Molecular and Crystal Structures of *N*-Phenylsuccinimides, and their Fungicidal Activities

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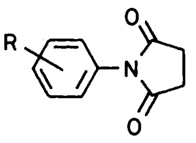
The crystal structures of seven *N*-phenylsuccinimides have been determined: *N*-phenyl- (**I**), *N*-(2-fluorophenyl)- (**II**), *N*-(2-bromophenyl)- (**III**), *N*-(3-fluorophenyl)- (**IV**), *N*-(3-bromophenyl)- (**V**), *N*-(4-fluorophenyl)- (**VI**), and *N*-(4-bromophenyl)- (**VII**). The molecules showed marked twisting around the C(6)–N(7) bond: The torsion angle between the least-squares planes of the benzene and succinimide rings was never 0°, being 59.6° [for (**I**)], 63.5° (**II**), 69.8° (**III**), 54.5° (**IV**), 59.8° (**V**), 55.9° (**VI**), or 62.2° (**VII**). The relation of torsion angle to fungicidal activity against *Botrytis cinerea* is discussed.

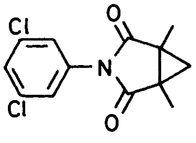
Cyclic imides such as *N*-phenylsuccinimides (**1**), procymidone (**2**), and vinclozolin (**3**) show fungicidal activity against *Sclerotinia sclerotiorum* and *Botrytis cinerea*.[1–4] To elucidate the structural features in *N*-phenylsuccinimides which induce these activities, we wished to examine whether the torsion angle between the benzene and succinimide rings of *N*-phenylsuccinimides (**1**) is changed by introduction of substituents into the benzene ring, and, if so, whether there is any relation between this angle and the biological activity.

X-Ray analysis is a good method for elucidating the influence of steric and electronic effects of substituents on stereo structure in the crystal state. However, there have been few *X*-ray studies on the changes of geometry of bioactive compounds caused by introduction of substituents, or on the relation of such changes to biological activity.[5,6] Some crystal structures of cyclic *N*-phenylimides have been reported, but without consideration of biological activity[7–9] in relation to molecular geometry.

We report here the crystal and molecular structures of the seven *N*-phenylsuccinimides (**I**)—(**VII**). The structural features necessary for fungicidal activity are also discussed.



(**1**)



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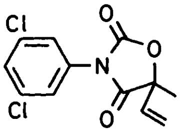

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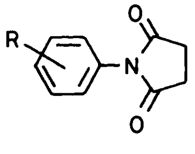


(I) R = H
(II) R = 2-F
(III) R = 2-Br
(IV) R = 3-F
(V) R = 3-Br
(VI) R = 4-F
(VIII) R = 4-Br

Experimental

Compounds (**I**)—(**VII**) were synthesized as reported previously;[4] the crystals used were grown from benzene solution.

X-Ray measurements were performed with a Rigaku four-circle diffractometer AFC-6B, using graphite-monochromated Mo-K_α radiation. A single crystal was mounted on the diffractometer and the unit-cell dimensions were determined by least-squares calculations using 25 automatically centred reflections in the range of $15° < 2\theta < 25°$. The intensity data for each compound were collected by the ω-scan technique and corrected for Lorentz and polarization effects, but not for absorption.

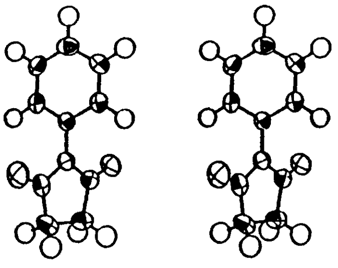
The initial structure was obtained by direct methods.[10], by the heavy-atom method, or by the isomorphous replacement method. A preliminary determination of the structure of compound (**VII**) has been reported already,[8] but in this study we determined its structure independently without using the reported structural parameters. The structures of compounds (**I**)—(**VII**) were developed by difference Fourier syntheses and/or block-diagonal least-squares calculations. Successive refinements were performed using the anisotropic thermal parameters for non-hydrogen atoms. The positional parameters of hydrogen atoms were calculated using values from standard geometries of C–H bonds. The positional and isotropic thermal parameters of the hydrogen atoms of compound (**I**) were refined by least-squares calculations, but those of other compounds were used only in the calculation of structure factors, not in the least-squares calculations. The isotropic thermal parameters of the carbon atoms, to which hydrogen atoms were attached, were used as the parameters of these hydrogen atoms for compounds (**II**)—(**VII**). The refinements were continued until values of parameter shifts converged to within their deviations. The crystal data and *X*-ray experimental details are listed in Table 1.

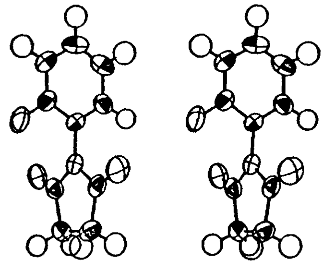
All calculations were performed by application of program packages [RASA (supplied with AFC 6B), MULTAN,[11] X-STANP (written by Z. T.), and ORTEP[12]] on the PANAFACOM U-1400 computer in Tokushima Bunri University and at the computer centre of the University of Tokushima. The atomic scattering factors used were taken from International Tables for *X*-Ray Crystallography.[13]

Table 1. Crystal data and experimental details for *N*-phenylsuccinimides

Compound	(I)	(II)	(III)	(IV)	(V)	(VI)	(VII)
Formula	$C_{10}H_9NO_2$	$C_{10}H_8FNO_2$	$C_{10}H_8BrNO_2$	$C_{10}H_8FNO_2$	$C_{10}H_8BrNO_2$	$C_{10}H_8FNO_2$	$C_{10}H_8BrNO_2$
M	175.19	193.18	254.08	193.18	254.08	193.18	254.08
Lattice	Monoclinic	Orthorhombic	Orthorhombic	Monoclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	$P2_1/a$	$Pca2_1$	$Pca2_1$	$P2_1/n$	$P2_1/a$	Cc	$P2_12_12_1$
a/Å	12.975(3)	11.064(2)	10.534(2)	18.818(5)	15.179(4)	10.588(3)	7.843(3)
b/Å	5.628(3)	10.271(2)	11.638(2)	6.313(1)	6.232(2)	11.943(4)	19.719(3)
c/Å	11.898(3)	8.053(2)	8.104(2)	7.779(2)	10.666(3)	7.574(3)	6.419(2)
β/°	101.77(2)	90	90	99.83(2)	105.66(2)	107.55(3)	90
V/Å^3	850.6(5)	915.1(4)	993.5(4)	910.6(4)	971.6(5)	913.2(6)	992.7(5)Å^3
Z	4	4	4	4	4	4	4
D_x/g cm^{-3}	1.368	1.402	1.698	1.409	1.737	1.405	1.700
F(000)	368	400	504	400	504	400	504
μ(Mo-K_α)/mm^{-1}	0.104	0.121	4.357	0.122	4.455	0.122	4.360
Crystal size (mm)	0.2 × 0.3 × 0.6	0.2 × 0.2 × 0.5	0.2 × 0.4 × 0.5	0.3 × 0.4 × 0.4	0.3 × 0.3 × 0.4	0.4 × 0.6 × 0.6	0.2 × 0.3 × 0.6
Scan mode	ω	ω	ω	ω	ω	ω	ω
Scan rate (min^{-1})	4	4	4	4	4	4	4
$2\theta_{max.}$/°	55	60	60	60	60	60	50
No. of unique reflections	2 328	1 627	1 756	3 051	3 301	1 512	1 767
No. of observed reflections[a]	1 049	670	779	1 185	1 131	1 017	747
R	0.039	0.063	0.045	0.085	0.060	0.066	0.051
R_w	0.037	0.061	0.046	0.090	0.064	0.065	0.054
Structure solution[b]	D	D	I	D	D	D	H

[a] Reflections with $F_0 > 6\sigma$ (F_0) were considered observed. [b] D, I, and H denote direct methods, isomorphous replacement method, and heavy-atom method, respectively.


(I)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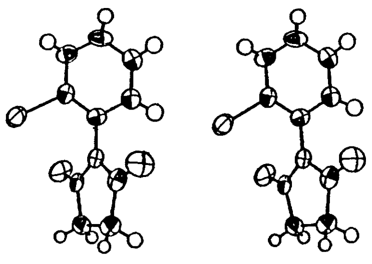
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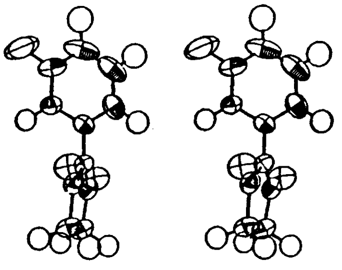
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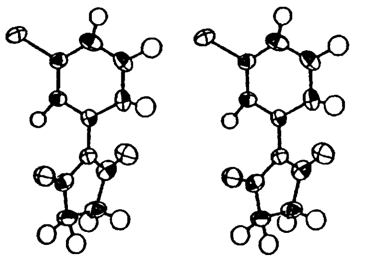
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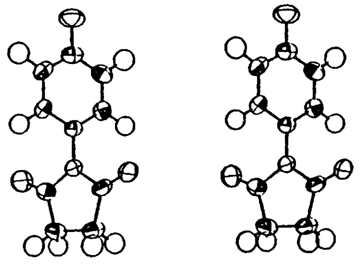
(VI)

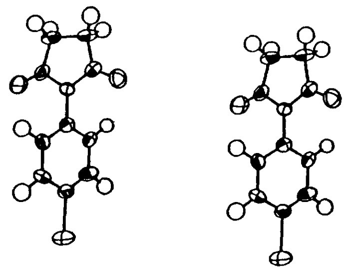
(VII)

Figure 1. Stereoview of *N*-phenylsuccinimides (**I**)—(**VII**); thermal ellipsoids are shown at the 50% probability level

Table 2. Atomic co-ordinates (× 10^4) with e.s.d.s in parentheses and equivalent temperature factors B_{eq} (× 10^2 in Å)

$$B_{eq} = \frac{3}{4}\sum_i\sum_j(a_ia_j\beta_{ij})$$

(I)	*x*	*y*	*z*	B_{eq}
C(1)	7 684(2)	9 033(5)	1 485(2)	360
C(2)	8 413(2)	9 106(5)	781(2)	415
C(3)	9 122(2)	7 280(6)	797(2)	429
C(4)	9 114(2)	5 351(5)	1 513(2)	403
C(5)	8 384(2)	5 240(5)	2 214(2)	344
C(6)	7 683(2)	7 086(5)	2 197(2)	296
N(7)	6 921(2)	6 983(4)	2 909(2)	316
C(8)	6 863(2)	8 644(5)	3 768(2)	378
C(9)	5 904(2)	8 045(6)	4 241(2)	436
C(10)	5 528(2)	5 644(6)	3 729(2)	444
C(11)	6 159(2)	5 217(5)	2 815(2)	351
O(12)	7 479(2)	10 235(4)	4 037(2)	544
O(13)	6 052(2)	3 648(4)	2 116(2)	484
(II)				
C(1)	303(7)	3 722(7)	−2 627(10)	426
C(2)	289(8)	5 033(10)	−2 935(12)	566
C(3)	1 247(10)	5 758(7)	−2 276(12)	600
C(4)	2 125(8)	5 217(8)	−1 316(12)	588
C(5)	2 118(7)	3 872(7)	−1 006(11)	455
C(6)	1 212(6)	3 141(6)	−1 674(9)	332
N(7)	1 150(5)	1 761(5)	−1 397(8)	339
C(8)	235(7)	1 157(7)	−472(10)	407
C(9)	532(7)	−280(7)	−427(11)	462
C(10)	1 734(8)	−425(7)	−1 328(12)	494
C(11)	2 068(6)	911(7)	−1 956(10)	388
O(12)	−590(5)	1 711(5)	−146(8)	517
O(13)	2 914(5)	1 247(5)	−2 762(9)	603
F	−556(4)	2 972(4)	−3 278(7)	666
(III)	*x*	*y*	*z*	B_{eq}
C(1)	154(9)	3 525(9)	−2 521(15)	335
C(2)	221(11)	4 681(8)	−2 886(13)	360
C(3)	1 204(12)	5 324(8)	−2 234(15)	415
C(4)	2 112(9)	4 819(9)	−1 253(14)	365
C(5)	2 028(9)	3 658(9)	−879(15)	353
C(6)	1 024(9)	2 994(8)	−1 519(13)	295
N(7)	964(7)	1 821(7)	−1 119(11)	276
C(8)	67(9)	1 356(8)	−47(14)	288
C(9)	302(9)	88(9)	14(15)	341
C(10)	1 489(10)	−135(8)	−963(14)	330
C(11)	1 831(10)	1 021(9)	−1 710(13)	330
O(12)	−725(7)	1 899(6)	653(11)	482
O(13)	2 699(8)	1 233(6)	−2 611(12)	505
Br	−1 207(1)	2 669(1)	−3 462(4)	475
(IV)				
C(1)	5 888(3)	8 650(11)	8 094(8)	445
C(2)	5 184(4)	9 294(14)	7 469(11)	644
C(3)	4 929(4)	11 226(16)	7 715(13)	796
C(4)	5 383(5)	12 704(13)	8 612(11)	732
C(5)	6 103(4)	12 173(11)	9 307(9)	535
C(6)	6 336(3)	10 140(10)	9 038(7)	367
N(7)	7 055(2)	9 519(8)	9 696(6)	340
C(8)	7 227(3)	7 675(10)	10 683(7)	401
C(9)	8 027(3)	7 332(12)	10 833(8)	495
C(10)	8 318(3)	9 256(12)	9 995(9)	487
C(11)	7 663(3)	10 510(11)	9 244(7)	421
O(12)	6 801(2)	6 630(8)	11 268(6)	549
O(13)	7 633(3)	12 106(8)	8 388(6)	626
F	4 747(3)	7 882(11)	6 562(8)	1 119

(V)	*x*	*y*	*z*	B_{eq}
C(1)	6 898(6)	1 182(15)	7 587(8)	277
C(2)	6 265(6)	1 669(16)	8 288(9)	301
C(3)	6 301(7)	3 587(18)	8 944(9)	378
C(4)	6 984(7)	5 004(17)	8 938(9)	388
C(5)	7 639(6)	4 576(16)	8 261(9)	338
C(6)	7 583(6)	2 623(15)	7 596(8)	260
N(7)	8 237(5)	2 123(12)	6 903(7)	273
C(8)	8 773(6)	261(18)	7 148(8)	335
C(9)	9 270(6)	123(18)	6 119(9)	393
C(10)	9 011(7)	2 112(19)	5 293(10)	415
C(11)	8 331(7)	3 268(17)	5 850(9)	371
O(12)	8 817(5)	−922(11)	8 039(7)	450
O(13)	7 935(5)	4 912(13)	5 465(7)	527
Br	5 331(1)	−326(2)	8 283(1)	462
(VI)				
C(1)	3 862(6)	−9 636(5)	1 661(9)	354
C(2)	2 505(6)	−9 706(5)	1 307(9)	405
C(3)	1 858(6)	−8 854(6)	1 861(8)	395
C(4)	2 499(6)	−7 904(6)	2 760(10)	422
C(5)	3 855(6)	−7 833(5)	3 118(9)	366
C(6)	4 527(5)	−8 701(5)	2 592(8)	310
N(7)	5 930(4)	−8 628(4)	2 951(6)	294
C(8)	6 824(6)	−9 469(5)	3 889(9)	390
C(9)	8 186(6)	−9 109(6)	3 908(10)	431
C(10)	8 008(6)	−7 967(6)	2 896(10)	422
C(11)	6 539(6)	−7 762(5)	2 287(9)	370
O(12)	6 519(5)	−10 289(4)	4 536(8)	595
O(13)	5 948(5)	−7 027(4)	1 353(8)	576
F	531(4)	−8 923(4)	1 528(7)	609
(VII)				
C(1)	6 165(17)	6 442(5)	8 263(17)	350
C(2)	6 468(17)	7 069(5)	9 313(19)	419
C(3)	5 877(15)	7 150(5)	11 287(17)	334
C(4)	5 057(15)	6 640(5)	12 341(21)	327
C(5)	4 807(16)	6 026(5)	11 383(17)	306
C(6)	5 349(14)	5 947(5)	9 371(18)	289
N(7)	5 105(11)	5 294(4)	8 322(13)	269
C(8)	4 172(14)	5 211(5)	6 550(18)	299
C(9)	4 493(17)	4 496(5)	5 704(21)	403
C(10)	5 436(15)	4 151(4)	7 521(25)	407
C(11)	5 925(15)	4 709(5)	9 005(19)	340
O(12)	3 272(12)	5 635(4)	5 774(13)	432
O(13)	6 832(12)	4 673(4)	10 486(15)	537
Br	6 388(2)	7 979(1)	12 674(3)	585

Results and Discussion

Fractional atomic co-ordinates for compounds **(I)**—**(VII)** are given in Table 2. Their molecular structures are presented as ORTEP[12] stereodrawings in Figure 1, and their bond lengths and angles are listed in Tables 3 and 4, respectively. The results are not corrected for thermal motion effects, but these effects

Table 3. Bond lengths (Å) with e.s.d.s in parentheses

	(I)	(II)	(III)	(IV)	(V)	(VI)	(VII)
C(1)–C(2)	1.386(12)	1.369(12)	1.379(14)	1.391(13)	1.401(21)	1.382(12)	1.428(15)
C(1)–C(6)	1.385(4)	1.398(10)	1.372(14)	1.387(12)	1.371(13)	1.392(13)	1.368(15)
C(2)–C(3)	1.376(4)	1.400(14)	1.383(16)	1.336(13)	1.378(15)	1.361(12)	1.359(17)
C(3)–C(4)	1.380(4)	1.360(14)	1.375(16)	1.372(15)	1.363(15)	1.391(13)	1.372(15)
C(4)–C(5)	1.385(12)	1.404(11)	1.387(15)	1.411(15)	1.404(22)	1.380(13)	1.371(15)
C(5)–C(6)	1.378(4)	1.363(10)	1.409(14)	1.384(9)	1.399(14)	1.382(11)	1.369(16)
C(6)–N(7)	1.429(12)	1.436(8)	1.405(12)	1.418(12)	1.423(20)	1.429(11)	1.465(13)
N(7)–C(8)	1.398(3)	1.402(10)	1.393(13)	1.402(8)	1.401(13)	1.415(16)	1.362(14)
N(7)–C(11)	1.390(4)	1.413(9)	1.389(13)	1.400(10)	1.370(13)	1.391(11)	1.392(13)
C(8)–C(9)	1.504(10)	1.513(10)	1.497(14)	1.505(9)	1.492(22)	1.500(10)	1.531(15)
C(8)–O(12)	1.200(5)	1.185(10)	1.191(12)	1.188(10)	1.190(12)	1.183(10)	1.203(13)
C(9)–C(10)	1.521(6)	1.522(12)	1.503(15)	1.523(11)	1.510(17)	1.548(10)	1.540(19)
C(10)–C(11)	1.508(12)	1.508(10)	1.518(14)	1.496(13)	1.507(21)	1.503(16)	1.504(16)
C(11)–O(13)	1.201(4)	1.190(9)	1.196(14)	1.203(8)	1.202(14)	1.181(14)	1.189(15)
C*–F[a]		1.331(9)		1.331(13)		1.353(11)	
C*–Br[a]			1.904(11)		1.885(10)		1.904(10)

[a] C* denotes the carbon atom to which the substituent F or Br is attached.

Table 4. Bond angles (°) with e.s.d.s in parentheses

	(I)	(II)	(III)	(IV)	(V)	(VI)	(VII)
C(6)–C(1)–C(2)	118.5(4)	121.8(8)	122.1(10)	116.3(8)	118.8(10)	118.9(10)	116.8(10)
C(1)–C(2)–C(3)	120.4(4)	116.5(8)	119.0(10)	124.1(8)	121.3(10)	119.0(7)	119.0(10)
C(2)–C(3)–C(4)	120.4(6)	122.6(8)	120.7(9)	119.1(8)	119.0(13)	123.0(7)	122.3(10)
C(3)–C(4)–C(5)	119.9(4)	119.9(8)	119.9(10)	120.4(9)	121.7(10)	118.1(10)	119.5(11)
C(4)–C(5)–C(6)	119.1(3)	118.4(7)	120.1(9)	118.1(6)	118.1(10)	119.5(7)	118.6(10)
C(5)–C(6)–C(1)	121.5(6)	120.6(6)	118.2(9)	121.9(6)	121.1(12)	121.4(6)	123.7(10)
C(5)–C(6)–N(7)	119.7(3)	121.1(6)	118.8(9)	120.6(6)	119.8(9)	119.7(7)	119.5(9)
C(1)–C(6)–N(7)	118.8(4)	118.2(6)	122.9(9)	117.4(8)	119.1(9)	118.9(9)	116.7(10)
C(6)–N(7)–C(8)	123.6(4)	123.6(6)	123.5(8)	122.9(7)	122.4(8)	123.5(9)	124.0(8)
C(6)–N(7)–C(11)	123.2(3)	121.7(6)	122.9(8)	123.8(5)	123.6(11)	123.0(8)	121.6(9)
C(8)–N(7)–C(11)	113.2(7)	114.5(5)	113.6(8)	112.8(6)	113.6(12)	113.3(5)	114.3(8)
N(7)–C(8)–C(9)	107.2(7)	106.7(6)	106.9(8)	107.2(8)	107.1(9)	107.3(9)	108.5(9)
N(7)–C(8)–O(12)	124.2(6)	124.5(7)	124.5(9)	124.3(6)	124.5(12)	124.8(6)	125.3(9)
C(9)–C(8)–O(12)	128.6(3)	128.7(7)	128.5(10)	128.5(7)	128.3(10)	127.9(9)	126.1(10)
C(8)–C(9)–C(10)	105.8(4)	105.9(6)	106.9(8)	106.2(7)	106.2(9)	105.9(10)	102.5(10)
C(9)–C(10)–C(11)	104.7(3)	106.5(6)	104.7(8)	104.9(5)	105.1(11)	104.8(10)	106.2(8)
C(10)–C(11)–N(7)	108.0(5)	106.2(6)	107.5(8)	108.6(5)	107.9(12)	108.5(7)	106.8(9)
C(10)–C(11)–O(13)	127.9(3)	129.7(7)	127.4(10)	128.1(7)	127.2(10)	128.1(11)	128.0(10)
N(7)–C(11)–O(13)	124.1(6)	124.0(6)	125.1(9)	123.4(7)	124.9(12)	123.3(6)	125.2(10)
C–C–X[a]		118.8(6)	120.3(7)	117.0(9)	118.6(8)	119.2(7)	117.7(8)
X–C–C[a]		119.3(7)	117.6(8)	118.8(7)	120.0(11)	117.8(10)	119.8(8)

[a] X is F or Br.

should be small, as shown by the equivalent thermal parameters B_{eq} in Table 2.

Figure 2 shows the bond lengths and angles as means of the values for all seven compounds. All the bond lengths and angles had normally accepted values, except the C(2)–C(3) bond in compound **(IV)** which is exceptionally short (1.336 Å) as compared with the values in the other compounds (1.359—1.400 Å). This value was therefore omitted in the calculation of mean values. This short bond length may be ascribed to the expanded thermal motional effect of C(2) and C(3) in compound **(IV)**. The thermal ellipsoids of these atoms in the ORTEP drawing (Figure 1), and the large values (6.44 and 7.96 Å^2) for the equivalent thermal parameters B_{eq} of C(2) and C(3), respectively (Table 2), suggest large thermal librations for these two atoms. As expected from the molecular structures, the mean values of the bond lengths and angles in Figure 2 show a complete two-fold rotational symmetry around the C(6)–N(7) bond. In the benzene ring, the mean bond lengths between carbon atoms and the mean internal angles are similar, being very close to the corresponding standard values. Furthermore, the sum of the three bond angles around the carbon atom to which a substituent (N, F, or Br) is attached is in the range 359.9—360.0°, indicating that the benzene ring of the *N*-phenylsuccinimides **(I)**—**(VII)** is essentially planar and that the substituents lie in the plane. These data were confirmed by least-squares plane calculations as described later.

The mean length (1.429 Å) of the C(6)–N(7) bond (Figure 2) is less than the sum of the single-bond radii of the C and N atoms[14] (1.47 Å), and within the lower limit of the range (1.431—1.483 Å) of C–N bond lengths of aniline derivatives.[15–18] This value is also less than the conjugated N–C(α) bond length (1.45 Å) in the peptide linkage.[19] Sheldrick *et al.*[20] have reported that the lengths of the two C–N bonds in 1,3-diphenylspiro[imidazolidine-2,2′-indan]-1′,3′-dione have small values (1.378 and 1.433 Å), owing to their double-bond character (complete and partial double-bond characters, respectively). The bond length of C(6)–N(7) (1.429 Å) for the *N*-phenylsuccinimides is very similar to this partial double bond length, suggesting that the C(6)–N(7) bond participates in the conjugated system of the benzene ring.

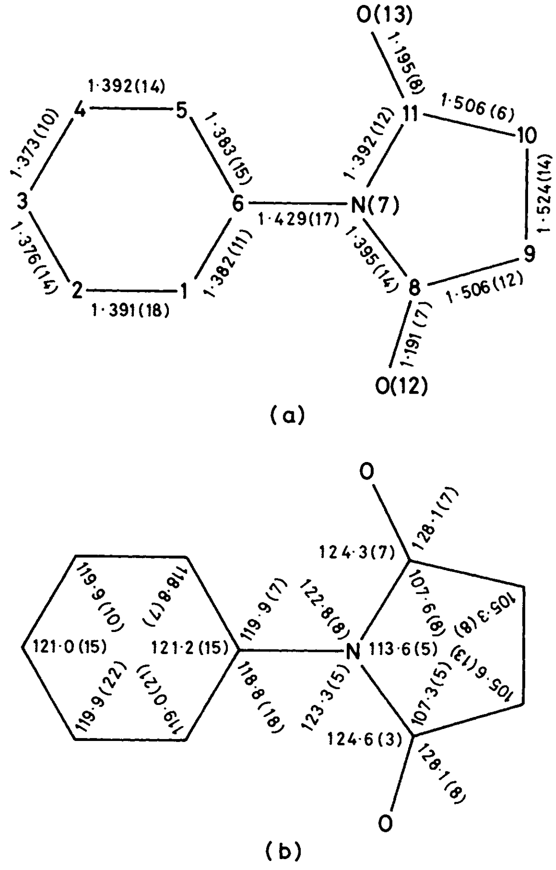

Figure 2. Atomic numbering, mean bond lengths (a), and mean bond angles (b) of *N*-phenylsuccinimides; mean values are the averages for compounds (**I**)—(**VII**); values in parentheses are standard deviations

The sums of the bond angles around the atoms N(7), C(8), and C(11) were 359.8, 360.0, and 360.0°, respectively, indicating that these atoms assume planar sp^2 hybridization. The lengths (1.191 and 1.195 Å) of the carbonyl bonds C(8)–O(12) and C(11)–O(13), respectively, are shorter than the corresponding value of 1.24 Å for a peptide linkage.[19] The lengths (1.395 and 1.392 Å) of the N(7)–C(8) and N(7)–C(11) bonds, respectively, are longer than that (1.32 Å) for a peptide linkage.

From these results, the features of the C–N bonds in these succinimides may be summarized as follows. (i) The C(6)–N(7) bond is shorter than a normal single C–N bond, and longer than a normal C=N double bond, probably as a result of sp^2 hybridization between C(6) and N(7). (ii) The N(7)–C(8) and N(7)–C(11) bonds are shorter than a C–N bond in a peptide linkage. (iii) The C(8)–O(12) and C(11)–O(13) bonds are shorter than a C=O bond in a peptide linkage. (iv) The bonds around N(7), C(8), and C(11) are all planar. These results suggest that the O(12)–C(8)–N(7)–C(11)–O(13) bond system in the succinimide ring is not fully conjugated, and is not conjugated with the benzene ring. The bonds C(8)=O(12), N(7)–C(6), and C(11)=O(13) appear to be somewhat isolated, and to have a partial resonance structure.

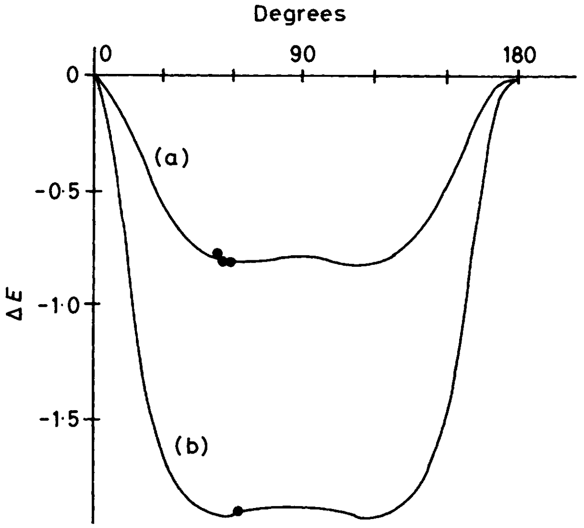

Figure 3. Conformational energy profiles around the C(6)–N(7) bond in compounds (**I**), (**II**), (**IV**), and (**VI**); curve (a) is for (**I**), (**IV**), and (**VI**), and curve (b) for (**II**); Filled circles (●) denote the energy at the angle determined by *X*-ray analysis

Next, we consider the differences in molecular structures of compounds (**I**)—(**VII**). The geometry of the carbon hexagon in the benzene ring is known to be deformed by introduction of a substituent, the deformation being most marked at the substituted carbon atom: the internal angle of a substituted carbon atom may differ considerably from 120°, to about 114 or 125°.[21–23] Deformations of this type were observed in the *N*-phenyl succinimides (**I**)—(**VII**). Although all the mean internal angles of the unsubstituted carbon atoms of the benzene ring were very close to 120°, those of the halogen-substituted carbon atoms were greater than 120°, indicating deformation: the increments in the internal angle from 120° brought about by substitution with fluorine were 1.8 (**II**), 4.1 (**IV**), and 3.0° (**VI**), and those observed on substitution with bromine were 2.1 (**III**), 1.3 (**V**), and 2.3° (**VII**) (see Table 4). Thus the effect of substitution by a fluorine atom was greater than that by a bromine atom, probably because of the greater electronegativity of the former. On the other hand, the bond lengths between carbon atoms in the benzene ring were very similar, as observed with monosubstituted benzenes.[21–23]

The least-square planes of the benzene and succinimide rings were determined by equation (1) (Table 5). Values of the coefficients of equation (1) and the deviations from the plane are summarized in this Table. Since the absolute maximum deviation from the least-squares plane of the benzene ring for the seven compounds was very small (0.017 Å), the benzene ring can be regarded as essentially planar in all cases. Furthermore, the coplanarity of halogen and N atoms attached to the benzene ring is very high, consistent with the internal bond angles shown in Figure 2.

Deviation from planarity in the succinimide ring is greater than that in the benzene ring in all these compounds. This deviation is very great in compounds (**I**) and (**VII**) but less than the estimated standard deviation (e.s.d.) by a factor of 3 in the other cases. Furthermore, the exocyclic atoms C(6), O(12), and O(13) attached to ring nitrogen or carbon can also be regarded as coplanar with the succinimide ring. The deviations for compounds (**I**) and (**VII**) were three times the e.s.d.s. Thus, the conformation of the five-membered ring of these compounds is deformed from a planar structure, to give an envelope form puckered at C(9).

As summarized in Table 5, the torsion angle between the benzene and succinimide rings depends on the nature and position of the substituent in the benzene ring. In the unsubstituted compound (**I**), the torsion angle is 59.6°. Substitution of a fluorine or bromine atom at the *ortho*-position increased this angle, and the effect of bromine (about 10° increase) was greater than that of fluorine (about 4° increase). However, substitutions of fluorine atoms at the *meta*- and *para*-

Table 5. Least-squares planes and deviations (Å) of the atoms from the planes; atoms used in calculating the least-squares planes by equation (1) are denoted by asterisks

$$Ax + By + Cz = D \quad (1)$$

	Planes	(I)	(II)	(III)	(IV)	(V)	(VI)	(VII)
(a) Phenyl group								
	A	6.619	6.033	5.848	8.145	5.753	−1.505	6.890
	B	2.620	−1.580	−2.457	1.920	−2.687	5.401	−6.572
	C	7.186	6.635	6.520	−7.079	7.317	6.683	2.198
	D	8.518	1.338	0.860	0.718	9.212	5.740	1.840
	C(1)*	0.001	0.000	0.007	0.008	−0.008	−0.007	−0.010
	C(2)*	−0.002	−0.011	0.001	0.001	0.009	−0.001	0.017
	C(3)*	0.000	0.015	−0.008	−0.009	−0.006	0.006	−0.009
	C(4)*	0.003	−0.007	0.007	0.008	0.002	−0.003	−0.007
	C(5)*	−0.004	−0.004	0.000	0.001	−0.001	−0.005	0.014
	C(6)*	0.002	0.008	−0.007	−0.009	0.005	0.010	−0.004
	F or Br		0.032	0.034	0.016	0.004	0.020	0.103
	N(7)	−0.017	0.004	−0.014	−0.008	0.008	0.000	0.027
(b) Succinimide group								
	A	6.414	−5.614	−6.192	−0.612	9.359	−1.663	6.467
	B	−2.973	−1.615	−1.972	3.283	3.190	−5.789	5.107
	C	6.841	6.823	6.411	6.585	4.368	6.572	−3.229
	D	4.360	0.018	−0.250	9.084	11.404	−4.057	3.292
	N(7)*	−0.007	0.005	0.011	−0.006	−0.002	0.015	0.026
	C(8)*	0.049	−0.015	−0.029	0.028	0.012	−0.003	−0.047
	C(9)*	−0.064	0.019	0.036	−0.035	−0.016	−0.009	0.068
	C(10)*	0.058	−0.017	−0.029	0.027	0.016	0.017	−0.085
	C(11)*	−0.036	0.008	0.011	−0.015	−0.009	−0.020	0.037
	O(12)	0.155	−0.063	−0.095	0.096	0.066	−0.002	−0.162
	O(13)	−0.115	0.029	0.009	−0.053	−0.023	−0.110	0.127
	C(6)	−0.036	−0.063	−0.001	−0.191	−0.152	−0.030	0.179
(c) Torsion angles between the two planes								
	θ/°	59.6	63.5	69.8	54.5	59.8	55.9	62.2

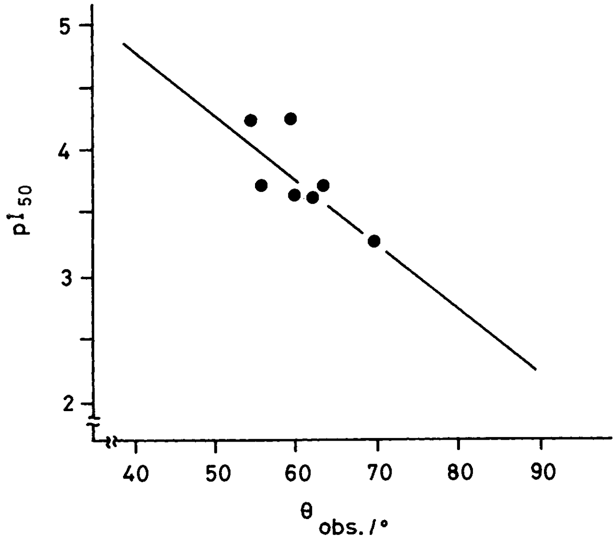

Figure 4. Relationship between the torsion angle $\theta_{obs.}$ and fungicidal activity of *N*-phenylsuccinimides. The angle $\theta_{obs.}$ is that between the least-squares planes of the benzene and succinimide rings. Fungicidal activity, pI_{50}, is the negative logarithmic value of the molar concentration required for 50% inhibition of mycelial growth of *Botrytis cinerea*

positions decreased the torsion angle to similar extents (both about 4°), whereas bromine atoms at these positions had little effect. It is noteworthy that the benzene and succinimide rings are not coplanar but are twisted around the C(6)–N(7) bond.

As just described, the major difference among the seven *N*-phenylsuccinimides is in the torsion angles between the benzene and succinimide rings. These values were determined for the crystal state, but it was important to know the relation between the structure in the crystalline state and the stable molecular conformation determined by molecular orbital calculation. We have therefore calculated the dependence of the total energy (*E*) of *N*-phenylsuccinimide (**I**) and its fluoro derivatives (**II**), (**IV**), and (**VI**) on the torsion angle (θ) by the extended Hückel method;[24] changes of *E* with increments of 5° of θ were calculated. As shown in Figure 3, the energy profiles of (**I**), (**IV**), and (**VI**) are the same, but different from that of (**II**). In all cases, the torsion angle found in the crystal state, $\theta_{obs.}$, was at or near the θ value for minimum energy, indicating that the observed torsion angle corresponds to the most stable conformation determined by molecular orbital calculation. Thus, we may expect that *N*-phenylsuccinimides have the same structure in the crystal state as under the conditions in which they exhibit biological activity.

Takayama and Fujinami[4] have determined the fungicidal activities of *N*-phenylsuccinimides against *Botrytis cinerea*. Figure 4 shows the relationship between activity and the torsion angle $\theta_{obs.}$. Interestingly, the activity tends to increase with decrease in $\theta_{obs.}$, suggesting that the planar conformation is favourable to fungicidal activity.

References

1 A. Fujinami, T. Ozaki, and S. Yamamoto, *Agric. Biol. Chem.*, 1971, **35**, 1707.

2 A. Fujinami, T. Ozaki, K. Nodera, and K. Tanaka, *Agric. Biol. Chem.*, 1972, **36**, 318.

3 H. Ohkawa, Y. Hisada, N. Fujiwara, and J. Miyamoto, *Agric. Biol. Chem.*, 1974, **38**, 1359.

4 C. Takayama and A. Fujinami, *Pestic. Biochem. Physiol.*, 1979, **12**, 163.

5 E. Eckle and J. J. Stezowski, *J. Med. Chem.*, 1985, **28**, 125.

6 P. Luger, G. Griss, R. Hurnaus, and G. Trummlitz, *Acta Crystallogr., Sect. B*, 1986, **42**, 478.

7 W. Wong and S. F. Watkins, *J. Chem. Soc., Chem. Commun.*, 1973, 888.

8 M. J. Barassin, *Ann. Chim. (Paris)*, 1963, **8**, 637.

9 O. Kirino, C. Takayama, A. Fujinami, K. Yanagi, and M. Minobe, *J. Pestic. Sci.*, 1984, **9**, 351.

10 M. Kaftory, *Acta Crystallogr., Sect. B*, 1980, **36**, 597.

11 P. Main, L. Lessinger, M. M. Woolfson, G. Germain, and J. P. Declercq, 'MULTAN 77, A Program for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data,' University of York, 1977.

12 C. K. Johnson, ORTEP, Report ORNL-3794, Oak Ridge National Laboratory, Tennessee, 1965.

13 'International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, 1974, vol. IV.

14 L. Pauling, 'The Nature of Chemical Bond,' Cornell University Press, Ithaca, 1960, 3rd edn., p. 224.

15 I. Van Bellingen, G. Germain, P. Piret, and M. Van Meerssche, *Acta Crystallogr., Sect. B*, 1971, **27**, 553.

16 I. Van Bellingen, G. Germain, P. Piret, and M. Van Meerssche, *Acta Crystallogr., Sect. B*, 1971, **27**, 560.

17 R. Hulme and J. C. Scruton, *J. Chem. Soc. A*, 1968, 2448.

18 A. F. Berndt and E. O. Schlemper, *Acta Crystallogr., Sect. B*, 1982, **38**, 2493.

19 R. E. Marsh and J. Donohue, 'Advances in Protein Chemistry,' ed. C. B. Anfinsen, Jr., M. L. Anson, J. T. Edsall, and F. M. Richards, vol. 22, 1967, p. 235.

20 W. S. Sheldrick, A. Schonberg, and E. Singer, *Acta Crystallogr., Sect. B*, 1982, **35**, 1355.

21 A. Domenicano, P. Mazzeo, and A. Vaciago, *Tetrahedron Lett.*, 1976, 1029.

22 A. Domenicano and P. Murray-Rust, *Tetrahedron Lett.*, 1979, 2283.

23 A. Domenicano, P. Murray-Rust, and A. Vaciago, *Acta Crystallogr., Sect. B*, 1983, **39**, 457.

24 R. Hoffmann, *J. Chem. Phys.*, 1963, **39**, 1397.

Received 21*st September* 1987; *Paper* 7/1682