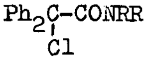
Tetrahedron Letters No. 2, pp 93 - 96, 1975. Pergamon Press. Printed in Great Britain.

SODIUM BORODEUTERIDE REDUCTION OF *N*,*N*-DIMETHYL-α-CHLORO-α,α-DIPHENYL-ACETAMIDE AND THE MECHANISM OF THE "NORMAL" REACTION OF α-CHLORO-α,α-DIPHENYLACETAMIDES WITH NUCLEOPHILES

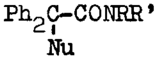
Gy. Simig and K. Lempert
Research Group for Alkaloid Chemistry of the Hungarian Academy of Sciences,
and J. Tamás and P. Miklós
Central Institute for Chemistry of the Hungarian Academy of Sciences,
Budapest

(Received in UK 23 October 1974; accepted for publication 29 November 1974)

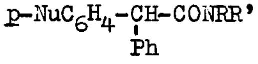
The reaction of α-chloro-α,α-diphenylacetamides /**1**/ with nucleophiles such as amines and *N*-cyanoanilide anions is known to yield either normal α- /**2**/ and/or anomalous *p*-substitution products /**3**/.[1] In order to get some insight into the mechanism of these reactions, the $NaBH_4$ reduction of **1a**


$Ph_2C(Cl)\text{-}CONRR'$

1


$Ph_2C(Nu)\text{-}CONRR'$

2

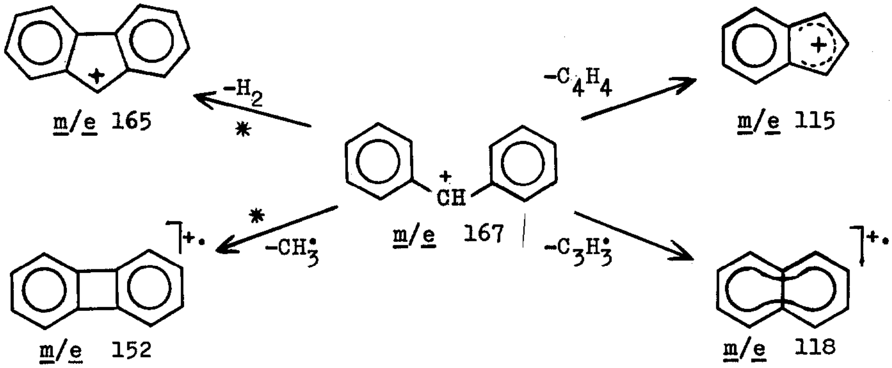

$p\text{-}NuC_6H_4\text{-}CH(Ph)\text{-}CONRR'$

3

/= **1**, R = R' = Me/ was studied with the aid of the isotopic tracer method.

When an ethereal solution of **1a** was stirred at r.t. with an aqueous solution of $NaBH_4$ /7 moles/, the reduction product **2a** /= **2**, R = R' = Me, Nu = H; 63%/,[2] and the hydrolysis product **2b** /= **2**, R = R' = Me, Nu = OH; 19%/[3] were obtained after chromatographic work-up. When the reagent was replaced by $NaBD_4/D_2O$, 35 % of monodeutero-**2a**, 14 % of /presumably *O*-deuterated/ **2b** and *non*-deuterated starting material were obtained. When **1a** was reduced with $NaBH_4$ in D_2O, only *non*-deuterated **2a** and **1a** were obtained in addition to *O*-deuterated **2b** /total recovery: 71 %/. No H-D exchange was observed when an ethereal solution of **2a** was stirred at r.t. with $NaBH_4/D_2O$.

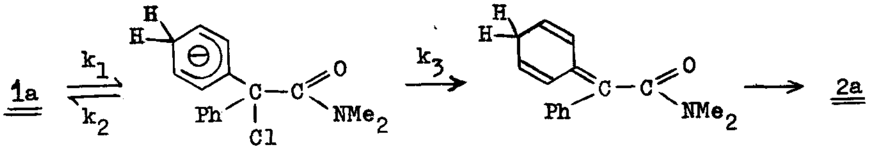
The distribution of the D-label in the monodeutero-**2a** ions was established on the basis of the mass spectrum /70 eV, direct inlet system, source temperature: 120 $^{\circ}C$/. The crucial fragment of *non*-deuterated **2a** is the *m/e* 167 ion /$Ph_2\overset{+}{C}H$/ which is known[4] to be transformed under elimination of one *ortho* proton, each, of the phenyl rings into the *m/e* 165 and 152 ions.



In addition, elimination of a $C_3H_3^{\bullet}$ and a C_4H_4 fragment from the *m/e* 167 ion give rise to the formation of the *m/e* 128 and 115 ions, respectively. The *m/e* 167 and 165 peaks in the mass spectrum of monodeutero-**2a** are shifted to *m/e* 168 and 166, respectively, and peaks at *m/e* 153, 129 and 116 are present in addition to the *m/e* 152, 128 and 115 peaks, respectively. The corrected ionic abundances are shown in the table. From the intensity ratio I^{153}/I^{152} in the mass spectrum of monodeutero-**2a** it can be seen that approximately 2/3 and 1/3 of the *m/e* 168 ions and, consequently, of the monodeutero molecules have the D-label in *p*- and α-position, respectively.

The intensity ratios I^{129}/I^{128} and I^{116}/I^{115} are approximately identical with the I^{153}/I^{152} ratio which indicates that in the course of the formation of the *m/e* 128 and 115 ions the α-CH group is incorporated in both cases into the C_nH_n neutral fragment while the *p*-CH groups are retained in the resulting ions, and corroborates the result concerning the distribution of the D-label deduced from the value of I^{153}/I^{152}.

All our observations are accomodated by the following mechanism of the reduction:



with $k_3 \gg k_2$, which incorporates the two limiting cases $k_2 = 0$ /first step irreversible/ and $k_3 \rightarrow \infty$ /concerted reaction/. Whether the deuterum distribution in monodeutero-2a is the result of only the operation of the H/D kinetic isotope effect or, in addition to the latter, of part of the α--deutero compound being formed by direct $D:^{\ominus}$ attack at the α-position of 1a is not clear at present. The hydrogen migration in the last step of the sequence, on the other hand, undoubtedly does <u>not</u> take place by a deprotonation-protonation mechanism.

Ionic abundances* in the mass spectra of 2a and monodeutero-2a

m/e	unlabelled	labelled
240		36
239	40	1,5
168		<u>100</u>
167	<u>100</u>	10
166	5	31
165	30	4
153		11
152	12	6
129		2
128	2	1
116		3
115	4	1,5

---

* Corrected for natural isotope abundances

If the reason of the hydride anion to attack mainly /or exclusively/ the *p*-position of one of the phenyl rings of **1a** is steric crowding at the α-carbon atom, then it may be assumed that the attack of more bulky nucleophiles /such as amines and *N*-cyanoanilide anions/ at the *p*-position must be even more favoured and that the "normal" substitution products with such nucleophiles are also formed *via* *p*-attack and subsequent rearrangement.

References

1. K. Nagarajan, C. L. Kulkarni and A. Venkatesvarlu, *Tetrahedron Letters* 1387 /1967/; K. Lempert, Gy. Simig and Sz. Vezér, *ibid*. 805 /1972/
2. V. G. Gokhale, N. L. Phalnikar and B. V. Bhide, *J. Univ. Bombay* **16**, 32 /1948/; *Chem. Abstr*. **43**, 1144d /1949/
3. Gy. Simig and K. Lempert, *Tetrahedron*, accepted for publication
4. R. A. W. Johnstone and B. J. Millard, *Z. Naturforsch*. **21a**, 604 /1966/