

Synthesis, Structure, and Spectral Behavior of Donor-Acceptor Substituted Biphenyls¹

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Reaction of the activated halonitrobenzenes **2a-f** with the bis- and tris(dialkylamino)benzenes **1a-e** affords, via a direct nucleophilic substitution, the highly substituted biphenyls **3a-o**; the lesser substituted biphenyls **5** and **6** were prepared by an Ullmann reaction. All these biphenyls are deeply colored; the dark red color can be assigned to an intramolecular charge transfer. A crystal structure determination was carried out for 2,4,6-tripyrrolidino-2',4',6'-trinitrobiphenyl (**3a**): space group *C2/c*, *a* = 16.071 (2) Å, *b* = 14.545 (1) Å, *c* = 20.177 (2) Å, β = 91.361 (9)°, *Z* = 8 (temperature \approx 120 K). The dihedral angle between the two arene rings was found to be only 52.5°, despite the four bulky substituents in the *o,o'*-positions. With this far-from-orthogonal torsional angle about the biphenyl linkage, the strong intramolecular charge transfer from the π system of the donor into the π system of the acceptor arene becomes easily understandable. A PPP calculation with the torsional angles taken from the X-ray structure analysis satisfactorily reproduces the experimental absorption spectrum of **3a**. The shift of the long-wavelength absorption between the individual biphenyls **3a-o**, **5**, and **6** likewise is accounted for satisfactorily by the calculation; it depends primarily on the intrinsic donor strength of the different NR₂ moieties (pyrrolidino > dimethylamino > piperidino > morpholino). The ¹H NMR spectra (in dilute solution) likewise mirror this gradation in NR₂ donor capacity; they also show that steric hindrance at the biphenyl linkage is mainly the result of interaction between the *o*-dialkylamino groups and the C₆ skeleton of the acceptor arene. This is borne out by the crystal structure analysis.

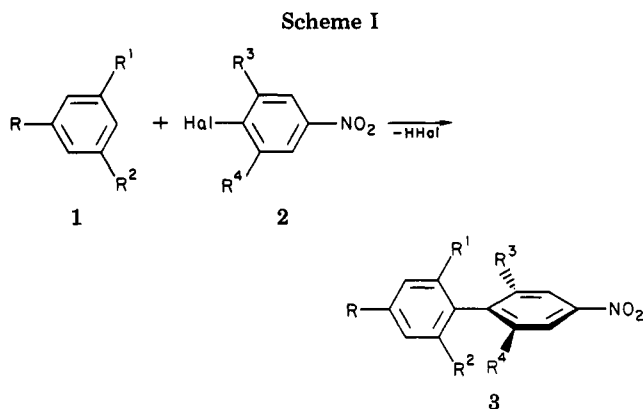
In a preliminary paper³ we have reported the facile synthesis of donor-acceptor substituted biphenyls via nucleophilic aromatic substitution of activated haloarenes by electron-rich aminobenzenes. These biphenyls are isolated as lustrous crystals which are surprisingly deep red to almost black. Because of the bulky substituents in *o*- and *o'*-positions, one would expect a nearly orthogonal orientation, and thus negligible mesomeric interaction, of the two phenyl rings. The dark red color had to be attributed to intramolecular charge-transfer processes, though, on the basis of the spectroscopic data and of calculations.⁴

It seemed desirable to test the scope of the new biphenyl synthesis, beyond those examples already reported,^{3,4} with respect to the reactivity limits for the amino- as well as the halobenzene components. This would allow for a systematic substituent variation in both the donor and acceptor moieties of the biphenyls, a prerequisite for a definitive study of the low-energy absorption, and thence of the bonding in these compounds.

We now report the preparation of a fairly wide range of donor-acceptor substituted biphenyls, together with the crystal structure analysis of one representative member, 2,4,6-tripyrrolidino-2',4',6'-trinitrobiphenyl. The ¹H NMR spectra are discussed in terms of ground-state solution conformation, and the nature of the long-wavelength electronic transition is established unequivocally on the basis of SCF-CI calculations.

Synthesis of Donor-Acceptor Substituted Biphenyls via Nucleophilic Aromatic Substitution

A decisive factor in the formation of the biphenyls **3** via this synthetic route is the aryl carbon nucleophilicity of



the aminobenzene substrate **1**; it strongly depends on number and relative positions of the amino substituents on the ring as well as on the nature of the NR₂ moieties. We have demonstrated in the course of extensive investigations on mono-, di- and triaminobenzenes⁵ that the mesomeric interaction of amino groups with an aromatic π system, and concomitantly the aryl-C nucleophilicity, decreases in the order pyrrolidino > dimethylamino > piperidino > morpholino. Meta orientation (rather than ortho or para) of the individual NR₂ substituents in polyaminobenzenes provides the best stabilization of the cationic reaction intermediate as substituent effects are approximately additive for meta derivatives.⁶ In the case of the second reactant, the 4-halonitrobenzenes **2**, reactivity parameters are known for a number of additional substituents.⁷

The limit for a polar formation of a biphenyl linkage, set by the relative reactivity of the components **1** and **2**, should easily be established with the help of these data.

(1) Aminobenzenes. 16. For part 15 see: Effenberger, F.; Menzel, P.; Seufert, W. *Chem. Ber.* **1979**, *112*, 1660-1669.

(2) (a) Universität Stuttgart. (b) Universität Konstanz.

(3) Effenberger, F.; Nagel, K.; Agster, W. *Angew. Chem.* **1971**, *83*, 619. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 566.

(4) Daltrozzo, E.; Effenberger, F.; Fischer, P. *Angew. Chem.* **1971**, *83*, 621-622. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 567-568.

(5) Effenberger, F.; Fischer, P.; Schoeller, W. W.; Stohrer, W. D. *Tetrahedron* **1978**, *34*, 2409-2417.

(6) Jaffé, H. H. *Chem. Rev.* **1953**, *53*, 191-261.

(7) (a) Miller, J.; Parker, A. J. *Aust. J. Chem.* **1958**, *11*, 302-308. (b) Berliner, E.; Monack, L. C. *J. Am. Chem. Soc.* **1952**, *74*, 1574-1579.

Reaction of 2,4,6-tripiperidino- and 2,4,6-trimorpholinoiodobenzene (**6c,d**), respectively, with 4-iodonitrobenzene in the presence of metallic Cu yielded only the symmetrical hexamino- and dinitrobiphenyls **7c,d** and **8** (Scheme III), apart from dehalogenated triaminobenzenes **1c,d**. With Cu₂O/quinoline, only **1** and **7**, but no trace of **8**, could be isolated. Attempts to prepare 2,4,6-tripiperidino-4'-nitrobiphenyl via a Gomberg reaction from tripiperidino-benzene **1c** and *p*-nitrophenyldiazonium salts failed in both homogeneous and heterogeneous phases.

¹H NMR Spectra

Since NMR spectra reflect upon molecules in a state which is practically unperturbed energetically, ¹H and ¹³C NMR of the biphenyls **3** and **5** should afford some insight into the effective charge transfer from the amino- (donor) to the nitrophenyl (acceptor) unit in the molecular ground state. Decomposition of the biphenyls **3** thwarted all attempts to obtain satisfactory ¹³C spectra which would have provided a much more powerful probe for changes in π charge density. ¹H spectra were run with 0.1 M solutions to minimize solute-solute interactions. The extremely constant residual solvent proton resonances (CHCl₃, CD₂HCN) indicate the absence of bulk medium effects; the chemical shift values in Table II may consequently be considered to be significant to at least ± 0.003 ppm.

For the 4-(dialkylamino)-2',4',6'-trinitrobiphenyls **5a,c,d**, the high-field shift of the 3',5'-protons in the acceptor moiety (both in CDCl₃ and CD₃CN; see Table II) clearly mirrors the increasing donor potential of the individual NR₂ moieties (mor < pip < pyr⁵). Introduction of two further dialkylamino donors in positions 2 and 6 of the donor arene does not alter this trend, $\delta(3',5'\text{-H})$ again moving upfield in the expected order: **3d** (mor) \rightarrow **3c** (pip) \rightarrow **3b** (NMe₂) \rightarrow **3a** (pyr). The absolute values, however, are not shifted to substantially higher field, as expected from the presence of three donor functions, but rather to slightly lower field. The effect is small for the pyrrolidino but clearly pronounced for the piperidino and morpholino derivatives ($\Delta\delta = 0.20$ ppm). Since these six-membered cyclic amines are nonplanar and thus bulkier, the (unexpected) downfield shift is very likely sterically induced. It cannot be distinguished, though, whether this is due to increased torsion about the biphenyl linkage (and a concomitant decrease in charge transfer) or simply to a larger twist of the *o*-NO₂ functions relative to the plane of the acceptor arene which would result in a change in the anisotropy field at the two meta protons 3',5'-H.

The assumption that steric effects are responsible for the observed deshielding is supported by the fact that it is 3-4 times larger in the H-donor solvent CDCl₃ than in CD₃CN; solvation of the NR₂ lone pairs and/or the N \rightarrow O dipoles of the NO₂ groups is expected to be much stronger for D-CCl₃, thus increasing the effective size of the respective substituents. That steric factors are indeed operative (which in turn are much more stringent for the piperidino than for the pyrrolidino group) receives additional confirmation from the following: relative to **5a**, 3',5'-H are shifted downfield by only 0.01 ppm in the 2,4-dipyrrolidino derivative **3e** and by 0.11 ppm in the 2,4,6-tripyrrolidino derivative **3a**. In the piperidino series, on the other hand, the first and second *o*-pip functions shift $\delta(3',5'\text{-H})$ downfield by 0.08 and 0.13 ppm each. These steric effects are clearly mirrored in the electronic spectra, the bathochromic shift of the long-wavelength absorption appearing much attenuated upon introduction of the third NR₂ group (see Table III, Figure 4).

The 3,5-H signals of the tripyrrolidinobiphenyls with one, two, and three NO₂ groups in the acceptor unit, in

contrast, respond to the increasing acceptor potential of the nitrophenyl ring in a straightforward manner, moving downfield by 0.04 ppm each from **3h** to **3g** and from **3g** to **3a**. The linear gradation indicates that in this series the two *o*-NO₂ functions do not contribute significantly to the steric hindrance about the biphenyl linkage. This also is borne out by the fairly monotonic bathochromic shift of the long-wavelength absorption in the series **3h** \rightarrow **3g** \rightarrow **3a** (see Table III, Figure 3). The decisive factor for the actual torsion about the C-1/C-1' bond, and thus the effective ground-state charge transfer, seems to be the steric interaction between the dialkylamino groups in 2- and 6-positions of the donor and the C₆ skeleton of the acceptor unit. This observation is supported by the crystal structure analyses of **3a** and of methyltripyrrolidinobenzene (see below).

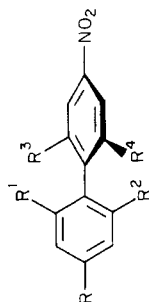
In all our biaryls, the N-CH₂ protons of the amino functions ortho to the biaryl linkage are shifted upfield by more than 0.5 ppm relative to those of the respective para functions (see Table II). This cannot be due to special mesomeric demand on the *p*-NR₂ moiety since the chemical shift difference is more than 20 times the $\Delta\delta$ value for the aryl protons and since the β -CH₂ protons of the *o*-dialkylamino groups likewise experience 0.3-ppm high-field shifts. Rather, the *o*-NR₂ groups must be assumed to lie well within the diamagnetic screening cone of the nitrophenyl ring. The even larger upfield shift (-0.75 ppm) for the α -piperidino signals shows that these protons intrude still deeper into the region of the anisotropic ring current; this is not unreasonable on consideration of the chair conformation of the piperidino substituent, in contrast to the quasi-planar structure of the pyrrolidino ring. The *p*-N-CH₂ signal remains unchanged within the series mono-, di-, trinitrotripyrrolidinobiphenyl (**3h** \rightarrow **3g** \rightarrow **3a**), i.e., the *p*- α -CH₂ protons do not feel the electron demand of the nitroarene moiety to any significant degree. The *o*-N-CH₂ signals are shifted to lower field by only 0.05 ppm in this series, due probably to some anisotropic deshielding by the NO₂ groups. The small shift rules out appreciable steric interaction between nitro and dialkylamino functions in positions ortho to the biphenyl linkage, respectively.

The *p*-N-CH₂ resonance again is not affected in the series mono-, di-, tripyrrolidinotrinitrobiphenyl (**5a** \rightarrow **3e** \rightarrow **3a**); the *o*-N-CH₂ signal in **3**, though, appears deshielded by 0.13 ppm relative to **3a**. This might be rationalized in terms of an increase in the C¹-C^{1'}-C^{2'} bond angle, removing the *o*-pyrrolidino function somewhat from the screening region of the nitrophenyl ring.

Electronic Spectra

The dark red color of all our donor-acceptor substituted biphenyls is due to a specific, long-wavelength absorption; its energy depends, as the compilation of $\tilde{\nu}_{\text{max}}$ values in Table III demonstrates, on both the kind and number of the individual substituents. For the biphenyls **3**, the high *o,o'*-substitution suggests an orthogonal orientation of the two arene systems (characterized by a torsional angle Θ of 90°). Three different intramolecular charge-transfer processes (i-iii) had originally been considered⁴ for the explanation of the long-wavelength absorption in this conformation. None of these, however, stands a more detailed, quantitative inspection.

(i) The first process was interaction of the "lone" electron pairs of both *o*-amino nitrogens with the p_z atomic functions in the 1'-position and, to a lesser degree, with those in positions 2' and 6', requiring a full twist between the donor nitrogen p orbital and the aminobenzene π system (torsional angle $\Phi = 90^\circ$). Numerical analysis shows that the overlap integral amounts to only 0.052 β_0 for sp² and

Table II. ¹H Chemical Shifts of Dialkylamino^a Nitro Biphenyls 3 and 5 (0.1 M in CDCl₃/CD₃CN, 25 °C)^b

compd	R	R ¹	R ²	R ³	R ⁴	3',5'-H ^c	3,5-H ^c	chemical shift, δ (Me, Si)			
								R ¹ , R ² (ortho) ^d		R (para) ^d	
								N-CH ₂ (α)	CH ₂ (β)	N-CH ₂ (α)	CH ₂ (β)
3a	pyr	pyr	pyr	NO ₂	NO ₂	8.773/8.742	6.013/6.021	2.78 ₀ /2.71 ₀	1.72 ₀ /1.66 ₀	3.34 ₀ /3.31 ₀	2.01 ₅ /1.99 ₅
3b	NMe ₂	NMe ₂	NMe ₂	NO ₂	NO ₂	8.817	6.205	2.58 ₀		3.04 ₀	
3c	pip	pip	pip	NO ₂	NO ₂	8.901/8.858	6.407/6.424	2.61 ₅ /2.59 ₅	1.34 ₅ /1.32 ₅	3.25 ₅ /3.25 ₅	1.63 ₅ /1.64 ₀
3d	mor	mor	mor	NO ₂	NO ₂	8.921/8.825	6.459/6.500	2.67 ₅ /2.63 ₀	3.48 ₀ /3.39 ₀	3.27 ₀ /3.24 ₀	3.88 ₅ /3.79 ₀
3e	pyr	pyr	H	NO ₂	NO ₂	8.679/8.731	6.056/6.083 (3-H), 6.192/6.180 (5-H), 6.829 (6-H)	2.91 ₅ /2.86 ₅	1.76 ₅ /1.72 ₀	3.33 ₅ /3.30 ₀	2.01 ₀ /1.99 ₅
3f	pip	pip	H	NO ₂	NO ₂	8.774/8.827	6.611/6.717 (3-H), 6.632/6.727 (5-H), 6.908 (6-H)	2.71 ₀ /2.69 ₅	1.39 ₀ /1.36 ₅	3.29 ₀ /3.31 ₀	1.66 ₀ /1.66 ₀
3g	pyr	pyr	pyr	NO ₂	H	8.692 (3'-H), 8.296 (5'-H), 7.700 (6'-H)	5.975/5.974	2.73 ₀ /2.68 ₅	1.69 ₀ /1.64 ₅	3.33 ₅ /3.29 ₅	1.99 ₅
3h	pyr	pyr	pyr	H	H	7.594 (2'-H), 8.138 (3'-H)	5.942	2.72 ₀	1.63 ₅	3.34 ₅	1.99 ₅
5a	H	pyr	H	NO ₂	NO ₂	8.668/8.774	7.062 (2-H), 6.573/6.614 (3-H)			3.33 ₀ /3.30 ₅	2.03 ₀ /2.00 ₅
5c	H	pip	H	NO ₂	NO ₂	8.695/8.801	7.079 (2-H), 6.915/6.969 (3-H)			3.29 ₅ /3.28 ₅	1.66 ₅ /1.64 ₀
5d	H	mor	H	NO ₂	NO ₂	8.773/8.822	7.134 (2-H), 6.924/6.987 (3-H)			3.26 ₀ /3.21 ₅	3.88 ₅ /3.78 ₅

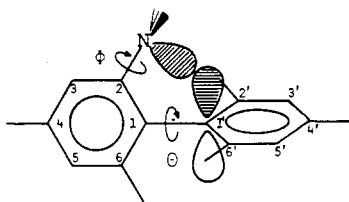
^a Pyr = pyrrolidino, NMe₂ = dimethylamino, pip = piperidino, mor = morpholino. ^b Pulse fourier transform conditions: pulse width 560 μs (45° flip angle), 16K interferograms, spectral width 892.8571 Hz ± 0.001 ppm digital resolution. ^c Shift data for other than singlet aryl proton spectra are from iterative analyses (Nicolet program ITRCL1/2, NIC 17-30712). ^d Position of the intense center line of the individual characteristic CH₂ multiplets.

Table III. Long-Wavelength Absorption of the Donor-Acceptor Substituted Biphenyls 3 and 5 (in CHCl₃, Ambient Temperature)

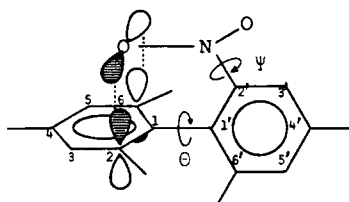
compd	$\tilde{\nu}_{\max}^1$, cm ⁻¹	λ_{\max} , nm	ϵ_{\max} , L mol ⁻¹ cm ⁻¹	$\Delta\tilde{\nu}_{1/2}^a$, cm ⁻¹
3a	17 000	588	5800	5600 (4200)
3c	18 250	548	4400	6400 (4600)
3e	17 600	568	7200	5700 (4250)
3f	19 200	521	4500	10600 (4800)
3g	19 100	524	6300	6200 (4600)
3h	21 900	457	6600	5900 (5200)
3i	20 500	488	7500	5200 (5200)
3k	20 500	487	7300	5500
5a	19 850	504	8100	5250 (4500)
5c	21 000	476	5200	7000 (5400)
5d	22 700	440	5100	6800 (5200)

^a The numerical values of $\Delta\tilde{\nu}_{1/2}$ are taken directly from the spectra. These data do not always present the true picture, though, since there are further electronic transitions in the region of the long-wavelength absorption, the number and intensity of which are both substituent dependent. The widths at half-height for the first electronic transition, given in parentheses, have been determined by a band analysis, based on the long-wavelength slope of the first absorption band.

0.0725 β_0 for sp³ hybridization of the NR₂ nitrogen (with 280 pm as a reasonable distance between N and C-1').



(ii) The second process was interaction between an oxygen n-electron pair of an o'-nitro group and the p_z orbitals at C-2 and C-6 in the donor arene. No additional rotation of the NO₂ group relative to the plane of the acceptor arene (torsional angle $\Psi = 0^\circ$) is required for this process. It likewise is ruled out by the negligible overlap integral⁹ and also for reasons of orbital symmetry.



(iii) The third process was interaction of the p_z orbitals of one arene with a pseudo- π orbital of the other arene, made up from the " σ " orbitals of the C-1/C-2 and C-1/C-6 or the C-1'/C-2' and C-1'/C-6' bonds, respectively. The large energy difference between the interacting orbitals eliminates such a straightforward intramolecular charge transfer between an electron-rich donor and an electron-deficient acceptor arene as the source of the long-wavelength absorption.

This leaves only a genuine π - π^* transition, polarized along the long molecular axis, as the origin of the deep color of the biphenyls 3 and 5, such as one would expect for all nonorthogonal conformations ($\Theta < 90^\circ$). Even with

(9) An overlap integral of 0.016 β_0 is calculated between the oxygen p orbital and the p_z lobes at C-2 and C-6 [with $r = 260$ pm, $\beta(p_x) = 0.075\beta_0$, and $\beta(p_z) = 0.001\beta_0$ as plausible limiting conditions].

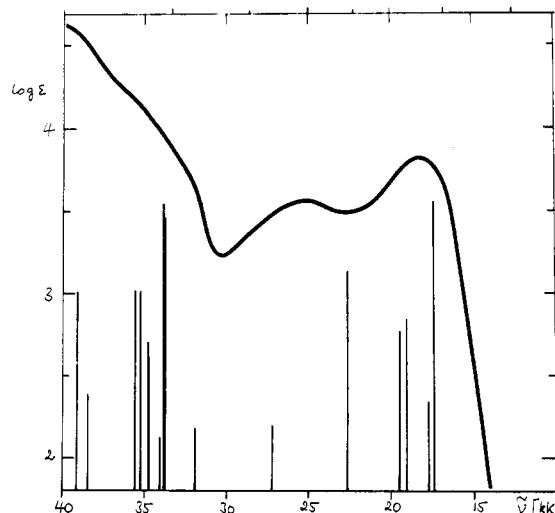


Figure 1. Absorption spectrum of 3a. The solid line represents the experimental spectrum in methylcyclohexane/isopentane (1:3) at ambient temperature. The calculated spectrum is presented as a stick spectrum (PPP calculation for a twisted geometry, with the torsional angles $\Theta = 52.5^\circ$, $\Phi = 53.9^\circ$, and $\Psi = 40.5^\circ$ from the X-ray structure analysis of 3a).

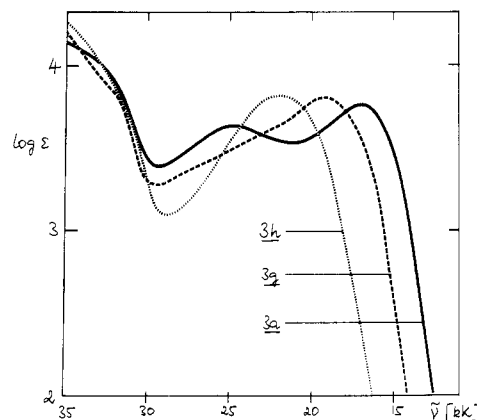


Figure 2. Dependence of the absorption spectra of 2,4,6-tripyrrolidinobiphenyls on the number of nitro groups in the 2', 4', and 6'-positions (3h \rightarrow 3g \rightarrow 3a; in CHCl₃, ambient temperature).

an 80° torsion between the donor and acceptor π systems, the effective overlap (0.1736 β_0) is large compared with the overlap integrals calculated for the hypothetical mechanisms i and ii. For "push-pull"-substituted biphenyls, the long-wavelength absorption thus represents an intramolecular CT transition by which electric charge is effectively transferred from the π -donor to the π -acceptor groups via the biaryl π system.

The (hexasubstituted) biphenyls 3, however, present some additional complexities compared to other, only 4,4'-disubstituted biaryls. Additional high-lying donor and low-lying acceptor terms are introduced into the molecules with the second and/or third π -donor and π -acceptor groups in the 2,2'- and 6,6'-positions. This alone could explain the bathochromic band shift observed in going from 4,4'-di- to 2,2',4,4',6,6'-hexasubstituted biphenyl derivatives (see Table III and also the supplementary material).

At the same time, the steric interaction between the ortho substituents increases the torsion about the biphenyl linkage. For 4-amino-4'-nitrobiphenyl, a hypsochromic band shift is calculated with increasing torsional angle Θ . This effect is much attenuated for the higher substituted biphenyls 3 and 5; for 3a, even a slight bathochromic shift

Table IV. Fractional Atomic Coordinates with Estimated Standard Deviations

atom	x	y	z	atom	x	y	z
C11	0.32748 (7)	0.25564 (8)	0.36815 (6)	O422	0.71669 (8)	0.31535 (9)	0.4355 (1)
C21	0.28279 (7)	0.32875 (8)	0.33856 (6)	N62	0.43398 (7)	0.10803 (7)	0.31537 (6)
C31	0.19623 (7)	0.32751 (8)	0.33611 (6)	O621	0.46222 (7)	0.03051 (7)	0.32498 (6)
C41	0.15207 (7)	0.25185 (8)	0.36172 (6)	O622	0.38199 (7)	0.12752 (7)	0.27190 (5)
C51	0.19731 (7)	0.17696 (8)	0.38863 (6)	H31	0.168 (1)	0.378 (1)	0.3148 (9)
C61	0.28371 (7)	0.17922 (8)	0.39285 (6)	H51	0.169 (1)	0.123 (1)	0.4076 (8)
C12	0.41871 (7)	0.25784 (8)	0.37594 (6)	H32	0.573 (1)	0.380 (1)	0.4419 (9)
C22	0.46340 (8)	0.32948 (8)	0.40736 (6)	H52	0.586 (1)	0.124 (1)	0.3536 (9)
C32	0.54896 (8)	0.32891 (9)	0.41893 (7)	H2111	0.333 (2)	0.335 (2)	0.219 (1)
C42	0.59252 (8)	0.25166 (9)	0.39998 (7)	H2112	0.420 (1)	0.342 (2)	0.259 (1)
C52	0.55407 (8)	0.17778 (9)	0.36814 (7)	H2121	0.354 (1)	0.469 (1)	0.168 (1)
C62	0.46930 (7)	0.18385 (8)	0.35561 (6)	H2122	0.446 (1)	0.479 (2)	0.204 (1)
N21	0.32957 (7)	0.40130 (7)	0.31039 (5)	H2131	0.334 (1)	0.596 (1)	0.2401 (9)
C211	0.3708 (1)	0.3779 (1)	0.24789 (8)	H2132	0.404 (1)	0.562 (1)	0.294 (1)
C212	0.38735 (9)	0.4697 (1)	0.21383 (7)	H2141	0.280 (1)	0.520 (1)	0.342 (1)
C213	0.3565 (1)	0.54264 (9)	0.26208 (8)	H2142	0.239 (1)	0.489 (1)	0.2715 (9)
C214	0.2902 (1)	0.49127 (9)	0.30018 (8)	H4111	0.042 (1)	0.164 (1)	0.4369 (9)
N41	0.06726 (7)	0.25072 (7)	0.36074 (6)	H4112	0.019 (1)	0.123 (1)	0.3675 (9)
C411	0.01843 (8)	0.17846 (9)	0.39194 (7)	H4121	-0.073 (1)	0.254 (1)	0.4364 (8)
C412	-0.06888 (8)	0.2197 (1)	0.39549 (7)	H4122	-0.113 (1)	0.173 (1)	0.392 (1)
C413	-0.07198 (8)	0.2880 (1)	0.33809 (7)	H4131	-0.080 (1)	0.255 (1)	0.2945 (9)
C414	0.01550 (8)	0.32905 (8)	0.34039 (6)	H4132	-0.117 (1)	0.334 (1)	0.3444 (9)
N61	0.33093 (6)	0.10752 (7)	0.42324 (5)	H4141	0.034 (1)	0.353 (1)	0.2967 (8)
C611	0.29855 (8)	0.01324 (8)	0.42119 (6)	H4142	0.018 (1)	0.379 (1)	0.3713 (8)
C612	0.36016 (8)	-0.03715 (8)	0.46677 (7)	H6111	0.300 (1)	-0.008 (1)	0.3769 (8)
C613	0.3722 (1)	0.0311 (1)	0.52364 (7)	H6112	0.240 (1)	0.006 (1)	0.438 (1)
C614	0.3641 (1)	0.12563 (9)	0.49120 (7)	H6121	0.413 (1)	-0.047 (1)	0.443 (1)
N22	0.41990 (7)	0.41051 (7)	0.43411 (6)	H6122	0.338 (1)	-0.095 (1)	0.481 (1)
O221	0.35534 (7)	0.39794 (7)	0.46397 (5)	H6131	0.327 (2)	0.023 (2)	0.556 (1)
O222	0.45391 (7)	0.48557 (7)	0.42743 (6)	H6132	0.426 (1)	0.026 (1)	0.547 (1)
N42	0.68294 (8)	0.24713 (9)	0.41207 (7)	H6141	0.327 (1)	0.167 (1)	0.517 (1)
O421	0.71924 (7)	0.17634 (9)	0.39771 (8)	H6142	0.422 (1)	0.155 (1)	0.489 (1)

with increasing θ is calculated. In addition to θ , one has to consider the dihedral angle Φ between the π -symmetrical *o*-N donor orbital and the aminobenzene π system and the dihedral angle Ψ between the two π systems of the *o*-nitro group and the acceptor benzene. A change even in one of these torsional angles will influence the experimental absorption in a complicated manner since θ , Φ , and Ψ are mutually interdependent.

A calculation (PPP approximation) with the torsional angles from the crystal structure analysis of **3a**, $\theta = 52.2^\circ$, $\Phi = 53.9^\circ$, and $\Psi = 40.5^\circ$, yields a spectrum which is in satisfactory agreement with the experimental absorption spectrum of **3a** (Figure 1). The spectral band shifts observed within the series **3a** \rightarrow **3g** \rightarrow **3h** and **3a** \rightarrow **3e** \rightarrow **5a** (see Figures 2 and 3) are likewise reproduced satisfactorily by the calculation (excitation energies, oscillatory strengths, and polarization of the transitions for the individual compounds are given in the supplementary material).

All the biphenyls investigated consequently exist in a twisted, chiral conformation, with an energy minimum for $\theta < 90^\circ$. Torsion about the C-1/C-1' biphenyl linkage is best represented by a double minimum potential. The form of the potential, i.e., minimum potential position, energy difference ΔE between E_{\min} and E_{90° , and steepness of the potential well, depends on the nature of the individual substituents and the respective torsional angles Φ and Ψ .

Only torsional, i.e., steric effects have been considered so far for the different biphenyl derivatives. The gradation of the broad long-wavelength absorption bands strikingly illustrates the hierarchy of the various +M substituents; their donor strength increases in the order OCH_3 ($\bar{\nu}$ 29 500 cm^{-1}) $<$ morpholino $<$ piperidino $<$ pyrrolidino (see Table III). The bathochromic band shifts within the series **3c** \rightarrow **3a** and **5d** \rightarrow **5c** \rightarrow **5a** probably are due to increasingly higher lying donor terms. The larger band width and

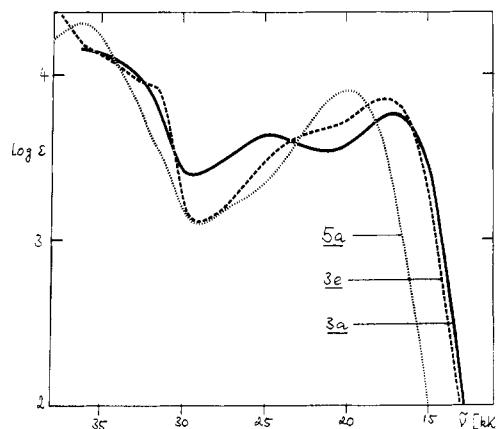


Figure 3. Dependence of the absorption spectra of 2',4',6'-trinitrobiphenyls on the number of pyrrolidino moieties in the 2-, 4-, and 6-positions (**5a** \rightarrow **3e** \rightarrow **3a**; in CHCl_3 , ambient temperature).

reduced band integral of **3c** relative to those of **3a** can be interpreted in terms of greater steric demand of the piperidino relative to the pyrrolidino moiety.

Crystal Structure Analysis of **3a**

The structure determination of **3a** reveals a conformation different from what might be expected for a biphenyl with four bulky ortho substituents. The torsion angle between the two aryl subunits, as determined by the angle between the normals of least-squares mean planes, fitted to the phenyl ring carbons, is 52.5° . Comparable values for perfluoro^{10a} and perchlorobiphenyl^{10b} are 59.6° and 86.6° , respectively. A stereoscopic projection of crystalline

(10) (a) Gleason, W. B.; Britton, D. *Cryst. Struct. Commun.* 1976, 5, 483-488. (b) Pedersen, B. F. *Acta Crystallogr., Sect. B* 1975, B31, 2931-2933.

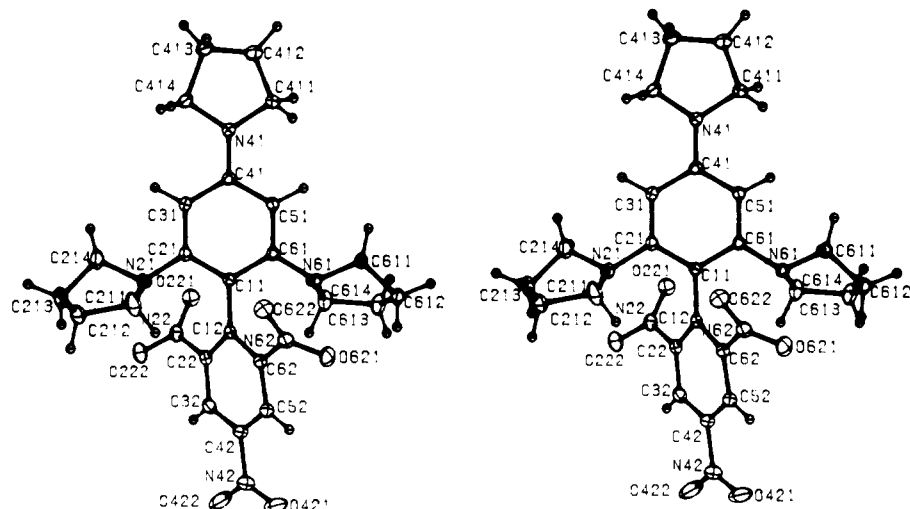


Figure 4. Stereoscopic projection¹³ of one molecule of **3a**.

Table V. Selected Bond Distances,^a Angles, and Dihedral Angles for 1-Methyl-2,4,6-tripyrrolidinobenzene (**9**)^b

bond	distance, Å	bond angle		dihedral angle	
		atoms	angle, deg	atoms	angle, deg
C1-C2	1.412	C2-C1-C6	117.5	C6-C1-C2-C3	7.1
C2-C3	1.398	C1-C2-C3	121.0	C5-C6-C1-C2	-4.8
C3-C4	1.403	C2-C3-C4	120.6	C1-C2-N2-C24	-8.5
C2-N2	1.415	C3-C4-C5	118.7	C1-C2-N2-C21	117.9
C4-N4	1.372	C2-N2-C21	117.4	C3-C4-N4-N41	6.4
N2-Cpy	1.471	C2-N2-C24	119.0	C3-C4-N4-C44	174.9
N4-Cpy	1.455	C21-N2-C24	106.4	C5-C6-N6-C61	2.1
Cpy-Cpy	1.530		(Σ 342.8)	C5-C6-N6-C64	-133.3
		C4-N4-C41	123.2		
		C41-N4-C44	112.6		

^a Where appropriate, average values are given for bonds related by molecular, not crystallographic, symmetry. ^b The locant numbering has been chosen to correspond to that for the biphenyls; correct name: 2-methyl-1,3,5-tripyrrolidinobenzene.

3a is displayed in Figure 4 (for the refined fractional atomic coordinates see Table IV; for the bonding geometry see the supplementary material).

Each phenyl ring of **3a**, together with the respective substituents in 2,4,6-position, has approximate C_2 symmetry. The two local symmetry axes pass through the carbon and nitrogen atoms in positions 1 and 4; they differ from colinearity by 8.3°. The *o*-nitro groups are twisted by 40.5° and the *o*-pyrrolidino groups by 53.9° with respect to their parent arene rings; the corresponding average interplanar angles, on the other hand, for the *p*-pyrrolidino and *p*-NO₂ substituents are only 5.4° and 5.0°. The two phenyl rings which constitute the biphenyl **3a** carry, respectively, strongly σ -electron-withdrawing substituents (NO₂) or substituents which are recognized as weak σ but extremely good π electron donors (pyrrolidino groups).⁵ In benzene derivatives, the deformation of the endocyclic bond angle of the substituted carbon atom (defined as α) and the compensatory change in the endocyclic bond angles at the two adjacent carbon atoms (β) have been correlated with the σ -electron-withdrawing or -releasing character of the individual substituents.¹¹ Thus, a σ -electron-donating substituent causes a decrease in α and an increase in β ; for σ -electron-withdrawing groups, the opposite effect is observed. The magnitude of the angular deformation can be correlated, at least semiquantitatively, with the substituent group electronegativity.¹¹ For substituents with the same electronegativity as the C₆H₆ ring,

and bonded by an atom of a first-row element, e.g., CH₃, α has a standard value of 117.7°.

1-Methyl-2,4,6-tripyrrolidinobenzene (**9**) provides a suitable structural reference for the donor subunit of **3a**; relevant averaged bonding geometry parameters from a high precision structure determination of **9**¹² are summarized in Table V. The angle α at the methyl-substituted ring carbon C-1 is 117.5°; this close-to-standard value demonstrates that the pyrrolidino groups in positions 2, 4, and 6 have no significant effect upon the endocyclic bond angle at C-1. So, from the bond angle α of 119.5° established for the ring carbon atom C-1 of **3a**, the σ -electron-withdrawal character of the trinitrophenyl moiety can be compared straightforwardly to that of CONH₂ and COOH (α 119.8°) or that of OCH₃ (α 119.9°). The respective angle α at C-1' in the trinitrophenyl (acceptor) ring is 113.7°; this remarkable decrease, however, very likely contains a sizeable contribution from the two σ -electron-withdrawing *o*-nitro groups (decrease of β).

The clearly significant difference in inter-ring C-N bond distances between *o*- and *p*-pyrrolidino substituents is present in both **3a** and **9** (see Tables IV and V); the effect thus must be primarily steric. No evidence for through conjugation between the two phenyl subunits can be gleaned from the structural data of the donor-acceptor substituted biphenyl **3a**. The ¹H NMR data for the *p*-pyrrolidino functions likewise do not mirror the varying

(11) Domenicano, A.; Mazzeo, P.; Vaciago, A. *Tetrahedron Lett.* 1976, 1029-1032.

(12) Schöllkopf, K. Diplomarbeit, Universität Stuttgart, 1979.
(13) Johnson, C. K. "ORTEP-II", Technical Report ORNL-5138; Oak Ridge National Laboratory: Oak Ridge, TN, 1971.

Table VI

atom	$U_{\mu\mu}$	Z_{cor}	$\gamma_{\mu\mu}$	$\gamma_{\mu\nu}$	$\beta_{\mu\nu}$
—C=	0	1.0	9.0	5.1	1.0
—N=	-3.0	1.0	9.6	5.2	1.05
—N	-8.3	1.9	10.4	5.3	1.03
=O	-4.9	1.0	11.2	6.4	1.25
=O(NO ₂)	-4.9	1.0	11.2	5.8	1.0
—O—	-14.8	2.0	12.6	6.2	1.05

electron demand of the different nitrophenyl acceptor rings.

Experimental Section

General Methods. ¹H NMR spectra were recorded on a Bruker HX-90-E, equipped with a 15-in. magnet and a 20K Nicolet BNC-12 computer, by use of the pulse Fourier transform technique at a 90.0-MHz nominal frequency. The absorption spectra were measured with a Cary 118 and a Zeiss PMQ-3 spectrophotometer. Melting points were determined on a Büchi SMP-20 apparatus with a silicon bath and are uncorrected.

Calculations. The PPP calculations were performed with the approximations $\gamma_{\mu\nu} = 9.6/R_{\mu\nu}$ and $\beta_{\mu\nu} = 0$ for nonadjacent centers μ and ν . A β correction was made with $\beta_{\mu\nu} = -2.05 - 0.7p_{\mu\nu}$ (eV). A dielectric constant $\epsilon = 0.913 + 0.0158N$, dependent on the number, N , of centers, was used to account for the effect of molecular size on the respective parameters. The set of parameters¹⁴ shown in Table VI was employed.

In the first iteration step ("Hückel calculation"), a set of parameters specially adopted for Hückel calculations always had to be used since otherwise the high number of electrons caused nonconvergence (a general result independent of the set of parameters used¹⁴). In the CI part, all single-excited configurations resulting from the six highest occupied and the five lowest unoccupied orbitals were considered.

All calculations were performed on the TR-440 computer at Konstanz University Computer Center.

X-ray Structure Determination. A $0.5 \times 0.3 \times 0.3$ mm³ single crystal in a thin-walled glass capillary was used for all X-ray diffraction measurements. The quantitative measurements were carried out with the crystal cooled to ca. 120 K. The lattice parameters [$a = 16.071$ (2) Å, $b = 14.545$ (1) Å, $c = 20.177$ (2) Å, $\beta = 91.361$ (9)°] were determined by a least-squares refinement¹⁵ with the 2 θ values of 72 automatically centered reflections in the angular range $35.0^\circ \leq 2\theta \leq 45.5^\circ$. The space group is $C2/c$ with $Z = 8$. Intensity data were measured with a Syntex P1 autodiffractometer equipped with a low-temperature device (Syntex LT-1). The scan range was 0.75° , the scan rate was $2.0\text{--}24.0^\circ/\text{min}$, and background radiation was measured for half the total scan time on each side of the reflection ($\Delta\omega = 1.0^\circ$). Of the 14575 unique reflections measured ($2\theta_{\text{max}} = 80.0^\circ$, $\lambda = 0.71069$ Å), 6328 were classified as observed under the criterion $I \geq 3.0\sigma(I)$.

The initial structural model was determined by direct methods, with difficulties apparently resulting from pseudo face centering in the strongest E values. The model was developed by difference Fourier and least-squares refinement techniques; all hydrogen atom coordinates were determined from difference electron density maps. The refinement of 437 variables (all atomic coordinates, anisotropic temperature factors for C, N, and O atoms, isotropic temperature factors for H atoms, and a single crystal factor) with 10825 contributing reflections converged to $R = 0.054$, $R_w = 0.067$, and $\sigma = 1.01$.

Starting Materials. **2-Chloro-5-nitro-1,3-benzenedicarboxylic Acid.** 2-Chloroisophthalic acid¹⁶ (10.0 g, 49.8 mmol) was added in small portions at 20 °C to a stirred mixture of fuming nitric acid (51 mL) and 45% oleum (56.5 mol) and refluxed for 6 h. The cooled mixture was poured on ice, and the colorless

precipitate was separated by filtration, and recrystallized from water or ethanol: yield 10.5 g (86%); mp 187 °C. Anal. Calcd for C₈H₄ClNO₆ ($M_r = 245.6$): C, 39.12; H, 1.64; Cl, 14.43; N, 5.70. Found: C, 38.93; H, 1.75; Cl, 14.42; N, 5.48.

Dimethyl 2-Chloro-5-nitro-1,3-benzenedicarboxylate (2f). Dry hydrogen chloride was passed through a stirred solution of 2-chloro-5-nitro-1,3-benzenedicarboxylic acid (9.8 g, 40.0 mmol) in absolute methanol (50 mL) for 2 h; in the course of the exothermic reaction, the solution heated up to the boiling point. The solvent was stripped off, and the residue was taken up in water and, after basification with sodium carbonate, extracted with ether. The extract was dried over sodium sulfate and evaporated to dryness, and the residue was recrystallized from petroleum ether (bp 80–120 °C) to give **2f**: 9.58 g (88%); mp 100 °C. Anal. Calcd for C₁₀H₈ClNO₆ ($M_r = 237.6$): C, 43.89; H, 2.94; Cl, 12.95; N, 5.11. Found: C, 43.67; H, 3.63; Cl, 12.88; N, 5.31.

4-Iodopyrrolidinobenzene (4a). 1,4-Dibromobutane (4.31 g, 20.0 mmol) was added at room temperature to a stirred solution of 4-iodoaniline (4.38 g, 20.2 mmol) in benzene (10 mL) and *N,N*-diisopropylethylamine (5.16 g, 39.9 mmol). The reaction mixture was heated to 50 °C for 24 h, and the cooled suspension was filtered. The filter cake was washed with 2 N NaOH and recrystallized from ethanol, yielding **4a**: 4.43 g (81%); mp 108 °C. Anal. Calcd for C₁₀H₁₂IN ($M_r = 273.1$): C, 43.97; H, 4.42; I, 46.47; N, 5.13. Found: C, 44.26; H, 4.64; I, 46.24; N, 4.97.

4-Iodopiperidinobenzene (4c). 4-Iodoaniline (4.38 g, 20.2 mmol) in benzene (10 mL), *N,N*-diisopropylethylamine (5.16 g, 39.9 mmol), and 1,5-dibromopentane (4.60 g, 20.0 mmol) were treated as above to give **4c**: 2.67 g (46%); mp 77 °C. Anal. Calcd for C₁₁H₁₄IN ($M_r = 287.1$): C, 46.01; H, 4.91; I, 44.20; N, 4.88. Found: C, 46.21; H, 4.97; I, 44.25; N, 5.07.

4-Iodomorpholinobenzene (4d). Finely powdered iodine (10.15 g, 40.0 mmol) was added slowly at 12–15 °C to a stirred mixture of morpholinobenzene¹⁷ (6.25 g, 38.3 mmol) and sodium bicarbonate (5.04 g, 60.0 mmol) in water (50 mL). Stirring was continued at room temperature for 1 h, the dark solid separated by filtration and dissolved in ethanol, and the filtrate was discolored with an aqueous solution of sodium thiosulfate. **4d** was precipitated with water, and recrystallized from ethanol: 3.64 g (32%); mp 146 °C. Anal. Calcd for C₁₀H₁₂INO ($M_r = 289.1$): C, 41.54; H, 4.18; I, 43.89; N, 4.84. Found: C, 41.53; H, 4.22; I, 44.03; N, 4.85.

2,4,6-Tripiperidinoiodobenzene (6c). To a stirred mixture of 1,3,5-tripiperidinobenzene (**1c**)¹⁸ (1.64 g, 5.0 mmol) in methylene chloride (10 mL) and finely powdered sodium bicarbonate (1.26 g, 15.0 mmol) was added dropwise a solution of iodine chloride (0.81 g, 5.0 mmol) in methylene chloride (5 mL) at room temperature (the mixture heated to the boiling point). Methanol (5 mL) was added, stirring continued for 1 h at 40 °C, the reaction mixture filtered, and the filtrate evaporated to dryness. The brown-red residue was washed with water, purified by successive chromatography on silica gel (column 15 cm × 2 cm o.d.) and Merck Nr. 9385 silica gel (column 50 cm × 4 cm o.d.) with ethyl acetate (22 mL/min) as the eluent. First fraction: **6c**, 0.4 g (18%); mp 146 °C. Anal. Calcd for C₂₁H₃₂IN₃ ($M_r = 453.4$): C, 55.63; H, 7.11; I, 27.99; N, 9.27. Found: C, 55.53; H, 7.21; I, 27.80; N, 9.20. Second fraction: **1c**, 0.58 g; mp 183 °C (ref.¹⁷ mp 183–184 °C).

2,4,6-Trimorpholinoiodobenzene (6d). 1,3,5-Trimorpholinobenzene (**1d**)¹⁸ (1.66 g, 5.0 mmol), iodine chloride (0.81 g, 5.0 mmol), and sodium bicarbonate (1.26 g, 15.0 mmol) were reacted as described above. The crude product was recrystallized repeatedly from acetone/methanol (6:4) to give **6d**: 0.82 g (36%); mp 256 °C. Anal. Calcd for C₁₈H₂₆IN₃O₃ ($M_r = 459.3$): C, 47.07; H, 5.70; I, 27.63; N, 9.15. Found: C, 47.61; H, 5.81; I, 27.59; N, 8.87.

Biphenyls 3 (Tables I and VII). General Procedure. A solution of the 4-halonitrobenzene **2** in ethanol was added to a boiling solution of the aminobenzene **1** in chloroform, and the resulting dark red mixture was refluxed for 4 h. The solvents were evaporated, and the residue was dissolved in boiling ethanol. When the mixture cooled to room temperature, the product precipitated. The dark red crystals were filtered off and purified

(14) Kollmannsberger-von Nell, G., unpublished results.

(15) Stewart, J. M.; Machin, P. A.; Dickinson, C. W.; Ammon, H. L.; Flack, H.; Heck, H. "The XRAY System Version 1976", Technical Report TR-446; University of Maryland Computer Science Center: College Park, MD, 1976. Unless otherwise indicated, this program was used for all computerized calculations.

(16) Stapleton, G.; White, A. I. *J. Am. Pharm. Assoc.* **1954**, *43*, 193–200; *Chem. Abstr.* **1955**, *49*, 8968b.

(17) Shono, T.; Iikuni, T.; Oda, R. *Nippon Kagaku Zasshi* **1960**, *81*, 1625; *Chem. Abstr.* **1962**, *56*, 7188c.

(18) Effenberger, F.; Niess, R. *Chem. Ber.* **1968**, *101*, 3787–3793.

Table VII. Biphenyls 3 from Aminobenzenes 1 and 4-Halonitrobenzenes 2^{d,e}

aminobenzene (g, mmol)	in CHCl ₃ , mL	4-halonitrobenzene (g, mmol)	in EtOH, mL	biphenyl (yield, g)	recrystallized from ^a
1a ¹⁸ (5.71, 20.0)	15	2a (2.47, 10.0)	15	3a (3.77)	EtOH/PE (7:3)
1c ¹⁸ (6.55, 20.0)	15	2a (2.47)	15	3c (3.82)	EtOH/PE/C ₆ H ₆ (6:2:2)
1d ¹⁸ (6.66, 19.9)	30	2a (2.47)	15	3d (3.7)	EtOH/C ₆ H ₆ (7:3)
1e ²¹ (4.32, 20.0)	15	2a (2.47)	15	3e (3.16)	EtOH/PE (7:3)
1f ²¹ (4.88, 20.0)	15	2a (2.47)	15	3f ^{b,c} (2.96)	EtOH/C ₆ H ₁₂ /CH ₂ Cl ₂ (6:2:2)
1a (5.71)	15	2b (2.02, 10.0)	15	3g (3.34)	EtOH/PE (8:2)
1a (5.71)	15	2d (1.82, 10.0)	15	3i (2.61)	EtOH/PE (8:2)
1a (5.71)	15	2e (2.15, 10.0)	15	3k (2.2)	EtOH/C ₆ H ₁₂ (8:2)
1a (5.71)	15	2e' (1.99, 10.0)	15	3k (4.01)	
1a (5.71)	15	2f (2.73, 10.0)	15	3l (4.07)	EtOH/PE (8:2)
1a (1.427, 5.0)	7	2g (1.302, 5.0)	5	3m (0.55)	EtOH
1a (2.85, 10.0)	7	2h (1.57, 6.9)	5	3n (1.26)	EtOH/C ₆ H ₆ (4:1)
1e (28.0, 129.4)	60	2g (14.0, 53.7)	60	3o (20.0)	EtOH/PE (8:2)

^a PE = petroleum ether. ^b After 12 h of refluxing. ^c In a second preparation, 2a (0.62 g, 2.5 mmol) in ethanol (5 mL) was added to 1f (1.08 g, 4.5 mmol) in chloroform (10.0 g) at 70 °C. The mixture was refluxed for 10 min. Ethanol (50 mL) was added, the reaction mixture cooled to 0 °C, and the precipitate recrystallized from ethanol; yield 0.82 g (72%) of 3f as black crystals, mp 179 °C. ^d Satisfactory analytical data ($\pm 0.3\%$ for C, H, N) for all biphenyls (except as noted) were submitted for review. Exception: 3f, calcd for C₂₂H₂₅N₃O₆: C, 58.01; H, 5.53; N, 15.38. Found: C, 58.55; H, 5.38; N, 14.86. ^e For yields and melting points, see Table I.

by recrystallization (see Table VII).

2,4,6-Tris(dimethylamino)-2',4',6'-trinitrobiphenyl (3b). A solution of 1,3,5-tris(dimethylamino)benzene (1b;¹⁸ 4.34 g, 20.9 mmol) in chloroform (25 mL) was added to a solution of 2a (2.47 g, 10.0 mmol) in ethanol (25 mL). The resulting dark red solution was refluxed for 10 min and allowed to cool to room temperature, and the precipitate was separated by filtration and recrystallized from benzene/ethanol (1:3) to give 3b: 2.5 g (60%); mp 258 °C. Anal. Calcd for C₁₈H₂₂N₆O₆ (M_r = 418.4): C, 51.67; H, 5.30; N, 20.09. Found: C, 51.88; H, 5.41; N, 19.94.

2,4,6-Tripyrrolidino-4'-nitrobiphenyl (3h). Compound 1a (5.71 g, 20.0 mmol) and 4-fluoronitrobenzene (2c'; 1.41 g, 10.0 mmol) were heated in a sealed tube to 120 °C for 20 h. The dark reaction mixture was taken up in hot methylene chloride, the solvent evaporated, and the dark residue recrystallized from ethyl acetate/ethanol. The red precipitate was recrystallized from cyclohexene to give 3h: 0.54 g (13%); mp 236 °C. Anal. Calcd for C₂₄H₃₀N₄O₂ (M_r = 406.5): C, 70.91; H, 7.44; N, 13.78. Found: C, 70.43; H, 7.22; N, 13.35.

Ullmann Reactions for the Preparation of 4-Amino-2',4',6'-trinitrobiphenyls 5. General Procedure. A mixture of 1,3,5-trinitrobenzene (2.13 g, 10.0 mmol), 4-iodoaminobenzene 4 (10.0 mmol), and Cu₂O (0.72 g, 5.0 mmol) in absolute quinoline (25 mL) was slowly heated to 180 °C with vigorous stirring and kept at 180 °C for 1 h. After the mixture cooled to room temperature, 200 mL of ether was added, the resulting suspension was filtered, and the yellow filter cake was carefully washed with ether. The ether was evaporated to dryness, and the resulting deep red oily residue was purified by chromatography on silica gel (column 50 cm \times 1.5 cm o.d., eluent benzene). The red fraction was evaporated and the residue recrystallized from methylene chloride/cyclohexane.

4-Pyrrolidino-2',4',6'-trinitrobiphenyl (5a). Reaction with 4a (2.73 g) yielded 5a: 0.86 g (24%); mp 205 °C. Anal. Calcd for C₁₆H₁₆N₄O₆ (M_r = 358.3): C, 53.63; H, 3.94; N, 15.64. Found: C, 54.14; H, 3.79; N, 15.67.

4-Piperidino-2',4',6'-trinitrobiphenyl (5c). Reaction with 4c (2.87 g) yielded 5c: 0.48 g (13%); mp 152 °C. Anal. Calcd for C₁₇H₁₆N₄O₆ (M_r = 372.3): C, 54.84; H, 4.33; N, 15.05. Found: C, 54.84; H, 4.40; N, 15.28.

4-Morpholino-2',4',6'-trinitrobiphenyl (5d). Reaction with 4d (2.89 g) yielded 5d: 0.42 g (11%); mp 245 °C. Anal. Calcd for C₁₆H₁₄N₄O₇ (M_r = 374.3): C, 51.34; H, 3.77; N, 14.97. Found: C, 51.40; H, 3.75; N, 14.96.

Reaction of 6c with 4-Iodonitrobenzene. A stirred mixture of 4-iodonitrobenzene (1.24 g, 5.0 mmol), 6c (2.26 g, 5.0 mmol), and activated copper (1.5 g, see below) was heated slowly to 250 °C and kept at this temperature for 1 h. After cooling to room temperature, the reaction mixture was extracted repeatedly with methylene chloride. The dark extract was washed several times with aqueous hydrochloric acid, and the organic layer was

evaporated to dryness, taken up with a little warm benzene, filtered, and kept at room temperature; after 2 days, 0.114 g of 4,4'-dinitrobiphenyl (8) was isolated by filtration: mmp 235 °C (lit.¹⁹ mp 237 °C). The aqueous phase was made basic with 2 N NaOH and extracted with methylene chloride. The methylene chloride was stripped off and the gray residue treated with methanol to give 1c [82 mg; mmp 181 °C (lit.¹⁸ mp 183–184 °C)] and 132 mg of 2,2',4,4',6,6'-hexapiperidinobiphenyl (7c), mmp 318 °C (lit.²⁰ mp 320–322 °C).

The activated copper was prepared by treating copper with a 2% solution of iodine in acetone for 10 min. After filtration, the residue was treated with a mixture of hydrochloric acid and acetone. The activated copper was filtered off, washed carefully with acetone, dried in vacuo, and used immediately.

In a second preparation, a mixture of 4-iodonitrobenzene (1.24 g, 5.0 mmol), 6c (2.26 g, 5.0 mmol), Cu₂O (0.72 g, 5.0 mmol), and quinoline (25 mL) was heated slowly with stirring to 180 °C and kept at 180 °C for 1 h. Quinoline was distilled off, and the residue repeatedly extracted with warm methylene chloride. The extracts were filtered and concentrated, the dark oily residue was treated with aqueous hydrochloric acid, and the resulting solution was filtered, made basic (2 N NaOH), and extracted with chloroform. Evaporation of the chloroform phase yielded a gray product (600 mg), which was identified as a mixture of 1c and 7c by ¹H NMR and TLC.

Reaction of 6d with 4-Iodonitrobenzene. 4-Iodonitrobenzene (1.24 g, 5.0 mmol), 6d (2.29 g, 5.0 mmol), and activated copper (1.5 g) were treated as above. The methylene chloride extract yielded 80 mg of 8, mmp 235 °C, (lit.¹⁹ mmp 237 °C). From the aqueous phase, 384 mg of a gray solid were obtained which yielded, after repeated treatment with chloroform, 1d [130 mg; mp 308 °C (lit.¹⁸ mp 308–312 °C)] and 254 mg of 2,2',4,4',6,6'-hexamorpholinobiphenyl (7d), mmp 334 °C (lit.²⁰ mp 344–346 °C).

Registry No. 1a, 16857-93-5; 1b, 16857-99-1; 1c, 16857-95-7; 1d, 16857-97-9; 1e, 27594-18-9; 1f, 27594-19-0; 2a, 88-88-0; 2b, 97-00-7; 2c', 350-46-9; 2d, 16588-02-6; 2e, 6307-82-0; 2e', 2965-22-2; 2f, 87350-69-4; 2g, 2213-79-8; 2h, 27697-45-6; 3a, 33931-06-5; 3b, 87350-70-7; 3c, 87350-71-8; 3d, 87350-72-9; 3e, 33949-03-0; 3f, 87350-73-0; 3g, 33949-02-9; 3h, 87350-74-1; 3i, 33949-06-3; 3k, 87370-87-4; 3l, 87350-75-2; 3m, 33949-04-1; 3n, 33931-07-6; 3o, 33931-13-4; 4a, 87350-76-3; 4c, 55376-34-6; 4d, 87350-77-4; 5a, 87350-78-5; 5c, 87350-79-6; 5d, 87350-80-9; 6c, 87350-81-0; 6d, 87350-82-1; 2-chloro-5-nitro-1,3-benzenedicarboxylic acid,

(19) Ullmann, F.; Frenzel, L. *Ber. Dtsch. Chem. Ges.* 1905, 38, 725–729.

(20) (a) Effenberger, F.; Stohrer, W. D.; Steinbach, A. *Angew. Chem.* 1969, 81, 261–262; *Angew. Chem., Int. Ed. Engl.* 1969, 8, 280. (b) Steinbach, A. Dissertation, Universität Stuttgart, 1969, pp 230, 233.

(21) Effenberger, F.; Prossel, G.; Auer, E.; Fischer, P. *Chem. Ber.* 1970, 103, 1456–1462.

87350-83-2; 2-chloroisophthalic acid, 13049-16-6; 1,4-dibromobutane, 110-52-1; 4-iodoaniline, 540-37-4; 1,5-dibromopentane, 111-24-0; morpholinobenzene, 92-53-5; 1,3,5-trinitrobenzene, 99-35-4; 4-iodonitrobenzene, 636-98-6.

Supplementary Material Available: Figure 5a-c with the bonding geometry of 3a (selected bond distances, bond angles,

and dihedral angles), tabulated calculated and observed structure factors, and Table VIII, listing the results of the PPP calculations for 4-(dialkylamino)-4'-nitrobiphenyl and for the (dialkylamino)nitrobiphenyls 3a, e, g, h and 5a [excitation energies ($\bar{\nu}$, λ), oscillatory strengths, and polarizations (μ_x , μ_y , μ_z) are given for the individual electronic transitions] (95 pages). Ordering information is given on any current masthead page.

A Lewis Acid Catalyzed 1,2 Aryl Shift in α -Haloalkyl Aryl Acetals: A Convenient Route to α -Arylalkanoic Acids

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A new method for the synthesis of α -arylalkanoic acids is given, based on Lewis acid promoted rearrangement of acetals of primary and secondary α -haloalkyl aryl ketones (halo = Br, Cl) in hydrocarbon solvents. The reaction is selective, providing the esters of α -arylalkanoic acids in almost quantitative yields. The ability of "soft and borderline" Lewis acids in activating the carbon-halogen bond is compared with that of silver salts. The reaction mechanism is discussed. The present synthesis has been applied to some α -arylpropionic acids well-known as antiinflammatory drugs.

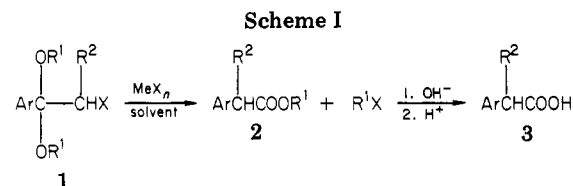
Introduction

The importance of α -arylalkanoic acids in the pharmaceutical industry is well-known:¹ some of them, like 2-(4-isobutylphenyl)propionic acid and 2-(6-methoxy-2-naphthyl)propionic acid, show potent antiinflammatory and analgesic activities. This class of compounds has thus attracted the attention of many research groups and many papers² and several patents³ have been published. Most of the syntheses of α -arylalkanoic acids start from aromatic acyl derivatives,¹ which can be prepared in high yields by selective electrophilic acylation and converted, by many different approaches, into α -arylalkanoic acids. Recently, we reported a synthesis of α -arylalkanoic acids starting from alkyl aryl ketones via halogenation, acetalization, and silver salts promoted rearrangement.^{2a,b} The reaction occurs smoothly in almost quantitative yield. However, the use of at least a stoichiometric amount of a silver salt makes the method less attractive for large-scale preparations and certainly not convenient for industrial manufacturing. This prompted us to seek ways of overcoming the synthetic limits related to the massive use of silver catalysts. The role of silver salts is that of polarizing the carbon-halogen bond of the α -haloalkyl aryl acetal without exerting a strong interaction on the carbon-oxygen bond of the acetal moiety, thus avoiding the conversion of the acetal into the corresponding ketone and/or enol ether. Consequently, the research was aimed at finding other catalysts that could exhibit a behavior similar to that of silver salts.

Results and Discussion

In light of the requirements stated above, attention was directed mainly toward the use of "soft and borderline"⁴ Lewis acids.

Zinc, tin, copper, mercury, palladium, cobalt, antimony, bismuth, and iron salts (MeX_n) were found to promote the conversion of alkyl acetals of α -haloalkyl aryl ketones into alkyl esters of α -arylalkanoic acids and into alkyl halides



(Table I, Scheme I). Hydrolysis of the esters 2 gives quantitatively the free acids 3. The reaction takes place in several different solvents, and among them the ones generally used in Friedel-Craft reactions are preferred.

The reaction temperature (20–200 °C) depends strongly on the catalyst and on the starting acetal. Among the "soft and borderline" Lewis acids, the halides of the above-mentioned metals have shown to be the catalysts of choice. In particular, zinc halides are among the most effective. For this reason, most of forthcoming considerations are relative to experiments with zinc halides in toluene. "Hard" Lewis acids are able to catalyze the rearrangement, but they are less attractive since, in some cases, the con-

(1) Lednicer, D. and Metscher, L. A. "The Organic Chemistry of Drugs Synthesis"; Wiley: New York, 1977; Chapter 6. Shen, T. Y. *Angew. Chem.* 1972, 84, 512; *Angew. Chem., Int. Ed. Engl.* 1972, 6, 460. Ferreira, S. H.; Vane, J. R. "Antiinflammatory Drugs"; Springer-Verlag: New York, 1979; p 321; *Scrip World Pharm. News* 1980, 497, 10.

(2) (a) Giordano, C.; Castaldi, G.; Casagrande, F.; Abis, L. *Tetrahedron Lett.* 1982, 1385. (b) Giordano, C.; Castaldi, G.; Casagrande, F.; Belli, A. *J. Chem. Soc., Perkin Trans. 1* 1982, 2575. (c) Giordano, C.; Minisci, F. *Chim. Ind.* 1982, 5, 340. (d) Tsuchihashi, G.; Kitajima, K.; Mitamura, S. *Tetrahedron Lett.* 1981, 4305. (e) Tsuchihashi, G.; Mitamura, S.; Kitajima, K.; Kobayashi, K. *Ibid.* 1982, 5427. (f) Goosen, A.; McClelland, C. W. *J. Chem. Soc., Chem. Commun.* 1982, 1311. (g) Higgins, S. D.; Thomas, C. B. *J. Chem. Soc., Perkin Trans. 1* 1982, 235. (h) Gujji, K.; Nakao, K.; Yamauchi, T. *Synthesis* 1982, 456. (i) Myrbo, B.; Ila, H.; Junjappa, H. *Ibid.* 1981, 126. (j) Cekovic, Z.; Bosnjak, J.; Cvetkovic, M. *Tetrahedron Lett.* 1980, 2675. (k) McKillop, A.; Taylor, E. C. *Endeavour* 1978, 35, 88.

(3) (a) U.S. Patent 4 324 904, 1982 (The Upjohn Co.). (b) Eur. Patent Appl. 79 104 475.3, 1979 (Sagami Chemical Research Center). (c) Eur. Patent Appl. 81 304 154.8, 1981 (Sagami Chemical Research Center). (d) Ital. Patent Appl. 2 018 780, 1980. Eur. Patent Appl. 81 200 211.1, 1981 (Blasinachim S.p.A.). (e) Eur. Patent Appl. 81 200 210.3, 1981 (Blasinachim S.p.A.). (f) Brit. UK Patent Appl. 8 005 752, 1980 (Montedison S.p.A.).

(4) Tse-lok Ho *Chem. Rev.* 1975, 1, 1.

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