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REARRANGEMENT OF α-(*p*-NITROPHENYL)-ALLYL CHLORIDE

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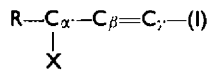
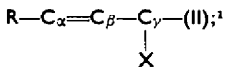
Abstract– α-(*p*-Nitrophenyl)-allyl chloride (IV) reacts with aliphatic amines yielding α-chloro-β-methyl-*p*-nitrostyrene (VI) as the major product and *p*-nitrophenyl-cinnamylamine (VII) corresponding to the amine employed. The unexpected formation of VI, involving a $C_\alpha \rightarrow C_\gamma$ proton transfer, is considered an electrophilic rearrangement on the basis of the reaction of IV with an N-deuterated amine. Kinetical studies of the rearrangement IV → VI are also reported.

SUBSTANCES containing an allylic system



frequently undergo a substitution reaction with amines, in which the product obtained is derived from the isomeric allylic system



a typical example is α-methylallyl chloride which condenses with diethylamine to N,N-diethyl-γ-methylallylamine.[2] The unusual reaction of an allylic halogenide of type I with amines, which yields, besides the allylic amine of type II, an isomer of the starting halogenide derived from a $C_\alpha \rightarrow C_\gamma$ proton transfer, is reported. During an investigation on unsaturated amines an attempt was made to prepare the unknown α-(*p*-nitrophenyl)-allyl chloride (IV). In the synthesis of IV, *p*-nitrocinnamaldehyde[3] was reduced with sodium borohydride to an 88% yield of *p*-nitrocinnamyl alcohol (III) which was then reacted with thionyl chloride in chloroform solution to yield 65% of IV and 15% of *p*-nitrocinnamyl chloride (V).[4] The structures of IV and V were established by the UV and the NMR spectra.[5]

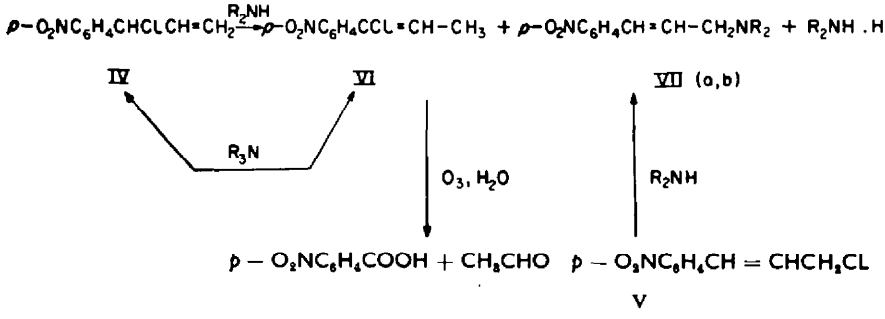
Condensation of IV (1 mole) with diisopropylamine (2 mole) yielded, in addition to diisopropylamine hydrochloride, 15% of N,N-diisopropyl-*p*-nitrocinnamylamine (VIIa) and 73% of a neutral product, $C_9H_8ClNO_2$, m.p. 62–63°, which was identified as α-chloro-β-methyl-*p*-nitrostyrene (VI). Evidence for this structure was obtained by the UV spectrum [λ_{max}^{MeOH} 305 mμ (14,000)] and the NMR spectrum [δ 2·02 (doublet, —CH_3), 6·45 (quadruplet, =CH—), 7·95 (quadruplet, four aromatic protons)].

[1] For a review see: R. H. De Wolfe and W. C. Young, *Chem. Revs.* **56**, 753 (1956).
[2] W. C. Young, I. D. Webb and H. L. Goering, *J. Amer. Chem. Soc.* **73**, 1076 (1951).
[3] S. G. Waley, *J. Chem. Soc.* 2008 (1948).
[4] The *p*-nitrocinnamylalcohol (III) contained about 1% unreacted *p*-nitrocinnamaldehyde. Surprisingly, when pure III was employed for the reaction with $SOCl_2$, the major product (over 70%) was V, whereas only 10–15% of the isomer IV was isolated.
[5] NMR spectra were taken into $CDCl_3$ at 60 Mc/s and chemical shifts are given as δ values (ppm, TMS = 0).

Additional chemical support for VI was based on its unreactivity towards amines (in agreement with the stability of a halogen attached to an ethylenic bond) and on the ozonolysis to *p*-nitrobenzoic acid and acetaldehyde (isolated as 2,4-dinitrophenylhydrazone).

The rearrangement IV → VI also occurs when IV is condensed with piperidine.[6] In this case the greater reactivity of the base—due to the absence of steric hindrance—results in a shorter reaction time and higher yields of VII. In order to rule out the hypothesis that the isomerization IV → VI is purely thermal and that the amines VII could arise from a rearrangement of IV to V before substitution, the stability of IV under the reaction conditions in absence of amines, was ascertained. The structure of compounds VII (a, b) was further confirmed by the identity (m.p. and IR spectrum) with the products isolated by condensing V with the appropriate amines.

It is interesting to note that by allowing IV to react with a tertiary amine (triethylamine), only VI is obtained.

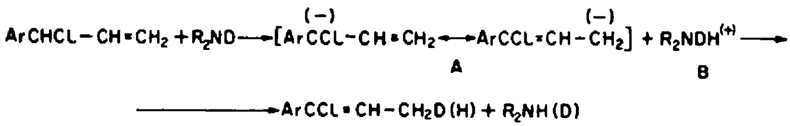


The behavior of IV seems to depend on two competitive factors: the release of the proton at the α-carbon due to the electron attracting *p*-nitrophenyl- and vinyl-groups and the chlorine atom, all attached at this carbon; and the reactivity of the chlorine atom enhanced by the adjacent ethylenic bond. In such a system, two driving forces for rearrangement are therefore possible, inducing, the first, a proton transfer $C_\alpha \rightarrow C_\gamma$ and, the second, an abnormal substitution of the halogen with the amine.

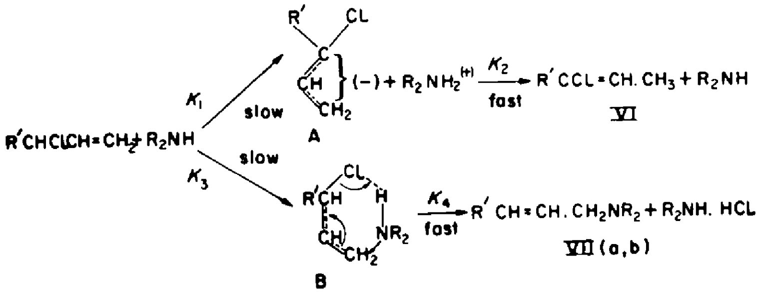
Based on the literature data concerning the condensation of allylic halogenides with amines, the reaction IV → VII may follow an abnormal nucleophilic second order mechanism (S_N2'). For the electrophilic rearrangement IV → VI the hypothesis of an intramolecular mechanism was considered and IV was condensed with a monodeuterated secondary amine. The neutral product obtained showed, after crystallization, the same melting point as VI. However, its NMR spectrum displayed at δ 6·45 an absorption, not well defined and interpreted as due to an overlapping of the =CH—CH_3 one proton quadruplet and the =CH—CH_2D one proton triplet, and an intensity ratio of the —CH_3 and =CH— bands showing the presence of approximately 60% deuterated VI. These results suggest a preliminary base catalysed removal of the C_α-proton of IV with formation of the hybrid carbanion (A) and of the ion R_2NDH^+ (B). Recombination of both the hydrogen and deuterium of B with A occurs on the resonance structure bearing the ethylenic double bond conjugated with

[6] Similar results were observed by employing other primary or secondary amines and solvents like acetone, ethanol, or carbon tetrachloride. (G. Cignarella, E. Occelli and E. Testa, to be published.)

the aromatic ring to give a mixture of deuterated and non-deuterated VI.



An intramolecular mechanism, therefore, seems to be excluded. The following scheme can then explain both competitive reactions IV → VI and IV → VII by assuming the carbanion (A) and the cyclic transition state (B) as intermediate steps for VI and VII respectively.



$R_2 = (iC_3H_7)_2, (CH_2)_5$; $R' = p-O_2NC_6H_4-$

It should be pointed out that when the base is a tertiary amine, the transition state B cannot form and therefore VI is the sole reaction product.

Kinetic studies on the isomerization IV → VI were carried out in benzene in presence of triethylamine, the reaction course being followed by measuring the changing UV absorption. The plot of the logarithm of the substrate concentration (C) at different initial values of C, the base concentration being constant, is reported in Fig. 1. The straight lines obtained suggest that the reaction follows a first order course; the same slope for C ranging from 5×10^{-3} to 5×10^{-2} mol/l. shows that in this range the rate constant (K) is independent of the initial concentration of the substrate ($K = 1{\cdot}2 \times 10^{-2}$ min^{-1}), but for higher C values ($C = 12{\cdot}5 \times 10^{-2}$) it slightly increases. The rate constant is furthermore proportional to the base concentration, as is shown in Fig. 2, where the logarithm of K is plotted against the base concentration, the concentration of the substrate being constant. These features indicate that the isomerization IV → VI is a reaction of pseudo first order.

Proton transfer rearrangements have been described in allylic systems concerning only non-halogenated hydrocarbons (X = H), typical examples being the base-catalysed isomerization of allylbenzene to propenylbenzene[7] and of 3-phenyl-1-butene to 3-phenyl-2-butene[8]. The isolation of VI is, as far as can be ascertained, the first example of prototropic rearrangement involving a carbanion intermediate in a α-substituted allylic halogenide.

EXPERIMENTAL

p-Nitrocinnamyl alcohol (III)

To a solution of 34 g (0·192 mole) *p*-nitrocinnamaldehyde[3] in 1 l. ethanol at 50°, a solution of 2·96 g (0·0778 mole) $NaBH_4$ in 50 ml ethanol was added dropwise. The reaction mixture was stirred

[7] L. Bateman and J. I. Cunneen, *J. Chem. Soc.* 2283 (1951).

[8] D. J. Cram and R. T. Uyeda, *J. Amer. Chem. Soc.* **84**, 4358 (1962).

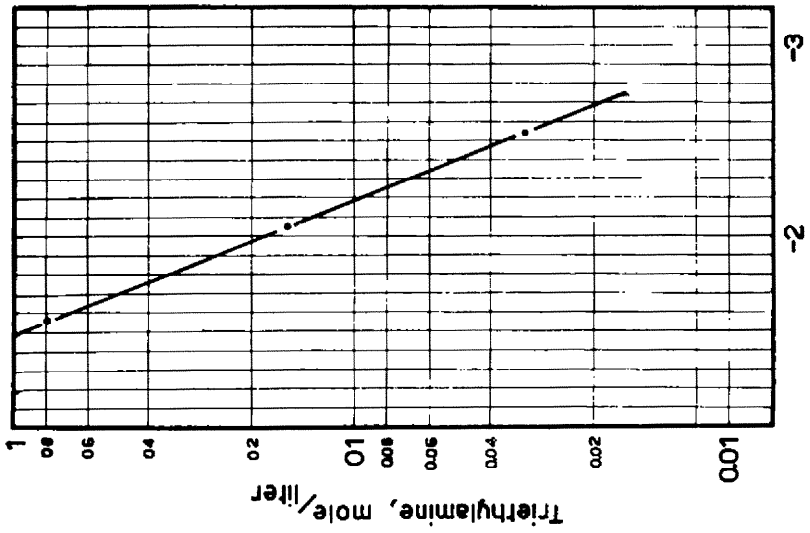


FIG. 2. Dependence of the IV → VI reaction rate from the base concentration (IV = 0·162 mole/l.)

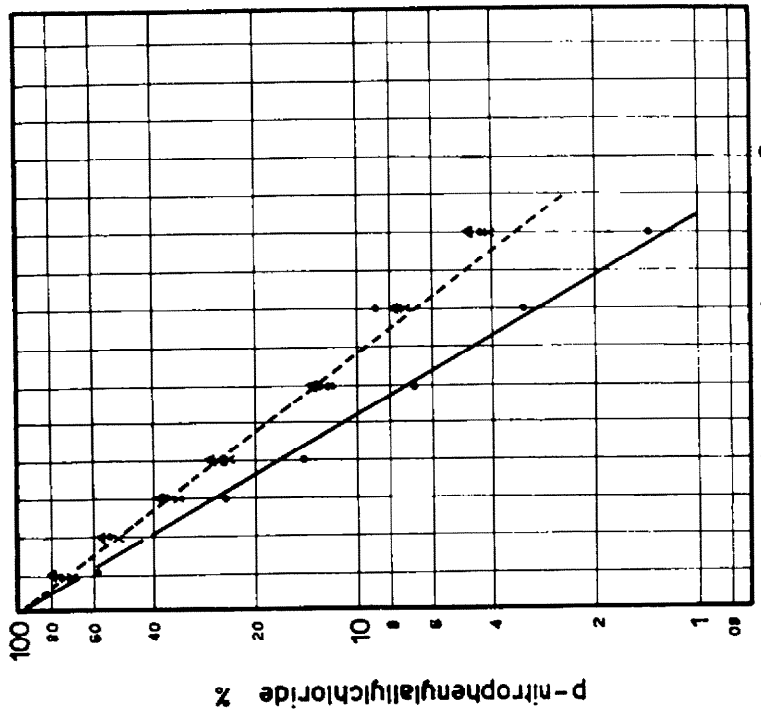


FIG. 1. Isomerization of IV at different concentrations in triethylamine 0·61M.
——— 0·125 mole/l.
- - - × - - - 0·051 mole/l.
- - - △ - - - 0·0155 mole/l.
- - - ○ - - - 0·0054 mole/l.

3 hr at room temp, acidified to Congo red with conc. HCl aq., the inorganic salts filtered off and the filtrate evaporated under red. press. The residue was treated with water and extracted with ether. The extract was dried (Na_2SO_4), decolourized with charcoal and the solvent evaporated. The solid residue was triturated with pet. ether, filtered and dried at 50° *in vacuo* to yield 30·2 g (88%) p-*nitrocinnamyl alcohol*, m.p. 125–127°. The product was used without further purification.[4] A sample, after crystallization from benzene, m.p. 127–129°; λ_{max}^{MeOH} 309 mμ (ε 15,500). (Found: C, 60·32; H, 5·21; N, 7·94. $C_9H_9NO_3$ requires: C, 60·33; H. 5·02; N, 7·82%).

Reaction of p-*nitrocinnamyl alcohol with thionyl chloride*

To a solution of 34 g (0·19 mole) III[4] in 300 ml chloroform, a solution of 29 ml $SOCl_2$ in 50 ml chloroform was added with stirring. The reaction mixture was kept 1 hr at room temp and 3 hr at 50–60°. The solvent and excess $SOCl_2$ were evaporated *in vacuo* and the oily residue distilled to give 24·4 g (65%) of a fraction b.p. 107–108° (0·5 mm) identified as α-(p-*nitrophenyl*)-*allylchloride* (IV); λ_{max}^{MeOH} 269 mμ (ε 10,700); δ[6] 5·21 (multiplet, ClCH), 5·49 (multiplet, =CH), 6·25 (multiplet, —CH=) and 7·88 (quadruplet, four aromatic protons); IR bands at 936 cm^{-1} (=CH_2 out of plane deformation) and at 980 cm^{-1} (=CH— out of plane deformation). (Found: C, 54·50; H, 4·19; N, 6·75; Cl 17·53. $C_9H_8ClNO_2$ requires: C, 54·70; H, 4·08; N, 7·09; Cl, 17·94%).

A second fraction, b.p. 120–125° (0·5 mm) which solidified on standing was crystallized from ether–pet. ether to yield 6·3 g (16·8%) p-*nitrocinnamyl chloride* (V); λ_{max}^{MeOH} 304 mμ (ε 16·700); δ 4·26 (doublet, —CH_2Cl), 6·64 (multiplet, —CH=CH—) and 7·87 (quadruplet, four aromatic protons); IR bands (nujol) at 960–974 cm^{-1} (s) (*trans* CH=CH out of plane deformation). (Found: C, 54·59; H, 4·28; N, 6·96; Cl, 17·67. $C_9H_8ClNO_2$ requires: C, 54·70; H, 4·08; N, 7·09; Cl, 17·94%).

Reaction of α-(p-*nitro-phenyl*)-*allyl chloride with amines*

(a) *With diisopropylamine.* A mixture of 1·5 g (0·0076 mole) IV, 1·54 g (0·0152 mole) diisopropylamine and 10 ml benzene was refluxed 15 hr. After cooling, 10 ml ether was added and the diisopropylamine hydrochloride (0·2 g) filtered off. The filtrate was shaken in a separatory funnel with 2 × 10 ml 10% HCl aq., the organic layer dried (Na_2SO_4) and the solvent evaporated. The solid residue was crystallized from pet. ether to give 1·1 g (73%) of α-*chloro*-β-*methyl*-p-*nitrostyrene* (VI), m.p. 62–63°; λ_{max}^{MeOH} 305 mμ (ε 14,000); δ 2·02 (doublet, —CH_3), 6·45 (quadruplet, =CH—), 7·95 (quadruplet, four aromatic protons.) (Found: C, 54·78; H, 4·13; N, 7·05; Cl, 17·79. $C_9H_8ClNO_2$ requires: C, 54·70; H, 4·08; N, 7·09; Cl, 17·94%).

The aqueous acid layer was concentrated *in vacuo*, the residual solution basified with 50% NaOH aq. and the oil extracted with ether. The extract was dried (Na_2SO_4), evaporated *in vacuo* and the solid residue crystallized from ethanol to give 0·30 g (15%) of N,N-*diisopropyl*-p-*nitrocinnamylamine* (VIIa), m.p. 74°; λ_{max}^{MeOH} 305 mμ (ε 16,100); δ 1·02 (doublet, four-CH_3), 3·05–3·06 (multiplet, >N—CH<), 3·28 (doublet, —CH_2—), 6·45 (multiplet, =CH—), 7·76–7·78 (doublet, four aromatic protons).

The product is identical (mixed m.p., IR and NMR spectra) with that synthesized in 30% yield by refluxing for 16 hr a benzene solution of V and diisopropylamine.

(b) *With piperidine.* Compound IV was condensed with piperidine in refluxing benzene, under the same conditions described under (a). The UV analysis after 4 hr showed the presence of only phenyl conjugated ethylenic bonds. The reaction mixture yielded, 40% VI and 32% N-*p*-nitrocinnamylpiperidine (VIIb) hydrochloride, from ethanol; m.p. 236° (dec). (Found: N, 10·01; Cl, 12·40. $C_{14}H_{19}ClN_2O_2$ requires: N, 9·90; Cl, 12·54%).

(c) *With triethylamine.* A mixture of 0·01 mole IV, 0·02 mole triethylamine and 15 ml benzene was refluxed for 4 hr. The clear solution was evaporated and the solid residue crystallized from pet. ether to give 92% VI, m.p. 62–63°.

p-*Nitrocinnamylamines from* p-*nitrocinnamyl chloride.*

Typical procedure. A mixture of 0·7 g (0·0035 mole) V, 0·6 g (0·007 mole) piperidine and 5 ml benzene was refluxed 4 hr. After cooling, 5 ml ether was added, the pideridine hydrochloride (0·4 g) filtered off and the filtrate shaken with 2 × 5 ml 10% HCl aq., the acid layer concentrated *in vacuo*

to a small volume, basified with 50% NaOH aq. and extracted with ether. The extract was dried (Na_2SO_4), decolourized with charcoal and the solvent evaporated. The oily residue (0·65 g) was dissolved in ethanol and transformed to the hydrochloride with dry HCl gas, yield 0·75 g (70%) of VIIb hydrochloride from ethanol m.p. 236 (dec), identical (mixed m.p. and IR spectrum) with the amine isolated by allowing IV to react with piperidine.

Reaction of IV *with monodeuteropiperidine*

A mixture of 1·6 g (0·0081 mole) IV, 2·08 g (0·0243 mole) monodeuteropiperidine and 10 ml benzene was refluxed for 4 hr, and the reaction mixture worked up to yield 70% VI and 23% VII. Examination of the NMR spectrum of VI showed an absorption, not well defined at 6·45 δ assigned to the one proton quadruplet of the $=CH—CH_3$ group overlapping with the one proton triplet of the $=CH—CH_2D$ group. In addition, the ratio between the intensities of the $—CH_3$ and $=CH—$ bands is 2·4 corresponding to a mixture of 60% of deuterated and 40% of non-deuterated VI.

*Ozonolysis of α-chloro-β-methyl-*p*-nitrostyrene*

Through a solution of 1 g VI in 20 ml ethyl acetate, cooled at −5°, a 0·5% O_3 current was bubbled for 3 hr. At the end of the reaction 20 ml water and 5 g Zn dust were added and the mixture stirred for 5 hr at 0–5°. After filtration, the aqueous layer was treated with 2,4-dinitrophenylhydrazine to give a yellow precipitate of acetaldehyde-2,4-dinitrophenylhydrazone, m.p. 149–151° (ethanol). Since different m.ps are reported for this derivative, the structure was confirmed by NMR spectrum which showed a doublet at δ 1·47 in accordance with a $CH_3—CH=$ group. The organic layer was evaporated and the residue was refluxed with 10% $NaHCO_3$ aq. until a clear solution was obtained. By acidification, a product, m.p. 232–233°, was obtained which was identical (mixed m.p. and IR spectrum) with a sample of *p*-nitrobenzoic acid.

Kinetics

The kinetics of the reaction IV → VI was carried out using UV spectroscopy. A multicomponent system method, based on the absorptions of IV, $\lambda_{max} = 269$ mμ, $E^{1\%}_{1cm} = 537$ and of VI, $\lambda_{max} = 305$ mμ, $E^{1\%}_{1cm} = 707$, was adopted to analyse the solutions. In each run IV and trietylamine were dissolved in benzene and the solution kept refluxing in a thermostat at 85°. At desired time intervals, a suitable amount of solution was removed, cooled and evaporated to dryness under red. pres. Methanol was then added in amounts appropriate for the spectrophotometric determination.

*Stability of α-(*p*-nitrophenyl)-allyl chloride*

(a) A solution of 5 g IV in 50 ml dry benzene was refluxed 2 days. The solvent was evaporated and the residue distilled. A main fraction of 4·5 g (95%), b.p. 105–106° (0·5 mm), of the unchanged halogenide was recovered. The IR spectrum was identical with that of an authentic sample.

(b) A suspension of 3 g IV in 10 ml 10% HCl aq. was stirred for 30 min at room temp. The mixture was extracted with ether, the solvent was dried (Na_2SO_4), evaporated and the residue distilled to give 2·75 g (92%) unchanged IV.

*Stability of α-chloro-β-methyl-*p*-nitrostyrene towards amines*

A solution of 3·95 g (0·02 mole) VI, 3·4 g (0·04 mole) piperidine and 20 ml benzene was refluxed 24 hr. The clear solution was evaporated under red. press. and the solid residue crystallized from pet. ether to give 3·48 g (88%) of a product m.p. 60–62°, not depressed in mixture with an authentic sample of VI.

Acknowledgement—We are indebted to Mr. E. Occelli for the technical assistance, to Mr. P. Radaelli for the kinetical measurements and to Dr. A. Vigevani for the NMR spectra.