EA. The extract was dried over $MgSO_4$, evaporated in vacuo, and the residue was chromatographed on a SiO_2 column. Elution with EA gave 0.21 g (39%) of (IVb), mp 212-214° (from alcohol), R_f 0.32. Ultraviolet spectrum: 260 nm. Infrared spectrum (ν, cm^{-1}): 1700 (C=O), 2800-3400 (CH, NH). PMR spectrum (δ, ppm): 2.01 s (CH_3), 6.00 s (HC—C), 11.26 s (2 NH). Found: C 46.47; H 3.78; S 20.32%. $C_6H_6N_2OS$. Calculated: C 46.66; H 3.90; S 20.40%. The value given in [3] for the UV spectrum of (IVa) is 262 nm.

1,3-Diacetyl-4-ethyl-5-(α-keto-ε-carbethoxyamyl)imidazolin-2-one (Ic). The treatment of 0.8 g of 4-ethyl-5-(α-keto-ε-carbethoxyamyl)imidazolin-2-one [5] with Ac_2O as described above gave 0.95 g (90%) of (Ic) (oil, R_f 0.84). The compound and those described below were used as such in the next steps.

1,3-Diacetyl-4-(α-bromoethyl)-5-(α-keto-ε-carbethoxyamyl)imidazolin-2-one (IIc). Similar to (IIb), the bromination of 0.95 g (0.0026 mole) of (Ic) with 0.6 g (0.003 mole) of NBS in 10 ml of CCl_4 gave 1.14 g (98%) of (IIc) as an oil with R_f 0.72.

1,3-Diacetyl-4-(α-acetylmercaptoethyl)-5-(α-keto-ε-carbethoxyamyl)imidazolin-2-one (IIIc). With stirring, to 1.14 g (0.0026 mole) of (IIc) in 5 ml of acetone was gradually added a solution of AcSK (from 0.5 g (0.0089 mole) of KOH and 1 ml (0.014 mole) of AcSH in 2 ml of water), the mixture was stirred for another hour at 20°, evaporated in vacuo, and the residue was treated with water and extracted with EA. The extract was dried over $MgSO_4$ and evaporated in vacuo to give 0.85 g (74%) of (IIIc) as an oil with R_f 0.42 (1:1 EA—benzene).

2-Oxo-2,3-dihydro-4-methyl-6-(δ-carbomethoxybutyl)-1H-thieno[3,4-d]imidazole (IVc). Similar to (IVb), the treatment of 0.85 g of (IIIc) in 6 ml of MeOH with 3 ml of BF_3 etherate gave 0.2 g (38%) of (IVc), mp 155-157° (from alcohol), R_f 0.40. Ultraviolet spectrum: 260 nm. Infrared spectrum (ν, cm^{-1}): 1700 (C=O), 1730 (COOMe), 2800-3400 (CH, NH). PMR spectrum δ, ppm): 1.45 m (CH_2CH_2), 2.05 m ($CH_3C{=}C$, CH_2COOCH_3), 2.70 m ($CH_2C{=}C$), 3.35 s (CH_3O), 11.11 s (2NH). Found: C 53.78; H 6.10; N 10.40; S 11.92%. $C_{12}H_{16}N_2O_3S$. Calculated: C 53.70; H 5.99; N 10.44; S 11.90%.

2-Oxo-2,3-dihydro-3-methyl-6-(δ-carbmethoxybutyl)-1H-thieno[3,4-d]imidazole (VI). Similar to the above, the treatment of 1 g of 1-methyl-4-(α-keto-ε-carbethoxyamyl)-5-(acetylmercaptomethyl)imidazolin-2-one (V) in 6 ml of MeOH with 3 ml of BF_3 etherate gave 0.66 g (85%) of (VI), mp 92-93°, R_f 0.56. Ultraviolet spectrum: 260 nm. Infrared spectrum (ν, cm^{-1}): 1700 (C=O), 1730 (COOMe), 2800-3400 (CH, NH). PMR spectrum (δ, ppm): 1.40 m (CH_2CH_2), 2.00 m (CH_2COOMe), 2.44 m ($CH_2C{=}C$), 2.93 s (MeN), 3.28 s (MeO), 6.10 s (HC=C). Found: C 53.47; H 6.22; N 10.03; S 12.29%. $C_{12}H_{16}N_2O_3S$. Calculated: C 53.60; H 6.21; N 10.04; S 12.40%.

1,3-Dimethyl-2-oxo-2,3-dihydro-4-(δ-carbomethoxybutyl)thieno[3,4-d]imidazole (VIII). With periodic stirring, a mixture of 1.2 g (0.0048 mole) of 2-oxo-2,3-dihydro-4-(δ-carboxybutyl)-1H-thieno[3,4-d]imidazole (VII) [3], 3 ml (0.048 mole) of MeI, and 4 g (0.029 mole) of dry, finely ground K_2CO_3 in 10 ml of dry DMF was kept for 360 h at 20°, after which it was diluted with water and extracted with EA. The extract was dried over $MgSO_4$, evaporated, and the residue was chromatographed on a SiO_2 column. Elution with a 1:4 EA—benzene mixture gave 0.56 g (40%) of (VIII) as an oil with R_f 0.64 (1:4 EA—benzene). Ultraviolet spectrum: 260 nm. Infrared spectrum (ν, cm^{-1}): 1710 (C=O), 1730 (COOMe), 2800-3400 (CH, NH). PMR spectrum (δ, ppm): 1.51 m (CH_2CH_2), 2.10 m (CH_2COOMe), 2.60 m ($CH_2C{=}C$), 3.00 s (MeN), 3.11 s (MeN), 3.43 s (MeO), 6.03 s (HC=C).

1,3-Dibenzyl-2-oxo-2,3-dihydro-4-(δ-carbobenzyloxybutyl)thieno[3,4-d]imidazole (IX). Similar to the above, the treatment of 0.5 g (0.002 mole) of (VII) in 10 ml of DMF with 2.5 ml (0.021 mole) of $PhCH_2Cl$ and 4 g (0.029 mole) of K_2CO_3 gave 0.36 g (35%) of (IX), mp 62-64° (from alcohol), R_f 0.37 (1:1 EA—benzene). Ultraviolet spectrum: 260 nm. Infrared spectrum (ν, cm^{-1}): 1710 (C=O), 1730 ($COOCH_2Ph$), 2800-3400 (CH, NH). PMR spectrum (δ, ppm): 1.27 m (CH_2CH_2), 2.03 m (CH_2COOCH_2Ph), 2.35 m ($CH_2C{=}C$), 4.76 s ($2PhCH_2N$), 5.01 s ($PhCH_2O$), 6.05 s (HC=C), 7.36-7.48 ($3C_6H_5$). Found: C 72.53; H 5.55; N 5.31; S 5.78%. $C_{31}H_{30}N_2O_3S$. Calculated: C 72.50; H 5.80; N 5.50; S 6.23%.

CONCLUSIONS

1. The reaction of N-substituted 4-acyl-5-(α-acetylmercaptoalkyl)imidazolin-2-ones with methanol in the presence of BF_3 etherate leads to 2-oxo-2,3-dihydro-1H-thieno[2,3-d]-imidazole derivatives.

2. The alkylation of 2-oxo-2,3-dihydro-4-(δ-carboxybutyl)-1H-thieno[3,4-d]imidazole with either excess methyl iodide or benzyl chloride proceeds at the carboxyl group and both of the nitrogen atoms.

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