TABLE II

6-ALKYLACRIDIZINIUM SALTS, III

R_1	R_2	R′	M.P., °C.	Formula	C Calcd.	C Obsd.	H Calcd.	H Obsd.	N Calcd.	N Obsd.
				Picrates						
CH_3	CH_3	CH_3	239–241 (dec.)[a]	$C_{22}H_{18}N_4O_9$	54.80	55.02	3.76	3.91	11.62	12.04
C_2H_5	C_2H_5	CH_3	205–206[b]	$C_{24}H_{22}N_4O_9 \cdot {}^1/_2H_2O$	55.00	54.81	4.46	4.72	10.79	10.65
C_2H_5	C_2H_5	C_2H_5	197–199[c]	$C_{25}H_{24}N_4O_9$	57.25	57.43	4.62	4.92	10.69	10.50
—CH_2—		CH_3	235–236[d]	$C_{21}H_{14}N_4O_9$	54.09	54.03	3.03	3.19	12.01	11.99
				Perchlorates						
CH_3	CH_3	CH_3	288–291[e]	$C_{16}H_{16}ClNO_6$	54.10	54.39	4.57	4.59	3.86	4.32
C_2H_5	C_2H_5	CH_3	272–274[f]	$C_{18}H_{20}ClNO_6 \cdot 3/2H_2O$	52.98	53.13	5.67	5.72	3.44	3.68
C_2H_5	C_2H_5	C_2H_5	269–270[g]	$C_{19}H_{22}ClNO_6$	57.69	57.31	5.56	5.66	3.56	3.75

[a] Needles from acetone. [b] Well formed needles from acetone-ethanol. [c] Flakes from acetone-ethanol. [d] Granules from ethanol. [e] All of the perchlorates formed needles which melted with decomposition. [f] From acetone-water. [g] From acetone-ethanol.

quinolizinium derivatives,[5–8] but also a further example of aromatic cyclodehydration,[9] one involving electrophilic attack on aromatic nitrogen rather than the usual carbon.

EXPERIMENTAL[10]

2-(3′,4′-Methylenedioxybenzyl)pyridine (II) (R_1 — R_2 = —O—CH_2O—) was prepared essentially as in the case of the known 2-(3,4-dimethoxybenzyl)pyridine[11] (II, R_1 = R_2 = OCH_3). To a solution of butyllithium prepared from 30.5 g. of *n*-butyl chloride, and maintained at a temperature of −50°, 40 g. of 2-bromopyridine was added in dry ether. The reaction mixture was stirred for 15 min., and then 42.7 g. of piperonal in dry ether was added. The temperature of the mixture was maintained at 0° for 1 hr. longer, and then allowed to come to room temperature. The reaction mixture was poured into dilute acid, the acid layer separated and made basic, and the resulting oil taken up in ether. The ethereal solution was washed, dried and concentrated and the crude residue was used directly for the reduction. A solution of the residue in 300 ml. of benzene was cooled and treated with 38 g. of thionyl chloride, the temperature being kept below 25°. After the mixture had stood for an additional hour, it was made basic with sodium hydroxide solution. The benzene layer was separated, wahed, dried and concentrated. The residue was dissolved in 250 ml. of glacial acetic acid and while this was heated on the steam bath during a 6 hr. period, 36 g. of zinc powder was added in small portions. The excess zinc was removed by filtration, the acetic acid was evaporated under reduced pressure, and the residue made alkaline with sodium hydroxide. The oil which separated was taken up in ether, and the ethereal extract washed, dried and concentrated. The residue was fractionated yielding 13.2 g. (28%) of an oil, b.p. 185–196° (3 mm.).

A *picrate* was prepared for analysis as fine yellow granules from ethanol, m.p. 143–145°.

Anal. Calcd. for $C_{19}H_{13}N_4O_9$: C, 51.70; H, 2.97; N, 12.70. Found: C, 52.00; H, 3.59; N, 12.66.

2-(3′,4′-Diethoxybenzyl)pyridine (II, R_1 = R_2 = OC_2H_5). Essentially the same procedure was used except that the aldehyde was 3,4-diethoxybenzaldehyde. The yield of 2-(3′,4′-diethoxybenzyl) pyridine, b.p. 170–180°(3 mm.) was 12.5%.

The *picrate*, prepared for analysis, crystallized from ethanol as bright yellow clusters, m.p. 157–158°.

Anal. Calcd. for $C_{22}H_{22}N_4O_9$: C, 54.40; H, 4.56; N, 11.51. Found: C, 54.36; H, 4.84; N, 11.79.

Acetylative cyclization of the benzylpyridine derivatives. One gram of the benzylpyridine derivative (II) was dissolved in 20 ml. of acetic or propionic anhydride containing 0.8 ml. of concentrated sulfuric acid. The mixture was heated on the steam bath for 2 hr., after which it was cooled, and the salt precipitated by addition of ether. The organic solvents were separated from the salt either by filtration or decantation. The crude sulfoacetate salt was dissolved in water, and perchloric acid added to precipitate the product as a *perchlorate* salt which was crystallized from an acetone-ethanol mixture.

The *picrate* was prepared by addition of an alcoholic solution of picric acid to an aqueous solution containing the crude sulfoacetate salt. The results are summarized in Table II.

DEPT. OF CHEMISTRY
DUKE UNIVERSITY
DURHAM, N. C.

(5) R. B. Woodward and B. Witkop, *J. Org. Chem.*, **71**, 379 (1949).

(6) R. B. Woodward and W. M. McLamore, *J. Org. Chem.*, **71**, 379 (1949).

(7) A. Richards and T. S. Stevens, *Chem. and Ind.* **1954**, 905.

(8) A. Richards and T. S. Stevens, *J. Chem. Soc.*, 3067 (1958).

(9) *Cf.*, C. K. Bradsher, *Chem. Revs.*, **38**, 447 (1946).

(10) All melting points were taken on a Fisher-Johns hot stage and are uncorrected. All analyses were by Micro Tech Laboratories, Skokie, Illinois.

(11) N. Sugiomoto, *J. Pharm. Soc. Japan*, **76**, 1045 (1956).

Benzo[*b*]quinolizidine Derivatives[1]

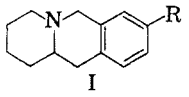
C. K. BRADSHER AND NANCY L. YARRINGTON

Received August 18, 1959

It was shown earlier[2] that benzo[*b*]quinolizidine derivatives (I, R = H) can be produced by the catalylic reduction of the acridizinium nucleus. As part of a study of the relation between structure

(1) This investigation was supported by a research grant (H-2170) from the National Heart Institute of the National Institutes of Health.

(2) C. K. Bradsher and L. E. Beavers, *J. Am. Chem. Soc.*, **77**, 4812 (1955).



I

and hypotensive activity, we have prepared a few benzo[*b*]quinolizidine derivatives. It has been found that sodium borohydride may be used for the reduction of acridizinium bromide to I (R = H).

EXPERIMENTAL[3]

2-Aldoximino-1-(3-methoxy)benzylpyridinium bromide. To a flask containing 5 ml. of dimethyl formamide, 4.88 g. of pyridine 2-aldoxime and 8.04 g. of *m*-methoxybenzyl bromide were added. The flask was warmed gently on the steam bath until solution was complete, then stoppered and allowed to stand for 24 hr. at room temperature. The colorless crystals were triturated with ethyl acetate and collected. The yield was 11.41 g. (88%), m.p. 178–182°. The analytical sample melted at 180–182°.

Anal. Calcd. for $C_{14}H_{15}BrN_2O_2$: C, 52.03; H, 4.68; N, 8.67. Found: C, 52.44; H, 4.84; N, 8.55.

8-Methoxyacridizinium perchlorate. To a solution containing 1 g. of the oximino quaternary salt in 8 ml. of absolute alcohol, 6 ml. of concentrated hydrochloric acid was added, and the mixture refluxed for 5 hr. After vacuum evaporation of the solvents the residual yellow solid was washed with ethyl acetate and then dissolved in a small quantity of water. The perchlorate was precipitated by addition of perchloric acid. Recrystallization of the product from methanol yielded 0.41 g. (44%) of yellow platelets, m.p. 222–224° (lit.[4] 218–219°).

8-Hydroxyacridizinium bromide. The oximino quaternary salt (5.9 g.) was placed in 30 ml. of 48% hydrobromic acid and the mixture refluxed for 45 min. The mixture was vacuum evaporated and the residue crystallized from a concentrated ethanol solution. The yield was 3.9 g. (97%),[5] m.p. 246–248° (lit.[4] 250–252°).

8-Methoxybenzo[b]quinolizidine (I, R = OCH_3) *hydroperchlorate.* To a suspension of 5.2 g. of 8-methoxyacridizinium perchlorate in 300 ml. of methanol, 100 mg. of platinum oxide was added and hydrogenation was carried out at room temperature and atmospheric pressure until the theoretical amount of hydrogen had been absorbed. The solution was filtered, concentrated, and cooled; 4.4 g. (83%) of colorless crystals, m.p. 175–177° was obtained.

Anal. Calcd. for $C_{14}H_{20}ClNO_4$: C, 52.92; H, 6.35; N, 4.41. Found: C, 53.10; H, 6.07; N, 4.50.

8-Methoxybenzo[b]quinolizidine (I. R = OCH_3) was recrystallized from ethanol, m.p. 50–51°.

Anal. Calcd. for $C_{14}H_{19}NO \cdot {}^1/_3H_2O$: C, 75.30; H, 8.88; N, 6.27. Found: C, 75.58; H, 8.69; N, 6.15.

8-Hydroxybenzo[b]quinolizidine (I. R = OH) *hydrochloride.* The reduction of 1.7 g. of the 8-hydroxyacridizinium salt was carried out as in the case of the methyl ether. Concentration of the methanol solution yielded 1.51 g. (88%), decomposes 268–290°. The analytical sample consisted of colorless prisms, decomposes 276–318°.

Anal. Calcd. for $C_{13}H_{18}ClNO$: C, 65.13; H, 7.57; N, 5.81. Found: C, 65.37; H, 7.69; N, 5.70.

8-Hydroxybenzo[b]quinolizidine (I. R = OH) was obtained as a colorless powder, m.p. 230–231°.

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.82; H, 8.43; N, 6.90. Found: C, 76.51; H, 8.35; N, 7.04.

The *methiodide* was prepared in 92% yield by refluxing a methanol solution of the base for 1 hr. with excess methyl iodide. It formed colorless needles from ethanol, m.p. 274–275°.

Anal. Calcd. for $C_{14}H_{20}INO$: C, 48.72; H, 5.84; N, 4.06. Found: C, 48.56; H, 5.91; N, 4.25.

Benzo[b]quinolizidine (I. R = H) *methiodide.* (a) *From the hydrobromide.* Benzo[b]quinolizidine hydrobromide[2] was converted to the free base by action of ammonia, and the crude base obtained by ethereal extraction was methylated with methyl iodide. The product was obtained from ethanol as colorless irregular crystals, m.p. 290–291°.

(b) *From the sodium borohydride reduction product.* To a solution of 2 g. of acridizinium bromide in 45 ml. of water an aqueous suspension 0.68 g. of sodium borohydride was added. The mixture was heated on the steam bath until the evolution of hydrogen ceased and a red oil separated. The oil was taken up in ether, the solution dried and concentrated, and the residue heated with methyl iodide on the steam bath for 2 hr. The product melted at 267–268° and the melting point did not change on recrystallization. When a sample of the product was dissolved in ethanol and seeded with a single crystal of product obtained by Procedure a, the entire material crystallized in irregular clusters, m.p. 290–291°. The infrared spectrum of this material was identical with that of the product obtained by Procedure a.

Anal. Calcd. for $C_{14}H_{20}IN$: C, 51.07; H, 6.12; N, 4.25. Found[6]: C, 51.27, 50.97; H, 5.85, 5.96; N, 4.13, 4.55.

DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY
DURHAM, N. C.

(3) All melting points were taken on a Fisher-Johns hot stage and are uncorrected. All analyses were performed by Drs. Weiler and Strauss, Oxford, England.

(4) C. K. Bradsher and J. H. Jones, *J. Am. Chem. Soc.*, **79**, 6033 (1957).

(5) Only a 37% yield of 8-hydroxyacridizinium was reported earlier [ref. (4)] for the cyclization of crude 1-(3-methoxybenzyl)-2-formylpyridinium bromide.

(6) Values are for the product of Procedure *a* and for the low-melting form (m.p. 267–268°) obtained by Procedure *b*.

9(11)-Dehydrocortical Steroids. Synthesis of 9(11)-Anhydro-17α-hydroxycorticosterone Acetate and 9(11)-Anhydrocorticosterone Acetate

E. M. CHAMBERLIN, E. W. TRISTRAM, T. UTNE, AND J. M. CHEMERDA

Received July 27, 1959

The elimination of the 11β-hydroxyl group from the steroidal nucleus to give 9(11)-dehydro compounds is easily accomplished because of the favorable conformation of the 11β-hydroxyl group and the 9α-hydrogen atom (di-axial-trans).[1] Reichstein and his co-workers[2] have reported the conversion of 11β-hydroxylated cortical steroids without a 17α-hydroxyl function to 9(11)-anhydro derivatives using phosphorus oxychloride and pyridine or refluxing acetic-hydrochloric acid mixtures. In the

(1) W. A. Cranshaw, H. B. Henbest, and E. R. Jones, *J. Chem. Soc.*, **73** (1954); H. L. Herzog, C. C. Payne, and E. B. Hershberg, *J. Am. Chem. Soc.*, **76**, 930 (1954).

(2) (a) C. W. Shoppee, *Helv. Chim. Acta*, **23**, 740 (1940); (b) C. W. Shoppee and T. Reichstein, *Helv. Chim. Acta*, **24**, 351 (1941); (c) P. Hegner and T. Reichstein, *Helv. Chim. Acta*, **26**, 715 (1943); (d) C. W. Shoppee and T. Reichstein, *Helv. Chim. Acta*, **26**, 1316 (1943).