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CONSECUTIVE [1,5]-SIGMATROPIC AND DISSOCIATION-RECOMBINATION PROCESSES IN REARRANGEMENTS OF 3-SUBSTITUTED 3-ACYL-3H-INDAZOLES TO 1-ACYLINDAZOLES

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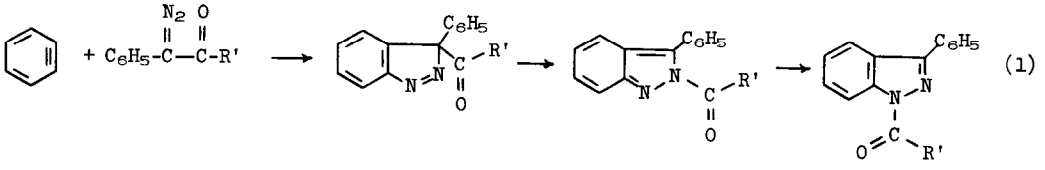
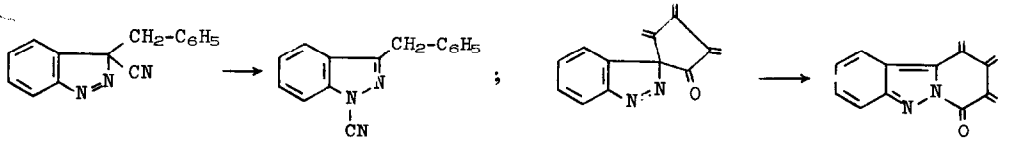
Benzyne (1) reacts with azibenzil (2) at 41° to yield 1-benzoyl-3-phenylindazole (2c);[1a] the 1,3-dipolar adduct (2a) presumably formed initially undergoes 1,3-rearrangement or/and successive 1,2-migrations of its benzoyl group to give 2c.[1a,b] Thermal isomerization of 3-benzyl-3-cyanoindazole (3) is analogous to that presumed for 2a in that 3-benzyl-1-cyanoindazole (3a) is produced;[1c] 3-benzyl-2-cyanoindazole is not observed in the rearrangement sequence. α-Diazocycloalkanones also add to 1; the intermediate spiroindazoles (such as 4) are not detectable because they convert so rapidly to 2-acylindazoles (4a)[1b] or bimolecular or polymolecular derivatives.[1d] Spiroindazoles such as 4 cannot undergo 1,3-rearrangement because of strain in the products. The facile isomerizations of 4 to 4a have led to the supposition that their 1,2-rearrangements are of the [1,5]-sigmatropic type.[1b,d]



(1)

1	2, R'=C_6H_5	2a	2b	2c
	5, R'=p-CH_3O-C_6H_4	5a	5b	5c
	6, R'=CH_3	6a	6b	6c



3 3a 4 4a

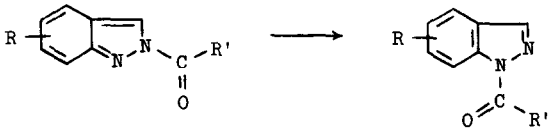
A study is now reported of (1) reactions of various acyclic α-diazoketones with 1 and (2) the products, kinetics, and pathways of isomerization of 2-acylindazoles to 1-acylindazoles. The objectives of this investigation are to provide information with respect to the mechanisms of isomerization of 3-substituted 3-acyl-3H-indazoles.

The behavior of 2 with 1,[2] as generated from benzenediazonium carboxylate in methylene chloride, has been reexamined. In all experiments 2c (mp 168-169°; >C=O at 1690 cm^{-1}) is the principal product (60-90%) and 2a could not be observed. At 25° and 2 hr reaction times, however, 2-benzoyl-3-phenylindazole[3] (2b, mp 120-122°; >C=O at 1720 cm^{-1}) can be isolated (4%). On warming 2b isomerizes quantitatively to 2c.[4a]

Addition of p-anisoylphenyldiazomethane (5) to 1 was then studied. 3-p-Anisoyl-3-phenyl-3H-indazole (5a) might be isolable and 2-p-anisoyl-3-phenylindazole (5b)[3] might isomerize so slowly that it would be a major product. Indeed reaction of 5 and 1 yields 5b as the principal product along with 1-p-anisoyl-3-phenylindazole[3] (5c, 14%; mp 130.5-132°, >C=O at 1750 cm^{-1}). Indazole 5a was not observable however, and it was not clear whether 5c was formed by rearrangement of 5a or/and 5b. Isomerization of 5b to 5c does occur (~ 100%) on heating.

1-Diazo-1-phenyl-2-propanone (6) reacts with 1 at 41° to give 2-acetyl-3-phenylindazole (6b, 67%; mp 100-100.5°, >C=O at 1755 cm^{-1});[3] neither 3-acetyl-3-phenyl-3H-indazole (6a) nor 1-acetyl-3-phenylindazole[3] (6c) is obtained. Heat rearranges 6b to 6c (mp 59-61°). Exclusive conversion of 6 and 1 to 6b provides strong support to the proposal[1b] that 1,2-rearrangement of indazoles such as 6a occurs by an intramolecular [1,5]-sigmatropic process.

The mechanisms of rearrangement of 2-acylindazoles were then studied.[4] 2-Acylindazoles 7-10 isomerize quantitatively to 1-acylindazoles 11-14, respectively, on heating. The rearrangements are not affected by light, oxygen, or cumene and do not exhibit behavior for free



7	R=H; R'=CH_3	11
8	R=5-NO_2; R'=CH_3	12
9	R=6-NO_2; R'=CH_3	13
10	R=6-NO_2; R'=C_2H_5	14
18	R=3-C_6H_5; R'=C_2H_5	19

radical processes. The isomerizations of 6b and 7-10, respectively, to their corresponding 1-acylindazoles (6c and 11-14) are followable by nmr methods and obey first order kinetics for conversions to products up to 70-90% in various solvents at temperatures ranging from 35-162°. The first order rate constants for rearrangement of 6b and 7-9 are summarized in Table 1. Nitroindazoles 8 and 9 isomerize more rapidly than does 7 and their rate constants for

Table 1

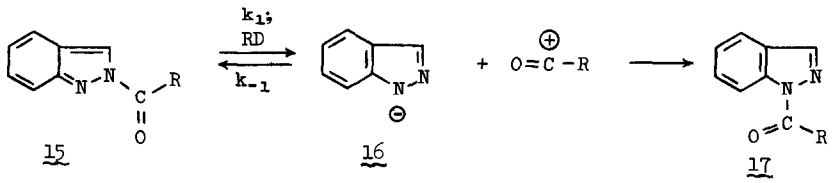
Rate Constants ($k_1 \times 10^{-3}$ min^{-1}) for Isomerization of 2-Acylindazoles to 1-Acylindazoles

Solvent, °	6	7[a]	8	9
C_6H_5Cl, 132°	5.75	8.8	--	6.22
$C_6H_5NO_2$, 132°[b]	7.20	11.4	21.5	21.0
DMSO-D_6, 25°[c]	v. slow	v. slow	109	4.6
C_9H_7N, 132°[c,d]	--	--	--	--

[a]The rate constants for 7 are high because of its response to trace acid catalysts. [b]The relative rate constants for 9 and 7 at 153° and 162° are 1.4 and 1.1, respectively. [c]These rearrangements may involve initial attack of the nucleophilic solvents on the 2-acylindazoles. [d]Quinoline.

rearrangement are significantly increased as the solvent becomes more polar. Isomerization of 2-acylindazoles is catalyzed by carboxylic acids and by boron trifluoride in ethyl ether. In acetic acid as solvent, 9 undergoes accelerated rearrangement by a first order process.

A mechanism for thermal rearrangement of 2-acylindazoles (15) which fits the above observations involves ionization-recombination with appropriate solvent assistance as in Eq 2. Data consistent with this mechanism are that mixtures of 6b and 10 in chlorobenzene at 132° yield (by nmr) the 1-acylindazoles 6c and 14 and the cross-over products 3-phenyl-1-propionylindazole (19), 13, and the 2-acylindazole 9 along with 6b and 10.[5] Under these conditions the 1-acylindazoles formed (6c, 13, 14, and 19) do not isomerize or interchange. The fact that 3-phenyl-2-propionylindazole (18) is not produced from redistribution of 6b and 10 is attributable to steric effects in propionylation of the 3-phenylindazolyl anion and agrees with the observation that 6b has not been preparable from 3-phenylindazole or its conjugate base by acetylation methods.



15 16 17 (2)

The present results thus imply that 3-substituted 3-acyl-3H-indazoles undergo [1,5]-sigmatropic rearrangement to 2-acylindazoles which then isomerize to 1-acylindazoles by heterolytic dissociation-recombination.[6] Intramolecular processes might be preferred by 3-acylindazoles because of favorable sp^3 stereochemistry at the 3-positions for migration of their acyl groups and the much greater nucleophilicity of nitrogen than of carbon. Such processes are not as available to 2-acylindazoles because of the sp^2 stereochemistry at their 2-positions and their migration origins and termini are both nitrogen. As a result of these disadvantageous factors and because of the weakness of their N-acyl bonds, 2-acylindazoles isomerize preferably by ionization-recombination mechanisms.[7]

REFERENCES

1. (a) G. Baum, Ph.D. Thesis, The Ohio State University, Columbus, Ohio, 1965; Diss. Abstr., 27, 97B (1966); 2c (mp 42°) was initially assigned incorrectly as 2a by W. Reid and M. Schon, Ann., 680, 141 (1965); (b) T. Yamazaki and H. Shechter, Tetrahedron Lett., 4533 (1972); (c) R. E. Bernard and H. Shechter, ibid., 4529 (1972); (d) T. Yamazaki and H. Shechter, ibid., 1417 (1973); (e) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, Inc., 114 (1970).
2. L. Friedman and F. M. Logullo, Org. Syn., 48, 12 (1968).
3. All new isolable compounds of the present work gave proper analyses and appropriate ir, uv, nmr, and mass spectra.
4. (a) K. v. Auwers, A. Ernecke, and E. Walter, Ann., 478, 154 (1930) observed that 2-acylindazoles isomerize thermally to 1-acylindazoles and presumed that these rearrangements are intramolecular; (b) prepared by acylation of silver salts of indazole; J. Elguero, A. Fruchier, and R. Jacquier, Bull. Soc. Chim. France, 3041 (1966).
5. Indazoles 7 and 10 exchange at 162° in chlorobenzene or quinoline to products analogous to those from 6b and 10.
6. M. Franck-Neumann and C. Buchecker, Tetrahedron Lett., 937 (1972) report single [1,5]-sigmatropic rearrangements of 3-acyl-3H-pyrazoles to N-acylpyrazoles. The isomerizations of 3-acyl-3H-indazoles are more complex than those of 3-acyl-3H-indazoles.
7. The mechanism of isomerization of 2-acylindazoles is thus quite different from that of sigmatropic rearrangements of N-nitropyrazoles and N-nitro-1,2,4-triazoles to their 3-nitro derivatives; (b) J. W. A. M. Janssen and C. L. Habraken, J. Org. Chem., 36, 3081 (1971); (c) C. L. Habraken and P. Cohen-Fernandes, Chem. Commun., 37 (1972).

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