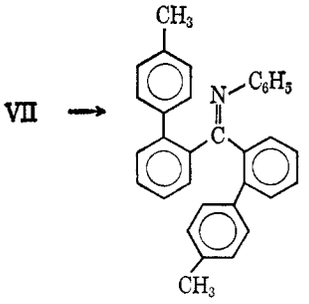

VIII

A side reaction in the preparation of VII was the further conjugate addition of *p*-tolyl Grignard reagent to VII, providing what appears to be 2,2′-di(*p*-tolyl)-benzophenone anil (VIII), on the basis of elemental analysis and nmr spectroscopy. The methyl groups in VIII are magnetically nonequivalent ($\Delta\nu$ = 4.3 Hz at 60 HMz) at room temperature, but the signals coalesce upon heating the sample, since facile *syn–anti* interconversion produces identical environments for both methyl groups. Cooling the sample to room temperature produced the original pair of methyl singlets. The coalescence temperature is 53°, at which k is calculated[6] to be 9.6 sec^{-1}, corresponding to $\Delta F^*_{326°} \sim 18$ kcal/mole. The inversion rate for VIII is similar in magnitude to recent data of Curtin, *et al.*,[7] on *p,p′*-dimethoxybenzophenone anil ($k_{62°}$ = 10.9 sec^{-1}).

When V was heated in PPA,[2] a mixture of 2-methyl-9-fluorenone and 8-methyl-6-phenylphenanthridine (III) was obtained in a ratio of *ca.* 8:1. Since III has mp 90° and III picrate has mp 280°, whereas 3-methyl-6-phenylphenanthridine (IV) melts at 119° and IV picrate has mp 245°,[8] it was not difficult to show that III was the correct structure for the phenanthridine product. Thus, the pathway to these products is that in which the oxime polyphosphates[3,4] rearrange with simultaneous aryl migration to give iminocarbonium ions (mechanism A) as postulated by Smith.[2] There is no evidence that iminium ions are formed from V. Since Smith's *o*-phenylbenzophenone oxime was a mixture of stereoisomers of unknown composition,[2] as was probably the case with V, which melted over a 10° range, it is not possible to say whether the fluorenone anil–phenanthridine ratios reflect the oxime isomer distribution (assuming stereospecific *trans* migration) or whether oxime isomerization occurs prior to rearrangement. However, the preponderance of fluorenone anils does seem to be consistent with the preferred *anti*-phenyl conformations of *ortho*-substituted benzophenone oximes.[9]

Experimental Section[10]

o-(p-Tolyl)benzophenone Anil (VII).—An ether solution (100 ml) of *p*-tolylmagnesium bromide, prepared as usual from *ca.* 0.06 mole each of *p*-bromotoluene and magnesium was added dropwise to a solution of 4.0 g (14 mmoles) of *o*-methoxybenzophenone anil[5] (VI) in 100 ml of benzene. The nitrogen-flushed reaction mixture was refluxed for 20 hr, cooled, and hydrolyzed with aqueous ammonium chloride solution. The product was extracted into ether, dried, and concentrated to an amorphous residue. Chromatography over alumina, using petroleum ether–benzene (with gradually increasing portions of the latter), afforded initially the expected *o*-(*p*-tolyl)benzophenone anil (VI) in 63% yield, mp 113–4° (from petroleum ether), as pale yellow crystals, ν_{max} 1634 cm^{-1} (>C=N–).

Anal. Calcd for $C_{26}H_{21}N$: C, 89.9; H, 6.1. Found: C, 89.8; H, 6.2.

Further elution yielded 2,2′-di(*p*-tolyl)benzophenone anil (VIII), mp 167–168° (ethanol), whose nmr spectrum showed the expected 21:6 integration ratio of aromatic (6.3–7.2 ppm) to methyl (2.2, 2.3 ppm) proton signals.

Anal. Calcd for $C_{33}H_{27}N$: C, 90.6; H, 6.2; N, 3.2. Found: C, 90.0; H, 6.4; N, 3.6.

o-(p-Tolyl)benzophenone Oxime (V).—A solution of 2.03 g of VII in 16 ml of hydrochloric acid and 100 ml of ethanol was refluxed for 1.5 hr, during which time the bright yellow color faded. Upon cooling and quenching in ice water, a white precipitate (1.48 g, 93%) of the parent ketone, mp 79–80° (ethanol), was obtained. A carbonyl band appeared in the infrared spectrum at 1667 cm^{-1}.

Anal. Calcd for $C_{20}H_{16}O$: C, 88.2; H, 5.9. Found: C, 87.8 H, 5.9.

The oxime (V) was prepared in the usual manner using ethanol pyridine as solvent and a 24-hr reflux period. The oxime of mp 151–161° (and –OH band at 3280 cm^{-1} together with disappearance of >C=O stretching) was used for the PPA reaction. An analytical sample, mp 164.5–165.5°, was obtained upon recrystallization from methanol.

Anal. Calcd for $C_{20}H_{17}NO$: C, 83.6; H, 6.0; N, 4.9. Found: C, 83.7; H, 6.0; N, 5.1.

Beckmann Reaction of V in Polyphosphoric Acid.—A mixture of 1.63 g of oxime V and 45 g of PPA was heated at 125–140° for 15 min, then cooled and poured into 250 g of ice water. The solution was made alkaline with ammonium hydroxide and extracted with benzene. The benzene solution was then extracted with concentrated hydrochloric acid and the latter solution neutralized to give an oil, which was chromatographed on alumina. Elution with 1:1 petroleum ether–benzene gave 0.14 g of 8-methyl-6-phenylphenanthridine, mp 91.5–92° (lit.[8] mp 90°), which formed a picrate having mp 280.5–281.5° (lit.[8] 280°). The remaining benzene solution was dried over magnesium sulfate and evaporated to yield 0.88 g of 2-methylfluorenone, mp 92° (lit.[11] mp 92.5–93.5°), which showed carbonyl absorption at 1721 cm^{-1} (Nujol) and $\lambda_{max}^{CH_3OH}$ 405 mμ (lit.[11] $\lambda_{max}^{i\text{-}PrOH}$ 400 mμ).

Registry No.—V, 13124-60-2; V (parent ketone), 13124-61-3; VII, 13124-62-4; VIII, 13135-42-7.

(6) J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 63.

(7) D. Y. Curtin, E. J. Grubbs, and C. G. McCarty, *J. Am. Chem. Soc.*, **88**, 2775 (1966).

(8) R. H. B. Galt and J. D. Loudon, *J. Chem. Soc.*, 885 (1959).

(9) P. A. Smith and E. P. Antoniades, *Tetrahedron*, **9**, 210 (1960).

(10) Melting points were taken on a Mel-Temp capillary tube apparatus and are uncorrected. Infrared spectra were taken on a Beckman IR-5A spectrometer, using Nujol mulls. Elemental analyses were by Dr. A. Bernhardt, Mülheim, Germany. Nuclear magnetic resonance spectra were obtained on a Varian Associates A-60 spectrometer equipped with a variable-temperature probe and an A-6040 temperature controller. Column chromatography was done using Merck alumina and 30–60° petroleum ether.

(11) G. G. Smith and R. P. Bayer, *Tetrahedron*, **18**, 323 (1962).

The Synthesis of Oximes. II[1]

BRENNIE E. HACKLEY, JR.,

Research Laboratories, Physiology Department, U. S. Army Edgewood Arsenal, Edgewood Arsenal, Maryland,

AND FRANCIS A. DANIHER

Ash Stevens Inc., Detroit, Michigan

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The successful conversion of various 2-chloromethylpyridines to the corresponding 2-pyridine aldoximes by direct reaction with hydroxylamine prompted us to

(1) Part I: F. A. Daniher, B. E. Hackley, Jr., and A. B. Ash, *J. Org. Chem.*, **31**, 2709 (1966).

consider a similar conversion of sulfonate esters of 2-pyridinemethanol to the corresponding 2-pyridine aldoximes.

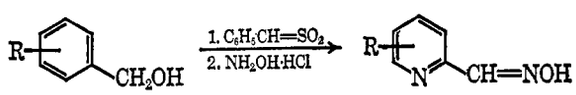
Reaction of 5-ethyl-2-pyridinemethanol with a molar excess of methanesulfonyl chloride in dry tetrahydrofuran containing an equivalent amount of pyridine yielded a crude, impure mesylate as an oil showing three spots on thin layer chromatography. Since the mesylate was unstable, decomposing to a dark red oil in minutes at room temperature, the product was treated directly with a buffered solution of 5 equiv by hydroxylamine hydrochloride in aqueous ethanol on a steam bath for 2 hr.[1] Work-up gave a 31% yield of oxime. The same procedure was applied to 6-methyl-2-pyridinemethanol to afford the oxime in an identical yield of 31%.

As an alternate approach to the preparation of the sulfonate esters, the reaction of phenylsulfene with the carbinol[2] was investigated. Phenylsulfene was generated *in situ* by the reaction of benzylsulfonyl chloride and triethylamine in dry tetrahydrofuran in the presence of 5-ethyl-2-pyridinemethanol. Thin layer chromatographic examination of the reaction product showed one spot with complete disappearance of starting material. The sulfonate ester was treated directly with hydroxylamine hydrochloride as before to give a 45% yield of oxime. The procedure was applied to a series of oximes to give yields of product ranging from 34 to 59%.

The effect of the leaving group was investigated by substitution of *p*-nitrophenylsulfene[3] in the esterification step. Examination of the esterification reaction by tlc indicated complete conversion to the sulfonate ester. Oxime conversion was performed as described above. The results of these studies, summarized in Table I, indicate that there is no significant

TABLE I

CONVERSION OF PYRIDINE METHANOLS TO OXIMES WITH PHENYL- AND *p*-NITROPHENYLSULFENE REAGENTS



R	Yield, %: A[a]	B[b]	Mp, °C
5-CH_3	46	46	157–158.5[c]
6-CH_3	59	58	168–170[d]
5-C_2H_5	45	50	149–150[e]
4-OCH_3	47		183–185[f]
4-$N(CH_3)_2$	34	36	260–261

[a] A, phenylsulfene. [b] B, *p*-nitrophenylsulfene. [c] Reference 4. [d] S. Ginsberg and I. B. Wilson, *J. Am. Chem. Soc.*, **79**, 481 (1957). [e] Reference 1. [f] S. Furakawa, *Yakugaku Zasshi*, **77**, 11 (1957).

difference in yield between the two reagents. On the other hand, *p*-methylphenylsulfene[4] gave somewhat lower yields of oxime. Thus, with 6-methyl-2-pyridinemethanol, a 47% yield of oxime was obtained *vs.* 58% for the other reagents.

The procedure is comparable to the synthesis of substituted 2-pyridine aldoximes *via* the mesyl or tosyl chloride rearrangement of 2-picoline N-oxides as previously reported.[1] In the present instance, the starting 2-pyridinecarbinols may be prepared by the acetic anhydride rearrangement of the same 2-pyridine N-oxides.[5] In general, the over-all yields from the 2-picolines are comparable by the two routes. The present sulfonate route is preferred in the case of the 4-N,N-dimethylamino analog which fails in the sulfonyl chloride rearrangement of the corresponding 2-picoline N-oxide.[6] Further, where the 2-pyridine methanol is available, the present procedure avoids the use of oxidants such as selenium dioxide to obtain the oxime *via* the aldehyde.[7]

The oximation reaction mechanism is doubtless similar to that proposed for the direct conversion of 2-chloromethylpyridines to 2-pyridine aldoximes.[1] In this case a sulfonate anion instead of chloride ion is displaced to form the intermediate hydroxylamine, followed by conversion to aldimine and subsequent displacement of ammonia by a second molecule of hydroxylamine.

Experimental Section

Preparation of 6-Methyl-2-pyridine Aldoxime.—Methanesulfonyl chloride (2.3 g, 0.02 mole) was added dropwise to a stirred solution of 1.23 g (0.01 mole) or 6-methyl-2-pyridinemethanol and 0.75 ml of pyridine in 15 ml of dry tetrahydrofuran at room temperature. The solution was stirred for 18 hr. After solvent removal, the resulting oil was dissolved in saturated sodium bicarbonate solution and the solution was extracted with chloroform. The chloroform extract was dried over sodium carbonate and filtered and the solvent was removed. Thin layer chromatographic analysis of the oil showed four spots (benzene–methanol 4:1), two major and two minor, none of which corresponded to starting materials. This oil was dissolved in a solution of 20 ml of 50% aqueous pH 7 and heated on a steam bath for 2 hr. The solutions was cooled to yield 430 mg (31%), of oxime, mp 168–170°. The material was identified by comparison of its tlc behavior and infrared spectrum with those of an authentic sample.

Preparation of 6-Methyl-2-pyridine Aldoxime *via* Phenylsulfene.—A solution of 2.4 g (0.0125 mole) of benzylsulfonyl chloride in 10 ml of dry tetrahydrofuran was added dropwise to a stirred solution of 1.23 g (0.01 mole) of 6-methyl-2-pyridinemethanol and 1.25 g of triethylamine in 15 ml of dry tetrahydrofuran maintained at 0° by an ice bath. After addition was complete, the solution was stirred at 0° for 10 min. The solvent was removed at aspirator pressure at room temperature to give a semisolid residue. The residue was treated with hydroxylamine hydrochloride as before to produce 800 mg (59%) of product, mp 168–170°.

The same procedure employing *p*-nitrobenzylsulfonyl chloride gave a 58% yield of product, mp 168–170°.

4-Dimethylamino-2-pyridinemethanol.—A solution of 1.60 g of 4-chloro-2-pyridinemethanol[7] in 16 ml of 40% aqueous dimethylamine was heated in a sealed tube at 125° for 19 hr. The tube was cooled and opened, and 3.0 g of potassium carbonate was added to the reaction mixture. The solvent was gradually removed under reduced pressure until an oil started to separate. The oil was extracted with chloroform. The extracts were dried and the solvent was removed to yield 1.2 g (71%) of product, mp 106–109°. Recrystallization from acetone afforded an analytical sample, mp 110–112°.

Anal. Calcd for $C_8H_{12}N_2O$: C, 63.06; H, 7.94; N, 18.41. Found: C, 62.97; H, 8.19; N, 18.50.

Conversion of 4-dimethylamino-2-pyridinemethanol to the oxime by the above procedure gave a 34% yield of product, mp 260–261° dec.

Anal. Calcd for $C_8H_{11}N_3O$: C, 58.10; H, 6.71; N, 25.44. Found: C, 58.11; H, 6.91; N, 25.40.

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(6) Unpublished results, these laboratories.