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A NOVEL SYNTHESIS OF YNAMINES. COPPER CATALYZED OXIDATION OF PHENYLACETYLENE IN THE PRESENCE OF SECONDARY AMINES

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Ynamines (1-aminoacetylenes) are a relatively new class of organic compounds which were unknown until 1958. However, they have now become generally accessible through nucleophilic substitution on 1-haloacetylenes with lithium amides, by dehydrohalogenation of appropriately substituted haloethylamines, and by the base catalyzed isomerization of propargylamines (1). We now wish to report the first direct synthesis of ynamines from phenylacetylene and secondary amines by air oxidation in the presence of homogeneous copper catalysts.

The oxidation is effected by adding dropwise a solution of phenylacetylene (5.1 g., 0.050 mole) in 100 ml. of benzene over 30 minutes to a stirred solution of cupric acetate monohydrate(2.0 g., 0.010 mole) and dimethylamine (25.0 ml., 0.38 mole) in 100 ml. of benzene maintained at 5°. A stream of oxygen (1.0 ft.^{3}/hr) was passed continuously through the reaction mixture during addition of phenylacetylene and for another 30 minutes. Ice water (100 ml.) was added to the reaction mixture to precipitate the copper ions and the organic layer was separated, dried over Drierite and concentrated under vacuum. Gas chromatography (10' x 1/2" 410 gum rubber) showed only two materials in addition to solvent, namely, N,N-dimethyl-2-phenylethynylamine (I) and 1,4-diphenylbutadiyne (II) in a 1.5:1 ratio (ratio of peak areas), respectively; no phenylacetylene was detected. Preparative gas chromatography was the most successful means of isolating I since partial decomposition occurred on fractional distillation. If the product mixtures are worked up with dilute hydrochloric acid instead of water, the ynamine I

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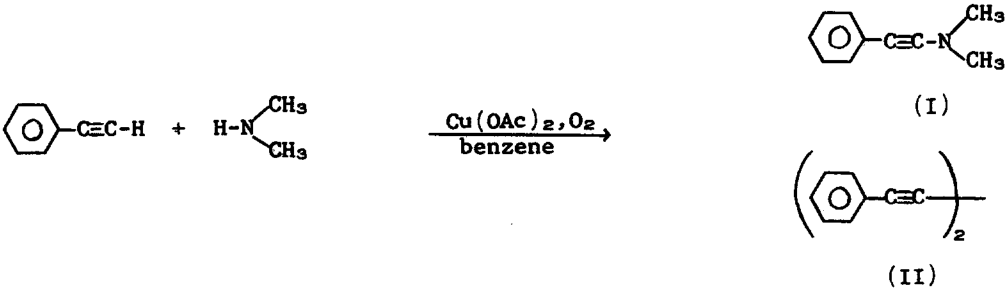
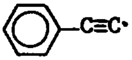
*Present address: Eastern Research Laboratory, The Dow Chemical Company, Wayland, Massachusetts 01778 is quantitatively converted to N,N-dimethyl-2-phenylacetamide by the acid catalyzed addition of water (2,3). Both I and the phenylacetamide were obtained in greater than 40% yield.

N,N-Dimethyl-2-phenylethynylamine isolated from the oxidation mixture exhibits two intense infrared absorption bands at 2205 and 2235 cm^{-1} and the nmr spectrum reveals resonance peaks at δ 7.14 (5.0 protons) and 2.73 (6.05 protons). These spectra were identical in all respects to those of an authentic sample prepared from chloroethynylbenzene and lithium dimethylamide (3). The Glaser coupling product II was identified by comparing its melting point (88°) and infrared spectrum with that of authentic material.

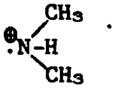


When dimethylamine is replaced by other secondary amines such as piperidine or diethylamine, the corresponding ynamines are obtained. If a primary amine such as ethylamine is employed under the same conditions, the anticipated secondary ynamine cannot be isolated but instead N-ethyl-2-phenylacetamide is found. Even under conditions which initially are anhydrous, enough water is formed in the oxidation process so that the amide presumably arises from hydration of N-ethyl-2-phenylethynylamine or its tautomer. This appears to be the first indication of the independent existence of a secondary ynamine.

Only catalytic amounts of the copper salt are required for the oxidation. For example, high conversions are achieved with reaction times of less than thirty minutes when the $[Cu^{++}]$/[phenylacetylene] ratio is only 0.02. The ynamine/1,4-diphenylbutadiyne ratio is sensitive to and varies in an inverse manner with the $[Cu^{++}]$/[phenylacetylene] ratio. As this latter ratio decreases from 1.0 to 0.10 to 0.02 the ynamine/1,4-diphenylbutadiyne ratio increases from 0.88 to 1.2 to 1.5, respectively. The formation of ynamine requires the presence of oxygen, for when the reaction is conducted with stoichiometric amounts of cupric ion in the absence of oxygen no ynamine is produced and only 1,4-diphenylbutadiyne is found. The yield of ynamine can be increased from 45% up to almost 90% if stoichiometric amounts (total amount added relative to phenylacetylene) of a reducing agent such as hydrazine, phenylhydrazine or pyridine-borane are added continuously during the course of the reaction. Problems are encountered, however, in isolating the ynamines from mixtures containing the oxidized reducing agents since the rate of hydration is enhanced under these conditions.



(III)



(IV)

The formation of N,N-dimethyl-2-phenylethynylamine can be viewed formally as the cross coupling of the phenylacetylenic radical (III) with an aminium radical (IV) derived from the secondary amine. The intermediacy of these two species is plausible since the acetylenic radical is the probable intermediate in the Glaser coupling reaction (4-6) and the aminium radical is well documented in the free radical addition of N-chloroamines to olefins and could be expected to arise from a one electron oxidation of the secondary amine.

The role of the reducing agent in enhancing yields and the mechanistic details will be the subject of future studies.

Acknowledgement

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3. Gas chromatographic analysis of the product mixtures gave erratic results apparently owing to decomposition of the ynamines in the injection port. However, good quantitative data could be obtained when these mixtures were worked up in the presence of acid. In these cases, g.l.c. analysis revealed only unreacted phenylacetylene, N,N-dimethylphenylacetamide and 1,4-diphenylbutadiyne in the product mixtures.

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