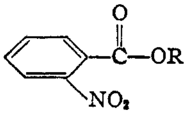
TABLE I

PHYSICAL CONSTANTS AND ANALYTICAL DATA FOR BENZOATES OF TYPE:



R	Yield, %	B.p., °C.	Mm.	$n^{20}D$	d^{20}_4	Sapn. equiv. Calcd.	Found	Nitrogen, %[a] Calcd.	Found
n-C_4H_9	69	110–113	0.13	1.5132	1.1423	223.2	221.2	6.28	6.02
i-C_4H_9	65	97–99.3	.09	1.5117	1.1507	223.2	221.2	6.28	6.00
s-C_4H_9	45	97.3–99.8	.05	1.5107	1.1572	223.2	227.4	6.28	6.15
n-C_5H_{11}	47	122.5–123.2	.08	1.5100	1.1222	237.3	240.0	5.94	5.75
i-C_5H_{11}	76	110.2–113.5	.08	1.5070	1.1211	237.3	237.7	5.94	4.99
$(CH_3)_2CH(CH_2)_2$	56	113.5–113.8	.07	1.5100	1.1324	237.3	235.7	5.94	5.72
n-C_6H_{13}	64	120.8–122	.04	1.5070	1.1191	251.3	249.9	5.58	5.75
Cyclohexyl	52	133.8–136.5[b]	.08	....	....	249.2	246.1	5.62	5.40
$CH_3O(CH_2)_2$	63	118–119.5	.07	1.5214	1.2510	225.2	216.2	6.22	6.11
$CH_2OC_4H_9CH_2$	55	132.5–135.3	.08	1.5059	1.1233	267.3	261.5	5.24	4.73
s-C_5H_{11}		113.3–114.6	.07	1.5075	1.1274	237.3	237.5	5.94	6.08

[a] Nitrogen content determined by a macro adaptation of the semi-micro Kjeldahl procedure of R. A. Harte, *Ind. Eng. Chem., Anal. Ed.*, **7**, 432 (1935). [b] M.p. 50–51° (corrected).

hours on a steam-bath. The resulting crude ester was extracted successively with water, 10% calcium chloride solution, water, 5% sodium bicarbonate solution, and finally with water. After standing over Drierite for 24 hours, the esters were distilled *in vacuo*. The benzoates were pale yellow oils.

A summary of the physical constants and analytical data is described in Table I.

Materials.—The alcohols were distilled from freshly crushed lumps of calcium oxide. A constant boiling fraction was taken for conversion to the *o*-nitrobenzoate. The *o*-nitrobenzoyl chloride used in these preparations had a f.p. of 19°.

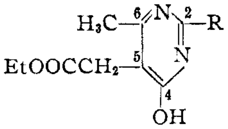
Acknowledgment.—The author expresses appreciation to Mr. Solomon C. Westbrook, Jr., and Dr. Carl M. Hill for assistance in this investigation.

DEPARTMENT OF CHEMISTRY
TENNESSEE AGRIC. AND INDUST. STATE COLLEGE
NASHVILLE 8, TENNESSEE
RECEIVED NOVEMBER 2, 1951

Derivatives of Pyrimidol-4 and Quinazolinol-4

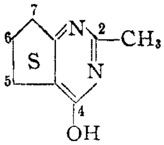
BY G. E. MCCASLAND AND JOHN R. G. BRYCE

In continuation of studies on pyrimidine derivatives[1,2] we wish to report the synthesis of two pyrimidines (I), one trimethylenepyrimidine (II), and two tetramethylenepyrimidines (tetrahydroquinazolines) III.

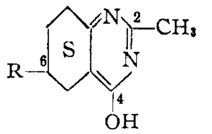


I

R = $-CH_3$, $-CH_2OH$



II



III

R = $-H$, $-OCH_3$

The reaction of diethyl acetosuccinate with acetamidine gave 5-carbethoxymethyl-2,6-dimethylpyrimidol-4 (I, R = $-CH_3$), and with hydroxyacetamidine gave 5-carbethoxymethyl-2-hydroxymethyl-6-methylpyrimidol-4 (I, R = $-CH_2OH$).

The reaction of acetamidine with 2-carbethoxycyclohexanone gave 2-methyl-5,6,7,8-tetrahydroquinazolinol-4 (III, R = $-H$); and with the corresponding cyclopentane ketoester gave 2-methyl-5,6-trimethylenepyrimidol-4 (II). The corresponding reaction with 2-carbethoxy-4-methoxycyclohexanone gave 6-methoxy-2-methyl-5,6,7,8-tetrahydroquinazolinol-4 (III, R = $-OCH_3$). Certain intermediates and products were isolated or characterized as dinitrophenylhydrazones, hydrochlorides or picrates.

Experimental

Melting points are corrected. Microanalyses by Mr. R. Pyke.

Condensation of the Amidine and Keto-Ester (General Procedure).—To a solution containing 2 to 5% excess of sodium ethoxide in warm absolute ethanol (21–83 ml. per gram of sodium) was added the solid acetamidine (or hydroxyacetamidine) hydrochloride. After ten minutes with shaking, sodium chloride was removed by filtration, and the keto-ester (one mole per mole of amidine) was added. Under anhydrous conditions, the mixture was allowed to stand and/or refluxed until reaction was nearly complete. If the product did not separate spontaneously after cooling, sufficient water was added to dissolve any precipitate, and the reaction mixture was adjusted to *p*H 4–6 by adding dilute hydrochloric acid and sodium bicarbonate solutions. The neutralized solution was vacuum-distilled to dryness, and the product separated from inorganic materials by extracting it with a suitable boiling solvent.

2-Methyl-5,6,7,8-tetrahydroquinazolinol-4 (2-Methyl-5,6-tetramethylenepyrimidol-4).—The general procedure was used with 12.5 ml. of ethanol, 2.38 g. of acetamidine hydrochloride (British Drug Houses, Toronto), and 4.25 g. of 2-carbethoxycyclohexanone[3] (b.p. 99–101° (9 mm.)). The reaction time was 24 hours at 25° plus four hours at reflux temperature. On cooling, long colorless needles separated. These were collected, washed with a limited amount of ethanol and dried, weight 1.9 g., m.p. 206–209.5°.

By extracting the evaporated filtrate with boiling benzene a second crop of 0.5 g., m.p. 205–209°, was obtained, making the total yield 2.4 g. (59%).

On recrystallization of a sample from benzene, for analysis, the m.p. was raised to 208–209°.

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.82; H, 7.37; N, 17.06. Found: C, 65.97; H, 7.87; N, 17.74.

4-Hydroxy-2-methyl-5,6,7,8-tetrahydroquinazolinium Picrate.—Addition of saturated benzene solution of picric acid to a boiling saturated benzene solution of the quinazoline gave an immediate yellow crystalline precipitate. The crystals after washing with benzene and drying, melted at 202–205.5°. After two recrystallizations from *n*-butanol a 61% yield of picrate, bright yellow crystals, m.p.

---

[1] G. E. McCasland, D. Stanley Tarbell, R. B. Carlin and Nancy Shakespeare, THIS JOURNAL, **68**, 2390 (1946).

[2] G. E. McCasland and D. Stanley Tarbell, *ibid.*, **68**, 2393 (1946).

[3] H. R. Snyder, L. A. Brooks and S. H. Shapiro, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 531.

207–208°, was obtained. A mixed m.p. of the picrate with the free base was depressed to 150–170°.

Anal. Calcd. for $C_{15}H_{15}N_5O_8$: N, 17.81. Found: N, 17.97.

2-Methyl-5,6-trimethylenepyrimidol-4 (2-Methyl-6,7-dihydrocyclopentapyrimidol-4).—The general procedure was used with 10 ml. of ethanol, 0.47 g. of acetamidine hydrochloride and 0.78 g. of 2-carbethoxycyclopentanone[4] (b.p. 99–100.5° (10 mm.)). The reaction time was 12 hours at 25° plus 3.5 hours at reflux temperature. The extraction solvent was ethyl acetate. On cooling, the extract deposited long colorless needles. These when collected, washed with a little ethyl acetate, and dried, weighed 180 mg., m.p. 208–212°. From the filtrate by partial evaporation 54 mg. more material, of m.p. 207–212°, was obtained, making the total yield 234 mg. (31%).

The material sublimed easily at 2 mm. (125° bath), but this did not improve the purity. Repeated recrystallization of the material from ethyl acetate raised the m.p. to 214.5–215.5°. Analysis indicated that the compound was still not entirely pure, but it gave a picrate of satisfactory purity.

Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.66. Found: C, 64.91; H, 7.10; N, 19.36.

4-Hydroxy-2-methyl-5,6-trimethylenepyrimidinium Picrate.—The crude picrate, prepared as described for the above quinazoline, was obtained in 51% yield, m.p. 178.5–182.5°. After recrystallization from *n*-butanol it melted at 184.5–185°.

Anal. Calcd. for $C_{14}H_{13}N_5O_8$: C, 44.33; H, 3.45; N, 18.47. Found: C, 44.11; H, 3.84; N, 18.29.

2-Carbethoxy-4-methoxycyclohexanone.—Hydrogenation[5] of commercial 4-methoxyphenol gave a *cis–trans* diastereomeric mixture of **4-methoxycyclohexanol**, b.p. 98–107° (15 mm.), in 89% yield.

The product was oxidized according to the procedure of Helfer[6] but to obtain the reported yield it was necessary to reduce the proportion of dichromate to a slight excess. **4-Methoxycyclohexanone** was obtained in 50–55% yield as a colorless liquid, b.p. 82–83° (13 mm.). A sample was converted to the 2,4-dinitrophenylhydrazone, m.p. 147–148° (reported[7] 150°).

The method of Cook and Lawrence[8] for the preparation of **2-carbethoxyformyl-4-methoxycyclohexanone** was modified as follows: The mixture of 4-methoxycyclohexanone (11.4 g.) and diethyl oxalate (14.7 g.) was added *to* the solution of sodium ethoxide in absolute ethanol (distilled from sodium). The reaction was conducted at 0–5° under dry nitrogen. After 2–3 hours stirring at 0°, the mixture was left overnight (with stirring), and after chilling to 0° was acidified and extracted.

The decarbonylation procedure[8] was modified by adding 100 mg. of powdered glass and 10 mg. of powdered iron to the entire batch of crude diketo-ester (a viscous oil), heated in a Claisen flask at 190°. The vigorous evolution of carbon monoxide was complete in 20 minutes, and 4.42 g. (25%, based on methoxycyclohexanone) of **2-carbethoxy-4-methoxycyclohexanone**, b.p. 128–135° (14 mm.), was obtained. On redistillation the product was obtained as a colorless liquid (3.69 g.), b.p. 139–141° (18 mm.) (reported[8] 131–133° (10 mm.)), n^{20}_D 1.4783, D_{20} 1.102, M^{20}_D 51.40 (theor. 49.50). The product gave a 2,4-dinitrophenylhydrazone of m.p. 125–128° dec., reported[8] 129–131° dec.

6-Methoxy-2-methyl-5,6,7,8-tetrahydroquinazolinol-4 Hydrochloride.—The general procedure was used with 0.47 g. of 2-carbethoxy-4-methoxycyclohexanone. The reaction time was three days at 25°. The extraction solvent was absolute ethanol. The hot filtered extract was cooled to 0°. Dry hydrogen chloride was passed into the solution for ten minutes. The colorless crystalline precipitate was collected, washed with ethanol and dried, giving 0.62 g. (54%) of product, m.p. 217–220° dec. After recrystallization of the product from absolute ethanol the m.p. was 221–222° dec.

Anal. Calcd. for $C_{10}H_{15}ClN_2O_2$: C, 52.06; H, 6.55; N, 12.15. Found: C, 52.24; H, 6.94; N, 12.15.

In earlier experiments the free base was isolated from the reaction mixture as colorless crystals, m.p. 129–137°. The yield was only 12% and purification was difficult.

5-Carbethoxymethyl-2,6-dimethylpyrimidol-4.—The general procedure was used with acetamidine hydrochloride (0.47 g.), 10 ml. of ethanol and 1.08 g. of diethyl acetosuccinate[9] (b.p. 103.5–106.5° (1 mm.), n^{20}_D 1.4348, M^{20}_D 52.22 (theor. 52.81). The reaction time was three days at 25°. The extraction solvent was ethyl acetate. The colorless crystals which separated from the extract were collected, washed (ethyl acetate) and dried, weight 159 mg. The filtrate on vacuum distillation to half-volume and dilution 1:1 with benzene gave 24 mg. more, making the total yield 182 mg. (18%), m.p. 177–179.5°. After recrystallization of the product from ethyl acetate–benzene (1:1) the m.p. was 181.5–182°.

Anal. Calcd. for $C_{10}H_{14}N_2O_3$: C, 57.13; H, 6.71; N, 13.33. Found: C, 57.80; H, 6.59; N, 13.39.

5-Carbethoxymethyl-2-hydroxymethyl-6-methylpyrimidol-4.—The general procedure was used with 1.10 g. of hydroxyacetamidine hydrochloride[3] (m.p. 147–148.5°), 22 ml. of ethanol and 2.16 g. of diethyl acetosuccinate.[9] (The amidine HCl was predissolved in half of the ethanol at the b.p.) The reaction time was 24 hours at 25° followed by 3 hours refluxing. The extraction solvent was 40 ml. of benzene (refluxed 20 minutes). The hot filtered extract on cooling deposited colorless needles which were collected, washed (benzene), and dried, giving 330 mg. (15%) of product, m.p. 137–142°. Repeated recrystallization of the product from benzene raised the m.p. to 143–144.5°.

Anal. Calcd. for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.39. Found: C, 52.48; H, 6.03; N, 11.61.

On heating with hydrazine hydrate the ester yields a colorless crystalline hydrazide, which can be recrystallized from ethanol and melts at about 225° (rapid heating), but which has not yet been purified sufficiently for analysis.

---

[4] R. P. Linstead and E. M. Meade, *ibid.*, p. 119.

[5] E. M. Van Duzee and H. Adkins, This Journal, **57**, 147 (1935).

[6] L. Helfer, *Helv. Chim. Acta*, **7**, 950 (1924).

[7] C. S. Marvel and W. L. Walton, *J. Org. Chem.*, **7**, 88 (1942).

[8] J. W. Cook and C. A. Lawrence, *J. Chem. Soc.*, 58 (1938).

[9] H. Adkins, N. Isbell and B. Wojcik, ref. 3, p. 262.

Department of Chemistry
University of Toronto
Toronto, Canada

Received September 21, 1951

Anion Exchange Studies. IV.[1,2] Cobalt and Nickel in Hydrochloric Acid Solutions

By George E. Moore and Kurt A. Kraus

The anion exchange behavior of nickel(II) and cobalt(II) in 0.5 to 12 *M* hydrochloric acid was studied by measuring their elution constants $E = dA/V$, where d is the distance (cm.) an absorption band moves when V (cc.) of eluent have been passed through a column of A (cm.²) cross-sectional area.

Glass columns of the practically colorless resin Dowex-1 (a "strong base" quaternary amine polystyrene–divinylbenzene resin) were used, whose cross-sectional areas were 0.023 cm.². Since both nickel and cobalt are colored (the latter has a characteristic blue color on the resin) the band positions (and hence E) were determined visually. Approximately 1 mg. of Co and Ni were used per experiment. In addition a few experiments were carried out with tracer cobalt (Co^{60}) and d determined with the automatic scanner previously described.[3]

The results for cobalt are summarized in Fig. 1. E_{Co} rapidly decreases from approximately 2.5 in less than 3 *M* HCl to *ca.* 0.02 in 9 *M* HCl and

---

[1] This document is based on work performed for the Atomic Energy Commission at the Oak Ridge National Laboratory.

[2] Previous paper: K. A. Kraus and G. E. Moore, This Journal, **73**, 2900 (1951).

[3] K. A. Kraus and G. E. Moore, *ibid.*, **73**, 9 (1951).