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REGIOSELECTIVITY AND SPECIFICITY IN CYCLOADDITION OF DIPHENYLNITRILIMINE

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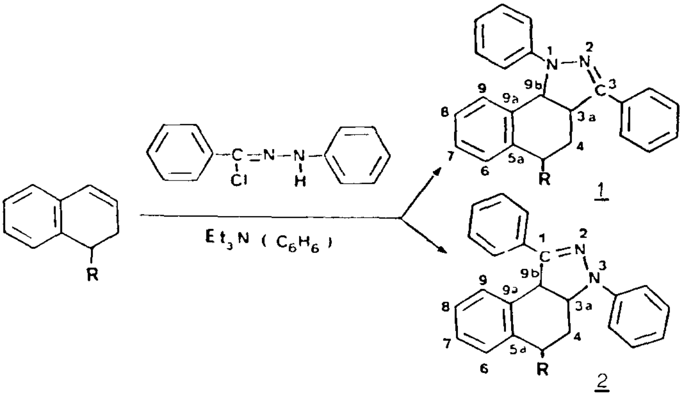
Diphenylnitrilimine cycloaddition reactions on 1,2-dihydronaphtalenes are only regioselective. Use of 1- or 2-tetralones enamines as dipolarophiles allows to attain regiospecificity.

According to HUISGEN et al. (1) cycloaddition of diphenylnitrilimine (DPNI) on 1,2-dihydronaphtalene should be regiospecific to give 1,3-diphenyl 3a,4,5,9b-tetrahydro benzo(g)indazole 1a.



1a : δH^{9b} = 5,01 ppm (d)
δH^{3a} = 3,93 ppm (ddd)
JH^{9b} - H^{3a} = 10,5 Hz

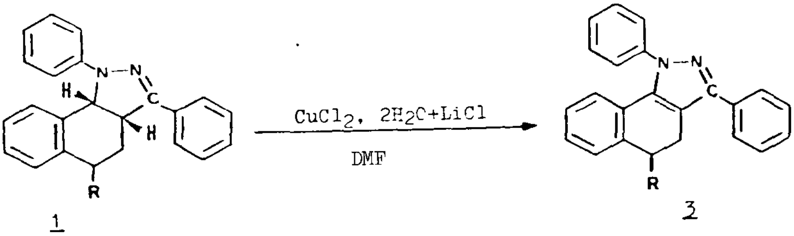
2a : δH^{9b} = 4,95 ppm (d)
δH^{3a} = 4,75 ppm (ddd)
JH^{9b} - H^{3a} = 11,5 Hz

R=H, mixture 1a (80) + 2a (20), m.p. 148-150 °C, yield 75 %
R=Me, mixture 1b (84) + 2b (16), m.p. 168-170 °C, yield 70 %
R=Ph, mixture 1c (80) + 2c (20), m.p. 186-187 °C, yield 50 %.

However, we observed that reaction is not regiospecific but regioselective. Thus, the high field H^1 NMR spectrum -CAMECA 250 MHz (2) of the reaction mixture dissolved in deuteriobenzene shows two types of signals corresponding to regioisomers 1a and 2a (80/20).

This regioselectivity also observed with monosubstitued 1,2-dihydronaphtalenes (R=Me, Ph) which give also a mixture of regioisomers 1 and 2. High field H^1 NMR spectrum of these mixtures presents in addition signals of a third product in small quantities. We assume that these signals implie the existence of two diastereoisomers (R exo and endo) of the predominant regioisomer (3).

Successive cristallisations allow separating predominant regioisomer 1, which treated with cupric chloride and lithium chloride according to HALTON and MORRISON (4), yields by heteroaromatization more than 90 % 1,3-diphenyl 4,5-dihydrobenzo(g)indazoles 3.



R=H 3a m.p. 172 °C
R=Me 3b m.p. 163 °C
R=Ph 3c m.p. 153 °C

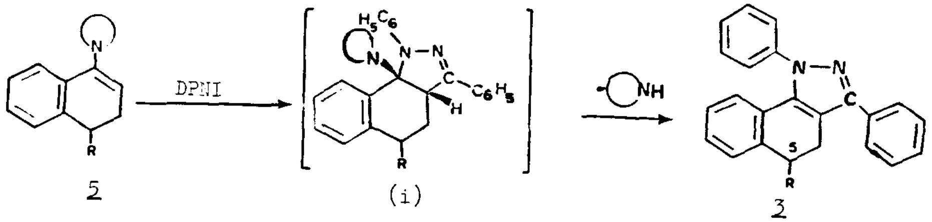
Treatment of cycloadducts (1+2) mixture by this reaction leads to the two products (3+4) in the same proportion. But the two diastereoisomers of one regioisomer lead to a single heteroaromatized compound since this reaction eliminates diastereoisomerism.

We, then, advantageously modified the dipolarophile to try at the same time :

- to make the reaction regiospecific,
- to obtain heteroaromatized benzoindazole by a "one step, one pot" reaction.

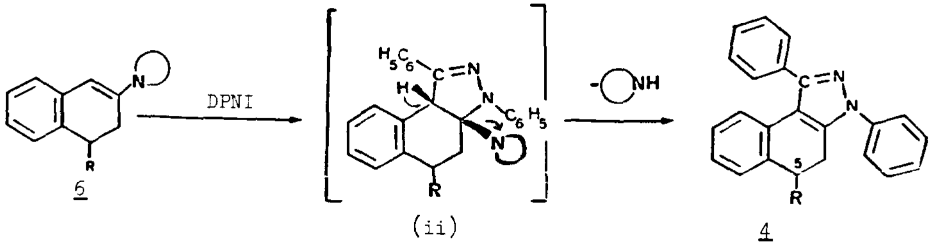
In order to obtain this double objective, we used 1- and 2-tetralones enamines as dipolarophiles. This choice was based on previous results (5,6) which shows that a secondary amino group is a very good leaving group in cycloaddition reactions.

1) DPNI-cycloaddition on enamines of 1-tetralones leads to benzo(g)indazoles 3 as follows :



R=H, 3a, m.p. 172 °C, yield 70 %
R=Me, 3b, m.p. 163 °C, yield 40 % after chromatography, δCH_3=1,33 ppm(d),JCH_3-H^5=7Hz.

2) DPNI-cycloaddition on enamines of 2-tetralones yields more than 70 % benzo(e)indazoles 4 :



R=H, 4a, m.p. 141 °C, yield 75 %
R=Me, 4b, m.p. 168 °C, yield 72 %, δCH_3=1,23 ppm (d), JCH_3-H^5=7 Hz.
R=Ph, 4c, m.p. 187 °C, yield 72 %.

It is interesting to note that whatever the amino group of the enamines, cycloaddition leads to the same result. The reactions were all carried out with either pyrolydinyl, morpholinyl and piperidinyl groups. 1-tetralones enamines 5 were prepared by the method of STORK et al. (7) and those of 2-tetralones 6 according to ELDLUND and BERGSON (8,9).

CONCLUSION

DPNI-cycloaddition reactions on 1,2-dihydronaphtalenes lead to mixtures of isomers (theoretically four) since these reactions are only regio- and diastereoselective. By oxydation of these mixtures, two isomers of dihydrobenzoindazole are obtained. The great interest in DPNI reactions on 1- or 2-tetralone enamines lies in the fact that it is possible to obtain regiospecifically and directly the dihydrobenzoindazole 3 or 4.

REFERENCES AND REMARKS

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(3) When there is a R-group at 1 on the dihydronaphtalene, it is necessary to assume two different approachs of the dipole. Then, the reaction is at the same time regio and diastereoselective. Stereoselectivity is now being studied.
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(9) Preparations of these enamines will be published soon.

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