Tetrahedron Vol. 37, No. 20, pp. 3503 to 3505, 1981
Printed in Great Britain

0040-4020/81/203503-03$02.00/0
Pergamon Press Ltd.

UNEXPECTED "HEAD TO HEAD" COURSE OF THE REACTION OF TWO MOLECULES OF BENZOYLACETANILIDE IN POLAR MEDIUM†

M. CIECHANOWICZ-RUTKOWSKA* and A. KONSUR
Regional Laboratory of Physicochemical Analysis and Structural Research, Kraków, Poland

and

S. DURAJ, A. KOLASA, L. L. LEDIBEA and W. ŻANKOWSKA-JANIŃSKA
Institute of Chemistry, Jagellonian University, Kraków, Poland

(*Received in the UK* 27 *January* 1981)

Abstract—The synthesis of 3,4-diphenyl-3,4-dichlorocyclobutanodicarbox-1,2-dianilides (new chloro-derivatives of truxinic acid) is reported. Structure elucidation based on IR, MS, ^{1}H NMR, ^{13}C NMR, Raman, and X-ray analysis clear up structural ambiguities as well as revealing the compound to be β-stereoisomer. A radical combination of two molecules of benzoylacetanilide in the presence of $POCl_3$ is postulated.

Since the isomeric diphenylcyclobutanodicarboxylic acids known as truxillic and truxinic acids, were isolated from the leaves of Erythroxylon coca,[1,2] many syntheses of their derivatives,[3] as well as numerous structural investigations concerning their stereochemistry, have been carried out. Very little, however, is known[4] about the synthesis of derivatives containing chlorine atoms in the cyclobutane ring.

In the previous paper[5] we ascertained that derivatives of benzoylacetanilide in the presence of the excess of $POCl_3$ yielded the compounds of that type. On the basis of IR, ^{1}H NMR, MS and UV spectra we established that two molecules of benzoylacetanilide reacted with each other, having methylene and benzoyl carbonyl groups involved in the reaction. $POCl_3$ not only led to this thermal cyclization, but also caused the substitution of OH groups by chlorine atoms. There are two possible pathways of ring closure: "head to head" leading to the truxinic (A) acid derivatives, and "head to tail" providing truxillic (B) acid derivatives.

The reaction led to a single isomer, out of six truxinic and five truxillic acid derivatives possible,[6] according to TLC followed by ^{1}H and ^{13}C NMR measurements (Table 1).

Of the eleven possible isomers, only the seven with twofold symmetry were allowed by the latter, and IR and Raman spectra (Table 2) determined on the solid phase eliminated[7] the truxillic derivative with a centre of symmetry.

Mass spectra were unhelpful, and X-ray analysis was therefore needed.

X-RAY ANALYSIS

A crystal suitable for single crystal X-ray diffraction was obtained by slow evaporation of dimethylsulphoxide solution of compound 1. Attempts to crystalize the product from other solvents like chloroform led to crystals in form of whiskers.

Crystal data for $C_{30}H_{24}Cl_2N_2O_2 \cdot C_2H_6OS$

F. W. = 985.599; orthorhombic, a = 9.259(2) Å, b = 24.911(3)Å, c = 25.934(3) Å, V = 5981 Å^3; d_{obs} = 1.25 g cm^{-3}, d_{calc} = 1.318 g cm^{-3}, Z = 8; F (000) = 2480; space group Pbca; μ(MoKα) = 2.75 cm^{-1}.

Data collection and reduction. The data were

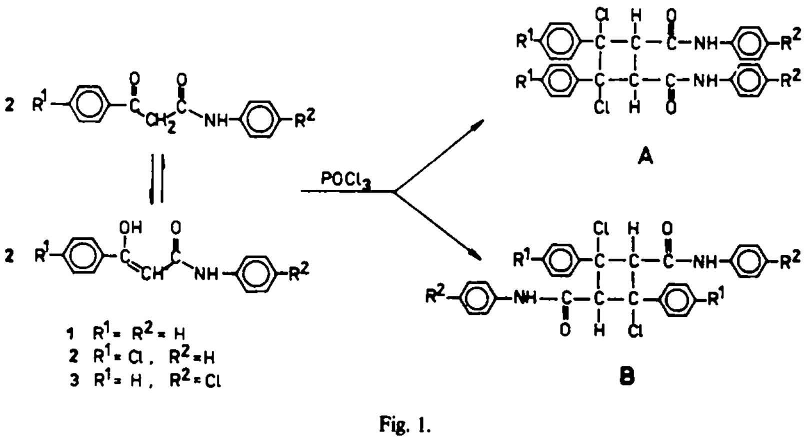

Fig. 1.

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†Data have been deposited with C.C.D.C.

Table 1. ^{13}C and ^{1}H NMR data for compound 1

	No	Intensity	δ [ppm]	Multiplicity	Assignment
^{13}C NMR	1	41	165.315	s	2 C (g)
	2	62	139.693	s	2 C (h)
	3	37	138.967	s	2 C (d)
	4	95	127.582	d	2 C (a)
	5	207	128.434	2 d	12 C (b, c, j)
	6	191	127.239	2 d	
	7	181	127.040	2 d	
	8	83	122.866	d	2 C (k)
	9	165	119.177	2 d	4 C (i)
	10	59	78.436	s	2 C (e)
	11	90	48.402	d	2 C (f)
^{1}H NMR	1		10.02	s	2 H NH
	2		6.90-7.70	m	20 H aromatic
	3		4.80	s	2 H alicyclic

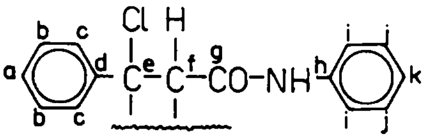

Table 2. Raman and IR data for compound 1

Raman $[\mathrm{cm}^{-1}]$	IR $[\mathrm{cm}^{-1}]$	Raman $[\mathrm{cm}^{-1}]$	IR $[\mathrm{cm}^{-1}]$
450 w	455 m	1220 vw	-
-	475 m	1255 m	1255 m
490 vvw	495 m	1300 w	-
510 vvw	510 mw	1315 m	1315 m
550 vvw	550 w	1345 vw	-
580 vvw	570 w	1360 vw	-
600 vw	600 w	1390 w	1390 w
615 w	620 w	1450 w	1445 vs
650 w	650 w	1500 w	1500 s
700 vvw	700 vs	1530 vw	1535 s
755 vw	755 s	1550 m	1550 s
805 vw	-	1600 vs	1600 vs
840 w	840 w	1670 m	1670 s
860 vvw	860 w	-	2840 w
870 vvw	870 vvw	-	2870 vw
-	875 w	-	2890 w
895 vw	900 w	2930 w	-
955 vw	955 vw	-	2950 w
990 w	990 w	2980 w	2980 m
1000 s	1000 w	-	3040 m
1040 w	1040 w	3070 s	3070 m
1090 vw	1080 w	-	3150 m
1110 vw	1110 vw	3200 vw	3200 m
1160 w	1160 w	-	3280 m
1180 w	1180 w	3330 w	3310 m
1195 w	-	-	3410 m
1210 m	1210 w		

w, weak; vw, very weak; vvw, very very weak; m, medium; mw, medium weak; s, strong; vs, very strong.

measured on CAD-4 diffractometer using graphite monochromated MoKα radiation. 6356 reflections up to $\theta = 22°$ were collected. There were 3487 independent reflections of which 385 with $F < 2$ were suppressed during structure refinement. The data were corrected for Lorentz, polarization, and absorption effects.

Structure determination and refinement. The structure was solved by direct methods using programs SHELX 76[8] and all non-hydrogen atoms of the molecule and the solvent, crystallizing with the molecule in the ratio 1:1, were localized from E-map. Hydrogen atoms of anilide groups were localized from difference Fourier map, others were placed in calculated positions and refined with isotropic thermal parameters. Full matrix least-squares anisotropic refinement converged at R = 0.059 and $R_w = 0.030$. Reflections 200 and 020 suffering from extinction were omitted in the last cycles of refinement. Final coordinates of non-hydrogen atoms and hydrogens of anilide groups, the anisotropic temperature factors, and the H atom positions together with thermal parameters are deposited with C.C.D.C. The final list of observed and calculated structure factors is deposited with the British Library, Lending Division.

RESULTS AND DISCUSSION

The molecular structure of the studied compound is that of β-truxinic acid derivative as shown in Fig. 2.

Deviations from the least squares plane through the cyclobutane ring atoms are given in Table 3. Both hydrogen atoms of the molecule form hydrogen bonds, one to the oxygen of solvent and another to the oxygen of neighbouring molecule; details in Table 4.

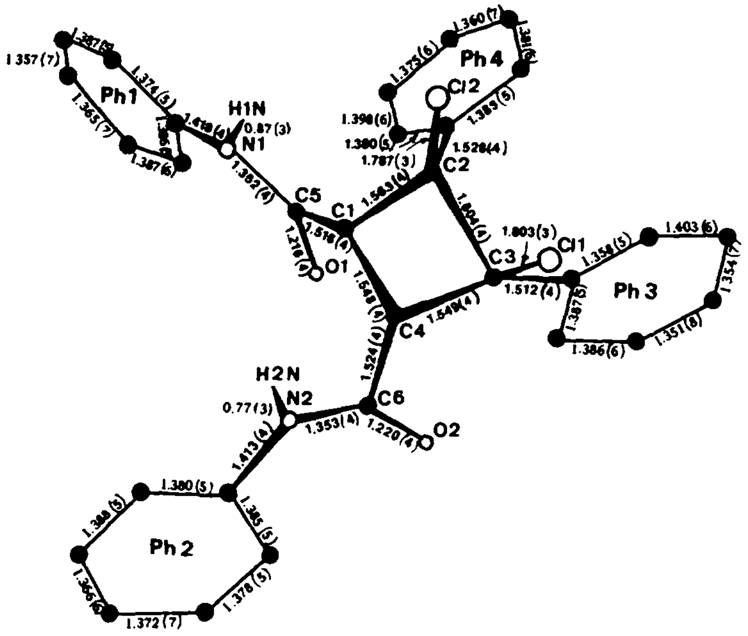

Fig. 2. Bond lengths (Å); the estimated standard deviations in parentheses

Table 3. Deviations from least squares plane (Å)[a] established by the first four atoms in the list

C1 (0.11), C2 (-0.10), C3 (0.10), C4 (-0.11), C5 (1.46),
N1 (1.52), O1 (2.40), Cl1 (1.79), C11 (2.62), C21 (1.22),
C31 (-0.84), C41 (-1.50), C6 (0.67), N2 (0.48), O2 (1.36),
Cl (1.13)

[a] The equation of the plane: $7.23x - 14.73y + 5.20z = -1.07$

Table 4. Hydrogen bond lengths

	oxygen in position	
N1.......O3	0.5+x, 0.5-y, 1-z	2.795
N2.......O2	0.5+x, y, 0.5-z	2.959

There is no intramolecular hydrogen bond in the product; it would be expected to exist if there was respective intermolecular linkage by hydrogen bond between two molecules of substrate.

CONCLUSIONS

The reaction of two molecules of benzoylacetanilide in an excess of boiling $POCl_3$ leads to 3,4-diphenyl-3,4-dichlorocyclobutanodicarbox-1,2-dianilide in the form of its β-stereoisomer. Its structure indicates a "head to head" course of this reaction and hence this proceeds by radical mechanism. That seems to be in accordance with the concept of the capto-dative substituent effects in syntheses with radicals.[9] The molecule of the substrate that takes part in cycloaddition contains two substituents, at the same double-bonded carbon, that can both act as electron-donors or acceptors.

EXPERIMENTAL

^{13}C NMR spectrum of 1 was recorded in DMSO-d_6 with TMS as internal standard on Varian 25.2 MHz spectrometer (*Laboratory for Organic Chemistry E.T.H., CH-8006, Zürich*). Raman spectra for compounds 1–3 were recorded at 4880 Å excitation in solid phase on Cary 82 apparatus (Regional Laboratory of Physicochemical Analysis and Structural Research, Kraków).

Acknowledgements—We wish to thank the Regional Laboratory of Physicochemical Analysis and Structural Research, Jagellonian University for making the CAD-4 diffractometer and Cary 82 apparatus available for measurements, and the Institute of Pharmacology, Polish Academy of Sciences, Kraków for financial support.

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