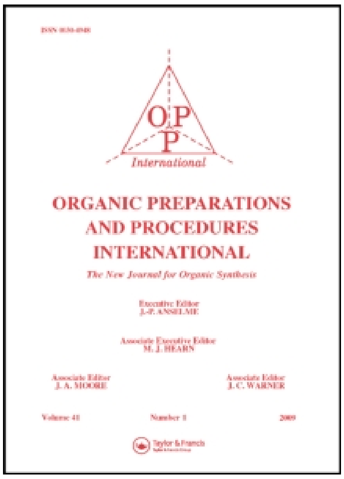

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4H-BENZPYRANO [3,4-d]OXAZOL-4-ONES AND 3-[N,N-BIS(CARBOXYMETHYL)AMINO]-4-HYDROXYCOUMARIN DERIVATIVES

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REFERENCES

1. D. J. Dunn and P. H. Plesch, Makromol. Chem., 175, 2821 (1974).
2. D. J. Dunn, Ph.D. Thesis, University of Keele, 1973.
3. S. M. McElvain and D. Kundinger, Org. Syn., Coll. Vol.III, 506 (1955).

4. As with other ketene acetals[3] it is advisable to wash all glassware with aqueous alkali prior to rinsing with water and drying. This treatment prevents the oligomerization of the ketene acetal caused by the acidic surface of the glass.
5. When this procedure was repeated on a larger scale (using *t*-butoxide from 200 g of potassium and 940 g of the bromoacetaldehyde acetal), the heat from the exothermic dehydrobromination reaction was not dissipated rapidly enough to avoid the loss of about one third of the contents of the flask during the subsequent violent boiling. When the boiling subsided, the distillation was continued normally to give 160 g of the ketene acetal.

4H-BENZPYRANO[3,4-d]OXAZOL-4-ONES AND 3-[N,N-BIS(CARBOXYMETHYL)AMINO]-4-HYDROXYCOUMARIN DERIVATIVES

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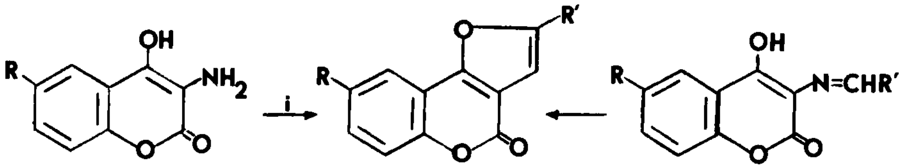
Some derivatives of 3-amino-4,7-dihydroxy-8-methyl coumarin (AHC),[1-3] a structural component of the antibiotic *novobiocin* as well as AHC itself have been reported as bactericidal and fungicidal agents.[4] In an effort to enhance the biological activity of AHC, the title compounds were synthesized. The oxazolone synthesis is based on the procedure of



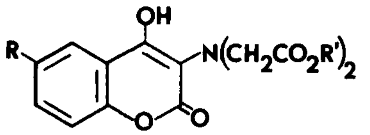
(AHC) (A) 1 (B)

i) R'CHO

a) R = Cl, R' = CH_3 b) R = Br, R' = CH_3 c) R = Cl, R' = Ph

Arndt and his group[5] who obtained oxazolones by heating AHC with acetic anhydride and that of Rao and Rao[6] who reacted AHC and an aromatic aldehyde in boiling nitrobenzene. In certain cases, the oxazolones were prepared using the preformed N-arylidene derivatives.

The carboxymethyl derivatives of AHC, 2a and 2c, resulted from the reaction of AHC and its 6-chloro derivative respectively, with chloroacetic acid in presence of a hydrohalide acceptor. The products were subsequently esterified to compounds 2b and 2d.



2a R = H, R' = H

2b R = H, R' = Et

2c R = Cl, R' = H

2d R = Cl, R' = Et

EXPERIMENTAL

All mp. are uncorrected. Ir spectra were obtained with a Perkin-Elmer M-377 infrared spectrophotometer using KBr pellets. Nmr spectra were recorded in dimethylsulfoxide with a Varian 60A instrument. All new compounds yielded satisfactory elemental analyses.

8-Chloro-2-methyl-4H-benzpyrano[3,4-d]oxazol-4-one (1a). -

A. 3-Amino-6-chloro-4-hydroxycoumarin, 0.5 g (2.36 mmoles) and 10 ml of acetic anhydride were refluxed for 2 hr., then poured onto 200 g of ice water. On standing in a refrigerator overnight the product separated as a solid. Recrystallization from ethanol gave 0.33 g (58.5%) of light gray crystals, mp. 208-209°.

B. The same procedure carried out with 3-benzilideneamino-6-chloro-4-hydroxycoumarin as the starting compound, and with the reflux time extended to 3 hr., yielded 0.17 g (71.5%) of recrystallized product, mp. 208-209°.

Both products gave identical ir and nmr data: IR, 1745 (CO), 1585, 1595, 1490, 1210 cm^{-1}; NMR, 2.74δ (s, CH_3), 7.53-7.82δ (m, arom.).

8-Bromo-2-methyl-4H-benzpyrano[3,4-d]oxazol-4-one (1b). - 3-Amino-6-bromo-4-hydroxycoumarin, (0.5 g, 2.49 mmoles), gave 0.42 g (60.3%) of purified product, mp. 188°, by route A.

8-Chloro-2-phenyl-4H-benzpyrano[3,4-d]oxazol-4-one (1c).[7] - A mixture of 0.4 g (1.34 mmoles) of 3-benzilideneamino-6-chloro-4-hydroxycoumarin and 40 ml of nitrobenzene was heated 3 hr. at 150°. The residue after removal of solvent by steam-distillation, was recrystallized from ethanol to give 0.05 g (12%) of brown crystals, mp. 165°; IR, 1776 (CO), 1630, 1605, 1550, 1265 cm^{-1}, (route B).

3-[N,N-bis(carboxymethyl)amino]-4-hydroxycoumarin (2a). - An aqueous solution (10 ml of H_2O) of 0.5 g (2.86 mmoles) of AHC, 0.5 g (5.3 mmoles) of chloroacetic acid, and 1 g (3.5 mmoles) of Na_2CO_3 was heated for 3 hr. at 120-130° in an oil bath.

Upon cooling and acidification a solid separated, which was recrystallized from water to give 0.8 g (75.8%) of white crystals, mp. 185-189°; IR 3250 (OH), 2900, 1730 (CO), 1600, 1550, 1250 cm^{-1}; NMR δ3.79 (s, CH_3), 4.00 (s, OH), 7.45-7.90 (m, arom.), 9.70 (s, COOH).

3-[N,N-bis(carboxymethyl)amino]-4-hydroxycoumarin diethyl ester (2b). - 2a (0.4 g, 1.30 mmoles) was dissolved in 30 ml of abs. ethanol. After addition of 3 ml of conc. HCl the solution was heated under reflux for 2 hr. The solid which separated on cooling was recrystallized from 50% ethanol to give 0.31 g (65%) of needle-like crystals, mp. 62-64°; IR 3265 (OH), 2980, 1740 (CO), 1720, 1685, 1620, 1200 cm^{-1}.

3-[N,N-bis(carboxymethyl)amino]-6-chloro-4-hydroxycoumarin (2c). - 3-Amino-6-chloro-4-hydroxycoumarin, (0.5 g, 2.36 mmoles), 0.5 g (5.3 mmoles) of chloroacetic acid, and 0.92 g (3.2 mmoles) of Na_2CO_3 was treated following the preceeding directions to yield 0.7 g (81%) of yellow crystalline solid, mp. 196-197°; IR 3342 (OH), 2920, 1696 (CO), 1625, 1435, 1230 cm^{-1}; NMR δ3.75 (s, CH_3), 4.02 (s, OH), 7.22-7.71 (m, arom.), 7.95 (s, COOH).

3-[N,N-bis(carboxymethyl)amino]-6-chloro-4-hydroxycoumarin diethyl ester (2d). - The preceeding procedure was carried out with 0.4 g (1.25 mmole) of 2b. The yield was 0.35 g (69%) of needle-like crystals, mp. 175-178°; IR 3062 (OH), 2980, 1752 (CO), 1723, 1628, 1295 cm^{-1}.

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REFERENCES

1. M. Dezelic, M. Trkovnik, R. Jovanovic and J. Grujic-Vasic, Glas. chem. tehnol. Bosne i Hercegovine, 12, 117 (1963); CA 63: 18009f (1965).
2. M. Dezelic and M. Trkovnik, Ind. Chim. Belge, 1967, 32 (Spec. No.), 256; CA 70: 87461t (1969).
3. H. Hoeksema, E. L. Caron and J. W. Hinman, J. Am. Chem. Soc., 78, 2019 (1956).
4. K. S. R. Krishna Mohan Rao and N. V. Subba Rao, Ind. J. Chem., 3, 522 (1965).
5. F. Arndt, L. Loewe, R. Ün and E. Ayca, Chem. Ber., 84, 319 (1951).
6. K. S. R. Krishna Mohan Rao and N. V. Subba Rao, Curr. Sci., 33, 614 (1964); CA 62: 1640a (1965).
7. Editor's Note: Attempted condensation using Procedure A yielded only compound 1a. A referee has suggested that the presence of moisture could generate sufficient acetic acid in this particular case to hydrolyze the benzylidene derivative.