(19%) of colorless prisms, m.p. 129.5–132°. Two additional recrystallizations from isopropyl alcohol gave the analytical sample, m.p. 134.5–135.5°.

The ultraviolet spectrum exhibits λ_{max} 271 mμ (ε 41,000) in 0.1 *N* methanolic sodium methoxide.

Anal. Calcd. for $C_{13}H_{18}N_2O_2 \cdot HCl$: C, 57.67; H, 7.02; N, 10.35; Cl, 13.12. Found: C, 57.64; H, 7.18; N, 10.15; Cl, 13.30.

N-Phenethylamidinoacetamide Hydrochloride (XIII).—A solution of 1.4 g. (5.0 mmoles) of ethyl N-phenethylamidinoacetate hydrochloride in 75 ml. of saturated ammoniacal ethanol was stirred at room temperature for 4 days and then concentrated under reduced pressure to a viscous oil, which slowly crystallized. Recrystallization from isopropyl alcohol afforded 0.6 g. (50%) of colorless needles, m.p. 168.5–169.5°. An additional recrystallization gave the analytical sample, m.p. 169.5–170.5°.

The ultraviolet spectrum exhibits λ_{max} 276 mμ (ε 10,000) in 0.1 *N* methanolic sodium methoxide.

Anal. Calcd. for $C_{11}H_{15}N_3O \cdot HCl$: C, 54.66; H, 6.63; N, 17.39; Cl, 14.70. Found: C, 54.57; H, 6.73; N, 17.38; Cl, 14.57.

N,N″-Diphenethylmalonamidine Dihydrochloride.—To a solution of 0.25 g. (0.011 g.-atom) of sodium in 15 ml. of anhydrous ethanol was added 2.5 g. (0.011 mole) of diethylmalonimidate dihydrochloride[2] and 1.3 g. (0.011 mole) of phenethylamine. The mixture was heated under reflux for 2.5 hr. and filtered. The filtrate was acidified with concentrated hydrochloric acid and concentrated under reduced pressure to an oily yellow solid. Recrystallization from water afforded 1.0 g. (48%) of colorless plates, m.p. 311–313° dec.

Anal. Calcd. for $C_{19}H_{24}N_4 \cdot 2HCl$: C, 59.84; H, 6.82; N, 14.70; Cl, 18.64. Found: C, 59.70; H, 6.93; N, 14.43; Cl, 18.47.

N,N′,N″,N‴-Tetraphenethylmalonamidine Dihydrochloride and Hydrochloride.—A solution of 4.6 g. (0.02 mole) of diethylmalonimidate dihydrochloride,[2] 12.0 g. (0.099 mole) of phenethylamine, and 0.099 mole of ammonia in 300 ml. of anhydrous ethanol was stirred at room temperature for 5 days. The solution was concentrated under reduced pressure to about 75 ml., and the white precipitate (5.3 g.) which separated was collected. This solid was partially dissolved in hot ethanol. The insoluble colorless crystals, m.p. 308–311° dec., amounted to 3.3 g. (43%). The melting point was not depressed upon admixture with authentic N,N″-diphenethylmalonamidine dihydrochloride. The ethanol-soluble fraction was recovered by concentration of the solution to dryness. Recrystallization of the solid residue from acetone, followed by recrystallization from isopropyl alcohol, afforded 0.05 g. (0.4%) of N,N′,N″,N‴-tetraphenethylmalonamidine dihydrochloride as colorless needles, m.p. 193–194°.

Anal. Calcd. for $C_{35}H_{40}N_4 \cdot 2HCl$: C, 71.31; H, 7.13; N, 9.51; Cl, 12.05. Found: C, 71.16; H, 7.31; N, 9.38; Cl, 12.12.

Concentration of the remainder of the original reaction solution under reduced pressure left oily crystals. Two recrystallizations from isopropyl alcohol afforded 1.6 g. (14%) of N,N′,N″,N‴-tetraphenethylmalonamidine hydrochloride as long colorless prisms, m.p. 155–156°. Two more recrystallizations gave the analytical sample, m.p. 157.5–158°.

Anal. Calcd. for $C_{35}H_{40}N_4 \cdot HCl$: C, 76.02; H, 7.42; N, 10.14; Cl, 6.43. Found: C, 75.71; H, 7.53; N, 10.15; Cl, 6.49.

The ultraviolet spectrum of N,N′,N″,N‴-tetraphenethylmalonamidine hydrochloride exhibits λ_{max}^{MeOH} 308 mμ (ε 21,200).

The monohydrochloride was converted to the dihydrochloride with ethanolic hydrogen chloride.

Phenethylbiguanide.—A solution of 2.30 g. (0.10 g.-atom) of sodium in 500 ml. of anhydrous ethanol was prepared, and 24.15 g. (0.10 mole) of phenethylbiguanide hydrochloride was added at room temperature with stirring. After 1 hr., the mixture was filtered, and the filtrate was concentrated to a colorless oil which crystallized on standing. Two recrystallizations from ethanol and three from acetonitrile afforded colorless prisms, m.p. 94–95°.

Anal. Calcd. for $C_{10}H_{15}N_5$: C, 58.51; H, 7.37; N, 34.12. Found: C, 58.21; H, 7.22; N, 34.07.

The ultraviolet spectrum exhibits λ_{max} 236 mμ (ε 17,100) in 10^{-5} *N* methanolic hydrochloric acid, 233 (ε 1410) in water, 235 μ (sh) in 0.04 *N* methanolic sodium methoxide, 232 (sh) in acetonitrile or dioxane.

Acknowledgment.—We wish to thank Mr. L. M. Brancone and associates for the analytical data and Mr. W. Fulmor and associates for ultraviolet spectra

Synthesis of Azoxy Compounds from Nitrosohydroxylamine Tosylates[1]

TRAVIS E. STEVENS

The Gorgas Laboratory, Rohm and Haas Company, Redstone Arsenal Research Division, Huntsville, Alabama

Received June 3, 1963

A convenient synthesis of azoxy compounds from organonitrosohydroxylamine tosylates, R—N(→O)=N—OTs, and Grignard reagents is outlined. Displacement on sulfur, with the expulsion of nitrosohydroxylamine anion and the formation of sulfones, predominated when the nitrosohydroxylamine tosylates were exposed to nucleophiles such as phenyllithium, alkoxides, and phenoxides. The azoxy ether structure, R—N(→O)=N—OR′, is assigned to the stable alkylation products of organonitrosohydroxylamines.

Unsymmetrical azoxy compounds usually are obtained by oxidation of an unsymmetrical azo compound,[2,3] by condensation of a nitroso compound and an hydroxylamine[4,5] or by selective substitution on an aromatic azoxy compound.[5,6] The first two methods often give a mixture of isomers.

More selective methods, such as the oxidation of indazole oxides[7] or the reaction of Grignard reagents, and the stable alkylation products of organonitrosohydroxylamines[8] also are reported.

An attractive approach to a general synthesis of azoxy compounds would be one where the R—N(→O)=N— group possessed a substituent capable of easy displace-

(1) This research was supported by the Advanced Research Projects Agency under Army Ordnance Contract No. DA-01-021 ORD-11909.

(2) See C.-S. Hahn and H. H. Jaffé [*J. Am. Chem. Soc.*, **84**, 949 (1962)] for references and a table of properties of substituted azoxybenzenes.

(3) Oxidation of hydrazones has produced many azoxy compounds: B. T. Gillis and K. F. Schimmel, *J. Org. Chem.*, **27**, 413 (1962).

(4) Y. Ogata, M. Tsuchida, and Y. Takagi, *J. Am. Chem. Soc.*, **79**, 3397 (1957).

(5) W. J. Hickinbottom, "Chemistry of Carbon Compounds," Vol. IIIA, E. H. Rodd, Elsevier Publishing Co., New York, N. Y., 1954, p. 314.

(6) J. J. Courtney, L. E. Geipel, and R. L. Shriner, *Proc. Iowa Acad. Sci.*, **62**, 264 (1955).

(7) L. C. Behr, *J. Am. Chem. Soc.*, **76**, 3672 (1954); L. C. Behr, E. G. Alley, and O. Levand, *J. Org. Chem.*, **27**, 65 (1962).

(8) M. V. George, R. W. Kierstead, and G. F. Wright, *Can. J. Chem.*, **37**, 679 (1959).

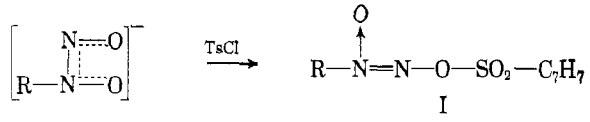
TABLE I

N-SUBSTITUTED N′-TOSYLOXYDIIMIDE N-OXIDES, R—N(→O)=N—OTs

R	M.p., °C.	Analysis, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
Phenyl	136[a]	53.41	4.14	9.59	53.66	4.43	9.44
p-Chlorophenyl	144[a]	47.78	3.39	8.57	47.25	3.24	8.67
p-Bromophenyl	150[a]	42.06	2.99	7.55	42.09	3.00	7.65
p-Tolyl	126[a]	54.89	4.61	9.15	54.95	4.62	8.98
Benzyl	92	54.89	4.61	9.15	54.70	4.74	8.94
Butyl	Oil	48.51	5.92	10.29	48.71	5.98	12.01
Methyl	86	41.73	4.38	12.17	41.76	4.35	11.92

[a] The melting of these samples usually took place with vigorous decomposition, and the temperature of this decomposition was dependent on the rate of heating.

ment. In order to test this preparation of azoxy compounds and to obtain more information on the alkylation products of nitrosohydroxylamines,[8] several *p*-toluenesulfonyl derivatives of organonitrosohydroxylamines were prepared. These tosylates, which are assigned the N-substituted N′-tosyloxydiimide N-oxide[9,10] structure (I) on the basis of the experiments to be outlined, are listed in Table I.



I

The aromatic nitrosohydroxylamine tosylates were prepared *via* tosyl chloride in aqueous bicarbonate solution, in acetone–aqueous sodium hydroxide mixtures, or in benzene solution with a preformed salt of the nitrosohydroxylamine; the same product was obtained in each case.

To prepare the tosylates of methyl and butyl nitrosohydroxylamine, the appropriate Grignard reagents were allowed to react with nitric oxide,[11] and the basic aqueous extract of this reaction mixture, containing the alkylnitrosohydroxylamine anion, was treated with tosyl chloride in the usual fashion. Details are given in the Experimental section.

However one views the multifunctional azoxy sulfonates (I), several potentially reactive sites are present. It was of some interest, then, to observe the center of nucleophilic attack, nitrogen or sulfur, in this ambient electrophile.[12]

Conversion of the aromatic nitrosohydroxylamine tosylates to azoxy compounds by means of Grignard reagents took place readily; there was no indication that sulfones, resulting from attack on sulfur and expulsion of the nitrosohydroxylamine anion, were formed. Tables II and III summarize the results of these reactions.

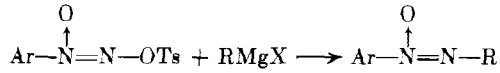


TABLE II

AROMATIC AZOXY COMPOUNDS, Ar—N(→O)=N—Ar′

Ar	Ar′	M.p., °C. Observed	M.p., °C. Reported	Yield, %
Phenyl	Phenyl	36	36[a]	71[b]
p-Chlorophenyl	Phenyl	82	62[c]	69
p-Bromophenyl	Phenyl	95	94[d]	69
Phenyl	*p*-Tolyl	50	50[a]	73
p-Chlorophenyl	*p*-Tolyl	109.5	*e*	83
p-Bromophenyl	*p*-Tolyl	125	122[d]	83
Phenyl	*p*-Chlorophenyl	68	68[c]	39
p-Tolyl	*p*-Chlorophenyl	107	*g*	57[h]
p-Bromophenyl	*p*-Chlorophenyl	160	*i*	46
Phenyl	*p*-Anisyl	72	68[f]	30
p-Chlorophenyl	*p*-Anisyl	145	*j*	51

[a] See ref. 8. [b] Azoxybenzene was obtained in 70% yield from the phenyl Grignard reagent–N-phenyl-N′-*p*-bromophenylsulfonoxydiimide N-oxide reaction. [c] See ref. 14. [d] See ref. 7. [e] *Anal.* Calcd. for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49; N, 11.36. Found: C, 63.65; H, 4.51; N, 11.28. [f] See ref. 2. [g] *Anal.* Calcd. for $C_{13}H_{11}ClN_2O$: C, 63.29; H, 4.49; N, 11.36. Found: C, 63.24; H, 4.60; N, 11.09. [h] Reaction conducted in methylene chloride solution. [i] *Anal.* Calcd. for $C_{12}H_8BrClN_2O$: N, 8.99. Found: N, 9.21. [j] *Anal.* Calcd. for $C_{13}H_{11}ClN_2O_2$: C, 59.43; H, 4.22; N, 10.67. Found: C, 59.65; H, 4.44; N, 10.83.

The reactions using aryl Grignard reagents were conducted in tetrahydrofuran solution for 2 to 5 hr. at 50–60°, but those involving alkyl Grignards were much cleaner when conducted in methylene chloride solution[13] at ambient temperature with a reaction time of 16 to 20 hr.

The azoxybenzenes were isolated by chromatography on silica gel, and yield figures given were based on the weight of the azoxy benzene fraction obtained from the column. One recrystallization from hexane produced

(9) The designation diimide oxide for azoxy compounds, as suggested by G. F. Wright,[8] appears to be a straightforward method of nomenclature for the azoxy derivatives to be discussed here.

(10) In assigning structure I to the nitrosohydroxylamine tosylates, structure ii was ruled out, since attack of the Grignard reagent on the —N=O function and displacement of the tosyloxy function would lead to azoxy

compounds isomeric with those actually obtained. A Grignard reagent and iii might be expected to produce a diimide dioxide (displacement of the sulfinate ion) or other products; in any event structure I explains the formation of azoxy compounds much more readily.

(11) M. H. Abraham, J. H. N. Garland, J. A. Hill, and L. F. Larkworthy, *Chem. Ind.* (London), 1615 (1962).

(12) Azoxysulfones, Ar—N(→O)=N—SO₂Ar′, are well-known compounds: W. V. Farrar and J. Masson Gulland, *J. Chem. Soc.*, 368 (1944). Diaryl azoxy compounds could not be obtained from these sulfones and aryl Grignard reagents under our experimental conditions.

(13) H. G. Viehe and M. Reinstein, *Ber.*, **95**, 2557 (1962).

TABLE III

AROMATIC AZOXYALKANES, Ar—$\overset{\overset{O}{\uparrow}}{N}$=N—R

Ar	R	$n^{20}D$ (m.p., °C.)	Yield, %	Analysis, % Calcd. C	Calcd. H	Calcd. N	Found[a] C	Found[a] H	Found[a] N
Phenyl	*n*-Butyl	1.5280	62	67.39	7.92	15.72	67.47	7.97	16.08[b]
p-Chlorophenyl	*n*-Butyl		56	56.77	6.21	13.17	56.46	6.16	13.68[b]
p-Chlorophenyl	Methyl	(40)	30	49.28	4.14	16.42	49.76	4.13	15.91[b]
Phenyl	Ethyl	1.5434	44	63.98	6.71	18.66	63.92	6.49	19.60[b]
Phenyl	Isopropyl	1.5296	30	65.82	7.37	17.06	65.46	7.47	17.45[c]
p-Chlorophenyl	Isopropyl	1.5438	30	54.41	5.58	14.10	54.08	5.65	14.35[d]

[a] Nitrogen analyses by the Dumas method often gave high results with these compounds, but the Kjeldahl method gave acceptable results. [b] Dumas value. [c] Kjeldahl value, Dumas result was 17.94%. [d] Kjeldahl value, Dumas result was 16.05%.

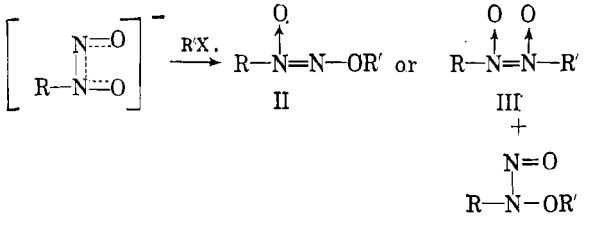
the melting point listed in the tables,[14] and the recovery of the azoxybenzene from the crude fraction usually was greater than 90%. The liquid azoxy compounds were purified by chromatography.

A small amount of the azobenzene corresponding to the azoxybenzene also was formed in these reactions. It undoubtedly arose from reduction of the azoxybenzene by the Grignard reagent.

Sulfone formation did occur when the preparation of the azoxy compounds was attempted from the aromatic tosylates and phenyllithium; only a small amount of diaryl azoxy compound was formed.

Unfortunately, alkazoxyalkanes could not be obtained from the alkylnitrosohydroxylamine tosylates. When these tosylates were treated with 2 equiv. of a Grignard reagent,[15] sulfone formation occurred and no sign of the azoxy compound could be found. No definite products could be obtained from reactions using aryllithium reagents.

In an earlier study of the alkylation of organonitrosohydroxylamines, structure III, rather than II, was preferred for the stable, α-alkylation products of nitrosohydroxylamines.[8] Another isomer, designated β, was

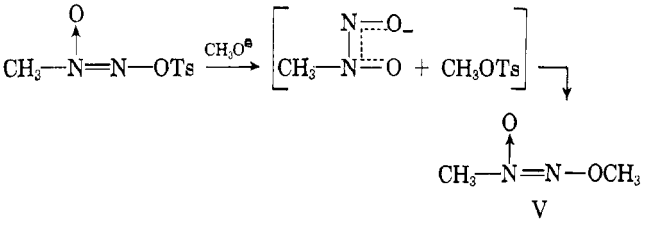


formed in these alkylations and was shown to have structure IV. As mentioned earlier, unsymmetrical azoxy compounds could be obtained from these α-alkylation products and Grignard reagents.[8] In view of the structure assigned to the nitrosohydroxylamine tosylates and of a recent n.m.r. study on azoxy compounds,[16] the α-alkylation products now are assigned the azoxy ether structure (II).[17]

Assignment of structure II to the α-alkylation products of nitrosohydroxylamines implied that the α-methylation products of organonitrosohydroxylamines should be available from the nitrosohydroxylamine tosylates (I) and methoxide ion presuming, of course, that displacement on nitrogen would occur.

Although both phenyl- and *p*-chlorophenylnitrosohydroxylamine tosylate and sodium methoxide in refluxing methanol indeed did produce the α-methylation products reported earlier,[8] all indications were that these methylated nitrosohydroxylamines arose from the interaction of the nitrosohydroxylamine anion and the methyl tosylate initially formed by displacement on sulfur. Not only was methyl tosylate isolated in high yield (79%) when the methoxide ion–phenylnitrohydroxylamine tosylate reaction was quenched early, but also ethoxide, phenoxide, and *p*-nitrophenoxide anions were observed to attack the nitrosohydroxylamine tosylates exclusively on sulfur.

However, the dimethylnitrosohydroxylamine obtained from sodium methoxide and methylnitrosohydroxylamine tosylate appeared to be N-methyl-N′-methoxydiimide N-oxide (V); the properties of this



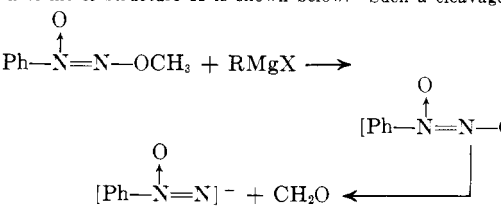
product were vastly different from those of dimeric nitrosomethane (III, R = R′ = CH_3).[18]

(14) A melting point of 62° is reported for 4-chloroazoxybenzene[6]; this material proved to be (infrared spectra, mixture melting points) a 1:1 mixture of 4- and 4′-chloroazoxybenzene. The author is indebted to Professor R. L. Shriner for supplying his samples of these azoxy compounds.

(15) The active hydrogen available to the organometallic reagents probably account for these results. However, the alkyl tosylates and 1 equiv. of the phenyl Grignard reagent gave tosyl bromide (displacement on sulfur by bromide ion) and phenyl tosylate (oxidation–reduction reaction). The details are outlined in the Experimental section.

(16) The n.m.r. evidence in favor of structure II was recently published: J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963).

(17) Almost overwhelming evidence [see B. G. Bownlock and W. Lüttke, *Quart. Rev.* (London), **12**, 321 (1958)] requires that structure III be reserved for nitroso dimers. The main reason structure III was preferred over II for the α-methylation product of phenylnitrosohydroxylamine (R = phenyl, R′ = methyl) was that the methylated product liberated methane when treated with a methyl halide Grignard reagent.[8] One explanation of this in terms of structure II is shown below. Such a cleavage is not without

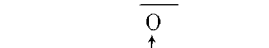
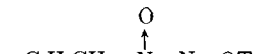
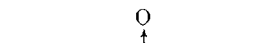


analogy; azoxy sulfones readily cleave in basic solution to give sulfonic acid and diazotate ion.[11]

(18) T. Emery and J. B. Neilands, *J. Am. Chem. Soc.*, **82**, 4903 (1960). The n.m.r. spectrum (Table IV) of this methyl azoxy methoxyl compound exhibits two peaks; *cis* and *trans* dimeric nitrosomethane each have only one n.m.r. peak at τ-values different from those of V.[18]

TABLE IV

N.M.R. SPECTRA OF AZOXY COMPOUNDS

Compound	Chemical shift (τ)[a]
	6.38[b]
	6.60
	6.22[c]
	6.03
	4.82
	5.95[b]
	6.06[d]
	6.07, 6.20[e]

[a] The spectra were measured on 10% solutions in carbon tetrachloride containing tetramethylsilane on a Varian Associates A-60 spectrometer. [b] Triplet. [c] Quadruplet, measurement reported is of the center. [d] Triplet, but integrated intensities confirmed that the indicated methyl and methylene groups absorbed at the same place. [e] Two single peaks, assignment uncertain.

Table IV summarizes some of the n.m.r. spectral data on the compounds prepared in this work. A recent publication[16] discussed in detail the n.m.r. spectra and structure of aliphatic azoxy compounds.

Experimental[19]

Preparation of Phenylnitrosohydroxylamine Tosylate.—A solution of 16 g. (0.10 mole) of cupferron (ammonium salt of N-phenyl-N-nitrosohydroxylamine, from Eastman Kodak) in 200 ml. of 10% aqueous sodium bicarbonate was stirred at ambient temperature while 20 g. (0.1 mole) of tosyl chloride was added in one portion; there was no noticeable exotherm of the reaction mixture. After 2 hr. an additional 2 g. of tosyl chloride was added. The mixture was stirred overnight, and then extracted with methylene chloride. The dark residue obtained by evaporation of the methylene chloride was stirred with 30 ml. of methanol, filtered, and the solid thus obtained was recrystallized from chloroform–hexane. A total of 19 g. of N-phenyl-N′-tosyloxydiimide N-oxide was obtained, m.p. 136–137° dec.

Preparation of Methylnitrosohydroxylamine Tosylate.—A mixture of 450 ml. of ether and 50 ml. of an ether solution of the methyl Grignard reagent (Arapahoe, about 3 *M*) was stirred at 20° while nitric oxide, diluted with nitrogen, was passed through the solution for 40 min. The reaction mixture was flushed with nitrogen, cooled to 5°, and 100 ml. of 2 *N* aqueous hydrochloric acid was added. The aqueous layer was separated, and the ether was washed with 130 ml. of 8% sodium hydroxide solution in three portions. All aqueous washes were combined, 18 g. of *p*-toluenesulfonyl chloride was added, and the mixture was stirred overnight. It then was acidified and extracted with methylene chloride. The residue obtained on evaporation of the methylene chloride was recrystallized from chloroform–hexane. A total of 9.05 g. of N-methyl-N′-tosyloxydiimide N-oxide was obtained, m.p. 86–88°.

Preparation of N-*p*-Chlorophenyl-N′-tosyloxydiimide N-Oxide.—N-*p*-Chlorophenylhydroxylamine (25 g.) was prepared and nitrosated according to the procedure of Wright.[8] The crude N-nitrosohydroxylamine thus obtained was dissolved in 220 ml. of acetone, and 35 g. of tosyl chloride was added in one portion. The solution was stirred in an ice bath while 90 ml. of 2.24 *N* aqueous sodium hydroxide was added dropwise. Stirring was continued for 15 min., then the ice bath was removed, 50 ml. of water was added, and stirring was continued for 30 min. After the addition of 125 ml. of water, the solution was filtered, and the filter cake was washed with a little methanol. The solid was recrystallized twice from chloroform–hexane to give the desired tosylate (18.2 g.), m.p. 144–145° dec.

Preparation of N-*p*-Tolyl-N′-tosyloxydiimide N-Oxide.—A solution of 52 g. of *p*-tolylhydroxylamine in 300 ml. of ether was cooled to 0°, and gaseous ammonia was passed into the solution at a rapid rate for 15 min. The ammonia flow was adjusted to a slow rate, and 46 ml. of butyl nitrite was added dropwise over a 20-min. period. The temperature of the mixture was not allowed to exceed 5°. After an additional 15 min. of stirring, the solution was filtered, and the precipitate was washed well with ether. The 30.5 g. of the ammonium salt of N-*p*-tolyl-N-nitrosohydroxylamine thus obtained was dissolved in 450 ml. of 10% aqueous sodium bicarbonate. The solution was stirred at ambient temperature while 35 g. of tosyl chloride was added over 1 hr. After stirring overnight the solution was filtered. The precipitate was recrystallized from ethanol to give the tosyloxydiimide, 30.5 g., m.p. 126° dec.

Reaction of *p*-Tolylmagnesium Bromide and N-Phenyl-N′-tosyloxydiimide N-Oxide.—A solution of 2.20 g. (7.5 mmoles) of the tosyloxydiimide N-oxide in 40 ml. of tetrahydrofuran was stirred at ambient temperature while 9 ml. of 1.2 *M* *p*-tolyl Grignard reagent (in tetrahydrofuran, THF) was added dropwise. The mixture was stirred at 50–60° for 2 hr., then cooled, and poured into an ice–dilute hydrochloric acid mixture. The organic product was isolated by extraction with methylene chloride. After concentration of the organic layer at reduced pressure, the residue was chromatographed on silica gel. Elution of the column with pentane–methylene chloride (3:1) gave 4-methylazobenzene, 0.06 g., m.p. 69–70°. Continued elution of the column with pentane–methylene chloride (2:1 and 1:1), gave 4′-methylazoxybenzene (N-phenyl-N′-*p*-tolyldiimide N-oxide), 1.16 g., 73%. After one recrystallization from hexane 1.05 g. of the azoxybenzene, m.p. 50–51°, lit.[8] m.p. 50–51°, was obtained.

Reaction of Phenylmagnesium Bromide and N-*p*-Bromophenyl-N′-tosyloxydiimide N-Oxide.—A solution of 2.23 g. (6.0 mmoles) of the tosyloxy diimide in 50 ml. of tetrahydrofuran was stirred at ambient temperature while 3 ml. of a 2.5 *M* ether solution of the phenyl Grignard reagent was added dropwise. After the mixture had been stirred at 50–60° for 2 hr., the mixture was processed as described above. The 4-bromoazoxybenzene fraction from the column weighed 1.14 g. (69%). This fraction was recrystallized from hexane to give N-*p*-bromophenyl-N′-phenyldiimide N-oxide, 1.04 g., m.p. 95–96°.

Reactions of the Butyl Grignard Reagent and N-Phenyl-N′-tosyloxydiimide N-Oxide.—A solution of 2.20 g. (7.5 mmoles) of the tosyloxydiimide in 40 ml. of methylene chloride was cooled while 3 ml. of about 3 *M* *n*-butylmagnesium chloride (Arapahoe) was added dropwise. The cooling bath was removed and the mixture was stirred at ambient temperature for 18 hr. The reaction was processed as usual, and the organic residue was chromatographed on silica gel. Pentane–methylene chloride (1:1) eluted phenylazoxybutane (N-phenyl-N′-*n*-butyldiimide N-oxide), a yellow oil, 0.834 g., $n^{20}D$ 1.5280; ultraviolet (cyclohexane), λ_{max} 245 mμ (ε 10,800).

Reaction of Phenyllithium and N-Phenyl-N′-tosyloxydiimide N-Oxide.—A solution of 2.92 g. (10 mmoles) of the tosyloxydiimide N-oxide in 50 ml. of THF was stirred at ice-bath temperature while 10 mmoles of phenyllithium in 7.2 ml. of ether was added slowly. The ice bath was allowed to melt, and the mixture was stirred overnight at ambient temperature. The reaction was processed in the usual way, and the organic residue obtained was chromatographed on silica gel. Pentane–methylene chloride eluted about 0.1 g. of azoxybenzene, identified by infrared spectrum, from the column. The major fraction was eluted by methylene chloride–ethyl acetate. After recrystallization from hexane–chloroform, this fraction, phenyl *p*-tolyl sulfone, weighed 1.75 g. (75%) and melted at 124–126°, lit.[20] m.p. 124.5°.

Reaction of Phenyllithium and N-*p*-Chlorophenyl-N′-tosyloxydiimide N-oxide.—The reaction of 1.63 g. (5 mmoles) of the

(19) Melting points are uncorrected.

(20) A. Michael and A. Adair, *Ber.*, **11**, 116 (1878).

tosyloxydiimide N-oxide in 30 ml. of THF and 6 mmoles of phenyllithium in 6 ml. of ether was carried out as described earlier. Chromatography on silica gel gave a trace of 4-chloroazoxybenzene (infrared spectrum) and 0.82 g. (71%) of phenyl *p*-tolyl sulfone, m.p. 124–126°.

Reaction of the Phenyl Grignard Reagent and Methylnitrosohydroxylamine Tosylate.—A solution of 1.15 g. (5.0 mmoles) of the tosylate in 25 ml. of methylene chloride was stirred at ice-bath temperature while 2.0 ml. of Arapahoe 3 *M* phenyl Grignard reagent was added. The mixture was stirred overnight at ambient temperature, and then was processed as usual. The residue was chromatographed on silica gel. Elution of the column was carried out with pentane–methylene chloride, methylene chloride, and ethyl acetate in methylene chloride. The first fraction eluted (after the biphenyl cut), 0.17 g., was identified as tosyl bromide by infrared spectrum, ultimate analysis, and m.p. 95–96°, lit.[21] m.p. 95–96°. The next fraction eluted, 0.365 g., was phenyl tosylate, m.p. 93–94°, lit.[22] m.p. 94–95°, identified by infrared spectrum and ultimate analysis. The last fraction from the column, eluted by ethyl acetate in methylene chloride, was recovered starting material, 0.188 g.

Reaction of the Phenyl Grignard Reagent and N-*n*-butyl-N′-tosyloxydiimide N-oxide.—A solution of 1.30 g. (5.0 mmoles) of the butylnitrosohydroxylamine tosylate in 35 ml. of methylene chloride was stirred at 3° while 12.2 ml. of 0.83 *M* phenyl Grignard in ether was added dropwise. The reaction was processed as usual and the residue was chromatographed on silica gel. The only fraction of the eluate that could be identified was that eluted by 10% ethyl acetate in methylene chloride. This was phenyl *p*-tolyl sulfone, 0.86 g., 74%, m.p. 126–127°.[20]

Reaction of N-Phenyl-N′-tosyloxydiimide N-Oxide and Sodium Methoxide.—A mixture of 5.84 g., (20 mmoles) of the above diimide N-oxide, 20 mmoles of sodium methoxide, and 75 ml. of methanol was stirred until the tosylate dissolved. The solution was refluxed for 1 hr., and then was cooled, poured into water, and extracted with methylene chloride. The residue was chromatographed on silica gel. Pentane in methylene chloride, methylene chloride, and ethyl acetate in methylene chloride were used to elute the column. The first fraction from the column was azobenzene (by infrared and melting point), 0.09 g.; the second was azoxybenzene (by infrared), 0.18 g. The infrared spectrum of the third fraction, 0.60 g., identified it as methyl tosylate (15%). Continued elution of the column gave N-phenyl-N′-methoxydiimide N-oxide, 1.24 g., 41%, m.p. 38–40° (from hexane), lit.[8] m.p. 39.5–40.5°. The infrared spectrum of this diimide was identical with that of a sample prepared from cupferron and dimethyl sulfate.[8]

When 10 mmoles of sodium methoxide in methanol was added slowly to a suspension of the tosyloxy diimide N-oxide in 50 ml. of methanol at ambient temperature, the tosylate dissolved slowly. As soon as solution was complete (*ca.* 15 min.), the methanolic solution was poured into water and processed as described before. A total of 1.48 g. (79%) of methyl tosylate and only a trace of N-phenyl-N′-methoxydiimide N-oxide was eluted from the silica gel column.

Reaction of Sodium Methoxide and N-Methyl-N′-tosyloxydiimide N-Oxide.—A mixture of 2.30 g. (10 mmoles) of the tosylate of methylnitrosohydroxylamine and 25 ml. of 0.49 *M* sodium methoxide (12 mmoles) in methanol was refluxed for 4 hr. The solution was cooled, diluted with 150 ml. of salt water, and extracted seven times with methylene chloride. The extract was dried over magnesium sulfate. After removal of all but about 2 ml. of the methylene chloride by distillation, the residual solution was distilled *in vacuo* through −30° and −80° traps. The −30° trap retained the N-methyl-N′-methoxydiimide N-oxide, 0.46 g., 51%. The sample was purified by preparative v.p.c. at 100° using a silicone (GE-SF-96) on Chromosorb column. A sample thus purified had $n^{20}D$ 1.4488; ultraviolet (cyclohexane), λ_{max} 238 mμ (ε 9730).

Anal. Calcd for $C_2H_6N_2O_2$: C, 26.66; H, 6.72; N, 31.10. Found: C, 27.03; H, 6.76; N, 32.35.[23]

Sodium Methoxide and N-*n*-Butyl-N′-tosyloxydiimide N-Oxide.—A mixture of 1.30 g. (5 mmoles) of the tosylate of *n*-butylnitrosohydroxylamine in 20 ml. of methanol and 12.0 ml. of 0.42 *M* sodium methoxide in methanol was refluxed for 3 hr. After the usual processing, the organic residue was chromatographed on silica gel. Methylene chloride eluted methyl tosylate, 0.08 g., 9%, identified by infrared spectrum; and 10% ethyl acetate in methylene chloride eluted N-*n*-butyl-N′-methoxydiimide N-oxide, 0.29 g., 44%, as a colorless oil. The n.m.r. spectrum is summarized in Table IV.

Anal. Calcd. for $C_5H_{12}N_2O_2$: C, 45.43; H, 9.15; N, 21.1. Found: C, 45.65; H, 9.27; N, 22.3.[23]

Potassium Phenoxide and N-Phenyl-N′-tosyloxydiimide N-Oxide.—A mixture of 2.92 g. (10 mmoles) of the tosylate of phenylnitrosohydroxylamine, 1.0 g. (11 mmoles) of phenol, 50 ml. of *t*-butyl alcohol, and 1.12 g. (10 mmoles) of solid potassium *t*-butoxide was refluxed for 3 hr. The mixture was cooled, poured into water, and extracted with methylene chloride. The methylene chloride was evaporated and the residue recrystallized from hexane yielding phenyl tosylate, 2.13 g., 86%, m.p. 94–95°.[22]

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(23) As mentioned in footnote *a*, Table III, high nitrogen values were often obtained on compounds of this type in the Dumas analysis.

Synthesis of Chonemorphine Stereoisomers

PING-LU CHIEN, WILLIAM E. MCEWEN,[1] ALBERT W. BURGSTAHLER, AND N. THANUKRISHNA IYER

Department of Chemistry, University of Kansas, Lawrence, Kansas

Received August 7, 1963

The four diastereoisomers of 3-amino-20-dimethylamino-5α-pregnane have been prepared by known reactions. One of these, the 3β,20α isomer, has been proved to be identical with the steroidal alkaloid chonemorphine. Some new observations on the stereoselectivity of reductions of 3-keto steroid oximes are reported and also some work on the preparation of $\Delta^{8(9)}$- and $\Delta^{8(14)}$-5α-pregnen-3β-ol-20-one acetates.

Chonemorphine is a steroidal alkaloid which has been isolated from the reputedly medicinal Indian herb, *Chonemorpha macrophylla*,[2] and from the similar Malayan plant, *Chonemorpha penangensis*.[3] In 1960 Chatterjee and Das[4] proposed that chonemorphine is a 3-amino-20-dimethylaminopregnene with the double bond possibly located at the 8,9-position.

Our initial work to establish the structure of this alkaloid was aimed at the synthesis of $\Delta^{8(9)}$- and $\Delta^{8(14)}$-3-amino-20-dimethylaminopregnenes having different stereochemical relationships at C-3 and C-20. 5,7-Pregnadien-3β-ol-20-one acetate, prepared by the action of N-bromosuccinimide on pregnenolone acetate with subsequent dehydrobromination,[5] was isomerized by acid to the corresponding $\Delta^{8,14}$-diene.[6] Hydrogenation

(1) Department of Chemistry, University of Massachusetts, Amherst, Mass.
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