Anal. Calcd. for $C_{15}H_{14}N_4O_7$: C, 49.72; H, 3.86; N, 15.46. Found: C, 49.86; H, 3.75; N, 15.36.

A styphnate melted at 212–214° dec.; **picrolonate**, m.p. 230–232° dec.

2-(2-Methyl-2-cyanoethyl)-cyclopentanone (VIII).—The pyrrolidine enamine of cyclopentanone (I) was prepared as before from 20 g. of cyclopentanone (0.24 mole) and 58 g. of pyrrolidine (0.82 mole). Nineteen grams (0.28 mole) of methacrylonitrile, prepared by dehydration of methacrylamide with P_2O_5, was then added to a solution of the enamine dissolved in 200 ml. of N,N-dimethylformamide. This solution was refluxed for 32 hours protected from moisture. After removal of solvent and hydrolysis, the product, recovered in the usual manner, was distilled *in vacuo* to give 12 g. (34%) of liquid boiling 126–128° (5 mm.), $n^{25.5}D$ 1.4624.

The semicarbazone prepared for analytical purposes melted at 195° dec.

Anal. Calcd. for $C_{10}H_{16}N_4O$: C, 57.69; H, 7.69; N, 26.92. Found: C, 57.23; H, 7.64; N, 26.76.

3-Methyl-octahydro-1,5-pyridine (IX).—2-(2-Methyl-2-cyanoethyl)-cyclopentanone (VIII) was reduced in the presence of Raney nickel as previously described. Several runs were combined and distilled through a 50-plate Todd column to give a colorless liquid, b.p. 84° (18 mm.), $n^{25.5}D$ 1.4820.

Anal. Calcd. for $C_9H_{17}N$: N, 10.07; neut. equiv., 139.2. Found: N, 9.83; neut. equiv., 139.2.

3-Methyl-6,7-dihydro-1,5-pyridine (X).—3-Methyl-octahydro-1,5-pyridine (IX) was dehydrogenated over Pd–C in the manner described before. A white solid collected in the dehydrogenation trap which was low melting and darkened on exposure to air. The solid melted at 39–41°, b.p. 222° (752 mm.).

Anal. Calcd. for $C_9H_{11}N$: neut. equiv., 133.2. Found: neut. equiv., 133.1.

A picrate prepared from equimolar quantities of picric acid and the amine in 95% ethanol after recrystallization from ethanol formed yellow needles, m.p. 204–206°.

Anal. Calcd. for: $C_{15}H_{14}N_4O_7$: C, 49.72; H, 3.86; N, 15.46. Found: C, 49.59; H, 4.20; N, 15.41.

The styphnate melted at 199–200.5° dec.; **picrolonate**, m.p. 210–212° dec.

AUSTIN 12, TEX.

[CONTRIBUTION NO. 1048 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Synthesis of Nitrogen-containing Ketones. VIII. The Acylation of 3-Picoline, 4-Picoline and Certain of their Derivatives[1-4]

BY STUART RAYNOLDS[5] AND ROBERT LEVINE

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3-Picoline, 4-picoline and certain of their derivatives have been acylated at their side chains to give high yields of the corresponding ketones containing pyridine rings. For the first time it has been possible to effect the direct acylation of 3-picoline with aliphatic esters to give alkyl 3-picolyl ketones using sodium diisopropylamide as the condensing agent.

In previous papers we reported that organolithium reagents can be used to effect the lateral acylation of 2-picoline,[6] 2-picoline homologs,[7] 4-picoline,[1] quinaldine,[8] lepidine[9] and 2,4-lutidine[9] and 2,6-lutidine[8] with aliphatic, aromatic and heterocyclic esters and thus good to high yields of the corresponding heterocyclic nitrogen-containing ketones have been prepared.

It has also been observed that although the acylation of 2-picoline with ethyl benzoate, using phenyllithium as the condensing agent, gave an 80% yield[6] of the expected 2-phenacylpyridine, the comparable reaction with 4-picoline gave, under optimum conditions,[1] a mixture of 4-phenacylpyridine (33%), and the azomethine addition products, 2-phenyl-4-methylpyridine (13%) and 2,6-diphenyl-4-methylpyridine (22%).

In contrast with the results which were obtained in the benzoylation of 2- and 4-picoline, 3-picoline is not acylated at its side chain by ethyl benzoate in the presence of phenyllithium. Instead, phenyllithium reacts with this base exclusively by azomethine addition.[10] However, 3-picoline is acylated by ethyl benzoate[10] to give 3-phenacylpyridine in 37 and 38% yield, respectively, using lithium diisopropylamide in ether and potassium amide in liquid ammonia as the condensing agents. Although it has been possible to acylate 3-picolylpotassium in low yields[10] with aromatic and heterocyclic esters, previous attempts to effect similar reactions with aliphatic esters failed.[10]

The present paper is concerned with the synthesis of a number of ketones by acylating 3-picoline, 4-picoline and certain of their derivatives with aliphatic and aromatic esters using phenylsodium and sodium diisopropylamide as condensing agents.

Although the interaction of 3-picoline (two equivalents), phenylsodium in benzene (two equivalents) and ethyl benzoate (one equivalent) gave only a slightly higher yield (45%) of 3-phenacylpyridine (IV) than was obtained (38%) earlier[10] when potassium amide was used as the condensing agent, the use of sodium diisopropylamide in benzene in place of phenylsodium gave a 78% yield of the desired ketone.

The over-all reactions which are involved are shown in the equations

$$C_6H_5Na + HN(i\text{-}C_3H_7)_2\ (I) \xrightarrow{C_6H_6} C_6H_6 + NaN(i\text{-}C_3H_7)_2\ (II) \quad (1)$$

(1) For paper VII in this series, see C. Osuch and R. Levine, *J. Org. Chem.*, **22**, 939 (1957).

(2) Part of this work was performed under Contract No. AT(30-1)-670 between the U. S. Atomic Energy Commission and the University of Pittsburgh.

(3) Presented, in part, before the Organic Division of the 135th National A.C.S. Meeting, Boston, Mass., April 5–10, 1959.

(4) This paper is based on part of the thesis presented by Stuart Raynolds to the Graduate Faculty of the University of Pittsburgh in partial fulfillment of the requirements for the Ph.D. degree.

(5) Monsanto Chemical Co. Research Fellow for the academic year 1958–1959.

(6) N. N. Goldberg, L. B. Barkley and R. Levine, THIS JOURNAL, **73**, 4301 (1951).

(7) C. Osuch and R. Levine, *J. Org. Chem.*, **21**, 1009 (1956).

(8) N. N. Goldberg and R. Levine, THIS JOURNAL, **74**, 2517 (1952).

(9) N. N. Goldberg and R. Levine, *ibid.*, **77**, 3647 (1955).

(10) A. D. Miller, C. Osuch, N. N. Goldberg and R. Levine, *ibid.*, **78**, 674 (1956).

TABLE I

3-PYRIDYL KETONES OF THE TYPE 3-$C_5H_4NCH(R)COR'$

Compound	R	R'	Yield, %	M.p. or b.p. °C.	Mm.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
				165–170[a]	2.5					
1	H	C_6H_5	78	47–48						
2	H	CH_3	47	80–81[b]	1	C_8H_9NO	71.07	70.87	6.71	6.71
3	H	C_2H_5	61	103–104	2.53	$C_9H_{11}NO$	72.45	72.23	7.43	7.41
4	H	$(CH_3)_2CH$	69	105–106	2	$C_{10}H_{13}NO$	73.59	73.56	8.03	7.68
5	H	$(CH_3)_3C$	79	110–111	2.48	$C_{11}H_{15}NO$	74.54	74.24	8.53	8.53
6	$(CH_2)_2N(CH_3)_2$	C_6H_5	64	148–152	0.29	$C_{17}H_{20}N_2O$	76.08	75.73	7.51	7.51
7	$(CH_2)_2N(CH_3)_2$	$(CH_3)_2CH$	55	101–103	0.27	$C_{14}H_{22}N_2O$	71.75	71.89	9.46	9.86
				Derivatives						
1a	Picrate			168.0–168.5[a]						
2a	Picrate[c]			154.0–155.1[d]		$C_{14}H_{12}N_4O_8$	46.16	46.26	3.32	2.94
3a	Picrate			111.2–112.2[d]		$C_{15}H_{14}N_4O_8$	47.62	47.61	3.73	3.75
4a	Picrate			132.8–133.6[d]		$C_{16}H_{16}N_4O_8$	48.99	49.22	4.11	4.10
5a	Picrate			152.1–152.8[d]		$C_{17}H_{18}N_4O_8$	50.25	50.20	4.46	4.49
6a	Dipicrate			223.0–224.0[e]		$C_{29}H_{26}N_8O_{15}$	47.94	47.95	3.61	3.54
7a	Dipicrate			186.6–187.6[d]		$C_{26}H_{28}N_8O_{15}$	45.09	44.86	4.07	3.84

[a] Literature values (see ref. 10): b.p. 170–175° at 3 mm. and m.p. 48.6–49.5°; picrate, m.p. 168.8–169.6°. [b] Literature value (see ref. 11): b.p. 119–123° at 1 mm. [c] This ketone also formed a semicarbazone in aqueous acetic acid solution, m.p. 183.0–184.2° (literature value, m.p. 184.5–185.0°, see ref. 11). [d] Recrystallized from 95% ethanol. [e] Recrystallized from a 1:1 acetone–95% ethanol mixture.

$$3\text{-}C_5H_4NCH_3 + II \longrightarrow I + 3\text{-}C_5H_4NCH_2Na\ (III) \quad (2)$$

$$III + C_6H_5CO_2C_2H_5 \longrightarrow NaOC_2H_5 + 3\text{-}C_5H_4NCH_2COC_6H_5\ (IV,\ 78\%) \quad (3)$$

It is interesting to note that the use of sodium diisopropylamide as the condensing agent with toluene rather than benzene as the reaction solvent gave a lower yield (46%) of 3-phenacylpyridine (IV). In addition, a 23% yield of desoxybenzoin (VI) was isolated. Apparently a portion of the toluene was converted to benzylsodium (V) by reaction with part of the phenylsodium and/or sodium diisopropylamide (equation 4). Then, V reacted with ethyl benzoate to give desoxybenzoin (VI, equation 5). Apparently benzylsodium is not a sufficiently strong base to effect the lateral metalation of 3-picoline under the reaction conditions since, if V were able to convert 3-picoline to 3-picolylsodium, no desoxybenzoin should have been formed.

$$NaN(i\text{-}C_3H_7)_2 \text{ and/or } C_6H_5Na + C_6H_5CH_3 \longrightarrow C_6H_5CH_2Na\ (V) + HN(i\text{-}C_3H_7)_2 \text{ and/or } C_6H_6 \quad (4)$$

$$V + C_6H_5CO_2C_2H_5 \longrightarrow NaOC_2H_5 + C_6H_5CH_2COC_6H_5\ (VI) \quad (5)$$

For the first time, the direct acylation of 3-picoline with aliphatic esters has been effected to give good yields of several alkyl 3-picolyl ketones, 3-$C_5H_4NCH_2COR$, by the sodium diisopropylamide method. These ketones are listed in Table I. Apparently, the only alkyl 3-picolyl ketone which is recorded in the literature is 3-acetonylpyridine. This ketone has been synthesized previously in low yields by two routes: (1) the reaction of 3-pyridylacetic acid (prepared from 3-picoline in six steps) with acetic anhydride and sodium acetate[11] and (2) the reaction of 2-methyl-3-chloropropene with 3-pyridylmagnesium bromide followed by ozonolysis of the resulting olefin.[12]

(11) A. Burger and C. R. Walter, Jr., THIS JOURNAL, **72**, 1988 (1950); the yield in the last step is 40% of theory.

(12) J. P. Wibaut and H. G. P. van der Voort, *Rec. trav. chim.*, **71**, 798 (1952), the over-all yield of the ketone based on 3-bromopyridine is 15%.

It is of interest to note that an attempt to prepare di-(3-picolyl)-ethylcarbinol, $(3\text{-}C_5H_4NCH_2)_2C(OH)C_2H_5$, by the reaction of 3-picolylsodium (prepared from 3-picoline and sodium diisopropylamide in benzene) with ethyl 3-picolyl ketone, 3-$C_5H_4NCH_2COC_2H_5$, gave only recovered starting materials. Although a vigorous reaction occurred when the ketone was added to the 3-picolylsodium, apparently the hydrogen atoms of the methylene group of the ketone are sufficiently acidic so that the 3-picolylsodium reacts with the ketone by a process of anion formation rather than by carbonyl addition.[13]

$$3\text{-}C_5H_4NCH_2COC_2H_5 + 3\text{-}C_5H_4NCH_2Na \longrightarrow \begin{cases} (3\text{-}C_5H_4NCH_2)_2C(ONa)C_2H_5 \\ (3\text{-}C_5H_4NCHCOC_2H_5)^-Na^+ + 3\text{-}C_5H_4NCH_3 \end{cases}$$

The 3-picoline derivative, 1-(3-pyridyl)-3-dimethylaminopropane,[14] $3\text{-}C_5H_4N(CH_2)_3N(CH_3)_2$, was also acylated with ethyl isobutyrate and ethyl benzoate using sodium diisopropylamide as the condensing agent. From these reactions (Table I) the previously unreported 1-dimethyl-

(13) The fact that anion formation apparently takes place rationalizes the observation that in the acylation of tar bases with esters to give ketones which can be converted to anions, maximum yields of products are obtained using a 2:2:1 molar ratio of tar base:condensing agent:ester. Thus, while the use of a 2:2:1 molar ratio of 3-picoline:potassium amide:ethyl benzoate gave a 38% yield of 3-phenacylpyridine, the yield dropped to 19% using a 1:1:1 molar ratio of reactants (see ref. 10).

(14) This compound was synthesized by the interaction of equivalents of β-dimethylaminoethyl chloride and 3-picolylsodium, which was prepared from 3-picoline and sodium diisopropylamide in benzene. The 29% yield of product, which was obtained when the halide was added to 3-picolylsodium, was increased to 45% when the 3-picolylsodium was added slowly to the halide. The present method of preparing 1-(3-pyridyl)-3-dimethylaminopropane is superior to that reported earlier (A. D. Miller and R. Levine, *J. Org. Chem.*, **22**, 167 (1957)) by which this amine was obtained in 34% yield by the interaction of one equivalent of β-dimethylaminoethyl chloride hydrochloride with three equivalents of 3-picolylpotassium, which was prepared from 3-picoline and potassium amide in liquid ammonia.

TABLE II

4-PYRIDYL KETONES OF TYPE 4-$C_5H_4NCHRCOR'$

R	R'	Yield, % C_6H_5Li		CH_3Li		LDIA[a]	C_6H_5Na	$NaNH_2$	SDIA[b]
H	C_6H_5	12(S.A.)[c,d,e]	33(R.A.)[c,e,f]	51(S.A.)[e,g]	49(R.A.)[e]			74[e]	80[h]
H	CH_3	22(R.A.)[e,i]		23(S.A.)[e,g]	27(R.A.)[e]			6[e]	55[h]
H	C_2H_5			55(S.A.)[e]				50[e]	77[h]
H	$(CH_3)_2CH$			66(S.A.)[e]				79[e]	78[h]
C_6H_5	C_6H_5[j]						56		78
C_6H_5	C_2H_5[k]	40				69	61		79
$(CH_2)_2N(CH_3)_2$	C_6H_5[l]								80
$(CH_2)_2N(CH_3)_2$	$(CH_3)_2CH$[m]								78

[a] LDIA = lithium diisopropylamide. [b] SDIA = sodium diisopropylamide. [c] S.A. = Standard Addition Method, *i.e.*, the tar base was added to the organolithium compound; R.A. = Reverse Addition Method, *i.e.*, the organolithium compound was added to the tar base. [d] A 39% yield of 2-phenyl-4-methylpyridine, A, and a 33% yield of 2,6-diphenyl-4-methylpyridine, B, were also obtained. [e] These are data of Osuch and Levine (see ref. 1). [f] A 13% yield of A and a 22% yield of B were also isolated. [g] A trace of 2,4-lutidine was also isolated. [h] The physical constants of this compound and of its picrate agree with those reported in ref. 1. [i] A 6% yield of A was also isolated. [j] B.p. 187–192° at 0.25 mm.; m.p. 119.8–120.8° (from 60–70° petroleum ether). *Anal.* Calcd. for $C_{19}H_{15}NO$: C, 83.49; H, 5.53. Found: C, 83.50; H, 5.57. Picrate, m.p. 166.5–167.2° (from 95% ethanol). *Anal.* Calcd. for $C_{25}H_{18}N_4O_8$: C, 59.76; H, 3.61. Found: C, 59.36; H, 3.79. [k] B.p. 144–145° at 0.28 mm. *Anal.* Calcd. for $C_{15}H_{15}NO$: C, 79.96; H, 6.71. Found: C, 79.70; H, 6.94. Picrate, m.p. 169.8–170.8° (from 95% ethanol). *Anal.* Calcd. for $C_{21}H_{18}N_4O_8$: C, 55.51; H, 3.99. Found: C, 55.58; H, 3.98. [l] B.p. 148–153° at 0.25 mm. *Anal.* Calcd. for $C_{17}H_{20}N_2O$: C, 76.08; H, 7.51. Found: C, 76.35; H, 7.35. Dipicrate, m.p. 154.7–156.2° (from 95% ethanol). *Anal.* Calcd. for $C_{29}H_{26}N_8O_{15}$: C, 47.94; H, 3.61. Found: C, 48.20; H, 3.63. [m] B.p. 110–112° at 0.26 mm. *Anal.* Calcd. for $C_{14}H_{22}N_2O$: C, 71.75; H, 9.46. Found: C, 71.86; H, 9.60. Dipicrate, m.p. 170–171° (from 95% ethanol). *Anal.* Calcd. for $C_{26}H_{28}N_8O_{15}$: C, 45.09; H, 4.07. Found: C, 44.70; H, 4.12.

amino - 3 - (3 - pyridyl) - 5 - methylhexanone-4 (55%) and 1-benzoyl-1-(3-pyridyl)-3-dimethylaminopropane (64%), respectively, were isolated.

Because it had been possible to acylate 3-picoline and 1-(3-pyridyl)-3-dimethylaminopropane in high yields using sodium diisopropylamide as the condensing agent, the study was extended to the 4-picoline series. The results which were obtained are found in Table II, in which the earlier data of Osuch and Levine[1] are included for purposes of comparison. It can be seen that sodium diisopropylamide is superior to any of the previously used condensing agents for effecting the acylation of 4-picoline. It will be noted that while the highest previously reported yield of 4-acetonylpyridine, $4\text{-}C_5H_4NCH_2COCH_3$, was 27%, the present method gives this compound in 55% yield. Furthermore, it can be seen that although the 4-picolyl ketones are often contaminated with trace to appreciable amounts of azomethine addition products when organolithium compounds are used as the condensing agents, only ketones are obtained when sodium amide and sodium diisopropylamide are employed.

Next, 4-benzylpyridine was acylated with ethyl benzoate and ethyl propionate using several condensing agents (Table II). Again it can be seen that sodium diisopropylamide is the condensing agent of choice. 4-Picoline and 4-benzylpyridine were then alkylated with β-dimethylaminoethyl chloride using sodium diisopropylamide as the condensing agent to give 1-(4-pyridyl)-3-dimethylaminopropane, $4\text{-}C_5H_4N(CH_2)_3N(CH_3)_2$, A, and 1-(4-pyridyl)-1-phenyl-3-dimethylaminopropane, $4\text{-}C_5H_4NCH(C_6H_5)(CH_2)_2N(CH_3)_2$, B, in yields of 80 and 88%, respectively.

The present route to B is more attractive than the previously published[15] synthesis. This involves the alkylation of phenylacetonitrile with β-dimethylaminoethyl chloride to give α-(β-dimethylaminoethyl)-phenylacetonitrile, which on reaction with 4-chloropyridine and sodium amide gives α-phenyl-α-(β-dimethylaminoethyl)-4-pyridylacetonitrile. On treatment with 75% sulfuric acid, this last compound is converted to B. When A was acylated with ethyl isobutyrate and ethyl benzoate, high yields of 1-dimethylamino-3-(4-pyridyl)-5-methylhexanone-4 (78%) and 1-benzoyl-1-(4-pyridyl)-3-dimethylaminopropane (80%) were obtained (Table II).

Attempts to acylate B with ethyl propionate and ethyl benzoate using phenyllithium or lithium diisopropylamide in ether, phenylsodium or sodium diisopropylamide in benzene or sodium amide in liquid ammonia as condensing agents did not give the expected ketones. Only traces of high boiling materials and high yields of recovered B were obtained. A satisfactory explanation for the failure of B to undergo acylation is not apparent at the present time.

Finally, attempts to prepare di-(4-picolyl)-ethylcarbinol from the reaction of ethyl 4-picolyl ketone with 4-picolylsodium and 1,3-diphenyl-1,3-di-(4-pyridyl)-2-ethylpropanol-2 by treating 1-(4-pyridyl)-1-phenylbutanone-2 with the sodium derivative of 4-benzylpyridine were unsuccessful and only starting materials were recovered. These reactions apparently failed for the same reason, *vide infra*, that a carbinol was not obtained from the reaction of 3-picolylsodium with ethyl 3-picolyl ketone.

Experimental[16]

Preparation of Sodium Dispersions.—The dispersions, which contain approximately 0.8 g. of sodium per milliliter of dispersing medium, were prepared essentially as described in the literature.[17] For each 200 g. of sodium to be dispersed, a mixture of 250 ml. of "mixed decanes"[18] (as the dispersing medium) with oleic acid (2 ml.) and pyridine (2 ml.) (as the dispersing aids) was used.

(15) N. Sperber, D. Papa, E. Schwenk, M. Sherlock and R. Fricano, THIS JOURNAL, **73**, 5752 (1951).

(16) The 3-picoline, 4-picoline and 4-benzylpyridine were supplied through the courtesy of Dr. F. E. Cislak, Reilly Tar and Chemical Corp.

(17) O. D. Frampton and J. F. Nobis, *Ind. Eng. Chem.*, **45**, 404 (1953).

(18) This is a paraffinic hydrocarbon mixture, b.p. 296–351°F., which was purchased from Phillips Petroleum Co.

Preparation of Condensing Agents. (a) **Phenylsodium.**—The procedure which was used for preparing phenylsodium was modeled after that described by Nobis and Moormeier.[19] Approximately 75 ml. of thiophene-free benzene and 0.23 mole of sodium dispersion, for each 0.1 mole of phenylsodium to be prepared, are introduced into the reactor. Then 2–3 ml. of a solution of bromobenzene (0.1 mole, 15.7 g.) in an equal volume of thiophene-free benzene was added followed by the addition of 1 ml. of a 10% solution of *t*-amyl alcohol in benzene maintaining the reaction temperature at 30°. More of the *t*-amyl alcohol–benzene solution was added every minute or two until the reaction between the bromobenzene and sodium was well started as indicated by a rise in temperature and a change in color of the reaction mixture from gray to black. The rest of the bromobenzene solution was added slowly and the reaction temperature was maintained at 30° using a cooling bath when necessary. The suspension of phenylsodium is stirred for 30 minutes after the addition of the bromobenzene is complete. The contents of the reactor are blanketed in a nitrogen atmosphere throughout the preparation of the sodium dispersion and its conversion to phenylsodium. The yield of phenylsodium, based on carbonation to benzoic acid, is greater than 95% of theory.

(b) **Sodium Diisopropylamide.**—Diisopropylamine (one equivalent), diluted with an equal volume of benzene, is added to the suspension of phenylsodium (one equivalent) at 5°. The mixture is stirred for an additional period of one hour and is then ready to be used. The conversion of diisopropylamine to sodium diisopropylamide is assumed to be quantitative.

(c) **Lithium Diisopropylamide.**—This condensing agent was prepared as described previously.[20] The procedure which was used in the one acylation (Table II) which was effected employing this base was the same as that involving the acylation of 2-picoline with esters using phenyllithium[6] as the condensing agent except that the phenyllithium was replaced by lithium diisopropylamide.

General Procedure for the Acylation of 3-Picoline, 4-Picoline and Their Derivatives Using Sodium Diisopropylamide as the Condensing Agent.—Two equivalents of the pyridine derivative, diluted with an equal volume of benzene, were added to two equivalents of a suspension of sodium diisopropylamide in benzene at 5° and the mixture was stirred for 30 minutes at 5°. One equivalent of the acylating ester, diluted with an equal volume of benzene, was then added and the mixture was stirred at 5° for an additional one-hour period. The mixture was then poured onto ice and filtered if any solid was present. It was then made strongly acidic with concentrated hydrochloric acid and was extracted with several portions of benzene to remove any unreacted ester. The aqueous phase was made basic with aqueous 20% sodium hydroxide solution and was extracted with several portions of ether or chloroform. The combined basic extracts were dried over anhydrous sodium sulfate, the solvents were removed by distillation at atmospheric pressure and the residue was fractionated in vacuum.

In those reactions which were effected using phenylsodium as the condensing agent, the procedure employed was the same as that described above except that phenylsodium was used in place of sodium diisopropylamide.

Alkylation of 4-Picoline and 4-Benzylpyridine with β-Dimethylaminoethyl Chloride Using Sodium Diisopropylamide as the Condensing Agent.—The procedure employed for these alkylations was the same as that described above for the acylations except that the esters were replaced by β-dimethylaminoethyl chloride and a 1:1:1 molar ratio of 4-picoline: or 4-benzylpyridine:sodium diisopropylamide:β-dimethylaminoethyl chloride was used. Thus, from the interaction of 0.5 mole each of 4-picoline, sodium diisopropylamide and β-dimethylaminoethyl chloride there was obtained 65.4 g. (80%) of 1-(4-pyridyl)-3-dimethylaminopropane, b.p. 80.0–80.5° at 1.59 mm. *Anal.* Calcd. for $C_{10}H_{16}N_2$: C, 73.12; H, 9.82. Found: C, 73.56; H, 10.40. This compound forms a dipicrate, m.p. 188.2–188.8° (from 95% ethanol). *Anal.* Calcd. for $C_{22}H_{22}N_8O_{14}$: C, 42.45; H, 3.56. Found: C, 42.45; H, 3.93.

From a similar experiment in which 0.2 mole each of 4-benzylpyridine, β-dimethylaminoethyl chloride and sodium diisopropylamide were used, there was isolated 42.2 g. (88%) of 1-phenyl-1-(4-pyridyl)-3-dimethylaminopropane, b.p. 144–146° at 1.0 mm.[15]

PITTSBURGH 13, PENNA.

(19) J. F. Nobis and L. F. Moormeier, *Ind. Eng. Chem.*, **46**, 539 (1954).

(20) M. Hamell and R. Levine, *J. Org. Chem.*, **15**, 162 (1950).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE INC.]

Quinazoline 3-Oxide Structure of Compounds Previously Described in the Literature as 3.1.4-Benzoxadiazepines[1]

BY L. H. STERNBACH, S. KAISER AND E. REEDER

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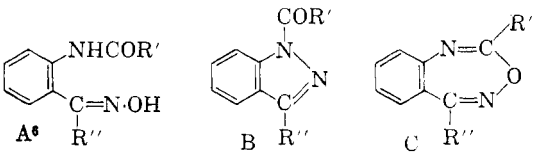
It has been shown that the compounds formed by the dehydration of *o*-acylaminobenzophenone oximes (I and XII) with a Beckmann mixture are quinazoline 3-oxides (II and XIII) and not, as formerly postulated, 3.1.4-benzoxadiazepines (C).[1]

A study has been made on the structure of compounds described in the literature as 3.1.4-benzoxadiazepines.[1] These heterocycles are obtained by dehydration of *o*-acylaminoaldoximes or ketoximes (A) with a Beckmann mixture. Auwers and F. v. Meyenburg[2] who had discovered and studied this reaction, initially considered these compounds to be acylindazoles (B). Later Bischler[3] postulated the structure C, which was accepted by other investigators[4] as well as by Auwers.[5] Ried and Stahlhofen[7] made the interesting observation that compounds of this type, on hydrogenation with a Raney nickel catalyst, absorb two moles of hydrogen and yield dihydroquinazolines. They postulated that the reaction proceeded *via* the intermediate D which lost the elements of water to form the dihydroquinazoline, and considered this result an additional proof for the seven-membered ring present in their starting material.



A[6] B C

(1) In the German literature these compounds are known as 4,5-benzo-[hept-1,2,6-oxdiazines].

(2) K. Auwers and F. von Meyenburg, *Ber.*, **24**, 2370 (1891).

(3) Aug. Bischler, *ibid.*, **26**, 1891, 1901 (1893).

(4) J. Meisenheimer and A. Diedrich, *ibid.*, **57**, 1715 (1924).

(5) K. von Auwers, *ibid.*, **57**, 1723 (1924).

(6) The structures discussed or described in the literature are marked with capital letters; compounds prepared in the course of this study with Roman numerals.

(7) W. Ried and P. Stahlhofen, *Chem. Ber.*, **87**, 1814 (1954).