seven less general routes[8] to **1** suffer from low over-all synthetic yield, low deuterium incorporation, or the use of costly lithium aluminum deuteride.

In contrast, the dithiane method incorporates deuterium derived from inexpensive deuterium oxide quantitatively and specifically at the aldehyde carbon in high over-all yield. This standard procedure is applicable to the rapid, large-scale preparation of a wide variety of 1-deuterioaldehydes.

In addition, 1-deuterioaldehyde precursors of type **4**, Ph = R, are readily and quite generally available from 1,3-dithiane by consecutive alkylation and deuteration.[2,3] Both operations may be carried out efficiently and conveniently in the same flask. Thus successive treatment of 1,3-dithiane with *n*-butyllithium, 2-iodopropane, *n*-butyllithium, and deuterium oxide provided 2-isopropyl-1,3-dithiane-2-*d* in 95% over-all yield.

Experimental Section

Melting points are corrected. Infrared spectra were observed in carbon tetrachloride on a Perkin-Elmer 237 grating spectrophotometer. Nmr spectra were observed in carbon tetrachloride on a Varian A-60 spectrometer; peaks are reported as parts per million downfield from internal tetramethylsilane reference. Mass spectra were taken on an AEI MS-9 double-focusing spectrometer at 11 and 70 ev; samples were introduced by sublimation at room temperature.

2-Phenyl-1,3-dithiane (**2**).—Dry hydrogen chloride was bubbled rapidly into a solution of 1,3-propanedithiol (40.0 ml, 0.395 mole) and benzaldehyde (40.0 ml, 0.393 mole) in chloroform (300 ml) until the mixture was saturated (5 min). The exothermic reaction was moderated by brief external cooling with ice–water. After standing 0.5 hr the mixture was washed with two 100-ml portions of water, three 100-ml portions of 10% potassium hydroxide solution, and two 100-ml portions of water; then it was filtered through anhydrous sodium sulfate and evaporated on a rotary evaporator. The residue was treated with charcoal and crystallized from 200 ml of methanol to furnish white needles (72.7 g, 94.5%), mp 69.0–69.8° (lit.[9] mp 70–71°), in three crops.

The infrared spectrum of **2** included strong bands at 3.38, 3.44, 6.88, 7.03, 7.85, 8.55, 10.97, 11.35, 14.4, and 14.8 μ. A band at 10.98 ± 0.04 μ is highly characteristic of the 1,3-dithiane ring.[3]

2-Phenyl-1,3-dithiane-2-*d* (**4**).—A solution of dithiane **2** (138.7 g, 0.705 mole) in anhydrous tetrahydrofuran (1.3 l.) was treated under nitrogen at −60 to −75° during 1 hr with a solution of *n*-butyllithium in hexane (Foote Mineral Co.; 500 ml, 0.80 mole). After standing 6 hr below −50° the solution was treated with deuterium oxide (>99.9% *d;* 90 ml) and warmed to room temperature; 0.05 *M* hydrochloric acid was added to the organic phase and tetrahydrofuran was removed on a rotary evaporator. The residue was shaken with 1:1 (v/v) dichloromethane–pentane; the organic phase was washed with sodium bicarbonate solution, water, and saturated salt solution and then dried over potassium carbonate. The residue after evaporation of solvent was crystallized from methanol to provide white needles (131.4 g, 94.5%), mp 68.8–69.8°, in three crops.

The nmr singlet at 5.07 ppm due to the proton at C-2 was absent. Deuterium incorporation at C-2 was 99.9 ± 0.1% by low voltage mass spectral comparison with nondeuterated **2**. The infrared spectrum was similar to that of **2**, except that the 8.55-μ band was absent, new bands were seen at 4.58 and 4.69 μ (weak; C–D stretch) and 14.1 μ, and the bands at 10.97 (dithiane) and 11.35 μ were shifted to 11.02 and 11.31 μ, respectively.

Benzaldehyde-1-*d* (**1**).—Treatment of a warm solution of dithiane **4** (9.87 g, 50.0 mmoles) in 9:1 (v/v) methanol–water (250 ml) with solid mercuric oxide (9.8 g, 45 mmoles) and a solution of mercuric chloride (27.2 g, 100 mmoles) in the same solvent mixture (50 ml) gave a voluminous white precipitate. The mixture was refluxed for 4 hr under nitrogen and then cooled. After filtration to remove the white solid, solvent was removed from the filtrate by distillation through a 20-cm Vigreux column under nitrogen until about 100 ml remained. Dichloromethane–pentane (100 ml), 1:1 (v/v), was added and the mixture was shaken twice with 100 ml of half-saturated ammonium acetate solution and twice with 100 ml of saturated salt solution and then dried over sodium sulfate. Most of the solvent was removed as before to furnish a colorless liquid that consisted of dichloromethane (53 mole %) and deuterioaldehyde **1** (47 mole %, 4.9 g, 92%) by nmr analysis. Distillation afforded a colorless liquid (4.32 g, 81%), bp 77–78° (27 mm), that was pure benzaldehyde-1-*d* by nmr; no aldehyde proton absorption was seen at 9.95 ppm.

2-Isopropyl-1,3-dithiane-2-*d*.—A solution of 1,3-dithiane (0.252 g, 2.1 mmoles) in anhydrous tetrahydrofuran (10 ml) was stirred at −25° under nitrogen while *n*-butyllithium solution (2.3 mmoles) was added. After 1.5 hr the solution was warmed to 0° and treated with 2-iodopropane (0.42 g, 2.5 mmoles). After 14 hr at 0° the solution was cooled to −25° and treated with *n*-butyllithium solution (2.7 mmoles). After 1.5 hr deuterium oxide (>99.9%, 1 ml) was added. The isolation procedure described for **4**, but using pentane as extraction solvent, furnished a colorless liquid (0.326 g, 95%) which microdistilled at a bath temperature of 58° (0.15 mm). Deuterium incorporation at C-2 was greater than 98% by nmr analysis.

Acknowledgments.—This work was supported in part by the National Science Foundation and the National Institutes of Health.

---

[8] K. B. Wiberg, *J. Am. Chem. Soc.*, **76**, 5371 (1954), along with C. R. Hauser, P. J. Hamrick, and A. T. Stewart, *J. Org. Chem.*, **21**, 260 (1956); G. P. Miklukhin and A. F. Rekasheva, *J. Gen. Chem. USSR*, **25**, 1099 (1955); J. Hampton, A. Leo, and F. H. Westheimer, *J. Am. Chem. Soc.*, **78**, 306 (1956); A. Streitwieser and J. R. Wolfe, *ibid.*, **79**, 903 (1957); J. D. McCollum and S. Meyerson, *ibid.*, **85**, 1739 (1963); L. Skattebøl and J. D. Roberts, *ibid.*, **80**, 4085 (1958), along with ref 7; T. Cohen and I. H. Song, *ibid.*, **87**, 3780 (1965).

[9] W. Autenrieth and K. Wolff, *Ber.*, **32**, 1375 (1899).

Nickel as an Alkylation Catalyst

William A. Bonner and Robert A. Grimm

Department of Chemistry, Stanford University,
Stanford, California 94305

Received June 2, 1966

This investigation was initiated in an attempt to learn more about the action on various substrates of "hydrogen-free Raney nickel" (RaNi-200°), prepared by degassing ordinary Raney nickel catalyst[1] at 200–250° under vacuum.[2,3] In particular, we wished to study the reactions of this catalyst with certain halogenated and oxygenated compounds of types not previously studied.

The usual reaction, if any, of ordinary Raney nickel with organic halides involves simple hydrogenolysis to the corresponding monomeric alkane derivative.[4–8] In a few instances,[7,8] however, especially when the catalyst/substrate ratio was low,[7] Raney nickel has been found to convert organic halides into dimeric coupling products—benzyl chloride, for example, yield-

---

[1] R. Mozingo, *Org. Syn.*, **21**, 15 (1941).

[2] H. Hauptmann and B. Wladislaw, *J. Am. Chem. Soc.*, **72**, 707, 710 (1950).

[3] H. Hauptmann, B. Wladislaw, L. L. Nazario, and W. F. Walter, *Ann.*, **576**, 45 (1952).

[4] W. E. Parham and R. Koncos, *J. Am. Chem. Soc.*, **83**, 4038 (1961).

[5] S. Imaizumi and S. Mitsui, *Bull. Chem. Soc. Japan*, **34**, 774 (1961).

[6] W. A. Bonner and J. A. Zderic, *J. Am. Chem. Soc.*, **78**, 3218 (1956).

[7] A. M. Grigorovskii and V. S. Fedorov, *Zh. Prikl. Khim.*, **21**, 529 (1948); *Chem. Abstr.*, **43**, 646*d* (1949).

[8] N. P. Buu-Hoi and N. Hoan, *J. Org. Chem.*, **14**, 1023 (1949).

ing both toluene and 1,2-diphenylethane,[7] and 1-chloro-1-*o*-methoxyphenylpropane affording 3,4-*o*-methoxyphenylhexane.[8] In view of the absence of information regarding the action of hydrogen-free Raney nickel on organic halides, however, experiments with this catalyst seemed worthy of investigation. By rough analogy, dimeric coupling products were anticipated.

When *t*-butyl chloride and RaNi–200° were heated in refluxing benzene, product isolation revealed substantial quantities of *t*-butylbenzene and 1,4-di-*t*-butylbenzene, and none of the anticipated 2,2,3,3-tetramethylbutane. Thus Friedel–Crafts alkylation of the solvent, rather than coupling, was the only reaction observed. Similar results were noted in *o*-xylene solvent, where 3,4-dimethyl-*t*-butylbenzene was the sole product. Analogous alkylation reactions occurred with *sec*-butyl chloride and RaNi–200°, whereby *sec*-butylbenzene and a mixture of (presumably) 1,2-dimethyl-*sec*-butylbenzenes were obtained, respectively, from refluxing benzene and *o*-xylene solvents. Alkylation of benzene or *o*-xylene under RaNi–200° catalysis was not observed, however, with *n*-butyl chloride or *n*-butyl bromide, and the catalyst was without action on bromobenzene. When benzyl chloride was refluxed with RaNi–200°, vigorous HCl evolution was noted and an amorphous, yellow solid, presumably polybenzyl, was obtained.

Nickel catalysts supported on alumina have frequently been observed to dealkylate alkylbenzenes[9–14] and alkylphenols[15,16] at elevated temperatures (350–450°), and similar reactions have been documented using Ni–Cr,[17,18] Ni–zeolite,[19] and Co[20] catalysts. While the reverse reaction, namely, the alkylation of benzene with methane over Ni–Al_2O_3 at 250–300°, has been recently reported,[21] we are not aware of nickel-catalyzed alkylations previously observed under the above gentle conditions with degassed Raney nickel. It was therefore decided to investigate such reactions further.

Spectrographic analysis of our RaNi–200° sample showed that it contained about 4% residual aluminum, and it seemed therefore possible that $AlCl_3$, formed by interaction of this residual aluminum with the alkyl halide substrate, might actually be the responsible catalyst in the above alkylations. A pyrophoric nickel catalyst was accordingly prepared by the pyrolysis under vacuum of nickelous formate. This catalyst proved to contain only 0.008% aluminum. When it was employed in place of RaNi–200° in reactions such as those above, using *t*-butyl, *sec*-butyl, and benzyl chlorides in refluxing benzene or *o*-xylene solvent, analogous alkylation products were again observed. *n*-Butyl chloride similarly failed to alkylate *o*-xylene, and benzoyl chloride was recovered unchanged in an aroylation experiment involving this catalyst. It would thus appear that the nickel itself, and not by-product $AlCl_3$, was the actual catalyst involved in these alkylations. Another "hydrogen-poor" nickel catalyst, formed by prolonged preliminary heating of ordinary Raney nickel in refluxing acetone solvent, proved similarly effective in promoting the alkylation of *o*-xylene with *t*-butyl, *sec*-butyl, and benzyl chlorides, but not with *n*-butyl chloride. That by-product nickel chloride was not the responsible catalyst was suggested by our failure to observe alkylation of benzene with *t*-butyl chloride using anhydrous nickelous chloride under similar conditions.

It appears probable to us that the above reactions involved conversion of the alkyl halides to a carbonium ion on the catalyst surface, and that this intermediate then alkylated the aromatic solvent in the usual electrophilic manner. The observed alkylations with benzyl, tertiary, and secondary halides, but not with primary halides accord with this tentative hypothesis, since carbonium ions are formed more readily from the former types of halides. By analogy, Isogai has recently found[22] that when alkyl halides were shaken under hydrogen with moist W-5 Raney nickel, tertiary halides were rapidly hydrogenolyzed (halide ion in the product filtrate), whereas secondary and particularly primary halides were hardly hydrogenolyzed at all, while Pd–C catalyst failed entirely to promote hydrogenolysis of any halides under similar conditions. Isogai also postulated an SN1 type of mechanism on the nickel catalyst surface to explain his observations.

The action of degassed Raney nickel on a variety of sulfur-[2,3,23,24] and selenium-containing[25] substrates has been extensively documented, and formation of the observed diaryl, diaryl sulfide or selenide, or analogous products has been rationalized in terms of free-radical coupling reactions.[2,3,23–25] Stilbene, for example, was the major product during reaction of benzaldehyde diethyl thioacetal with RaNi–200°, while formaldehyde diphenyl thioacetal afforded diphenyl sulfide.[2] Analogous reactions have not been attempted with ordinary acetals, however, although Hauptmann has found that phenyl benzoate was inert toward RaNi–200° under conditions where phenyl thio- or selenobenzoate reacted readily. More recently, on the other hand, Waki has observed[26] that degassed Raney nickel converted 1,8-cineole into limonene and other oxygen-free terpenes at 240°, while aromatization to *p*-cymene was the major reaction at 350°. We have accordingly studied the action of RaNi–200° in refluxing benzene

---

(9) A. Rieche, H. Seeboth, and H. Wolf, *Monatsber. Deut. Akad. Wiss. Berlin*, **6**, 364 (1964); *Chem. Abstr.*, **61**, 15993*a* (1964).

(10) N. I. Shuikin, N. F. Kononov, L. K. Kashkovskaya, and V. M. Akimov, *Zh. Obshch. Khim.*, **33**, 3871 (1963); *Chem. Abstr.*, **60**, 9169*d* (1964).

(11) N. I. Shuikin, N. F. Kononov, L. K. Kashkovskaya, and V. M. Akimov, *Zh. Obshch. Khim.*, **32**, 3595 (1962); *Chem. Abstr.*, **58**, 13821*f* (1963).

(12) N. I. Shuikin and H.-H. Tien, *Isv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 854 (1961); *Chem. Abstr.*, **55**, 22178*e* (1961).

(13) N. I. Shuikin and H.-H. Tien, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 2014 (1960); *Chem. Abstr.*, **55**, 13336*g* (1961).

(14) K. Morikawa and F. Nozaki, *Kogyo Kagaku Zasshi*, **64**, 898, 654 (1961); *Chem. Abstr.*, **57**, 6667*g*, 3325*b* (1962).

(15) L. Beranek, M. Kraus, and V. Bazant, *Collection Czech. Chem. Commun.*, **29**, 239 (1964); *Chem. Abstr.*, **60**, 6771*h* (1964).

(16) A. A. Balandin, T. A. Slovokhotova, and C.-Y. Yu, *Dokl. Akad. Nauk. SSSR*, **141**, 839 (1961); *Chem. Abstr.*, **56**, 14138*c* (1962).

(17) G. N. Maslyanskii, G. L. Rabinovich, and N. K. Avtanomova, *Neftekhimiya*, **4**, 421 (1964); *Chem. Abstr.*, **61**, 6832*c* (1964).

(18) G. N. Maslyanskii and G. L. Rabinovich, *Neftkhimiya*, **2**, 709 (1962); *Chem. Abstr.*, **58**, 6629*f* (1963).

(19) A. M. Okruzhnov, R. I. Izmailov, and R. A. Virobyants, *Neftekhimiya*, **4**, 850, 676 (1964); *Chem. Abstr.*, **62**, 11707*f*, 2724*a* (1965).

(20) D. Tamonova and A. Banner-Voigt, *Collection Czech. Chem. Commun.*, **29**, 1626 (1964); *Chem. Abstr.*, **61**, 5545*b* (1964).

(21) A. Rieche and H. Seeboth, *Angew. Chem.*, **75**, 861 (1963).

(22) K. Isogai, *Nippon Kagaku Zasshi*, **83**, 1238 (1962); *Chem. Abstr.*, **59**, 11226*h* (1963).

(23) H. Hauptmann, W. F. Walter, and C. Marino, *J. Am. Chem. Soc.*, **80**, 5832 (1958).

(24) A. Luttringhaus and R. Deckert, *Angew. Chem.*, **67**, 275 (1955).

(25) H. Hauptmann and W. F. Walter, *J. Am. Chem. Soc.*, **77**, 4929 (1955).

(26) T. Waki, *Nippon Kagaku Zasshi*, **81**, 131 (1960); *Chem. Abstr.*, **56**, 508*e* (1962).

TABLE I

ALKYLATION OF AROMATIC SUBSTRATES UNDER THE INFLUENCE OF NICKEL CATALYSTS[a]

Catalyst	Approx wt, g	Halide	Wt, g	Aromatic substrate	Vol, ml	Reflux time, hr	Product	Wt, g
A	10	$PhCH_2Cl$	27.5	None	...	0.2[b]	Cl-free polymer	15.1
B	4	$PhCH_2Cl$	11.0	*o*-Xylene	30	5	3,4-Dimethyldiphenylmethane	9.2[c]
C	15	$PhCH_2Cl$	5.0	*o*-Xylene	100	1	3,4-Dimethyldiphenylmethane	...
A	9	*t*-BuCl	8.5	Benzene	50	25.5[d]	*t*-Butylbenzene	6.4
							1,4-Di-*t*-butylbenzene[e]	0.7
A	18	*t*-BuCl	17.0	*o*-Xylene	40	1	3,4-Dimethyl-*t*-butylbenzene[f]	5.9
B	4	*t*-BuCl	17.4	*o*-Xylene	40	18	3,4-Dimethyl-*t*-butylbenzene	4.9
C	9	*t*-BuCl	8.5	*o*-Xylene	40	18	3,4-Dimethyl-*t*-butylbenzene	5.3
A	9	*sec*-BuCl	8.7	Benzene	50	25	*sec*-Butylbenzene[g]	3.1
A	9	*sec*-BuCl	8.7	*o*-Xylene	50	21	Two 1,2-dimethyl-*sec*-butylbenzenes[h]	4.4
B	4	*sec*-BuCl	8.7	*o*-Xylene	40	11	Two 1,2-dimethyl-*sec*-butylbenzenes	0.9
C	9	*sec*-BuCl	8.7	*o*-Xylene	40	15	Two 1,2-dimethyl-*sec*-butylbenzenes	4.8
A	6	*n*-BuCl	12.8	Benzene	50	60	No reaction	...
A	10	*n*-BuBr	22	Benzene	100	6	No reaction	...
A, B, or C	...	*n*-BuCl	...	*o*-Xylene	...	...	No reaction	...
RaNi alloy[i]	8	*t*-BuCl	17	*o*-Xylene	40	3	3,4-Dimethyl-*t*-butylbenzene	3.2
A	18	PhBr	37	None	...	3.5	No reaction	...
B	4	PhCOCl	12	Benzene	40	23[b]	No aroylation	...

[a] Catalysts: A, RaNi–200°; B, Ni–For; C, RaNi–Ac. [b] Under N_2 atmosphere. [c] Bp 165–170° (18 mm); 4.9 g of higher boiling product also obtained. [d] HCl evolution noted prior to heating. [e] Mp 77–78°; H. Meyer and K. Bernhauser [*Monatsh.*, **53**, 727 (1929)] report mp 76°. [f] Characterized by $KMnO_4$–pyridine oxidation to 2-methyl-4-*t*-butylbenzoic acid[3] [D. Nightengale and J. R. Janes, *J. Am. Chem. Soc.*, **66**, 154 (1944)], mp 141.5–142.5°. [g] Gas chromatography showed 50% unreacted *sec*-BuCl. [h] Bp 210–216°; poorly separated by gas chromatography. [i] Baked under vacuum at 250° for 2 hr.

on two acetals, acetaldehyde di-*n*-butyl acetal and diphenoxyacetic acid. In each case only starting material was recovered and no coupling products were noted. In accord with earlier >CHOH dehydrogenation reactions observed using ordinary Raney nickel,[27-29] we also found that RaNi–200° readily converted cyclohexanol into cyclohexanone in refluxing benzene.

Experimental Section

Nickel Catalysts. A. Vacuum-Degassed Raney Nickel (RaNi–200°).—Raney nickel was prepared by the usual procedure[1] and stored under ethanol until further treatment. A sample of the catalyst–ethanol paste was placed in a three-neck flask equipped with a reflux condenser and dropping funnel and attached to a vacuum line. The system was evacuated and the catalyst was freed of solvent by heating with warm water. When the sample appeared dry the water bath was replaced by a heating mantle and the temperature was gradually increased to 200–250°. Around 130° hydrogen evolved abruptly from the catalyst, accompanied by vigorous motion of the catalyst and a weak, orange luminescence. The residual catalyst powder was baked *in vacuo* for 0.25 to 2 hr, usually 1 hr. No apparent catalyst differences were noted if baking was conducted for 0.25–0.5 or 1–2 hr. The evacuated system was cooled, and the reaction mixture or reaction solvent was introduced through the dropping funnel. If air were introduced prior to the solvent, the catalyst reacted vigorously and exothermally, with emission of a dull orange glow. A spectrographic analysis[30] of a typical sample of degassed RaNi–200° showed the following additional constituents (as oxides): Al (4%), Co (0.03%), Fe (0.12%), Si (0.01%), Mn (0.003%), Mg (0.004%), Cu (0.015%), Co (0.005%), and Cr (0.001%). The above procedure is an adaptation of that of Hauptmann and co-workers.[2,3]

B. Nickel from Nickelous Formate (Ni-For).—Powdered nickelous formate (Baker technical, 6–7 g) was evacuated in the above apparatus and heated to 250–300°, turning black within 5–10 min. Residual undecomposed material on the sides of the flask was pyrolyzed by flaming with a bunsen burner. Heating was continued at 250–300° for 15–60 min, whereupon the cooled nickel (pyrophoric) was covered with the reaction mixture or solvent as before, prior to exposure to air. The following extraneous metals (as oxides) were found[30] by spectrographic analysis: Na (0.3%), Mg (0.05%), Al (0.008%), Si (0.01%), Ca (0.5%), Cr (0.003%), Mn (0.04%), Fe (0.15%), Co (0.10%), Cu (0.007%), Sr (0.005%), Ba (0.006%), and Pb (0.05%).

C. Acetone-Deactivated Raney Nickel (RaNi-Ac).—Ordinary Raney nickel was treated with acetone (*ca.* 50 ml per teaspoonful of catalyst paste), and the mixture was heated under reflux for 5 hr. The acetone was removed by decantation and rinsed with the appropriate reaction solvent, whereupon the indicated reactants (see below) were added.

Alkylation Experiments.—The catalyst samples, prepared as above, were treated prior to exposure to air with the aromatic substrate to be alkylated (Table I), and the appropriate alkyl halide was then added. The mixture was heated under reflux for the indicated time (Table I), whereupon the catalyst was filtered from the cooled mixture. With benzyl and *t*-butyl chlorides, hydrogen chloride evolution was noted within a few minutes, while gas evolution from mixtures containing *sec*-butyl chloride commenced only after 1 hr or more. The crude product mixtures were subjected to fractional distillation, and the appropriate fractions were characterized by comparison of gas chromatographic retention times, infrared spectra, and refractive indices with those of authentic samples. Data pertaining to these experiments are summarized in Table I.

Other Reaction Attempts.—An attempt was made to alkylate benzene with *t*-butyl chloride using anhydrous nickelous chloride catalyst. After 60 min of reflux no HCl was evolved and no other sign of reaction was observed. When Alcoa activated alumina (F-20, preheated at 250° for 12 hr) was used as catalyst with *t*-butyl chloride and benzene, a considerable amount of HCl was liberated during 8 hr of reflux. Chloride ion was subsequently found in the aqueous filtrate after treating the filtered catalyst with water. No alkylation of benzene was observed using *sec*-butyl chloride and the same alumina catalyst.

Attempts to fragment the two acetals, acetaldehyde di-*n*-butyl acetal and diphenoxyacetic acid, by heating them with RaNi–200° in refluxing benzene were unsuccessful. Only unchanged starting material was recovered in each case.

---

[27] R. Paul, *Compt. Rend.*, **208**, 1319 (1939).

[28] R. Paul, *Bull. Soc. Chim. France*, **8**, 507 (1941).

[29] E. C. Kleiderer and E. C. Kornfeld, *J. Org. Chem.*, **13**, 455 (1948).

[30] Performed by American Spectrographic Laboratories, Inc., San Francisco, Calif.

When cyclohexanol (10 ml) and RaNi-200° (9 g) were heated in refluxing benzene (40 ml) during 48 hr, gas chromatography of the product mixture showed the presence of cyclohexanone and cyclohexanol in a 35:65 ratio. The former ketone was characterized as its 2,4-dinitrophenylhydrazone, mp 160–161°, (lit.[31] mp 162°).

---

[31] N. R. Campbell, *Analyst*, **61**, 393 (1936).

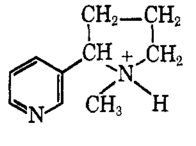
The Effect of Hydrogen Chloride on the Optical Rotation of Nicotine

AKIRA TOMITA, EI-ICHIRO OCHIAI, HIDEFUMI HIRAI, AND SHOJI MAKISHIMA

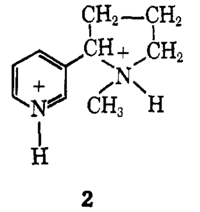
Department of Industrial Chemistry, Tokyo University, Tokyo, Japan

Received April 26, 1966

The optical rotatory dispersion curve of (−)-nicotine has been investigated by several workers,[1–3] and (−)-nicotine has been assigned the (*S*) configuration.[3] In a previous paper,[4] the effects of various Lewis acids on the optical rotation of nicotine have been shown, using dimethylformamide as a solvent. However, owing to the strong absorption band of dimethylformamide, the rotatory dispersion in ultraviolet region could not be studied. The study in this region was thought advisable, because it would clarify the mechanism of the optical rotational change of nicotine in detail. The present work was undertaken to determine the effect of hydrogen chloride (the simplest model compound of Lewis acid) on the optical rotatory dispersion and circular dichroism curves of (*S*)-nicotine. The protonated nicotine is easily soluble in transparent solvents (such as alcohol and water). Since the first and the second ionization constants of nicotine are sufficiently different, all species, *i.e.*, nicotine, nicotine monohydrochloride (1), and nicotine dihydrochloride (2), can be obtained separately in solution. Therefore, the difference between the effect of the protonation on the pyrrolidine nitrogen of nicotine and that of the protonation on the pyridine nitrogen would clearly be demonstrated. The fraction of species present at various hydrogen chloride concentrations can be calculated using the following pK_a values which were obtained from the pH titration at 15°: 6.28 and 2.37 in 95% alcohol, and 8.03 and 3.44 in water.[5] When equimolar amount of hydrogen chloride is added to nicotine, 97.6% of the nicotine is in the monoprotonated form 1 in 95% alcohol (pH 4.52), and 99.7% in water (pH 6.20). When hydrogen chloride is added in excess (HCl/nicotine = 5.0), 65.0% is as the diprotonated form 2 in 95% alcohol (pH 2.10), and 94.5% in water (pH 2.20).



1



2

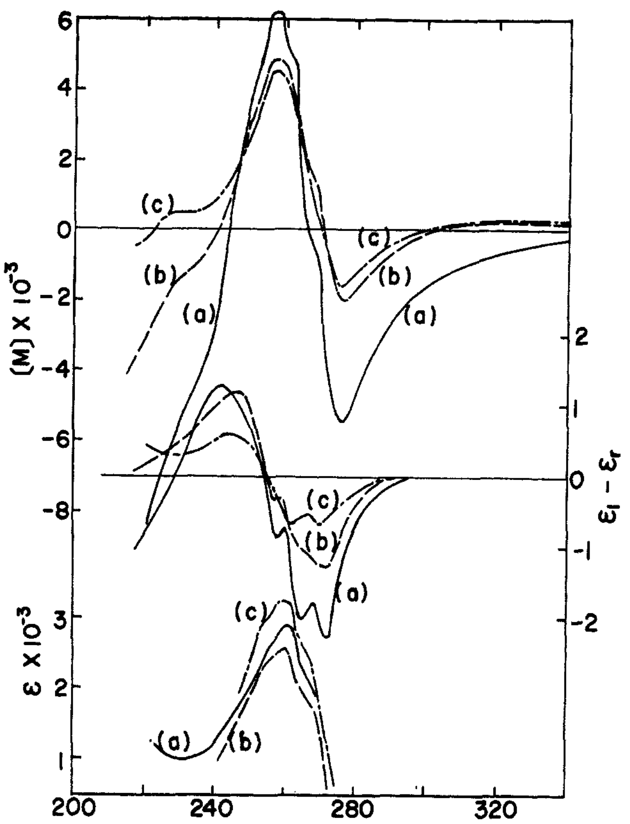


Figure 1.—Rotatory dispersion, circular dichroism, and absorption curves for nicotine–hydrogen chloride in 95% alcohol. Mole ratios of HCl/nicotine are (a) 0.0, (b) 1.0, (c) 5.0.

The rotatory dispersion, the circular dichroism, and the absorption curves of nicotine and its protonated species are shown as a function of the mole ratio (HCl/nicotine) in Figure 1. The established assignment of pyridine[6] and pyrrolidine[7] absorption spectra is applied in the following discussion. In view of the circular dichroism curves, the dispersion curves may be reasonably resolved into one plain curve and two anomalous dispersions, one of which shows a positive Cotton effect, centered at about 245 mμ, and the other, a negative Cotton effect at about 268 mμ. This negative Cotton effect may be assumed to arise from an optically active $\pi-\pi^*$ transition of the pyridine ring.[8] Since the magnitude of this negative Cotton effect is decreased by addition of equimolar amount of hydrogen chloride, it would appear that the transition in pyridine ring is influenced by protonation on the pyrrolidine nitrogen. The Cotton effect centered at 245 mμ is due to either the $2p_z$–3s transition in pyrrolidine nitrogen[7] or the $\pi-\pi^*$ transition in pyridine ring. In the latter case, Cotton effects at 245 and 268 mμ are at-

---

[1] T. S. Patterson and J. D. Fulton, *J. Chem. Soc.*, **127**, 2435 (1925).

[2] T. M. Lowry and W. V. Lloyd, *ibid.*, 1771 (1929).

[3] J. C. Craig and S. K. Roy, *Tetrahedron*, **21**, 401 (1965).

[4] A. Tomita, E. Ochiai, H. Hirai, and S. Makishima, *J. Inorg. Nucl. Chem.*, in press.

[5] Values of pK_a = 7.92 and 3.32 in water (at 25°) have been reported by R. T. Fowler, *J. Appl. Chem.*, **4**, 449 (1954).

[6] H. H. Jaffé and M. Orchin, "Theory and Application of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, Chapter 14.

[7] L. W. Pickett, M. E. Corning, G. M. Wieder, D. A. Semenov, and J. M. Buckley, *J. Am. Chem. Soc.*, **75**, 1618 (1953).

[8] Electronic transition within aromatic rings attached to asymmetric centers have been found to be optically active by other workers; see L. Verbit, *ibid.*, **87**, 1617 (1965); G. G. Lyle, *J. Org. Chem.*, **25**, 1779 (1960).