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SYNTHESIS OF ACETYLENES BY HOFMANN ELIMINATION OF QUATERNIZED ENAMINES

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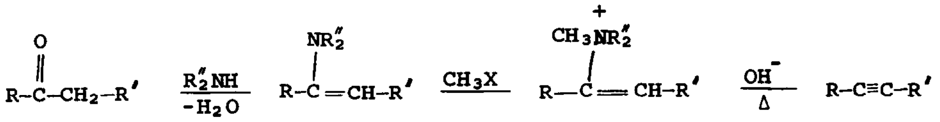
Despite isolated examples[1] heretofore, no systematic examination of the preparation of acetylenes by Hofmann elimination of quaternized enamines has been reported. The synthetic value lies in conversion of methylene ketones to acetylenes via enamines, i.e., I→II→III→IV.



$$R{-}\overset{\overset{O}{\|}}{C}{-}CH_2{-}R' \xrightarrow[-H_2O]{R''_2NH} R{-}\overset{\overset{NR''_2}{|}}{C}{=}CH{-}R' \xrightarrow{CH_3X} R{-}\overset{\overset{\overset{+}{CH_3NR''_2}}{|}}{C}{=}CH{-}R' \xrightarrow[\Delta]{OH^-} R{-}C{\equiv}C{-}R'$$

I II III IV

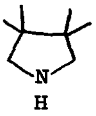
a, $R{=}R'{=}C_6H_5$

b, $R{=}C_6H_5$; $R'{=}H$

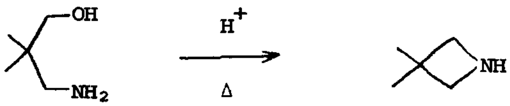
c, $R{=}C_6H_5CH_2$; $R'{=}C_6H_5$

d, $R{=}CH_2COOC_2H_5$; $R'{=}COOC_2H_5$

The presumed problems are: (1) assuring trans geometry in II for elimination, (2) exclusive N-methylation of the ambident enamine II, (3) competitive Hofmann elimination in R″ in III. Since initial trials in the deoxybenzoin series yielded more deoxybenzoin (40%) than diphenylacetylene (29%) on refluxing III a (pyrrolidine enamine) with 15% aqueous sodium hydroxide, we undertook to explore problem (3) with cyclic enamines bearing no β-hydrogens. To this end 3,3,4,4-tetramethylpyrrolidine(V) (mp 55-56°) was synthesized by lithium aluminum hydride reduction (refluxing tetrahydrofuran/one week/74%) of tetramethylsuccinimide.[2] Also 3,3-dimethylazetidine(VII) was synthesized by a shorter route than that used previously.[3] Lithium aluminum hydride reduction (refluxing ether/2 days/47%) of ethyl dimethyl-cyanoacetate[4] afforded VI (bp 185-6°) which was cyclodehydrated in hot aqueous sulfuric acid to yield the azetidine VII (37%; bp 88-91°; lit. 90°).[3]



V



VI VII

Using deoxybenzoin (Ia) as a model, we were able to prepare enamines of V and VII; the former (mp 79-81°) required 16 days refluxing in toluene (with catalytic p-toluenesulfonic acid and water separator); the latter(mp 53-55°) only 22 hours in refluxing benzene; both were formed in over 95% yield. N-methylation of the enamines was exclusive (> 95%) with neat methyl fluorosulfonate, as it was also with the simple pyrrolidine enamine; these quaternary enammonium salts are quite stable to aqueous acid or base unless heated.

The best conditions found for IIIa → IVa were 40% aqueous potassium hydroxide at reflux (2 hours), which yielded 86% diphenylacetylene, identified as dibromotolane (mp 210°), from the methylated pyrrolidine enamine. In no case, however, was any acetylene formed on pyrolysis with anhydrous potassium carbonate, 1,8-*bis*-dimethylaminonaphthalene or diazabicyclooctane. The tetramethylpyrrolidine, however, produced no diphenylacetylene and up to 40%

deoxybenzoin. This is interpreted as evidence for *trans*-stilbene geometry in the pyrrolidine enamine(**IIa**) but *cis*-stilbene for the more bulky tetramethylpyrrolidine enamine(**IIa**). In view of renewed interest in the *syn*-*anti* stereoelectronics of the Hofmann elimination,[5] the present comparison shows elimination occurring only with the *anti* example in two very similar enammonium salts.[6] The enamine from the azetidine(**VII**), however, produced neither diphenylacetylene nor deoxybenzoin under these conditions.

The N-methylation problem (2) afflicted the examples from acetophenone (**Ib**) and diethyl acetonedicarboxylate(**Id**). The former pyrrolidine enamine (**IIb**) yielded a mixture on methylation estimated as 2:1 C- to N-alkylation, and this mixture with 40% alkali produced very little phenylacetylene, the main products being acetophenone and propiophenone. Pyrrolidine enamine **IId** was exclusively methylated on carbon with methyl fluorosulfonate.

Pyrrolidine enamine **IIc** from diphenylacetone(Ic) was cleanly N-methylated to **IIc**, however, and subjected to hot 40% alkali. Diphenylacetone was isolated in 32% yield and diphenylallene (the product of base-catalyzed isomerization of 1,3-diphenylpropyne, **IVc**)[8] in 25% yield, identical with the authentic allene. In conclusion it appears that, while the reaction can be successful in some cases, it seems likely to have very limited usefulness owing to the several problems enumerated above.

References

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6. Identification of enamine geometry by nmr spectra has not been satisfactory; the vinyl proton signals for the *cis*- *trans*-morpholine enamines are 5.56 and 5.71 δ, respectively,[7] while those for the pyrrolidine and tetramethylpyrrolidine enamines are 5.35 and 5.22 δ, respectively.

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