Tetrahedron Letters No. 37, pp 3523 - 3524. 0040-4039/79/0908-3523$02.00/0

THE REACTION OF PROPARGYL ALCOHOL WITH AMINES A NOVEL ROUTE TO AMINOPROPANONES AND 2-METHYLQUINOXALINE

Yoshihisa WATANABE,* Mitsushige IDEI, and Yoshinobu TAKEGAMI
Department of Hydrocarbon Chemistry, Kyoto University, Kyoto 606

Propargyl alcohol reacts with a variety of amines in the presence of zinc acetate and cadmium acetate at reflux temperatures for 8-20 h to give aminopropanones in fairly good yields. *o*-Phenylenediamine gives 2-methylquinoxaline.

Enamines are useful compounds as the starting material in organic synthesis and can be readily prepared from secondary amines and carbonyl compounds.[1] Little attention, however, has been paid to the reaction of amines with alkynes, regarded as a possible way to enamines. Alkynes such as acetylene and propyne react with primary and secondary amines to give ethylidenimines and 1,1-dimethyl-2-butynylamines respectively.[2]

We now wish to report the reaction of propargyl alcohol with a variety of amines, affording a novel route to N,N-disubstituted aminopropanones from secondary amines and 2-methylquinoxaline from *o*-phenylenediamine.

Typically, an equimolar mixture of propargyl alcohol(100 mmol) and an amine (100 mmol) was stirred in the presence of zinc acetate(25-50 mg) and cadmium acetat (25-50 mg) under an argon atmosphere at 70-115°C for 8-20 h. The reaction products were separated by vacuum distillation and identified by IR, ^{1}H NMR, and elemental analysis. The reaction could be readily monitored by means of IR spectra. A band at 2200 cm^{-1} characteristic of the acetylenic bond disappeared gradually through the reaction and a new band at 1710 cm^{-1} appeared.

Propargyl alcohol reacts with a variety of secondary amines to give the corresponding N,N-disubstituted aminopropanones in fairly good yields. Typical results are shown in Table. Diethylamine, diallylamine, piperidine, N-methylbenzylamine, and N-methylcyclohexylamine can be applied for this reaction, while such secondary amines as dicyclohexylamine, diisopropylamine, and diphenylamine had little activity to be recovered unchanged in the reaction. This fact shows that the secondary amines with two bulky groups have a large steric hindrance in forming a 1 : 1 adduct with propargyl alcohol. The first step of the reaction appears to be the formation of N,N-disubstituted amino-1-propen-3-ol, an enamine with allyl alcohol type, according to Eq.

$$\text{>NH} + \text{HC}\equiv\text{C-CH}_2\text{OH} \longrightarrow \text{>N-CH=CH-CH}_2\text{OH} \longrightarrow \text{>N-CH}_2\text{-CH(O)-CH}_2 \longrightarrow \text{>N-CH}_2\text{COCH}_3$$

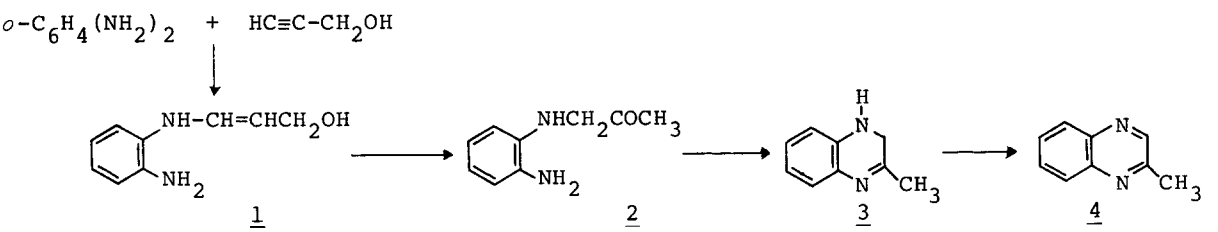
Table. The preparation of aminopropanones and 2-methylquinoxaline from propargyl alcohol and amines

Entry	Amine	Reaction condition[a]		Product	Isolated yield (%)
		Temp. (°C)	Time (h)		
1	Diethylamine	70	20	N,N-Diethylamino-propanone	39
2	Diallylamine	100	20	N,N-Diallylamino-	45
3	Piperidine	100	16	1-Azacyclohexyl-	38
4	Morpholine	115	16	4-Oxa-1-azacyclohexyl-	38
5	N-Methylbenzylamine	110	8	N,N-Methylbenzylamino-	51
6	N-Methylcyclohexylamine	90	20	N,N-Methylcyclohexylamino-	25
7	*o*-Phenylenediamine	85	24	2-Methylquinoxaline	43
8	Aniline	110	17	Tarry material	-

a) Propargyl alcohol 100 mmol, an amine 100 mmol, $Zn(OAc)_2$ 25-50 mg, and $Cd(OAc)_2$ 25-50 mg under an argon atmosphere.

The intramolecular rearrangement of the enamines seems to result in the formation of the final products, the aminopropanones, via epoxides. Although the mechanism of the reaction is not clear yet, this consideration is supported by the fact that epoxides undergo rearrangement to give allyl alcohols and ketones.[3)]

Primary amines such as aniline, toluidines, and propylamine also have a great activity for this reaction but give only resinous material. On the other hand, *o*-phenylenediamine reacts with propargyl alcohol to give 2-methylquinoxaline in good yields. This reaction appears to proceed as follows:



2-Methylquinoxaline (4) can be derived from several intermediates, an enamine (1), an aminoketone (2), and dihydro-2-methylquinoxaline (3) unstable for oxidation. This is a new method for the preparation of 2-methylquinoxaline.

References

1) A.G. Cook, Enamine, Marcel Dekker, New York and London(1969).
2) C.W. Krunse and R.F. Kleinschmidt, J. Am. Chem. Soc., 83, 213, 216(1961).
3) H. Yamamoto and H. Nozaki, Angew. Chem., 90, 180(1978), and references therein; M. Suzuki, Y. Oda, and R. Noyori, J. Am. Chem. Soc., 101, 1623(1979).

(Received in Japan 11 June 1979)