

Efficient Synthesis and Structural Characteristics of Zwitterionic Twisted π -Electron System Biaryls

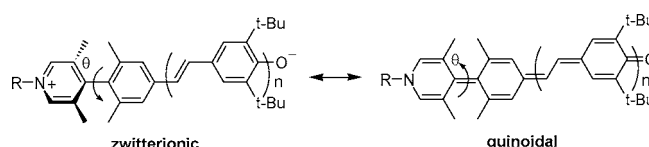
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ABSTRACT



A series of unconventional twisted π -electron system molecules has been synthesized via Suzuki cross-coupling of two sterically hindered arenes. Crystallographic analysis of these molecules reveals a large ring–ring dihedral twist angle (87°) and a highly charge-separated zwitterionic ground state. An efficient conversion of phenols into aryl halides is also reported.

Organic chromophores exhibiting very large hyperpolarizabilities have attracted considerable current research interest due to their potential applications in novel photonic technologies such as high-speed optical communications, optical data processing and storage, and integrated optics.¹ To date, most of the organic molecules developed for this purpose consist of extended *planar* π -conjugated systems end-capped with electron donor and acceptor substituents,² which are inherently elaborate structurally, complicating synthetic approaches, and frequently subject to chemical, thermal, and photochemical instability.³ Recent computational investigations⁴ indicate that relatively simple zwitterionic molecules with *twisted* π -electron systems, TICTOID (twisted intramo-

lecular charge transfer) structures (Figure 1), should exhibit very large hyperpolarizabilities and two-photon absorption

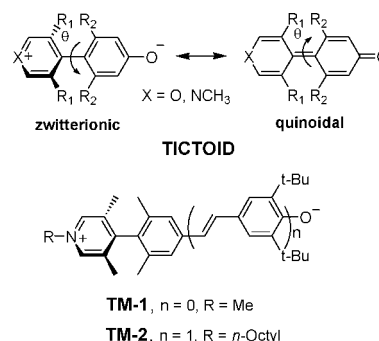


Figure 1. Twisted π -electron system chromophores.

cross-sections. The exceptional responses arise from the very strong sensitivity of the charge separation and excited-state

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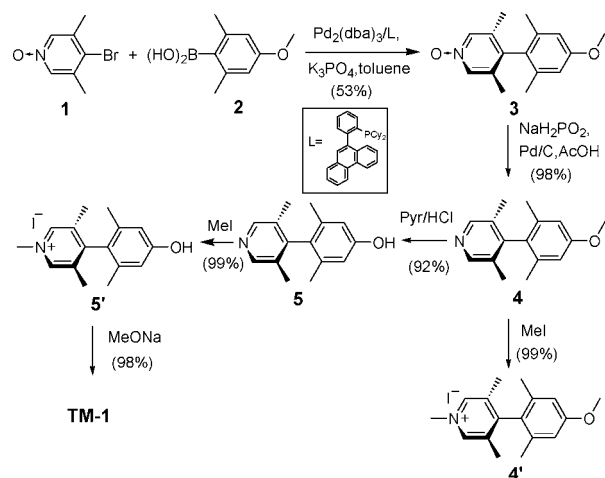
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charge redistribution to the inter-ring twist angle, which is tuned by introducing sterically encumbered R_1 and R_2 substituents. Notably, the mechanism of the response to the light field is distinctly different from the current models such as “bond length alternation”⁵ and “auxiliary donor and acceptor”.⁶ Synthetic access to such chromophores could therefore have a major impact on organic electro-optics.

The synthetic challenge posed by this type of chromophore is obvious: formation of highly hindered substitution patterns via the coupling of two arenes possessing bulky ortho substituents. In this contribution, we report the synthetic realization of the first twisted π -electron system molecules (**TM**s; Figure 1),⁷ merocyanine-based dyes containing a tetra-*ortho*-methylbiaryl core, and their molecular structural characteristics.

Among the catalytic cross-coupling reactions for unsymmetrical biaryl synthesis, limited success has been realized with Stille and Negishi protocols when coupling sterically hindered fragments,⁸ while the Suzuki method has shown more tolerance to steric effects.^{9,10} Recently, Buchwald et al. reported a highly active Pd(0)/phenanthrene-based phosphine Suzuki catalyst for the synthesis of tetra-*ortho*-substituted biaryls, with substituents such as methyl, primary alkyl, phenyl, and alkoxy groups accommodated.^{10a} In the case of electron-deficient heteroarenes, however, our initial attempts to couple 3,5-dimethyl-4-bromopyridine with 4-methoxy-2,6-dimethyl phenylboronic acid (**2**, Scheme 1) employ-

Scheme 1. Synthesis of Twisted π -System Molecule **TM-1**



ing this catalyst system were unsuccessful in affording the key tetra-*ortho*-methylbiaryl core under standard reaction

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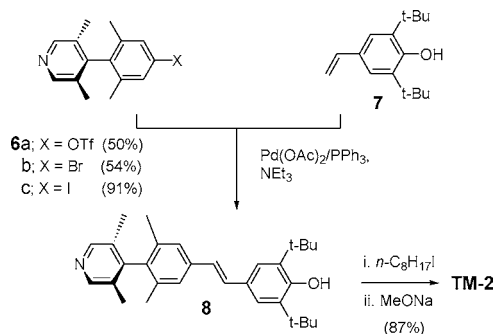
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(7) DFT/ZINDO computations predict hyperpolarizability (β_0) as -123×10^{-30} and -2552×10^{-30} esu for **TM-1** and **TM-2**, respectively (Keinan, S.; Ratner, M. A. Unpublished results).

conditions. Usually, electron-deficient pyridine halides are reactive with respect to oxidative addition processes, often turnover-limiting in the Suzuki catalytic cycle.¹¹ The sluggishness of the present coupling reaction implies that reductive elimination may be turnover-limiting, presumably due to slow formation of a requisite but sterically encumbered *cis*-Pd(II)(aryl)₂ intermediate. Such sluggishness in Suzuki coupling was also observed in hindered aryl halides possessing ortho electron-withdrawing groups using the same catalyst.^{10a} An alternative reason for this inertness in catalyzed coupling may be inhibition by pyridine,¹² displacing a phosphine ligand to form unproductive complexes in some Pd-catalyzed aminations.¹² To investigate this possibility, 4-bromopyridine *N*-oxide **1** was used as a coupling partner with boronic acid **2**, successfully affording the key tetra-*ortho*-methylphenylpyridine core **3** in 53% yield (Scheme 1). Interestingly, the *N*-oxide functionality does not appear to induce detrimental oxidation of the Pd(0) form of the catalyst. Pyridine *N*-oxide **3** was next reduced to **4** using Pd-catalyzed hydrogenation with sodium hypophosphite as the hydrogen source.¹³ This deoxygenation is facile and quantitative. Subsequent cleavage of the **4** methoxyl group affords pyridylphenol intermediate **5** in high yield, which was then quaternized with methyl iodide and deprotonated to afford chromophore **TM-1** almost quantitatively.

The synthetic approach to chromophore **TM-2** relies on Heck cross-coupling (Scheme 2), known to be efficient in

Scheme 2. Synthesis of Twisted π -System Molecule **TM-2**



forming C–C connections between sp^2 carbons and to be highly stereoselective for the (*E*)-stereoisomer.¹⁴ Styrenic coupling partner **7** was obtained from the thermal decar-

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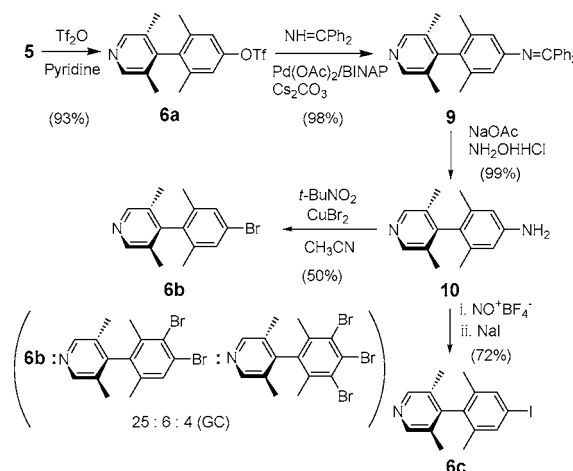
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boxylation of 3,5-di-*tert*-butyl-4-hydroxycinnamic acid in DMF.¹⁵ When the conventional Heck Pd(OAc)₂/PPh₃ catalyst system is employed, **7** undergoes coupling with various twisted triflate (**6a**), bromide (**6b**), and iodide (**6c**) substrates to afford the stilbene precursor **8** in moderate to excellent yields of 50, 54, and 91%, respectively. Precursor **8** was then quaternized with *n*-octyl iodide and deprotonated to afford **TM-2**.

Halide precursors **6b** and **6c** are important not only for facilitating the Heck coupling but also for facilitating introduction of stronger, more stable electron donor functionalities such as the dicyanomethanide group,¹⁶ which could not be introduced by triflate nucleophilic substitution at **6a**.¹⁷ Converting phenol **5** into aryl halides, which can undergo cross-coupling with active methylene compounds such as malononitrile in the presence of Pd catalysts,¹⁸ is thereby highly desirable. Few methods have been reported for direct conversion of phenols to aryl halides.¹⁹ Attempts to synthesize **6b** via thermolysis of the phenol-triphenylphosphine dibromide complex^{19a} were unsuccessful. The displacement of triflate by iodide or bromide is usually feasible in activated aryl triflates possessing ortho or para electron-withdrawing groups²⁰ but in the present case was unsuccessful in affording bromide **6b** and iodide **6c**. We therefore devised a new strategy to convert the phenol **5** to bromide **6b** and iodide **6c** by combining Pd-catalyzed aryl triflate amination²¹ with the arylamine-to-aryl halide conversion (Scheme 3). The conversion began with Pd-catalyzed coupling of triflate **6a** with benzophenone imine, leading to diphenyl ketimine adduct **9** in 98% yield. Subsequent quantitative hydrolysis of **9** to the primary aniline **10** was facilitated by hydroxylamine hydrochloride. Next, aniline **10** was converted into the corresponding halides via anhydrous Sandmeyer-like reactions,²² since conventional Sandmeyer methods in aqueous media²³ gave only low yields and complicated products. Aniline **10** was treated with *tert*-butyl nitrite and anhydrous

Scheme 3. Conversion of Phenol Intermediate **5** to Aryl Halides **6b** and **6c**



CuBr₂ in dry CH₃CN to produce bromide **6b** rapidly, accompanied by the formation of di- and tribrominated byproducts due to competitive oxidative CuBr₂ bromination.^{22a,24} The multibrominated byproducts, even in low yields, complicate purification and result in moderate yields of the desired monobrominated product (50%) after multiple recrystallizations. In contrast, treatment of **10** with nitrosonium tetrafluoroborate in dry CH₃CN and iodination of the corresponding diazonium salt with anhydrous NaI affords pure monoiodide **6c** in 72% yield. The overall yield of this four-step phenol-to-aryl iodide conversion is 65%. This method thereby represents an efficient general route for phenol-to-aryl halide conversion.

Single crystals of synthetic intermediates **3** and **5**, *N*-methyl pyridinium salts **4'** and **5'**, and chromophores **TM-1** and **TM-2** were obtained via slow evaporation of saturated solutions.²⁵ The most important feature revealed from the

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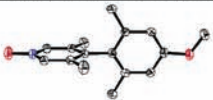
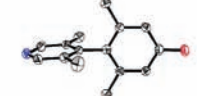
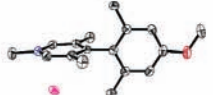

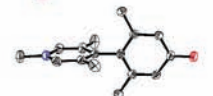
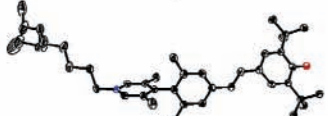
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(25) Crystal data for **3**: C₁₆H₁₉NO₂, *M* = 257.32, monoclinic, *C*2/*c*, *a* = 21.018(6), *b* = 8.137(3), *c* = 18.221(4) Å, β = 119.049(12)°, *V* = 2724.1(13) Å³, *Z* = 8, *D*_c = 1.255 g/cm³. Of the 12 351 reflections that were collected, 3314 were independent (*R*_{int} = 0.0351), 177 parameters, *R*₁ = 0.0525 (for reflections with *I* > 2σ(*I*)), *wR*₂ = 0.1552 (for all reflections); CCDC 274100. Crystal data for **5**: C₁₅H₁₇NO, *M* = 227.30, orthorhombic, *Fdd*2, *a* = 21.927(6), *b* = 29.244(4), *c* = 8.089(2) Å, *V* = 5187(2) Å³, *Z* = 16, *D*_c = 1.164 g/cm³. Of the 11 899 reflections that were collected, 3171 were independent (*R*_{int} = 0.0297), 162 parameters, *R*₁ = 0.0381 (for reflections with *I* > 2σ(*I*)), *wR*₂ = 0.1023 (for all reflections); CCDC 274101. Crystal data for **4'**: C₁₇H₂₂INO, *M* = 383.26, monoclinic, *P*2₁/*c*, *a* = 12.834(2), *b* = 17.241(3), *c* = 7.9026(13) Å, β = 100.799(11)°, *V* = 1717.6(5) Å³, *Z* = 4, *D*_c = 1.482 g/cm³. Of the 15 777 reflections that were collected, 4214 were independent (*R*_{int} = 0.0235), 187 parameters, *R*₁ = 0.0288 (for reflections with *I* > 2σ(*I*)), *wR*₂ = 0.0720 (for all reflections); CCDC 274103. Crystal data for **5'**: C₁₆H₂₂INO₂, *M* = 387.25, monoclinic, *C*2/*c*, *a* = 27.251(7), *b* = 11.5610(18), *c* = 11.868(3) Å, β = 109.661(15)°, *V* = 3521.1(13) Å³, *Z* = 8, *D*_c = 1.461 g/cm³. Of the 15 979 reflections that were collected, 4275 were independent (*R*_{int} = 0.0366), 199 parameters, *R*₁ = 0.0320 (for reflections with *I* > 2σ(*I*)), *wR*₂ = 0.0840 (for all reflections); CCDC 274102. Crystal data for **TM-1**: C₁₇H₂₂INNNO₂, *M* = 423.25, monoclinic, *P*2₁/*n*, *a* = 12.2350(7), *b* = 12.9850(7), *c* = 12.7805(7) Å, β = 110.2070(8)°, *V* = 1905.48(18) Å³, *Z* = 4, *D*_c = 1.475 g/cm³. Of the 17 558 reflections that were collected, 4664 were independent (*R*_{int} = 0.0261), 209 parameters, *R*₁ = 0.0236 (for reflections with *I* > 2σ(*I*)), *wR*₂ = 0.0634 (for all reflections); CCDC 274104. Crystal data for **TM-2**: C₄₂H₆₄NO₄, *M* = 646.94, monoclinic, *P*2₁/*c*, *a* = 14.551(2), *b* =

Table 1. Selected Crystallographic Data for Twisted π -Electron System Molecules (TMs) and Some Synthetic Intermediates

twisted molecule species	ORTEP drawing of the molecular structure ^a	(ring)C–C(ring) (Å)	(ring)C–O (Å)	twist angle (°) ^b
3		1.5006(18)	1.3767(16)	84.2
5		1.4932(18)	1.3579(17)	85.7
4'		1.496(3)	1.372(3)	87.9
5'		1.496(3)	1.364(3)	86.1
TM-1		1.489(2)	1.312(2)	86.9
TM-2		1.490(5)	1.305(4)	87.5

^a 50% probability ellipsoids. Hydrogen atoms and solvent molecules have been omitted for clarity. The iodide counterions are included in the drawings of **4'** and **5'**. ^b Average of four dihedral angles in the respective crystal structures.

crystallographic analysis of these molecules is the consistently large arene–arene dihedral twist angles (84–88°) (Table 1), suggesting that the tetra-*ortho*-methylbiaryl substitution pattern indeed provides sufficient steric encumbrance to achieve very large twist angles, a prerequisite for large molecular hyperpolarizabilities in such **TM** chromophores.⁴ Furthermore, it can be seen that the magnitude of this twist is governed primarily by sterics and is practically independent of chromophore architecture.²⁶ Indeed, neutral, positively charged, and zwitterionic molecules all exhibit comparable twist angles. The (ring)C–C(ring) distances in these molecules are slightly longer than in typical biaryls (~1.487 Å),²⁷ doubtless a result of the pronounced steric hindrance. On the other hand, the (ring)C–C(ring) and (ring)C–O distances in the two zwitterionic **TM** chromophores are only modestly shorter than those of the other species, probably a result of the very small contribution of quinoidal limit forms to the

ground state, due to the twist-induced intramolecular charge transfer. Thus, there is a pronounced reduction in inter-ring π -conjugation and a dominant zwitterionic ground state in the **TM** chromophores, evidenced by the departure from quinoidal structures where (ring)C=C(ring) \approx 1.349 Å and C=O \approx 1.222 Å.²⁷

In summary, synthetic approaches to the first examples of unconventional twisted π -electron system **TM** chromophores have been developed. Crystallographic analysis reveals large ring–ring dihedral twist angles (\sim 87°) and highly charge-separated zwitterionic ground states. The hyperpolarizability physical characteristics will be discussed elsewhere.

Acknowledgment. We thank DARPA/ONR (SP01-P7001R-A1/N00014-00-C), the NSF-Europe Program (DMR-0353831), and the NSF MRSEC program (DMR-0076077) for support of this research.

Supporting Information Available: Experimental procedures, characterization of new compounds, and crystallographic details (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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15.697(3), c = 18.554(3) Å, β = 103.107(2)°, V = 4127.3(12) Å³, Z = 4, D_c = 1.041 g/cm³. Of the 23 176 reflections that were collected, 5374 were independent (R_{int} = 0.0475), 455 parameters, R_1 = 0.0788 (for reflections with $I > 2\sigma(I)$), wR_2 = 0.2200 (for all reflections); CCDC 274105.

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