

Diels-Alder Reaction of 1-Methyl-4-substituted-2(1H)-pyridones with Alkyl-1,3-butadiene
 ----- A Novel Synthesis of Isoquinoline Derivatives -----

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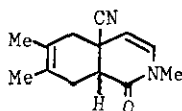
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We wish to report the first successful Diels-Alder reaction of 1-methyl-4-substituted-2(1H)-pyridones used as dienophiles. This reaction will be an advantageous synthetic method for isoquinoline derivatives.

Reaction of 4-cyano-1-methyl-2(1H)-pyridone (I) with 2,3-dimethyl-1,3-butadiene (II) at 170° for 96 hr gave cis-4a-cyano-4a,5,8,8a-tetrahydro-2,6,7-trimethyl-1(2H)-isoquinolone (III) in 71.6% yield and at 190° gave III (31.0%), trans-4a-cyano-4a,5,8,8a-tetrahydro-2,6,7-trimethyl-1(2H)-isoquinolone (IV) (7.5%), and 2,6,7-trimethyl-1(2H)-isoquinolone (17.6%). Heating of 4-methoxycarbonyl-1-methyl-2(1H)-pyridone (V) with II afforded cis-4a,5,8,8a-tetrahydro-4a-methoxycarbonyl-2,6,7-trimethyl-1(2H)-isoquinolone (VI) in 85.3% yield. [cf. H.Kato, R.Fujita, H.Hongo, and H.Tomisawa, *Heterocycles*, 12, 1(1979)].

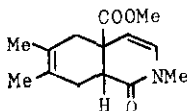
Reaction of I with isoprene (VII) at 190° for 96 hr gave four kinds of crystals, cis- and trans-4a-cyano-4a,5,8,8a-tetrahydro-2,7-dimethyl-1(2H)-isoquinolone and cis- and trans-4a-cyano-4a,5,8,8a-tetrahydro-2,6-dimethyl-1(2H)-isoquinolone, but the yields of these products were only 4.0%, 3.4%, 1.3%, and 1.7%, respectively. Heating of V with VII at 190° afforded cis-4a,5,8,8a-tetrahydro-4a-methoxycarbonyl-2,7-dimethyl-1(2H)-isoquinolone (VIII) in 50.5% yield. Treatment of VIII with LDA gave the more stable isomer, trans-4a,5,8,8a-tetrahydro-4a-methoxycarbonyl-2,7-dimethyl-1(2H)-isoquinolone (IX), in 68% yield. Dehydrogenation of VIII and IX afforded 2,7-dimethyl-1(2H)-isoquinolone.

The structures of these products were confirmed by their spectral comparisons and their stereochemical considerations (Alder-Stein rule, cis principle).

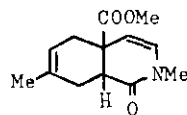


III : cis

IV : trans



VI



VIII