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AN ALUMINA CATALYZED ADDITION OF SECONDARY AMINES TO EXOCYCLIC α,β-UNSATURATED KETONES

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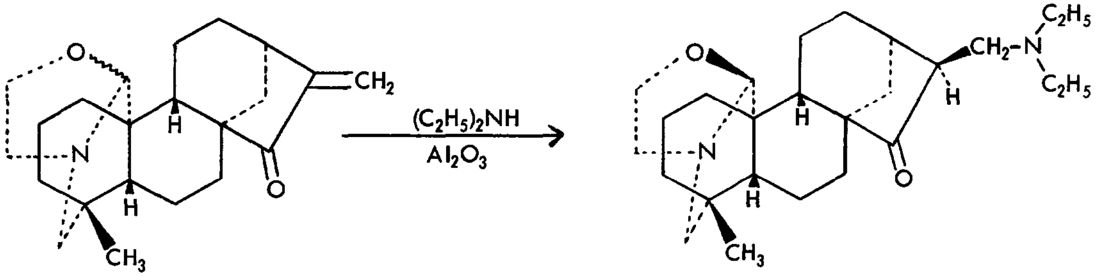
A Michael addition of secondary amines to exocyclic α,β-unsaturated ketones has been achieved in excellent yield in the presence of alumina. In the absence of alumina, the reaction does not proceed or takes place in low yield with many side products after a long reaction time.

Recently organic reactions on alumina surfaces have generated a great deal of interest among synthetic organic chemists because of their exceptionally high selectivity under mild reaction conditions.[1] Usually Michael addition of a secondary amine to α,β-unsaturated carbonyl-containing compounds proceeds in good yield without any catalyst, but we observed that in the case of exocyclic α,β-unsaturated ketones, the addition does not occur <u>or</u> takes place in low yield after a long reaction time.



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We now report an alumina-catalyzed Michael addition of secondary amines to exocyclic α,β-unsaturated ketones. During an investigation of C_{20}-diterpenoid alkaloids, we observed the addition of diethylamine in the presence of neutral alumina of activity III to the α,β-unsaturated ketone, veatchinone (1), to afford compound 2, $C_{26}H_{42}N_2O_2$, mp. 116-117°, in quantitative yield. This reaction did not proceed in the absence of alumina or in the presence of alumina of activity I. The structure of compound 2 was established by a single-crystal X-ray analysis (Figure 1) and other spectroscopic methods. Crystals of compound 2 were orthorhombic, space group = $P2_12_12_1$, $a = 10.643(1)$Å, $b = 12.825(1)$Å, $c = 17.528(2)$Å and dcalc = 1.12 g/cc for $Z = 4$. All reflections with $2\theta < 120^\circ$ were measured using ω-2θ scans and CuKα radiation and 978 (48.3%) of these were judged observed ($I < 3\sigma(I)$). The structure was solved by direct methods[2] and refined to R = 0.058[3]. The diethylamine side chain is disordered and its geometry is inaccurate, but the remaining bond distances and angles are within accepted ranges.[4]

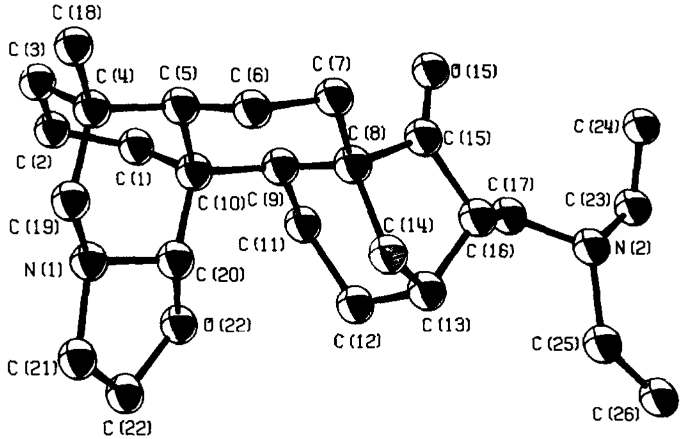
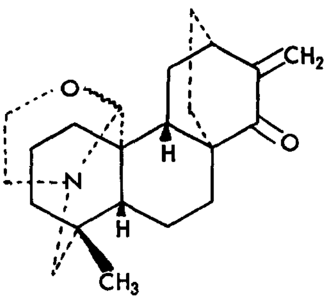


Figure 1. ORTEP Drawing of Compound 2.

Addition of diethylamine to atisinone (3) and dihydroatisinone (5) proceeded in quantitative yield to give compounds 4 (mp. 121–123°) and 6 (amorphous), respectively[5], in the presence of alumina. Veatchinone, atisinone, and dihydroatisinone did not react with diethylamine in the absence of alumina even after 48 hours at room temperature or after refluxing for 24 hours. In a typical experiment: A solution of veatchinone (100 mg) in 10% diethylamine in benzene (10 ml) was stirred in the presence of 200 mg of neutral alumina of activity III[6] for 15 hours at room temperature. Work-up of the reaction mixture afforded compound 2 in quantitative yield. No starting material or side product was detected after 15 hours.



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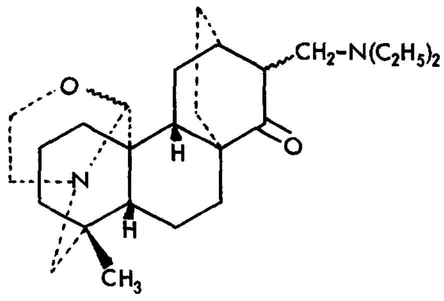

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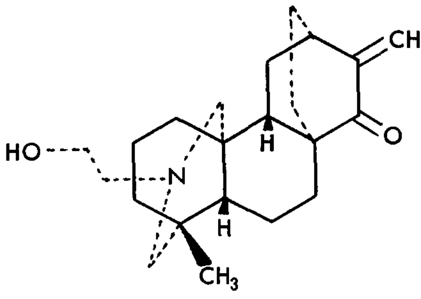

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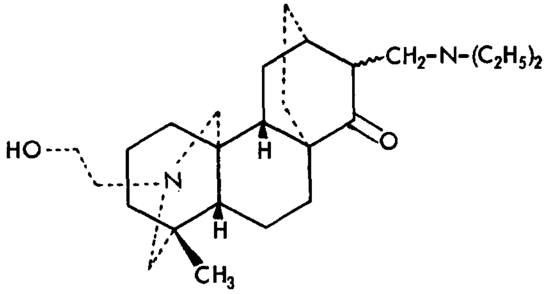

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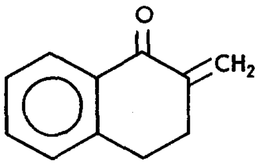
Treatment of 2-methylene-1-tetralone (7)[7] and 3-methylene-norbornanone (9)[8] with 10% diethylamine in benzene for 2 hours in the presence of alumina gave compounds 8 (HCl salt: mp. 123-124°) and 10 (oil), respectively, in quantitative yield. In the absence of alumina reaction was incomplete even after 72 hours and many side products were formed.



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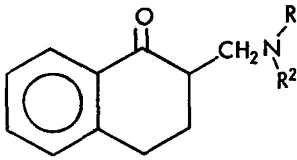
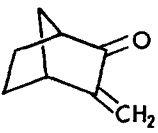


8 $R^1 = R^2 = C_2H_5$

13 $R^1 = R^2 = CH_2C_6H_5$

14 $R^1 = CH_3$; $R^2 = CH_2C_6H_5$



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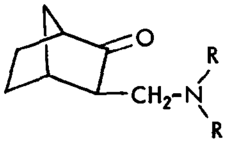

10 $R = C_2H_5$

11 $R = C_4H_9$

12 $R = CH_2C_6H_5$

Application of this alumina-catalyzed addition to several secondary amines suggests its general scope. For example, treatment of dibutylamine and dibenzylamine with 3-methylene-2-norbornanone (9) in the presence of alumina for two hours afforded the addition products 11 and 12 as oils in isolated yields of 68% and 59%, respectively. Similarly treatment of 2-methylene-1-tetralone with dibenzylamine and N-methyl benzylamine afforded compounds 13 (mp. 122.5-124.5°) and 14 (HCl salt: 223-236°dec.) in 90% yields, respectively. These reactions did not proceed within two hours in the absence of alumina.

Attempts to extend this alumina-catalyzed addition of diethylamine to various α,β-unsaturated carbonyl compounds (e.g., mestiyl oxide, itaconic ester, β-ionone, and coumarine) were unsuccessful. In the case of 2-cyclohexen-1-one, addition of diethylamine was five times faster in the presence of alumina than without. The results obtained from this study demonstrate that alumina acts as an efficient catalyst for the addition of secondary amines to exocyclic α,β-unsaturated ketones.

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REFERENCES AND NOTES

1. G. H. Posner, Angew. Chem. Int. Ed. Engl., 17, 487 (1978).
2. G. Germain, P. Main, and M. M. Woolfson, Acta Crystallogr., A27, 368 (1971).
3. J. M. Stewart, Ed., The X-Ray System - Version of June 1971 (Technical Report TR-446, Computer Science Center, University of Maryland, College Park).
4. Supplementry X-ray material is submitted for deposition at the Cambridge Crystallographic Data Centre.
5. New compounds were characterized by MS, IR, ^{1}H, and ^{13}C NMR spectra.
6. E. Merck neutral alumina (90 active 70-230 mesh) for column chromatography was adjusted to activity III by addition of the appropriate amount of water.
7. 2-Methylene-1-tetralone, mp. 43-45°, was prepared according to the method of Jean-Louis Gras, Tetrahedron Lett., 2111 (1978). It is unstable in solution and in the solid state, rapidly forming a dimer, mp. 107-108°. 2-Methylene-1-tetralone gave the following ^{13}C signals: 187.2, 144.0, 143.3, 133.3, 132.9, 128.4, 127.9, 126.8, 121.4, 31.5,and 29.5 ppm.
8. 3-Methylene-2-norbornanone was obtained from Aldrich Chemical Company, Inc., Milwaukee, Wisconsin.

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