thetical 3-hydroxydecahydroquinoline (IV). The former course of oxidation is analogous to the introduction of β-hydroxy groups into pyridine[1] and quinoline[2] on biological oxidation. The latter route would be comparable to the β-oxygenation of *trans*-decaline (→ β-decalone)[3]. The possible introduction of a hydroxy group in the 2-position is reminiscent of the oxidation of niacine[4] and quinine[5].

By contrast, $\Delta^{1(9)}$-octahydroquinoline, being a tertiary unsaturated amine with only one activated tertiary center for the attack of oxygen, easily forms, as do similar bicyclic systems of this type a beautifully crystalline hydroperoxide[6].

B. WITKOP

National Institutes of Health, Washington 14, D.C., April 21, 1954.

Zusammenfassung

Dem phenolischen Oxydationsprodukt, das beim Durchleiten von Sauerstoff durch geschmolzenes *trans*-Dekahydrochinolin entsteht, wird auf Grund der Analyse und spektrophotometrischen Daten die Konstitution III eines 3-Oxy-5, 6, 7, 8-tetrahydrochinolins beigelegt. Seine Entstehung erfolgt wahrscheinlich über das gleichfalls gebildete 5, 6, 7, 8-Tetrahydrochinolin.

[1] *Cf.* J. N. SMITH and R. T. WILLIAMS, Biochem. J. *56*, 325 (1954).
[2] L. NOVACK and B. B. BRODIE, J. Biol. Chem. *187*, 787 (1950).
[3] H. KLEINFELLER and C. ODEFEY, Angew. Chem. *62*, 342 (1950).
[4] *Cf.* M. E. PULLMAN and S. P. COLOWICK, J. Biol. Chem. *206*, 121 (1954).
[5] B. B. BRODIE, J. E. BAER, and L. C. CRAIG, J. Biol. Chem. *188*, 567 (1951).
[6] L. A. COHEN and B. WITKOP, J. Amer. Chem. Soc. (in preparation).

Spectrophotometric Differences between Aminoheterocyclic Bases and Their Salts

When an open or cyclic base of the SCHIFF type containing the element >C=N– passes into the cation >C=$\overset{\oplus}{\text{N}}$H– three major spectroscopic changes are observed in the ultraviolet and infrared absorption spectra:

(1) A bathochromic shift in the ultraviolet ranging between 1 and 50 mμ and more depending on the type of compound and the presence of auxochromic groups[1]. A hypsochromic shift on salt formation usually indicates the participation of the cation >C=$\overset{\oplus}{\text{N}}$H– in partial or complete *intra-* or *inter*molecular addition reactions[2]. Pyridine and its derivatives are not normally looked upon as cyclic SCHIFF bases, although a number of chemical reactions (1, 2-addition and reduction, such as addition of alkyl lithium, HAMMICK reaction, acyloin-like condensations with aldehydes, etc.) clearly indicate the independence of the "ammono-aldehyde" (MORTON) system. In other respects pyridine exhibits aromatic character. This dualistic behavior is reflected in the effect of salt formation on the ultraviolet absorption of pyridines which may vary from hypsochromic to bathochromic (Table I).

[1] *Cf.* B. WITKOP, J. B. PATRICK, and H. M. KISSMAN, Ber. dtsch. chem. Ges. *85*, 949 (1952).
[2] *Cf.* E. D. BERGMANN, Chem. Rev. *53*, 309 (1953).

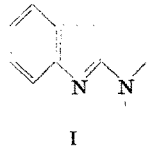
Table I

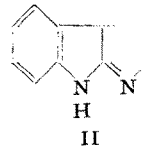
Influence of Salt Formation on the Ultraviolet Absorption of Some Pyridines (solvent ethanol if not stated otherwise).

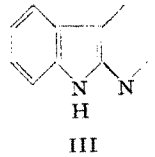
	λ_{max} free base	λ_{max} salt	$\Delta\lambda$
Pyridoxamine	308 (3·86)[a]	293 (3·95)	–15
Pyridoxal	300 (3·76)	288 (3·93)	–12
Pyridine[b]	257 (3·43)[c]	256 (3·73)	– 1
Nicotine[b]	262 (3·46)	260 (3·68)	– 2
2,6-Lutidine[b]	267 (3·48)[d]	272 (3·68)	+ 5
3-Vinylpyridine[b] . . .	278 (3·44)	287 (3·53)	+ 9
Nicotyrine[b]	288 (3·99)	310 (4·04)	+22

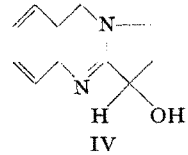
[a] Measured in 0·1 *N* NaOH: A. MEISTER, E. A. PETERSON, and H. A. SOBER, J. Amer. Chem. Soc. *76*, 169 (1954). [b] M. L. SWAIN, A. EISNER, C. F. WOODWARD, and B. A. BRICE, J. Amer. Chem. Soc. *71*, 1341 (1949), measured in 95% alcohol. [c] *Cf.* H. V. DAENIKER, Helv. chim. Acta *35*, 1955 (1952). [d] Measured in isooctane: R. A. FRIEDEL and M. ORCHIN, *Ultraviolet Spectra of Aromatic Compounds* (John Willey and Sons, Inc., New York, 1951), p. 106. – F. G. HERINGTON, Discussions of the Faraday Society *9*, 26 (1950).

α- and γ-aminopyridines are no longer formulated as α- or γ-pyridone imines but as cyclic (vinylogous) amidines; the true N-methyl pyridone imines which are only present in anhydrous inert solvents, absorb at much longer wave length than their tautomeric amidine cations; in this respect the salt formation has a hypsochromic effect. A slight hypsochromic effect is also observed when forming the salt of α-aminoindolenine, the properties of which (Table III) are best explained by formula I rather than II[1] or III[2], or of a cyclic amidine where the amino group forms part of a second ring as in vasicine (peganine, IV, Table III).


I


II


III

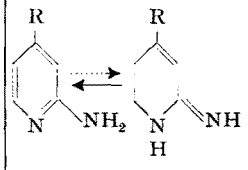
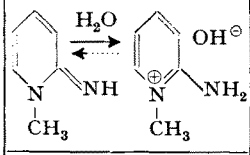
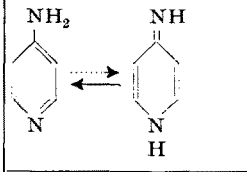
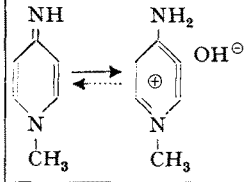
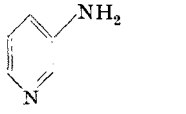
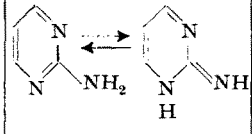

IV

(2) The infrared absorption of the >C=N– group (6·10–6·15 in aromatic SCHIFF bases, 6·24–6·28 in pyridines[3]) on salt formation invariably moves to shorter wave length (5·98–6·08 in SCHIFF bases, 6·07–6·13 in pyridines). This hypsochromic shift is even stronger in open and cyclic amidines (Table II and III) and clearly

[1] H. RINDERKNECHT, H. KOECHLIN, and C. NIEMANN, J. Org. Chem. *18*, 971 (1953).
[2] R. PSCHORR and G. HOPPE, Ber. dtsch. chem. Ges. *43*, 2543 (1910).
[3] The assignment of the band 6·28μ (1590 cm^{-1}) to the group >C=N– in pyridines (H. M. RANDALL, R. G. FOWLER, N. FUSON, and J. R. DANGL, *Infrared Determination of Organic Structures* [D. Van Nostrand Co., New York, 1949], p. 32) or pyrimidines (*Cf.* I. A. BROWNLIE, J. Chem. Soc. *1950* 3062), or other heterocycles is a simplification convenient for the purpose of comparison with the hydrochlorides. Normally no absolute assignments to >C=C< or >C=N– in conjugated systems can be made with certainty (*Cf.* E. R. BLOUT, M. FIELDS, and R. KARPLUS, J. Amer. Chem. Soc. *70*, 194 [1948]).

Table 11

The Effect of Salt Formation on the UV and IR Absorption Spectra of Aminopyridines and -Pyrimidine.

Tautomers	Compound (measured in N = Nujol, or C = Chloroform)	IR-Absorption: Immonium Bands	IR-Absorption: >C=N–	IR-Absorption: aromatic	Basicity pK_A	UV-Absorption λ_{max}	$\Delta\lambda$ λ_{max} cation $\overset{\oplus}{(>C=NH-)}$ λ_{max} base (>C=N–): IR (μ)	$\Delta\lambda$ λ_{max} cation $\overset{\oplus}{(>C=NH-)}$ λ_{max} base (>C=N–): UV (μ)
	α-aminopyridine (R = H) (C)	–	6·17[s] (6·18)	6·38[m a] (6·41)	6·86[b]	295[c]	–0·20	+5
	α-aminopyridine hydrochloride (N)	–	5·98[s]	6·11[s a]		300[c]		
	1-methyl-1,2-dihydro-2-iminopyridine (C)	–	6·05[s]	6·37[s e]	12·20[b]	353 (3·48)[d] in ether	–	~ –50
	1-methyl-2-amino-pyridinium hydroxide (in H_2O)	–				303 (3·65)[d] in aqueous diox.		
	γ-aminopyridine (C)	–	6·14[s]	6·24[s e]	9·17[b]	245[c]	–	+19
	γ-aminopyridine hydrochloride	–				264[c]		
	1,4-dihydro-4-amino-1-methylpyridine (C)	–	6·04[s]	6·48[s e]	12·5[b]	315 (3·46)[d] in aqueous diox.	–	~ –43
	1-methyl-4-amino-pyridinium hydroxide (in H_2O)	–				272 (4·45)[d]		
	3-aminopyridine (C)	–	6·16[s] (6·16)	6·29[s f] (6·31) 6·15[s]	6·6[c]	298 (3·59)ether[d] 304 (ethanol)[c]	–0·10	~ +12
	3-aminopyridine monohydrochloride (N)	–	6·06[s]	6·22[m]			–0·06	
	3-aminopyridine dihydrochloride (N)	4·80; 4·92; 5·14	6·10[m]	6·45[s]		316[c]		
	2-aminopyrimidine (C)	–	– 6·02[s]	6·23[s f] 6·19[s]	3·54[h]	292 (3·50)	–	~ +11
	2-aminopyrimidine hydrochloride (N)	–	6·02[s]	6·19[s]		303 (3·60)		

[a] The infrared data are those of the homologous 4-methyl-α-aminopyridine. The figures given below in parentheses are those of 2-aminopyridine observed by S. J. ANGYAL and R. L. WERNER, J. Chem. Soc. *1952*, 2911. [b] *Cf.* S. J. ANGYAL and C. L. ANGYAL, J. Chem. Soc. *1952*, 1461. [c] E. A. STECK and G. W. EWING, J. Amer. Chem. Soc. *70*, 3397 (1948). [d] L. C. ANDERSON and N. V. SEEGER, J. Amer. Chem. Soc. *71*, 340 (1949); 1-methyl-2-pyridonemethide absorbs at considerably longer wave length: 422 (3·18); 277 (3·25). [e] S. J. ANGYAL and R. L. WERNER, J. Chem. Soc. *1952*, 2911. [f] The figures in parantheses are those of S. J. ANGYAL and R. L. WERNER, J. Chem. Soc. *1952*, 2911. [g] D. J. BROWN and L. N. SHORT, J. Chem. Soc. *1953*, 331; $\Delta\lambda$ decreases on methylation: 2-methylaminopyrimidine $\Delta\lambda$ + 8 – 9; 2 dimethylaminopyrimidine + 6 – 7 mμ. The three analogous compounds in the 4-aminopyrimidine show the following negative $\Delta\lambda$: 4-aminopyrimidine — 22–23; 4-methylaminopyrimidine — 22–23; 4-dimethylaminopyrimidine — 26. [h] A. ALBERT, R. GOLDACRE, and J. PHILLIPS, J. Chem. Soc. *1948*, 2240.

distinguishes the cation of α- and γ-aminopyridine from the (double) cation of β-aminopyridine. The lowest absorption so far observed occurred in certain guanidinium cations, e.g., 5·65[s] and 5·64[s] in creatinine hydrochloride (measured in nujol).

(3) The infrared absorption of the cation $\overset{\oplus}{>C=NH-}$ always shows the broad ammonium band at 4·0–4·3 μ and one or several bands in the triple bond region 4·5–5·5 μ. These bands, which may be termed *immonium bands*, are characteristic of the salts of open and cyclic imines including heterocycles such as pyridine, quinoline, isoquinoline, etc. The neighborhood of a heteroatom of small basicity, e.g., oxygen, weakens the extinction of the immonium band, e.g., in benz-1,3-oxazines, or suppresses it completely as in acetiminoether hydrochloride. The presence of a second basic heteroatom, such as in the hydrochlorides of open or cyclic amidines, leads to the complete disappearance of these immonium bands. This observation is of diagnostic value, as can be seen from the comparison of the three aminopyridines: only the *di*hydrochloride of β-aminopyridine shows

Table III

The Effect of Salt Formation on the UV and IR Absorption Spectra of α-Aminoindolenine (I) and of Alkaloids of Partly Unknown Structure

Compound	Infrared Absorption				Basicity (pK_A and pK'_A)	Ultraviolet data (in neutral EtOH or N/10 ethanolic HCl)	$\Delta\lambda$ λ_{max} cation $\oplus$ (>C=NH—Ph) λ_{max} base (>C=NPh)	
	OH or NH	–C=N–	Aromatic	$CHCl_3$ (C) or Nujol (N)			IR (μ)	UV (mμ)
α-Aminoindolenine (I)	2·85 2·95 3·04	6·13[s] 6·01[s]	6·24[s] 6·22[w]	C N	~8·0 (R = H)[a] [~10·0 (R = Me)[a]]	[289 (3·50)] 267 (4·05)	—0·08	+1 (—7)
α-Aminoindolenine hydrochloride	(2·98)	5·93[s] 6·13[s]	6·24[s]	C	—	290 (3·40) 260 (3·96) 252 (3·95)		
Quebrachamine (*cf.* III)	2·88	—	—	C	6·76 (80% methyl cellosolve)	295 (3·85) 286 (3·88)	—	—5
Quebrachamine hydrochloride	3·15	—	6·18[s]	N	9·25 (75% EtOH)	290 (3·83) (methiodide)		
β-Hydroxyquebramidine (*cf.* I)[f]	2·79	—[e]	6·20[w]	C	11·0[d] (80% methyl cellosolve)	293 (3·52) 235 (3·96)	—	± 0
β-Hydroxyquebramidinehydrochloride	3·15	—[e]	6·18[s]	N	10·57[d] (7·43) (in H_2O)	293 (3·39) (methiodide or hydriodide)		
nor-C-Curarine-I (*cf.* I)	—	6·05[s]	6·25[s]	C	6·26 (EtOH)[b] 8·5 (H_2O)[b]	302 (3·75) (in alcoholic KOH)[c]	—0·01	—12
nor-C-Curarine-I hydrochloride	2·93	6·04[s]	6·23[s]	C	—	290 (3·68) 257 (3·87)		
Vasicine (peganine) IV	—	6·10[s]	6·23[s]	C	—	304 (3·66)	—0·20	—19
Vasicine hydrochloride	3·2	5·90[s]	6·15[m]	N	—	285 (3·51)		

[a] Private communication from Dr. S. J. ANGYAL, *cf.* S. J. ANGYAL, Australian J. Scient. Res. [A] *5*, 377 (1952). I am greatly indebted to Dr. ANGYAL for this communication and for a stimulating discussion. [b] P. KARRER and H. SCHMID, Helv. chim. Acta *29*, 1558 (1946). [c] H. SCHMID, A. EBNÖTHER, and P. KARRER, Helv. chim. Acta *33*, 1487 (1950). [d] These pK values are of limited value, since chemical changes (double bond tautomerism or hydrolysis) seem to occur during the titration. [e] Another indolenine of this type, 3-hydroperoxy-3-methyl-2-phenyl-(or 2-*p*-methoxyphenyl)-indolenine likewise lacks absorption in this region: B. WITKOP, J. B. PATRICK, and H. M. KISSMAN, Ber. dtsch. chem. Ges. *85*, 949 (1952). [f] *Cf.* B. WITKOP, Bull. Soc. Chim. France *1954*, 423.

immonium bands (Table II) but not the hydrochlorides of α-, β-, γ-aminopyridine or of α-aminoindolenine. Alkaloidal hydrochlorides can be assayed by this method (Table IV).

The hydrochlorides of the alkaloids listed in Table III do not show immonium bands. If β-hydroxyquebramidine and *nor*-C-cuarine-I hydrochlorides be accepted as indolenines, as a number of chemical and spectrophotometric indications seem to suggest[1], the absence of

[1] *Cf.* B. WITKOP and J. B. PATRICK, J. Amer. Chem. Soc. *75*, 4474 (1953); Angew. Chem. *65*, 467 (1953).

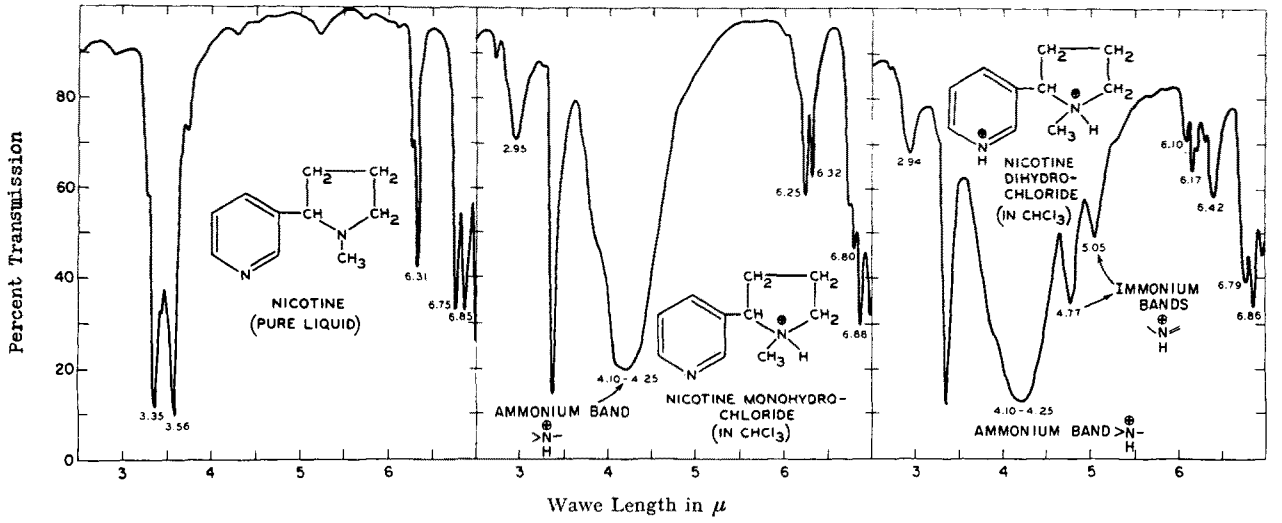


Fig. 1.—The effect of stepwise salt formation on the infrared spectrum of an alkaloid with a saturated and an unsaturated tertiary nitrogen function.

Table IV

Assay of Variouy Hydrochlorides for the Presence of "Immonium Bands"

Compound (measured in C = Chloroform, or N = Nujol)	Immonium Bands
Nicotine monohydrochloride (Fig. 1 (C)	–
Nicotine dihydrochloride (Fig. 1) (C) . .	$4{\cdot}77^{m}$; $5{\cdot}05^{m}$
Peganine (vasicine) hydrochloride (N) .	–
Pegadiene hydrochloride (C)	–
4-Quinazolone hydrochloride (N)[a] . . .	$4{\cdot}92^{vw}$; $5{\cdot}30^{vw}$
Febrifugine dihydrochloride (N)[a] . . .	$4{\cdot}86^{w}$; $5{\cdot}14^{m}$; $5{\cdot}43^{m}$

[a] It was expected that the weakly basic character of the amide nitrogen in position 3 would restore the independence of the cation

$$\underset{1}{\overset{\oplus}{N}}H=\underset{2}{CH}-\underset{3}{NH}-\underset{4}{CO}$$

by suppressing the contribution

$$\underset{1}{NH}-\underset{2}{CH}=\overset{\oplus}{\underset{3}{N}}H-\underset{4}{CO}.$$

Such an effect is operative and leads to the appearance of immonium bands, very weak in quinazolone hydrochloride, more distinct in the dihydrochloride of the quinazolone alkaloid febrifugine (an alkaloid from Hydrangea, *cf.* B. R. Baker, *et al.*, J. Org. Chem. *17*, 132 [1951]; I am greatly indebted to Dr. Baker for samples), where there must be bonded or non-bonded interaction between the three oxygen functions: desoxyfebrifugine dihydrochloride, where no such interaction is possible, lacks immonium bands.

immonium bands is unexpected and might be due to the direct or, less likely, vinylogous attachment of N^{b} to the $>C=N^{a}-$ group, in other words, an α-aminoindolenine type of structure (I). The substantiation of this concept is awaiting further chemical experiments. A full report on further uses of the immonium bands for diagnostic purposes (positional effect of alkyl substituents in pyridines and quinolines, shift to longer wave length in aromatic N-oxide hydrochlorides, ketimine-enamine tautomerism, etc.) will appear in the near future[1].

B. Witkop

National Institutes of Health, Washington 14, D.C., February 8, 1954.

Zusammenfassung

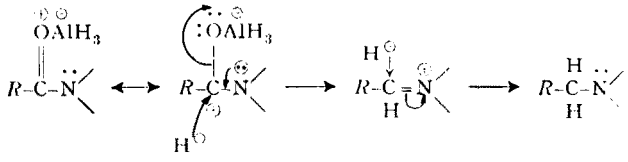
Bei der Salzbildung offener oder zyklischer Schiffscher Basen, eingeschlossen aromatische Heterozyklen, wie Pyridin, Chinolin, Benzoxazin, Indolenin usw., können die im UV.- und UR.-Spektrum auftretenden batho- oder hypsochromen Verschiebungen sowie das Auftreten oder Ausbleiben der für das Kation $>C=\overset{\oplus}{N}H-$ charakteristischen «Immonium-Banden» bei 4,5–5,5 μ zur Erkennung der Natur und der Position von Aminosubstituenten benutzt werden.

[1] The method has been utilized to advantage in the meantime: the tobacco alkaloid myosmine was found to be a Δ_1-pyrroline derivative as the free base as well as in the form of the mono- and dihydrochloride, B. Witkop, J. Amer. Chem. Soc. *76*, in press. Likewise, new structures had to be postulated for tetrahydropyridine and γ-coniceine (added in proof).

The Reduction of Amides with Lithium Aluminium Hydride[1]

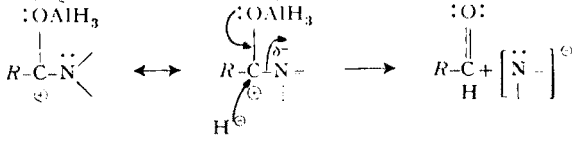
The reduction of carboxylic acid amides with lithium aluminium hydride generally yields the corresponding amine with the same number of carbon atoms[2]. However, in some cases, amides are cleaved to alcohols or aldehydes and amines[3].

The following mechanism has been proposed[4] for the reduction of amides and vinylogs of amides to yield the corresponding oxygen-free compounds:



The reactive species here is the aluminohydride ion $AlH_4^{\ominus}$ which, according to Paddock[5], exists in ether solution in equilibrium with aluminium hydride and the hydride ion. The attack of the hydride ion and the tendency of the nitrogen atom to donate its electron pair to the electron deficient carbon results in a cleavage of the carbon-oxygen bond to yield the amine, with a total consumption of one-half mole of lithium aluminium hydride.

When the electron-donating tendency of the nitrogen atom is decreased by stabilization, the adjacent carbon assumes a more positive character. The attack by the hydride ion alone or in conjunction with a shift of electrons from the oxygen atom results in a cleavage of the carbon-nitrogen bond to yield the carbonyl derivative and the starting amine.



The isolation of aldehydes generally requires the addition of one-quarter mole of lithium-aluminium hydride to a solution of amide. These conditions are fulfilled by the indicated mechanism. The aldehyde therefore does not arise as a result of the hydrolysis of an intermediate complex, as has been postulated[6], but is present in the reaction mixture prior to hydrolysis. The use of excess complex hydride causes a reduction of the aldehyde to the corresponding alcohol.

The mechanism has been experimentally verified. The benzamide of benzotriazole was treated with one-quarter mole of lithium aluminium hydride in ether, with inverse

[1] Contribution No. 13 from the Yerkes Research Laboratory.

[2] R. F. Nystrom and W. G. Brown, J. Amer. Chem. Soc. *70*, 3738 (1948). – A. Uffer and E. Schlittler, Helv. chim. Acta *31*, 1397 (1948).

[3] K. Banholzer, T. W. Campbell, and H. Schmid, J. Amer. Chem. Soc. *35*, 1577 (1952). – G. Wittig and P. Hornberger, Ann. Chem. *577*, 11 (1952). – N. G. Gaylord, J. Amer. Chem. Soc. *76*, 285 (1954). – V. M. Mićović and M. L. Mihailović, J. Org. Chem. *18*, 1190 (1953). – M. Mousseron, R. Jacquier, M. Mousseron-Canet, and R. Zagdoun, Bull. Soc. chim. France [5] *19*, 1042 (1952).

[4] N. G. Gaylord, Exper. *10*, 166 (1954).

[5] N. L. Paddock, Nature *167*, 1070 (1951).

[6] V. M. Mićović and M. L. Mihailović, J. Org. Chem. *18*, 1190 (1953). – M. Mousseron, R. Jacquier, M. Mousseron-Canet, and R. Zagdoun, Bull. Soc. chim. France [5] *19*, 1042 (1952).