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## Note

# Synthesis of 3-alkyl(aryl)-1-aryl-4-(D-*arabino*-tetrahydroxybutyl)-imidazoline-2-thiones*,†

F. GARCÍA GONZÁLEZ, J. FERNÁNDEZ-BOLAÑOS, J. FUENTES MOTA, AND M. A. PRADERA DE FUENTES

*Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Sevilla, and Instituto de Química Orgánica General, C.S.I.C., Sevilla (Spain)*

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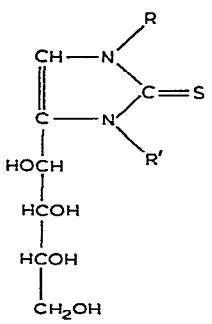
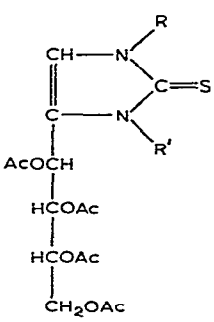
The 1-alkyl(aryl)-4-(D-*arabino*-tetrahydroxybutyl)imidazoline-2-thiones can be obtained[1–4] by the reaction of 1-alkyl(aryl)amino-1-deoxy-D-fructoses with ammonium(potassium) thiocyanate, and also by isomerization of 1-alkyl(aryl)-4,5-(1,2-D-glucofurano)imidazolidine-2-thiones, which are prepared by condensation of 2-amino-2-deoxy-D-glucose with alkyl(aryl) isothiocyanates.

The 3-methyl(aryl)-4-(D-*arabino*-tetrahydroxybutyl)imidazoline-2-thiones have been recently prepared[5] by the reaction of 1-amino-1-deoxy-D-fructose with methyl (aryl) isothiocyanates, and also by the reaction of 2-deoxy-2-methylamino-D-glucose hydrochloride with potassium thiocyanate.

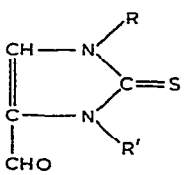
We now report the synthesis of 1-aryl-3-alkyl(aryl)-4-(D-*arabino*-tetrahydroxy-



1 R = *p*-$MeC_6H_4$, R′ = Me
2 R = *p*-$MeC_6H_4$, R′ = Et
3 R = *p*-$MeOC_6H_4$, R′ = Me
4 R = *p*-$MeOC_6H_4$, R′ = Et
5 R = *p*-$EtOC_6H_4$, R′ = Me
6 R = *p*-$MeC_6H_4$, R′ = Ph
7 R = *p*-$MeOC_6H_4$, R′ = Ph
8 R = *p*-$EtOC_6H_4$, R′ = Ph



9 R = *p*-$MeC_6H_4$, R′ = Me
10 R = *p*-$MeC_6H_4$, R′ = Ph
11 R = *p*-$MeOC_6H_4$, R′ = Ph
12 R = *p*-$EtOC_6H_4$, R′ = Ph



13 R = *p*-$MeC_6H_4$, R′ = Me
14 R = *p*-$MeOC_6H_4$ R′ = Ph

*Dedicated to Professor V. Deulofeu, in honor of his 70th birthday.
†Part 10 in the series "Thiolglucimidazoles". For Part 9, see Ref. 5.

TABLE I

3-ALKYL(ARYL)-1-ARYL-4-(D-*arabino*-TETRAHYDROXYBUTYL)IMIDAZOLINE-2-THIONES

| *Compound* | *M.p.* (°) | $[\alpha]_{546.1}$[a] (°) | *Yield* (%) | *Elemental analysis* | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | *Formula* | *Calculated* | | | | *Found* | | | |
| | | | | | *C* | *H* | *N* | *S* | *C* | *H* | *N* | *S* |
| **1** | 162–164 | −10 | 70 | $C_{15}H_{20}N_2O_4S$ | 55.53 | 6.22 | 8.64 | 9.88 | 55.48 | 5.95 | 8.87 | 9.79 |
| **2** | 155–156 | +5 | 72 | $C_{16}H_{22}N_2O_4S$ | 56.78 | 6.55 | 8.28 | 9.47 | 56.81 | 6.71 | 8.47 | 9.05 |
| **3** | 161–163 | −7 | 68 | $C_{15}H_{20}N_2O_5S$ | 52.93 | 5.92 | 8.23 | 9.42 | 52.93 | 6.18 | 8.33 | 9.46 |
| **4** | 133–135 | +5 | 70 | $C_{16}H_{22}N_2O_5S$ | 54.22 | 6.26 | 7.91 | 9.05 | 53.90 | 5.86 | 7.82 | 8.84 |
| **5** | 112–114 | | 68 | $C_{16}H_{22}N_2O_5S$ | 54.22 | 6.26 | 7.91 | 9.05 | 53.95 | 6.40 | 8.36 | 9.13 |
| **6** | 190–192 (dec.) | −21 | 14 | $C_{20}H_{22}N_2O_4S$ | 62.15 | 5.73 | 7.25 | 8.29 | 62.19 | 5.96 | 7.58 | 7.98 |
| **7** | 179 (dec.) | −13 | 26 | $C_{20}H_{22}N_2O_5S$ | 59.68 | 5.51 | 6.96 | 7.97 | 59.43 | 5.51 | 6.68 | 7.77 |
| **8** | 169–170 (dec.) | −8 | 20 | $C_{21}H_{24}N_2O_5S$ | 60.56 | 5.81 | 6.72 | 7.70 | 60.66 | 6.00 | 6.89 | 7.49 |

[a]Optical rotations determined in pyridine ($c \sim 1$) at 29° (**1–4, 6**), 19° (**7, 8**).

TABLE II

3-ALKYL(ARYL)-1-ARYL-4-(D-*arabino*-TETRAACETOXYBUTYL)IMIDAZOLINE-2-THIONES

| *Compound* | *M.p.* (°) | $[\alpha]_{546.1}$[a] (°) | *Yield* (%) | *Elemental analysis* | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | *Formula* | *Calculated* | | | *Found* | | |
| | | | | | *C* | *H* | *N* | *C* | *H* | *N* |
| **9** | 49–52 | −93 | 63 | $C_{23}H_{28}N_2O_8S$ | 56.08 | 5.73 | 5.69 | 56.29 | 5.92 | 5.58 |
| **10** | 165 | −103 | 83 | $C_{28}H_{30}N_2O_8S$ | 60.63 | 5.45 | 5.05 | 60.57 | 5.50 | 4.83 |
| **11** | 147 | −112 | 75 | $C_{28}H_{30}N_2O_9S$ | 58.93 | 5.30 | 4.91 | 58.60 | 5.50 | 5.01 |
| **12** | 151 | −108 | 89 | $C_{29}H_{32}N_2O_9S$ | 59.58 | 5.52 | 4.79 | 59.28 | 5.82 | 4.90 |

[a]Optical rotation determined in pyridine ($c \sim 1$) at 20° (**9, 10**), 21° (**11, 12**).

butyl)imidazoline-2-thiones (**1–8**) by the reaction of 1-arylamino-1-deoxy-D-fructoses with alkyl(aryl) isothiocyanates.

The structure of these compounds is supported by the following observations: Acetylation of **1**,**6**,**7**, and **8** gave the tetraacetates **9–12**, in agreement with a tetrahydroxybutyl chain; oxidation of **1** and **7** with lead tetraacetate gave the 4-formylimidazoline-2-thiones **13** and **14**; the u.v. spectra of **3**, **7**, and **11** have the characteristic wavelenght absorption[2,5,6] at ~265 nm of imidazoline-2-thiones.

## EXPERIMENTAL

*General.* — Optical rotations at 546.1 nm were determined with a Bendix-NPL Automatic Polarimeter 143C at $c \sim 1$ in pyridine. U.v. spectra were obtained on a Unicam SP-800 spectrophotometer in 1:1 ethanol–water and i.r. spectra on a Perkin–Elmer 621 instrument.

*1-Aryl-3-alkyl(aryl)-4-*(D-arabino-*tetrahydroxybutyl*)*imidazoline-2-thiones* (**1–8**). — A mixture of 1-arylamino-1-deoxy-D-fructose (3.6 mmoles) and alkyl(aryl) isothiocyanate (3.6 mmoles) in ethanol (10 ml) was heated with stirring at 100° for 45–60 min (90 min when compound **5** was prepared), acetic acid (1 ml) was added, and the solution heated at reflux for a further 45–60 min. The solvent was evaporated under reduced pressure to yield a syrup from which acetic acid was removed by several additions and evaporations of ethanol. The residue was crystallized from ethanol. Physical constants, yields, and analytical data of the products are given in Table I.

*1-Aryl-3-alkyl(aryl)-4-*(D-arabino-*tetraacetoxybutyl*)*imidazoline-2-thiones* (**9–12**). — Compounds (**1**,**6–8**, 0.5 g, each) were suspended in 1:1 acetic anhydride–pyridine (5 ml). After being kept for 24 h at room temperature, the reaction mixture was poured into ice–water (50 ml) and the acetates crystallized after scratching. Compound **9** was purified by precipitation from aqueous ethanol. Compounds **10–12** were washed repeatedly with water and recrystallized from ethanol. Physical constants, yields, and analytical data are given in Table II.

*4-Formyl-3-methyl-1-*p-*tolylimidazoline-2-thione* (**13**). — To a solution of **1** (0.5 g, 1.5 mmoles) in 9:1 benzene–methanol (2.5 ml) was added lead tetraacetate (1.3 g, 3 mmoles) and the mixture was stirred for 30 min. Benzene–acetic acid (1:1, 2 ml) and water (~10 ml) were added, the organic layer was filtered, washed with a saturated solution of sodium hydrogen carbonate, and water. Drying (calcium chloride) and evaporation afforded a residue which was crystallized from ethanol (0.1 g, 28%), m.p. 155–156°, i.r. datum: $\nu_{max}^{CHCl_3}$ 1675 $cm^{-1}$ (C=O)

*Anal.* Calc. for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.28; N, 12.03. Found: C. 62.04; H, 5.46; N, 11.84.

*4-Formyl-3-phenyl-1-*p-*methoxyphenylimidazoline-2-thione* (**14**). — To a solution of **7** (0.5 g, 1.2 mmoles) in 1:1 acetic acid–benzene (2.5 ml) was added lead tetraacetate (1.1 g, 2.5 mmoles) and the mixture was stirred for 30 min. Benzene (4 ml) and water (10 ml) were added, the organic layer was washed with water and with a saturated

solution of sodium hydrogen carbonate, filtered, and finally washed again with water and dried (calcium chloride). The solvent was evaporated and the residue crystallized from ethanol (0.1 g, 32%), m.p. 205–207°, i.r. datum: $\nu_{max}^{CHCl_3}$ 1681 $cm^{-1}$ (C=O).

*Anal.* Calc. for $C_{17}H_{14}N_2O_2S$: C, 65.79; H, 4.55; N, 9.03. Found: C, 65.74; H, 4.66; N, 8.89.

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