[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of Ketonization. V. *aci*-Nitro Tautomerism[1]

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2-Phenyl-1-*aci*-nitrocyclohexane (I) has been synthesized. Conversion of this highly unstable intermediate to the nitro isomer has been found to proceed by protonation of its conjugate base to yield preferentially *cis*-1-nitro-2-phenylcyclohexane (IIa). The analogy of *aci*-nitro–nitro tautomerism to enol ketonization is discussed.

Previous studies[2–5] of the ketonization reaction of enols have indicated that in situations where two stereoisomers may result, one frequently observes preferential formation of the less stable isomer, the reaction geometry being controlled by a transition state which closely resembles the enolic reactant and in which steric hindrance to prototopic attack is the controlling factor.

It was of interest to ascertain whether the same situation exists for the formally similar conversion of unstable *aci*-nitro compounds to their nitro tautomers. The 1-nitro-2-phenylcyclohexane system was chosen for this investigation since considerable information for comparison purposes was available from studies[2–5] of the carbonyl analogs.

As a starting material *trans*-4-phenyl-5-nitrocyclohexene (III)[6] proved convenient. This compound, readily obtained from the Diels–Alder reaction of β-nitro-styrene with butadiene, has been shown by Arnold to be *trans*.[7] Catalytic hydrogenation of III with platinum dioxide in acetic acid afforded *trans*-1-nitro-2-phenylcyclohexane (IIb), m.p. 124.0–124.5°.

trans-1-Nitro-2-phenylcyclohexane dissolved in alcoholic potassium hydroxide to yield the conjugate base IV of II. Acidification of this solution of IV with alcoholic sulfuric acid resulted in formation not of IIb but rather of its stereoisomer, *cis*-1-nitro-2-phenylcyclohexane (IIa), m.p. 58.0–58.5°.

Confirmation of these configurational assignments was found in experiments in which an equilibrium mixture containing 99% of IIb and 1% of IIa, as determined by quantitative infrared analysis, resulted by refluxing either IIa or IIb with 95% ethanol saturated with sodium bicarbonate (note runs 3, 4, 5 in Table I).

When the alcoholic solution of the conjugate base IV of 1-nitro-2-phenylcyclohexane was first diluted with water and then acidified at −10° there was precipitated 2-phenyl-1-*aci*-nitrocyclohexane (I), m.p. 82–85° dec. This structural assignment was supported by carbon–hydrogen analysis, by the infrared spectrum which exhibited both strongly bonded O–H stretching and C=N stretching bands and which differed markedly from that of the isomeric nitro tautomers IIa and b, and finally by its conversion (*vide infra*) to the 1-nitro-2-phenylcyclohexane. 2-Phenyl-1-*aci*-nitrocyclohexane (I) could be kept indefinitely by storing in Dry Ice, but was stable at room temperature for less than a day.

TABLE I

Run	Conditions	*cis* isomer, %
1	1-*aci*-Nitro-2-phenylcyclohexane + LiOAc buffer	98 ± 3
2	*cis*-1-Nitro-2-phenylcyclohexane + LiOAc buffer	100 ± 3
3	*cis*-1-Nitro-2-phenylcyclohexane + satd. ethanolic $NaHCO_3$; 4.5 hr. reflux	2 ± 3
4	*cis*-1-Nitro-2-phenylcyclohexane + satd. ethanolic $NaHCO_3$; 1 hr. reflux	1 ± 3
5	*trans*-1-Nitro-2-phenylcyclohexane + satd. ethanolic $NaHCO_3$; 4.5 hr. reflux	1 ± 3

Since *cis*-1-nitro-2-phenylcyclohexane (IIa) resulted from acidification of IV only when no water had been added and hence where 2-phenyl-1-*aci*-nitrocyclohexane (I) would not precipitate, it seemed likely that the *aci*-nitro compound was an intermediate in the formation of the *cis*-nitro isomer IIa. This was reasonable, for prototopic attack at oxygen might be expected to be rapid compared to the rate of attack at carbon.

However, when the *aci*-nitro compound was allowed to react in ethanolic sulfuric acid of varying concentrations or in ethanol alone, IIa did not result. Instead a mixture was obtained which was largely ketonic as determined from the infrared spectrum.

On the other hand, when compound I was dissolved in an ethanolic lithium acetate–acetic acid buffer, designed to convert I largely to its conjugate base, a very rapid and smooth formation of 1-nitro-2-phenylcyclohexane stereoisomers resulted with the complete absence of ketonic products. Quantitative infrared analysis of the product indicated this to contain 98 ± 3% *cis*-1-nitro-2-phenylcyclohexane (IIa) (note Table I).

Thus it is clear that it is the conjugate base IV of I and not I itself which undergoes prototopic attack to yield the nitro tautomer.[8,9a,b] This is not

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[1] Presented at the Organic Division, A.C.S. Meeting, New York, N. Y., September, 1957.

[2] H. E. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955).

[3] H. E. Zimmerman, THIS JOURNAL, **78**, 1168 (1956).

[4] H. E. Zimmerman and H. J. Giallombardo, *ibid.*, **78**, 6259 (1956).

[5] H. E. Zimmerman, *ibid.*, **79**, 6554 (1957).

[6] W. C. Wildman and R. B. Wildman, *J. Org. Chem.*, **17**, 581 (1952).

[7] R. T. Arnold and P. N. Richardson, THIS JOURNAL, **76**, 3649 (1954).

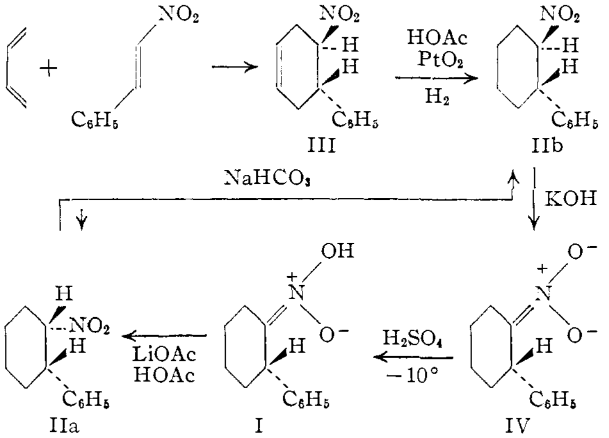
[8] R. G. Pearson and R. L. Dillon, *ibid.*, **72**, 3574 (1950), have presented kinetic evidence that tautomerism of *aci*-nitroethane proceeds by attack of a proton donor on the *aci*-nitro salt.

[9] (a) M. F. Hawthorne, *ibid.*, **79**, 2510 (1957), has shown that the Nef reaction is first order each in hydrogen ion and in *aci*-nitroalkane. Thus tautomerism is favored over Nef hydrolysis by increasing concentration of the *aci*-nitro conjugate base relative to the concentration of the *aci*-nitro compound itself; (b) N. Kornblum and G. Graham, *ibid.*, **73**, 4041 (1951) have pointed out the necessity of addition of the acid to the *aci*-nitro salt rather than the reverse for regeneration of the nitro compound from the salt.

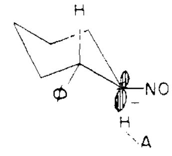
surprising, since attack of a proton donor on the α-carbon atom of an anionic species such as IV would be expected[10] to be rapid compared to attack on the neutral molecule (*e.g.*, I).

The formation, described above, of *cis*-1-nitro-2-phenylcyclohexane (IIa) by acidification over several minutes of the conjugate base IV with insufficient water present for precipitation of the intermediate 2-phenyl-1-*aci*-nitrocyclohexane (I) emphasizes the rapidity of the tautomerism process. Had the formation of IIa not been essentially complete by the end of the neutralization with sulfuric acid, the remaining unreacted molecules would have been trapped as 2-phenyl-1-*aci*-nitrocyclohexane (I) which has been shown (*vide supra*) not to yield nitro isomer in absence of the conjugate base (IV).

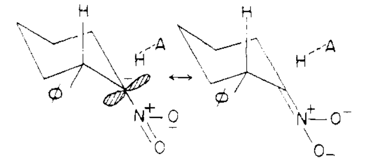
CHART I



Of interest is the preferential formation of the less stable stereoisomer Ia in analogy to the stereochemistry of ketonization. From this result it may be concluded that the transition state for protonation of the *aci*-nitro salt IV[11] is essentially sp^2-hybridized (as VI); thus delocalization of the bonding electrons is energetically important and these have not been localized in an incipient σ-orbital (as in V). Were this latter possibility correct the nitro group would demand the equatorial conformation. With trigonal hybridization, however, the nitro group does not compete sterically, leaving prototopic attack as the controlling factor.



V



VI

Experimental[12]

4-Phenyl-5-nitrocyclohexene was prepared essentially according to the method of Wildman and Wildman[6] from 30 g. of β-nitrostyrene, 60 g. of butadiene and 100 mg. of hydroquinone in 50 ml. toluene at 100° for 48 hours.

***trans*-1-Nitro-2-phenylcyclohexane.**—Hydrogenation of 9.72 g. of 4-phenyl-5-nitrocyclohexene in 75 ml. of ethyl acetate and 75 ml. of acetic acid with 40 mg. of platinum oxide was carried out in a modified Parr apparatus. After the theoretical uptake and a cessation of hydrogenation the solution was filtered and concentrated to yield 7.65 g. of material, m.p. 123.5–124.0°; an additional 2.00 g. was obtained by dilution of the filtrate with water. Recrystallization from ligroin (b.p. 86–100°) gave a total of 9.18 g. of *trans*-1-nitro-2-phenylcyclohexane, m.p. 124.0–124.5°.

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.30. Found: C, 69.96; H, 7.51.

***cis*-1-Nitro-2-phenylcyclohexane.**—One gram of *trans*-1-nitro-2-phenylcyclohexane was converted to the soluble potassium salt by swirling with 2.80 g. of 20% ethanolic potassium hydroxide for 15 minutes. The clear yellowish solution was cooled to −5° and with good stirring at this temperature was acidified with a 1:3 sulfuric acid–ethanol mixture until a congo red end-point was reached. After three minutes more the solution was diluted with 15 ml. of water and filtered. The crude product was crystallized from ether–hexane to yield 0.45 g. of material, m.p. 57.0–58.0°. Further crystallization brought the melting point of *cis*-1-nitro-2-phenylcyclohexane to 58.0–58.5°.

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.30. Found: C, 70.18; H, 7.39.

***aci*-Nitro Tautomer of 1-Nitro-2-phenylcyclohexane.**—One gram of *trans*-nitro-2-phenylcyclohexane was dissolved in 2.80 g. of 20% ethanolic potassium hydroxide. The clear yellow solution was diluted with 60 ml. of water and was cooled in a methanol–Dry Ice-bath to −10°. With mechanical stirring at this temperature, the solution was acidified to a congo red end-point with 1:3 sulfuric acid–ethanol. The resulting colorless crystalline material was filtered at once, washed once with cold water, taken up in chloroform, separated from the small amount of water present, diluted with hexane and chilled in Dry Ice. The material which crystallized was filtered. This weighed 0.3 g., m.p. 81–83° dec. Concentration of the cold chloroform filtrate to *ca.* 30% of its original volume and again cooling in Dry Ice gave an additional 0.4 g., m.p. 82–85° dec. Recrystallization of the combined material from chloroform–hexane by chilling in Dry Ice gave a yield of 0.60 g. of 2-phenyl-1-*aci*-nitrocyclohexane, m.p. 84.0–86.0° dec.

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.30. Found: C, 69.93; H, 6.91.

This material was stable indefinitely at Dry Ice temperatures, but decomposed within a day at room temperature. The infrared spectrum exhibited the expected broad, strongly bonded OH stretching absorption (2.9–3.8 μ) and C=N absorption at 6.01 μ.

Isomerization of *aci*-Nitro Isomer.—A lithium acetate buffer was prepared by dissolving 2.04 g. of lithium acetate and 0.12 g. of acetic acid in 10.0 ml. of 95% ethanol and

TABLE II

KNOWN MIXTURES

Run	Actual % *cis* isomer	$D_{11.11\mu}$	$D_{11.92\mu}$	Calcd., %
1	0	0.382	0.034	..
2	25.0	.328	.102	22.8
3	50.0	.260	.184	49.3
4	75.0	.187	.280	77.8
5	100	.131	.372	..

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[10] Proton transfer from a donor HA to the α-carbon atom of either I or IV may be envisioned as a nucleophilic attack of either I or IV on the hydrogen atom of HA with concerted loss of A^-. While it has not been established whether the rates of such processes are better related to the basicity or the nucleophilicity of the attacking species, it is nevertheless certain that IV, being a much stronger base and almost certainly a better nucleophile, will react at a greater rate than I.

[11] This transition state, which is depicted as involving protonation of the conjugate base of the nitro compound, differs from that for ketonization of enols as depicted by C. G. Swain (THIS JOURNAL, **72**, 4578 (1950)) and W. D. Emmons and M. F. Hawthorne (*ibid.*, **78**, 5593 (1956)) for the reverse reaction; the enolate is considered not to be an intermediate. This dichotomy is not unreasonable, for while the *aci*-nitro compound might be expected to ionize extensively (pK_A 2-*aci*-nitropropane = 4.41 (D. Turnbull and S. H. Maron, *ibid.*, **65**, 212 (1943)) the concentration of enolate ions available for anion protonation would be much smaller except in the presence of very strong bases (*e.g.*, pK_A acetone enol $\cong$ 14.4).

[12] All melting points were taken on a Fisher-Johns block checked with known compounds.

1.30 ml. of water. Then 0.0638 g. of the *aci*-nitro compound was dissolved in 7.5 ml. of the buffer solution. At the end of 15 minutes at room temperature the reaction mixture was diluted with 20 ml. of water, ether extracted, and the extracts washed with bicarbonate and then water. The dried extracts on concentration yielded material analyzing with quantitative infrared for 98% *cis*-1-nitro-2-phenylcyclohexane and free of carbonyl impurity.

Equilibration of the 1-Nitro-2-phenylcyclohexanes.—To 50 ml. of 95% ethanol was added 50 mg. of sodium bicarbonate and the mixture was heated to boiling; the saturated solution was decanted from undissolved solid. To 5.0 ml. of the saturated bicarbonate solution was added 45 mg. of *cis*-1-nitro-2-phenylcyclohexane. The solution was refluxed for four hours. Dilution with water followed by ether extraction, drying and concentration led to the equilibrated mixture which was analyzed by quantitative infrared. This indicated 99% *trans* isomer. Similar equilibration of the *trans* isomer gave a mixture containing 1% *cis* isomer and 99% *trans*.

The solubility of sodium bicarbonate in hot 95% ethanol (*ca.* 1 mg./25 ml.) was low enough to ensure the presence of only catalytic quantities.

Quantitative infrared analyses were performed by the method described previously.[5] The analytical wave lengths were 11.11 μ, characteristic of the *trans* isomer, and 11.92 μ, characteristic of the *cis* compound. All runs were made in chloroform in 0.10-mm. cells at a total concentration of 40 mg./0.20 ml. of solvent.

EVANSTON, ILLINOIS

COMMUNICATIONS TO THE EDITOR

TRIPHENYLCHROMIUM[1]

Sir:

We wish to report the preparation and properties of the first isolable[2] member of a series of covalent organo-chromium compounds, **triphenylchromium,** $(C_6H_5)_3Cr(III)$.[3] This blood-red crystalline substance is deposited from tetrahydrofuran, after reaction of chromic trichloride and phenylmagnesium bromide in a mole ratio of 1:3 at −20° in the same solvent, as a tetrahydrofuranate $(C_6H_5)_3$-$Cr(THF)_3$ (I) (*Anal.* Calcd.: Cr, 10.4. Found: Cr, 10.2), or combined with magnesium halide tetrahydrofuranate, $(C_6H_5)_3Cr(THF)_3 \cdot 3[MgBrCl(THF)]$ (II) (*Anal.* Calcd.: Cr, 4.58. Found: Cr, 4.62), depending upon the initial concentration of the reactants. The magnesium salt may be removed from II by diluting a tetrahydrofuran solution of II with diethyl ether which causes concurrent separation of I from the solution.

I and II are chemically similar in that they are inordinately sensitive to moisture, hydrolyzing instantaneously to green $Cr(H_2O)_6^{+++}$. In tetrahydrofuran solution they are cleaved rapidly by mercuric chloride and yield quantitatively three moles of pure phenylmercuric chloride, m.p. 266–267°, for each chromium atom present in I or II (*Anal.* 2.29 g. (2.02 mmoles) of II yields 1.94 g. (6.19 mmoles) of C_6H_5HgCl and 0.105 g. (2.02 mmoles) of Cr^{+++}. Calcd.: C_6H_5/Cr, 3/1; C_6H_5, 20.4; Cr, 4.58. Found: C_6H_5/Cr, $3.0_6/1$; C_6H_5, 20.8; Cr, 4.58), the red color of $(C_6H_5)_3Cr(THF)_3$ in either case changing to the violet color of $Cr(THF)_6^{+++}$. A sample of II has been found to be strongly paramagnetic to the extent of 3.89 Bohr magnetons in agreement with a chromium valency of 3.[4]

Further evidence for the identities of I and II is derived from the loss of tetrahydrofuran from these substances either by heating at atmospheric pressure, by vacuum at room temperature or by washing with diethyl ether. II loses 39.3% of its weight, corresponding to a loss of 6 moles (38.0%) of tetrahydrofuran, while I gives up 41.5% or 3 moles (43.3%) of tetrahydrofuran per mole of formula molecular weight. In both instances the red color of I and II is lost also, and a black solid is formed (from II, admixed with white magnesium salt) which on hydrolysis under nitrogen with oxygen-free water yields **bis-benzenechromium(0)** and **benzene-biphenylchromium(0)** directly in approximately equal amounts. Air oxidation of a benzene solution of these complexes permits their transference to aqueous solution as cations and precipitation as tetraphenylborates for yield and further identity determinations.

The rearrangement of I and II in diethyl ether to the completely reduced forms of the chromium complexes, showing that triphenylchromium has a short life in this solvent, has led to a re-examination of the original Hein reaction between chromic trichloride and phenylmagnesium bromide in diethyl ether.[5] The primary products of this reaction, after hydrolysis *under nitrogen*, are found to be the same completely reduced complexes. This remarkable rearrangement of a covalently bonded structure to that of a π-complex will be the subject of forthcoming papers.

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[1] Paper IV, "π-Complexes of the Transition Metals"; Paper III, M. Tsutsui and H. H. Zeiss, *Naturwissenschaften*, **44**, 420 (1957).

[2] F. A. L. Anet and E. Leblanc, THIS JOURNAL, **79**, 2649 (1957), report the existence of $Cr(H_2O)_5CH_2Ph^{++}$ in solution.

[3] This term was first applied by F. Hein and E. Markert, *Ber.*, **61**, 2255 (1928), to the compound now recognized to be benzene-biphenylchromium(0).

[4] We are indebted to Dr. R. B. Johannesen of the National Bureau of Standards, Washington, D. C., for this and other magnetic measurements.

[5] H. H. Zeiss and M. Tsutsui, THIS JOURNAL, **79**, 3062 (1957).

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RECEIVED NOVEMBER 15, 1957

FLAVONOIDS OF CITRUS. II. ISOLATION OF A NEW FLAVONOL FROM LEMONS

Sir:

The enzymatic (hemicellulase) hydrolysis of a preparation[1] of the flavonoid glycosides of lemon peel affords a complex mixture of aglycones.

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[1] "Calcium Flavonate Glycoside, Lemon," purchased from Sunkist Growers, Ontario, California. The use of this material is not intended as an endorsement by the Department of Agriculture.