Tetrahedron Letters No. 12, pp. 781-784, 1963. Pergamon Press Ltd.
Printed in Great Britain.

REARRANGEMENT OF N-CYANO-ANTHRANILIC ACIDS TO 1,2-DIHYDRO-2-IMINO-3,1,4H-BENZOXAZIN-4-ONES AND 2,4(IH,3H)-QUINAZOLINE-DIONES. REACTIONS OF 1,2-DIHYDRO-2-IMINO-3,1,4H-BENZOXAZIN-4-ONE WITH HYDROXYLIC REAGENTS.

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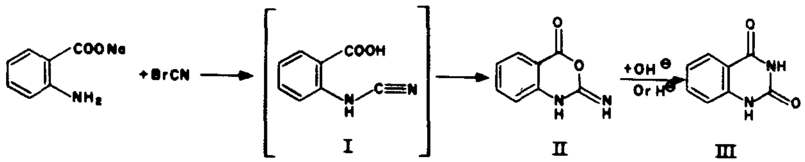
(Received 8 February 1963)

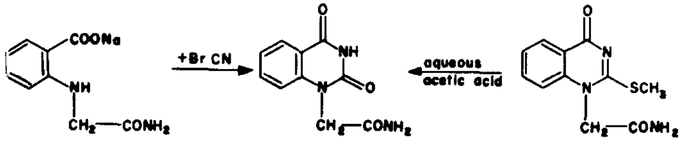
Reaction of sodium anthranilate with excess cold aqueous cyanogen bromide affords - evidently through rearrangement of transitionally formed N-cyano-anthranilic acid (I) - 1,2-dihydro-2-imino-3,1,4H-benzoxazin-4-one (II) mp.: 212°C, decomp., from ethyl acetate; found C 59,48 H 3,81 N 17,50; $C_8H_6N_2O_2$ = 162,1 requires C 59,26 H 3,73 N 17,28, the asymmetric imide of isatoic acid.



The structure of II follows 1) from its IR spectrum, which does not contain bands corresponding to a C = N or N = C = N group, however contains bands between 3440 and 3000 cm^{-1} corresponding to the different NH groups, bands at 1750 and 1690 cm^{-1} corresponding to the carbonyl vibration of a cyclic lactone and to the C = N band respectively; 2) from its UV spectrum which is closely similar to that of anthranilic acid and isatoic anhydride; and 3) from its reactions outlined below.

Treatment of II with excess hot aqueous-alcoholic potassium carbonate or with cold aqueous-acetonic potassium hydroxide or with hot 20% hydrochloric acid, as well as prolonged refluxing with acetic acid converts it to 2,4(IH,3H)-quinazolinedione (III) identified by mp. and mixed mp.

If the N-carbamoylmethyl derivative (IV) of sodium anthranilate is treated with cyanogen bromide under the conditions stated above, the corresponding derivative (V) mp: 331-332°C, decomp., from aqueous alcohol; found C 54,79 H 4,12 N 19,35; $C_{10}H_9N_3O_3$ = 221,2 requires C 54,79 H 4,14 N 19,15 of III is directly formed.

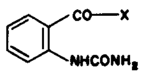


IV V VI

The structure of V has been proved 1) by its IR spectrum and 2) by independent synthesis from (1,4-dihydro-2-methylmercapto-4-oxo-1-quinazolinyl)-acetamide (VI)[1].

Treatment of II with 1 mole of cold aqueous-acetonic potassium hydroxide or short refluxing with 1 mole of aqueous potassium carbonate or even with aqueous dioxane as well as treatment with 50% acetic acid at room temperature converts it to 2-ureido-benzoic acid (VIIa) mp.: 173-174°C, decomp., from aqueous methanol; found: C 53,45 H 4,54 N 15,45; $C_8H_8N_2O_3$ = 180,2 requires: C 53,33 H 4,48 N 15,55, which on more energic treatment with alkali or acid, is cyclised to III.

Correspondingly, short refluxing with 50% aqueous methanol or ethanol converts II to 2-ureido-benzoic acid methyl (VIIb) mp.: 178-179°C[x] from methanol; found: C 55,80 H 5,15 N 14,25; $C_9H_{10}N_2O_3$ = 194,2 requires C 55,66 H 5,19 N 14,43 and ethyl ester (VII c) mp.: 179°C[x], from ethanol; found: C 57,99 H 5,70 N 13,58; $C_{10}H_{12}N_2O_3$ = 208,2 requires C 57,68 H 5,81 N 13,46 respectively.



VII

a: X = HO-
b: X = CH_3O-
c: X = C_2H_5O-
d: X = n-C_3H_7O-
e: X = n-C_4H_9O-
f: X = i-C_3H_7O-

Treatment of a solution of II in a mixture of dry dioxane and ether with dry gaseous hydrochloric acid yields the hydrochloride of II (mp.:260°C decomp.) C 48,59 H 3,65 N 14,12 Cl 17,65; $C_8H_7ClN_2O_2$ = 198,6 requires C 48,38 H 3,55 N 14,11 Cl 17,83.

The latter, on treatment with water or primary alcohols at room temperature, or with hot iso-propyl alcohol yields 2-ureido-benzoic acid and its corresponding esters (VIIb-f) (VIId) mp.: 144-145°C; from 70% methanol, found C 59,43 H: 6,38 N: 12,71; $C_{11}H_{14}N_2O_3$ = 222,2 requires C: 59,45 H: 6,35 N: 12,60 - VIIe mp.: 122-123°C, from benzene-petrol-

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[x] With foaming and resolidification; second mp.: about 330°C, corresponding to that of III.- For VIIb Grammaticakis[2] states mp.-s between 320-330°C, and for VIIc Weil and Syngierowna[3] state mp.: 342-343°C.

ether; found N 11,99; $C_{12}H_{16}N_2O_3$ = 236,3 requires N:11,86; - VIIf; mp.: 182-183°C from isopropyl alcohol-petrolether; found N: 12,90; $C_{11}H_{14}N_2O_3$ = 222,2 requires N: 12,60 respectively. Short refluxing of II.HCl with water or primary alcohols converts it to III.

The structures of VIIa-c have been proved 1) by the IR spectrum of VIIc which contains three ester bands at 1709, 1250 and 1095 cm^{-1} respectively, two bands at 3410 and 3320 cm^{-1} characteristic for the NH_2 group, the amide I band at 1670 cm^{-1}, the amide II band at 1590 cm^{-1} and a band at 3230 cm^{-1} characteristic for the secondary NH group; 2) by the UV spectra of VIIb and c which are closely similar to that of anthranilic acid and identical with the spectrum of VIIb published by Grammaticakis[2]; 3) by comparison of VIIa and B with authentic samples prepared according to Bogert and Scotchard[4].

Investigation of the reaction of II and II.HCl with amines is in progress.

REFERENCES

[1] K. Lempert and G. Doleschall: Chem. Ber. in press

[2] P. Grammaticakis: Compt. rend. 247, 2014 (1958)

[3] St. Weil and T. Syngierowna: Roczniki Chem. 8 177 (1928)

[4] M. T. Bogert and G. Scotchard: J. Amer. Chem. Soc. 41, 2056 (1919)