THERMAL TRANSFORMATIONS OF 7-ARYL-1,6-DIAZABICYCLO[4.10]HEPTANES AND 6,13-DIARYLPERHYDRODIPYRIDAZINO-[1,2-a:1',2'-d]-1,2,4,5-TETRAZINES*

Yu. B. Koptelov and A. I. Ukolov

The thermolysis of 7-aryl-1,6-diazabicyclo[4.1.0]heptanes in the absence of 1,3-dipolarophiles leads to dimers of the initially formed azomethineimines, namely, 6,13-diaryloctahydridipyridazino[1,2-a:1',2'-d]-1,2,4,5-tetrazines. The thermolysis of such diaziridines in the presence of N-arylmaleimides leads predominantly to the trans cycloaddition adducts. The trans adducts are the only products of the thermolysis in the presence of 2,6-disubstituted N-phenylmaleimides. The cis adducts predominated in the thermolysis of 6,13-diaryloctahydridipyridazino[1,2-a:1',2'-d]-1,2,4,5-tetrazines in the presence of N-arylmaleimides without substituents in the ortho position of the benzene ring.

**Keywords:** azomethineimine, N-arylmaleimide, 1,6-diazabicyclo[4.1.0]heptane, tetrazine, 1,3-dipolar cycloaddition.

Azomethineimines are a convenient synthone for obtaining five-membered heterocycles with two nitrogen atoms. These reagents undergo 1,3-dipolar cycloaddition, permitting the formation of polyfunctional pyrazole derivatives, including polycyclic systems already with several new chiral sites in a single synthetic step [1]. Readily available 1, (n+2)-diazabicyclo[n.1.0]alkanes serve as precursors for reactive azomethineimines: the thermal opening of the diaziridine fragment, for example, in 1,5-diazabicyclo[3.1.0]hexanes, which occurs above 100°C at the carbon–nitrogen bond, leads to unstable cyclic azomethineimines. Under the reaction conditions, these cyclic species may either isomerize to give the corresponding 2-pyrazolines [2] or, in the presence of active 1,3-dipolarophiles, give products of 1,3-dipolar cycloaddition [3-5]. The steric interactions between the reagent and substrate in the *endo* or *exo* approach of the 1,3-dipolarophile are probably the determining factor in the steric selectivity of the cycloaddition leading to *trans* isomers as the major products [6].

In the present work, we studied possible changes in the reactivity and direction of stabilization of the intermediate labile azomethineimines as well as the steric selectivity of the cycloaddition of N-arylmaleimides with increasing size of the N,N'-polymethylene bridge in going from 6-aryl-1,5-diazabicyclo[3.1.0]hexanes studied in our previous work to 7-aryl-1,6-diazabicyclo[4.1.0]heptanes 1a-c obtained according to Kuznetsov et al. [7].

* Dedicated to the memory of A. A. Potekhin.
The thermolysis of diaziridines 1a,b in p-xylene for 1 h gave good yields of 6,13-diarylocta- 
hydrodipyridazino[1,2-α:1′,2′-d]-1,2,4,5-tetrazines 2a,b instead of 1-arylmethyl-1,4,5,6-tetrahydrodipyridazines 
3a and 3b expected by analogy to the thermolysis of 1,5-diazabicyclo[3.1.0]hexanes. Nevertheless, the 1H NMR 
spectrum of the reaction mixture obtained in the thermolysis of 1b shows signals for benzylic protons 
(4.17 ppm) and imino group protons (6.74 ppm) of 3b present in trace amounts [8]; these signals correspond to 
the literature values.

The stabilization of the azomethineimines formed in the thermal opening of the diaziridine ring in 1a 
and 1b by dimerization rather than a [1,4-H] shift was somewhat unexpected since we observed dimerization 
for 1,5-diazabicyclo[3.1.0]hexanes only in the catalytic opening of the diaziridine fragment [9, 10]. According to 
literature data [11, 12], dimer 2b has been obtained in the reaction of benzaldehyde with hexahydropyridazine. 
We should note that, under conditions similar to those used for obtained 1a-c, a dimer of the corresponding 
azomethineimine, namely, 6,13-bis(4-methoxyphenyl)octahydrodipyridazino[1,2-α:1′,2′-d]-1,2,4,5-tetrazine (2c, 
R = OMe) was also obtained from anisaldehyde instead of the diazabicycloheptane.

Carrying out the thermolysis of diazabicycloheptanes 1a-c for 40 min in p-xylene at reflux in the 
presence of an equimolar amount of N-arylmaleimides 4a-g gave adducts 5a-m and 6a-d in total preparative 
yields of 66-91%.

The relative trans configuration of adduct 5m was established using the NOESY 2D 1H NMR spectrum. 
The major through-space interactions between the protons of this compound seen as the corresponding cross 
peaks are given in the scheme below. The most important such peak here is observed for the interaction between 
the proton at 3.60 ppm and the methyl protons at 2.16 ppm, which is possible only for the trans isomer.