

yield) of methyl 4-difluoramino-4-methylpentanoate, bp 56° (1.5 mm), and 1.9 g of recovered starting material.

*Anal.* Calcd for  $C_7H_{13}NF_2O_2$ : C, 46.43; H, 7.19; N, 7.74. Found: C, 46.60; H, 7.15; N, 7.43.

The proton nmr spectrum ( $CDCl_3$  solution) consisted of a singlet at  $\delta$  3.80 for  $OCH_3$ , a triplet ( $J = 1.8$  cps) at  $\delta$  1.32 for  $(CH_2)_2CNF_2^-$ , and a multiplet at  $\delta$  1.7–2.9 for  $CH_2$ . The infrared spectrum showed a carbonyl band at  $5.75 \mu$  and bands in the NF region at 10.50 (m), 10.71 (m), and 11.65  $\mu$  (s).

**4-Difluoramino-4-methylpentanoic Acid.**—A mixture of 1.20 g (0.00663 mol) of methyl 4-difluoramino-4-methylpentanoate and 10 ml of 2.5 N sodium hydroxide was heated intermittently in a 50° bath and agitated with a vortex mixer for 10 min to give a clear solution. Acidification with sulfuric acid, extraction with two 5-ml portions of ether, and distillation gave 0.79 g (71.3% yield) of 4-difluoramino-4-methylpentanoic acid, bp 72–73° (0.05 mm).

*Anal.* Calcd for  $C_8H_{11}NF_2O_2$ : C, 43.11; H, 6.60; N, 8.39. Found: C, 42.84; H, 6.41; N, 7.95.

The proton nmr spectrum ( $CDCl_3$  solution) consisted of a singlet at  $\delta$  11.02 for  $COOH$ , a triplet ( $J = 2$  cps) at  $\delta$  1.30 for  $CH_3$ , and a multiplet at  $\delta$  1.8–2.9 for  $CH_2$ .

**Registry No.**—Methyl 4-difluoramino-4-methylpentanoate, 22427-05-0; 4-difluoramino-4-methylpentanoic acid, 22427-06-1.

**Acknowledgment.**—The author is grateful to Mrs. Yoshie Kadota for the pK determinations of the carboxylic acids, to Mr. K. Inouye for elemental analysis, and to Dr. W. Woolfenden for nmr spectra.

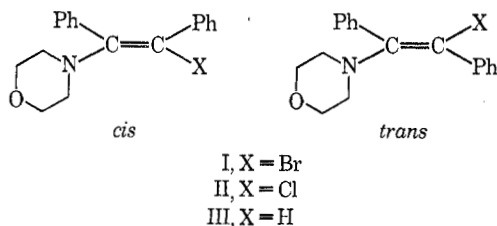
## Studies on Enamines. II. The Effect of the Amino Group on the Stabilities of Isomeric Vinyl Anions<sup>1,2</sup>

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Earlier we reported the synthesis and *cis-trans* isomerization of 1-bromo- and 1-chloro-2-(4-morpholino)-1,2-diphenylethene (I and II).<sup>1</sup> In the same article we also reported the easy heterolytic cleavage of the carbon-halogen bond to give a vinyl cation. We have now studied the reactions of I and II with phenyllithium and triphenylphosphine. In both cases the halo enamines were reduced to give 1-(4-morpholino)-1,2-diphenylethene (III) through a vinyl anion intermediate.



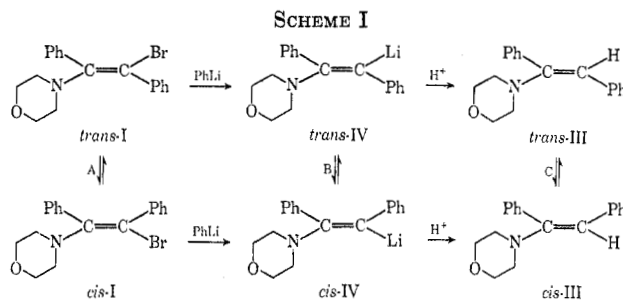
**Reaction with Phenyllithium.**—When treated with an equimolar amount of phenyllithium in benzene at room temperature, both I and II were converted into the enamine III (51% and 45%, respectively). A

(1) Part I: S. J. Huang and M. V. Lessard, *J. Amer. Chem. Soc.*, **90**, 2432 (1968).

(2) Abstracted from the Ph.D. dissertation of M. V. Lessard, University of Connecticut, 1969.

(3) University of Connecticut Predoctoral Fellow, 1966–1969.

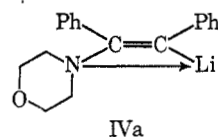
*cis-trans* 1:1 equilibrium mixture of I was converted quantitatively into III after reaction with twice the equimolar amount of phenyllithium. In all cases the enamine III formed was the pure *cis* form, as determined by nmr. Possible routes for converting *trans*-I into *cis*-III are shown in Scheme I.



According to Munk and Kim, the equilibrium mixture for enamine III is *cis-trans* (88:12).<sup>4</sup> Since we detected no *trans*-III and since the conditions necessary for the *cis*-III–*trans*-III isomerization are much more severe than those employed in our studies, we feel that the isomerization of products, route C, can be considered to be rather unlikely.

It is generally accepted that protonation of vinyl-lithium reagents occurs with retention of configuration.<sup>4–7</sup> There are then two remaining possible routes for the conversion of *trans*-I into *cis*-IV. In route A, *cis*-I reacts faster than *trans*-I with phenyllithium, and consequently the equilibrium *cis*-I–*trans*-I is shifted toward *cis*-I. Our study showed that the *cis*-I–*trans*-I isomerization reaches equilibrium after several hours in benzene at room temperature, showing that route A is possible. Alternatively, both *cis*-I and *trans*-I may react with phenyllithium at similar rates to give *cis*-IV and *trans*-IV, respectively, and a fast conversion of *trans*-IV into *cis*-IV may occur (route B). Since diarylvinyl lithium and triarylvinyl lithium are known to undergo *cis-trans* isomerization at rather fast rates,<sup>5–7</sup> it is reasonable to assume that *trans*-IV also isomerizes to *cis*-IV at a rather fast rate. Detailed kinetic studies will be necessary to estimate the relative importance of route A and of route B. However, attempts to study such kinetics have been frustrated, as *trans*-I can not be obtained in pure form; also the reaction rate of I with phenyllithium is too fast to be measured in an easy way.

The fact that only *cis*-III is formed in the above reactions (our nmr measurements are estimated to be accurate to  $\pm 2\%$ ) suggests that *cis*-IV is much more stable than *trans*-IV. We feel that intramolecular coordination of the nonbonded electrons of the morpholino nitrogen to the lithium metal probably is responsible for the relatively high stability of the *cis* form of IV, which may be more accurately represented as IVa rather than *cis*-IV. Such intramolecular coordination is not possible in the *trans* form of IV.



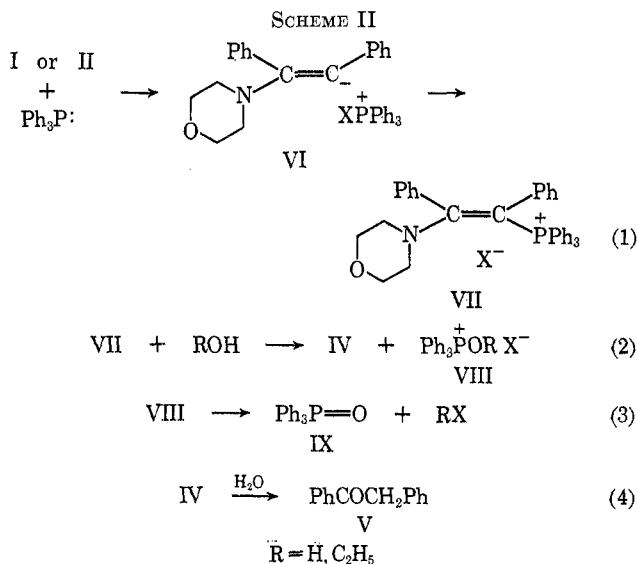
(4) M. E. Munk and Y. K. Kim, *J. Org. Chem.*, **30**, 3705 (1965).

(5) A. N. Nesmeyanov and A. E. Borisov, *Tetrahedron*, **1**, 158 (1957).

(6) D. Y. Curtin and J. W. Crump, *J. Amer. Chem. Soc.*, **80**, 1922 (1958).

(7) D. Y. Curtin and W. J. Koehl, Jr., *ibid.*, **84**, 1967 (1962).

**Reaction with Triphenylphosphine.**—Reaction of a mixture of the *cis* and *trans* forms of bromo enamine I with triphenylphosphine in benzene at room temperature yielded 37% of *cis*-III, 27% of deoxybenzoin (V, hydrolysis product of III), and a white, hygroscopic solid believed to be the triphenylphosphonium salt of the enamine. Reaction of a mixture of the *cis* and *trans* forms of the chloro enamine II with triphenylphosphine under the same conditions yielded 29% deoxybenzoin. A possible mechanism for the reaction is shown in Scheme II. A nucleophilic displacement of triphenyl-



phosphine on halogen yields the phosphonium salt VI, which may rearrange to give phosphonium salt VII (eq 1). Hydrolysis of the phosphonium salt VII by water present in the reaction system would yield enamine III [which may undergo further hydrolysis to give deoxybenzoin (V), eq 4] and phosphonium salt VIII (eq 2). Decomposition of VIII could then yield triphenylphosphine oxide (IX).<sup>8</sup> Support for this mechanism was provided by treating bromo enamine I with triphenylphosphine in benzene under anhydrous conditions, followed by addition of ethanol. The reaction yielded 86% *cis*-III, 9% deoxybenzoin (V), 92% triphenylphosphine oxide (IX), and 50% ethyl bromide. The fact that the bromo enamine I underwent a faster and more complete reaction than the chloro enamine II supported the postulated nucleophilic attack on halogen rather than on carbon.<sup>8-14</sup> Indeed, very similar mechanisms have been suggested by several workers on the reduction of halo ketones by triphenylphosphine.<sup>8-12</sup>

An alternative mechanism for formation of the phosphonium salt VII may involve addition of triphenylphosphine to the olefin followed by elimination of a halide ion. This mechanism may be ruled out by two considerations: (1) steric hindrance probably makes

the addition of the large triphenylphosphine molecule to the olefin very difficult; and (2) in an addition-elimination reaction one would expect that the chloro enamine II would react as easy as or more easily than the bromo enamine I. This was not the observed case.

Again, the fact that only *cis*-III was obtained suggests that internal coordination between the morpholino nitrogen and the cationic phosphorus makes the *cis* forms of VI and VII more stable than the *trans* forms.

### Experimental Section

All melting points were uncorrected and were taken on a Thomas-Hoover apparatus. Infrared spectra were recorded on a Perkin-Elmer Model 137B Infracord. Nuclear magnetic resonance spectra were determined using a Varian A-60 spectrometer and carbon tetrachloride solution containing tetramethylsilane was used as internal standard. Mass spectra were obtained on an AEI MS-12 mass spectrometer. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn., and Baron Consulting Co., Orange, Conn. Thin layer chromatography (tlc) was performed on 0.25-mm layers using silica gel GF 254 or PF 254 (Merck), Darmstadt, Germany. The silica gel used for column chromatography was obtained from Gerbrüder Hermann, Köln, Germany.

All solvents and reagents were purified according to standard procedures before use. All products were identified by melting point and spectroscopic methods.

**1-Bromo-2-(4-morpholino)-1,2-diphenylethene (I).**—To a solution of 15.0 g (57 mmol) of *cis*-1-(4-morpholino)-1,2-diphenylethene (III)<sup>4</sup> in 250 ml of dry benzene stirred under nitrogen was added 10.2 g (57 mmol) of N-bromosuccinimide in small portions. After completion of the addition of NBS (30 min) the mixture was stirred for 1.5 hr; after this time TLC showed that all of III had reacted. Filtration of the succinimide formed in a vacuum system followed by evaporation of solvent *in vacuo* resulted in a yellow-brown oil. The oil was crystallized from dry methanol to give 15.5 g (79%) of a *cis-trans* (3.4:1) mixture of I. Two more recrystallizations from methanol yield the pure *cis* isomer, mp 109–110°. The infrared spectrum showed the following peaks: 3030, 2940, 1590, 1140, 950, 740, 710, and 705 cm<sup>-1</sup>. The nmr spectrum was reported elsewhere.<sup>1</sup>

Anal. Calcd for C<sub>18</sub>H<sub>18</sub>BrNO: C, 62.79; H, 5.28; N, 4.07. Found: C, 63.06; H, 5.23; N, 4.03.

Attempts to isolate the pure *trans* form failed.

**1-Chloro-2-(4-morpholino)-1,2-diphenylethene (II).**—The enamine II was prepared in 70% yield from *cis*-III and N-chlorosuccinimide in a similar manner. The pure *cis*-II was obtained by recrystallization, mp 79–80°. The infrared spectrum showed the following peaks: 3030, 2940, 1590, 1575, 1110, 940, 745, and 700 cm<sup>-1</sup>. The nmr spectrum was reported elsewhere.<sup>1</sup>

Anal. Calcd for C<sub>18</sub>H<sub>18</sub>ClNO: C, 72.11; H, 6.03; N, 4.67. Found: C, 71.94; H, 6.08; N, 4.53.

Attempts to isolate the pure *trans* form failed.

**Reaction with Phenyllithium.**—Reactions were run on a 5-mmol scale. Phenyllithium (Alfa Inorganics) in benzene-ether was added to a stirred solution of an equilibrium mixture of I or II in dry benzene under nitrogen at room temperature. The reaction was instantaneous and the organometallic intermediate was hydrolyzed 1 hr later by addition of isopropyl alcohol (acid hydrolysis was not employed in order to avoid hydrolysis of enamine III). Removal of solid by filtration and evaporation of the solvent *in vacuo* gave a yellow oil. The nmr spectrum of the oil in carbon tetrachloride solution revealed the presence of only unreacted halo enamine and *cis*-III. Preparative TLC and column chromatography gave deoxybenzoin (hydrolysis product of III) and  $\alpha$ -halodeoxybenzoin (hydrolysis product of I or II). The result are listed in Table I.

TABLE I

REACTION OF THE  $\alpha$ -HALO ENAMINES WITH PHENYLLITHIUM

Reactants (ratio)	Yield of product, %	
	<i>cis</i> -III	<i>trans</i> -III
I and PhLi (1:1)	51	0
I and PhLi (1:2)	100	0
II and PhLi (1:1)	45	0

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**Reaction of I with Triphenylphosphine.** A.—To a solution of 2.28 g (8.7 mmol) of triphenylphosphine (Carlisle Chemical Co.) in 100 ml of benzene stirred under nitrogen was added a solution of 3.00 g (8.7 mmol) of the bromoamine I in 20 ml of benzene. After 1 hr of stirring at room temperature, tlc showed the absence of unreacted I. A white, hygroscopic precipitate, mp 128–130°, was filtered from the reaction mixture. An oil was obtained from the filtrate after removal of solvent. Hydrolysis of the oil with undried methanol gave 0.86 g (37%) of enamine III and 0.56 g (27%) of deoxybenzoin after fractional recrystallization from methanol. The white precipitate could not be purified, as it hydrolyzed rapidly in air to give enamine III, deoxybenzoin, and triphenylphosphine oxide.

B.—The same reaction was carried out in a carefully dried system. Instead of filtration of the precipitate, a different work-up procedure was employed. A mild exothermic reaction took place with the dissolution of the original precipitate when 1.8 times the equimolar amount of absolute ethanol was added to the reaction mixture. After having been stirred overnight, the mixture was fractionally distilled. Comparison of the nmr spectra of the distillate fractions with that of authentic ethyl bromide showed a 50% yield of ethyl bromide. An 85% yield of *cis*-III, a 9% yield of deoxybenzoin, and a 92% yield of triphenylphosphine oxide were obtained from the residue by fractional recrystallization from methanol.

**Reaction of II with Triphenylphosphine.**—The reaction was carried out in a manner similar to A above. After 24 hr of stirring tlc showed the presence of unreacted II. Column chromatography yielded 70% unreacted triphenylphosphine and 29% deoxybenzoin.

**Registry No.**—*cis*-I, 20735-65-3; *trans*-I, 20735-66-4; *cis*-II, 20735-67-5; *trans*-II, 20735-68-6; phenyllithium, 591-51-5; triphenylphosphine, 603-35-0.

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### The Coupling of Nitrophenyl Radicals and Anions To Form Anion Radicals

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Dimerization, disproportionation, and atom abstraction are among frequently reported reaction pathways for organic free radicals.<sup>1</sup> Evidence has been presented recently which shows that still another reaction pathway, the coupling of a radical with an anion, predominates for nitrobenzyl radicals in the presence of certain anions.<sup>2</sup> Similarly, the coupling of a phenyl radical with an anion has been suggested to rationalize the formation of biphenyl in the photolysis of a phenyllithium in ether solution.<sup>3</sup>

In the course of some of our earlier work we reported that the presence of iodide ion markedly altered the rate of halogenated nitrobenzene anion radical decomposition.<sup>4</sup> That observation suggested that further

(1) W. A. Pryor, "Free Radicals," McGraw-Hill Book Co., Inc., New York, N. Y., 1966.

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(4) J. G. Lawless and M. D. Hawley, *J. Electroanal. Chem.*, **21**, 365 (1969).

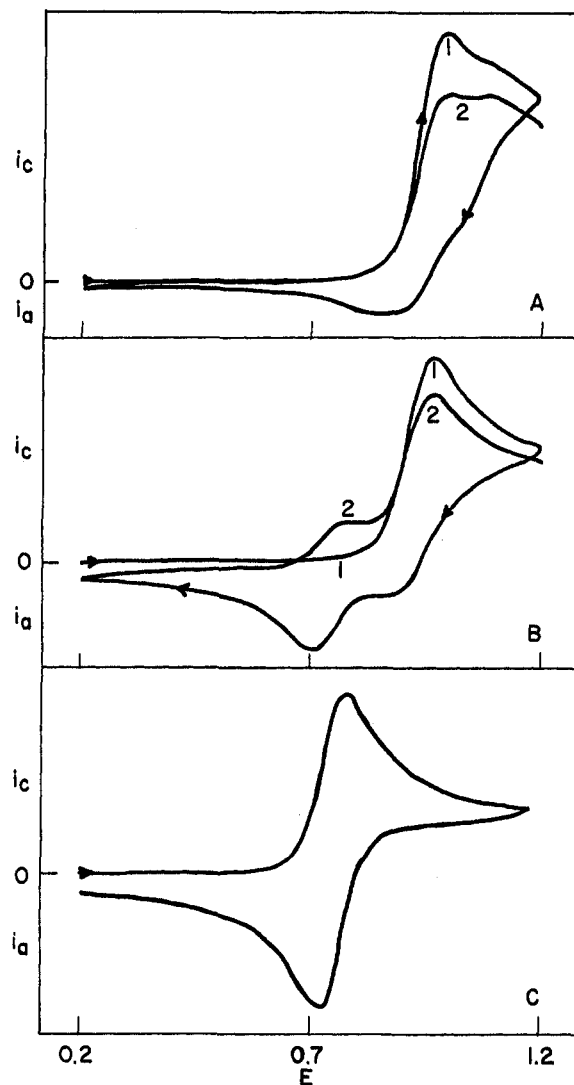


Figure 1.—Cyclic voltammograms in 0.1 M TEAP–DMSO at a scan rate of 80.6 mV/sec: (a)  $7.32 \times 10^{-3}$  M *p*-iodonitrobenzene; (b)  $7.32 \times 10^{-3}$  M *p*-iodonitrobenzene and 0.1 M NaCN; (c)  $5.82 \times 10^{-3}$  M *p*-nitrobenzonitrile. Numbers 1 and 2 represent cycles 1 and 2, respectively.

studies should be made into the reactions of phenyl radicals in the presence of anions. The results of such a study are reported herein.<sup>5</sup>

Evidence for a phenyl radical–anion reaction is shown in Figure 1. In the absence of a reactive anion, such as cyanide (Figure 1a), the nitrophenyl radical formed by the electrochemical reduction of *p*-iodonitrobenzene (cathodic peak near –1.0 V) abstracts a hydrogen atom from the solvent to form nitrobenzene. The nitrobenzene is then reduced in a one-electron process at slightly more negative potential (cathodic peak near –1.09 V) to its anion radical.<sup>6</sup> The absence of appreciable anodic current on the reverse, anodic sweep is the result of a solution oxidation–reduction reaction involving nitrobenzene anion radical and *p*-iodonitrobenzene.<sup>4</sup>

Hydrogen atom abstraction is virtually eliminated as a reaction pathway in dimethyl sulfoxide (DMSO)

(5) Since the completion of this work, the coupling of phenyl radical and nitrite ion was observed by esr spectroscopy in aqueous solution: A. L. J. Beckwith and R. O. C. Norman, *J. Chem. Soc., B*, 403 (1969).

(6) For additional applications of cyclic voltammetry to organic systems, see, e.g., R. N. Adams, "Electrochemistry at Solid Electrodes," Marcel Dekker, New York, N. Y., 1969.