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Ferrocenes Conjugated with Thiophene, Carbazole, and Pyrimidine Fragments: Synthesis and Properties

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Abstract—Ferrocenyl-containing chalcones containing π-excessive heterocyclic fragments capable of electrochemical polymerization (carbazole, thiophene, 2,4-ethylenedioxythiophene) were prepared by the Claisen–Schmidt reaction. 2,4,6-Trisubstituted pyrimidines derived from them were synthesized.

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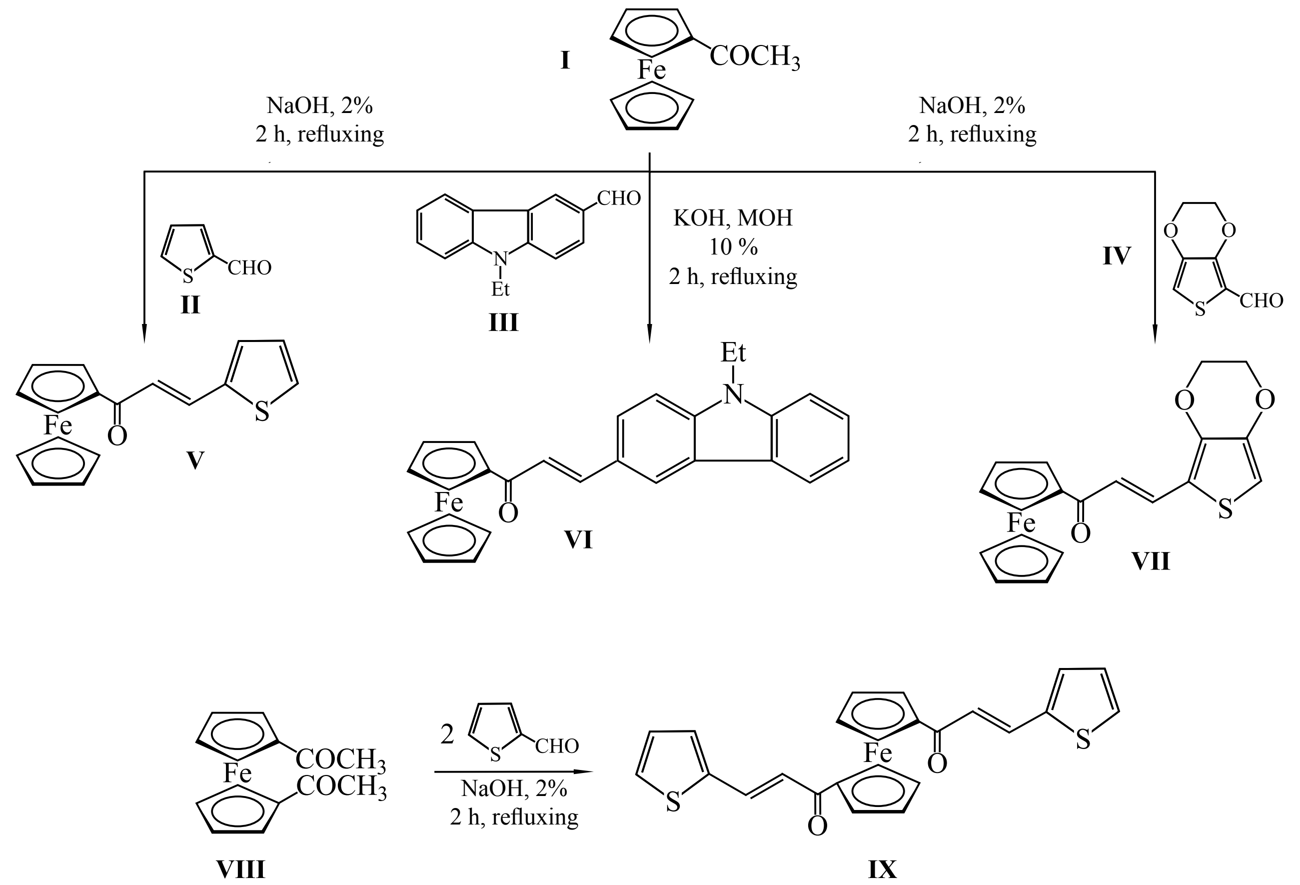
The properties of ferrocene and its derivatives attract steady interest of researchers in many fields of organic and organometallic chemistry. Wide range of studies of applied properties of ferrocene is due to its specific physical and chemical properties: unusually high (for organometallic compounds) thermal stability, high vapor pressure, low toxicity, good solubility in organic solvents, and diverse chemical transformations. The use of electrochemical properties of ferrocene is based on readiness and reversibility of one-electron redox processes. The ferrocene–ferricenium cation system is one of the most highly reversible redox systems. Thanks to this property, this redox couple has found wide practical use: as reversible electrodes in analytical chemistry and as electron-transfer agent in various systems (primarily in biochemical studies) [1, 2]. Recently there has been growing interest in the use of ferrocene-containing organic compounds in such fields as nonlinear optics [3] and chemosensorics [4]. It was also shown that compounds containing a ferrocene fragment can penetrate through cell membranes [5]. At the same time, it is known that such heterocycles as pyrrole, thiophene, and pyrimidine are widely used in fabrication of conducting and electroluminescent materials [6]. A combination of the properties of ferrocene and such heterocycles could lead to new unique properties of materials, i.e., nonlinear optical, magnetic, or electrochemical properties.

From acetylferrocene **I** and diacetylferrocene **VIII** prepared in advance, we synthesized ferrocene-containing chalcones containing unsubstituted thiophene (**V**, **IX**) and carbazole (**VI**) fragments, described previously [7], and 3,4-ethylenedioxythiophene fragment (**VII**) (Scheme 1). The Claisen–Schmidt condensation used in our study can be performed by diverse procedures. We used either refluxing of a mixture of aldehyde and ketone in 2% aqueous alkali solution (chalcones **V**, **VII**, **IX**) or heating in a 10% solution of KOH in methanol (chalcone **VI**). Relatively recently a procedure was described for preparing chalcone **VI** without solvent [8]. All the compounds obtained have bright color: red (**V–VII**, **X**) or violet (**IX**).

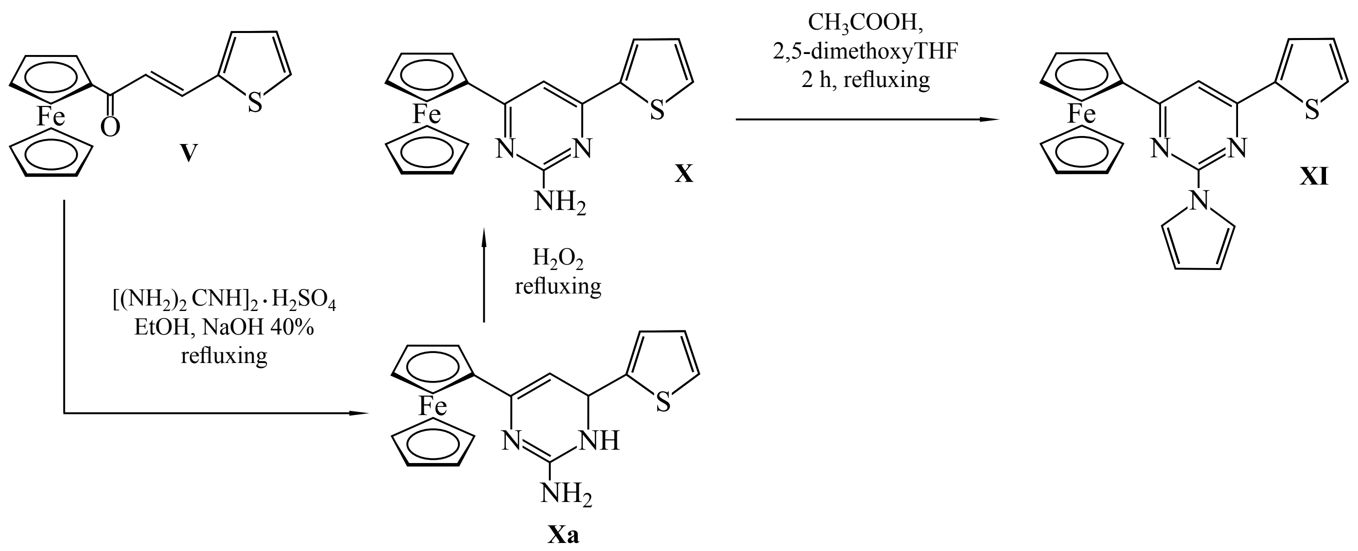
The chalcones prepared were subsequently used for synthesizing ferrocene-substituted pyrimidines by cyclization with guanidine sulfate in aqueous solution [9] or with guanidine nitrate in dioxane [10] in the presence of alkali. Under these conditions, we successfully synthesized previously unknown pyrimidine **X** (Scheme 2). The two other chalcones, **VI** and **VII**, cyclize under these conditions with a very low yield.

Then, by the reaction of 2-amino-6-(thiophen-2-yl)-4-ferrocenylpyrimidine **X** with 2,5-dimethoxy-tetrahydrofuran in acetic acid, we synthesized previously unknown substituted pyrimidine **XI** containing as

Scheme 1.



Scheme 2.



substituents three π-excessive fragments: ferrocene, thiophene, and pyrrole (Scheme 2).

All the compounds obtained were studied by cyclic voltammetry. Measurements were performed in a three-electrode cell with Ag/AgCl reference electrode, glassy carbon working electrode, and Pt wire auxiliary electrode. The conditions of electrochemical measurements were identical in all the cases: supporting electrolyte Et_4NClO_4, $c_{sup} = 0.1$ M; $c_{monomer} = 1 \times 10^{-3}$ M; $V_{scan} = 100$ mV s^{-1}; absolute CH_3CN as solvent. We showed that all the compounds under these conditions showed stable reversible oxidation of the ferrocene fragment to the ferricenium fragment. For the convenience of comparison, under the same conditions we recorded the cyclovoltammograms of unsubstituted ferrocene. The peak potentials E_p for the transitions $Fc^{2+} \rightarrow Fc^{3+}$ (E^1_{pa}) and $Fc^{3+} \rightarrow Fc^{2+}$ (E^1_{pc}) were 488 and 384 mV, respectively (see table). The peak potentials for the compounds synthesized are given in the table. For the convenience of comparison of the electron-donor properties of the compounds prepared, we also present the values of ΔE_p and $E_{p_{1/2}}$. As seen from the table, the half-wave potentials of the compounds synthesized are shifted toward more positive values relative to unsubstituted ferrocene (432 mV). This may be due to delocalization of the electron density in the conjugated systems. Delocalization of the electron density is more efficient in the case of chalcones, especially of dichalcone **IX**, which leads to the highest half-wave potential $E_{p_{1/2}}$: 951 mV. For all the compounds prepared, except dichalcone **IX**, the second peak of anodic oxidation, E^2_{pa}, is observed. It corresponds to the formation of a radical cation by oxidation of heterocyclic fragments present in the structure (carbazole, thiophene, pyrrole). For chalcone **VI**, the potential of this peak is 1304 mV, and this compound polymerizes under the conditions of cyclic voltammetry. The potential of the peak of the polymerization onset, E_{onset}, for this compound is 1047 mV, and in the process a bright violet film is formed on the electrode surface. Polymerization of pyrimidines **X** and **XI** under the above-indicated conditions was not observed, but on replacement of the solvent used (acetonitrile) by a mixture of boron trifluoride etherate and methylene chloride (3 : 2) [11] compound **XI** containing simultaneously ferrocene, pyrimidine, pyrrole, and thiophene rings also appeared to be capable of electrochemical polymerization.

Redox potentials of the compounds obtained

Ferrocene	E^1_{pa}	E^1_{pc}	ΔE_p	$E_{p_{1/2}}$[a]	E^2_{pa}, mV
	mV				
	484	381	103	432	
V	708	634	74	634	1393
VI	700	610	90	655	1304
VII	706	655	51	655	1584
IX	1008	894	114	951	
X	605	529	76	567	1290
XI	634	572	62	603	1198

[a] $E_{p_{1/2}} = E_p - \frac{\Delta E_p}{2}$.

The structure of **X** was confirmed by single crystal X-ray diffraction. The compound crystallizes in the tetragonal system, space group $I4_1$; unit cell parameters: $a = 21.5709(8)$, $b = 21.5709(8)$, $c = 13.4184(7)$ Å; $\alpha = \beta = \gamma = 90°$; unit cell volume $V = 6243.63$ Å^3.

There are short S···S contacts in the structure. The thiophene, pyrimidine, and one of the cyclopentadiene rings in the structure of the molecule are coplanar.

EXPERIMENTAL

The ^1H NMR spectra were recorded with a Mercury plus300 device, internal reference HMDS. Electrochemical studies were performed with an IPC-compact device equipped with an EM-04 electrochemical sensor. The results were processed with the IPC-compact 8.60F program. Mass-spectrometric analysis was performed with an Agilent Technologies 6890N/5975B gas chromatograph–mass spectrometer (HP-5ms column, 30 × 0.25 mm, 0.25 μm, carrier gas He, ionization by electron impact, 70 eV).

Acetylferrocene **I** was prepared by acetylation of ferrocene with acetic anhydride in the presence of orthophosphoric acid [13]. Diacetylferrocene was isolated as by-product.

9-Ethyl-9*H*-carbazole-3-carbaldehyde III was prepared by the procedure similar to that described in [14]. To a solution of 4.46 g (0.02 mol) of *N*-ethylcarbazole and 1.90 g (0.026 mol) of DMF in 40 ml of chlorobenzene, we added dropwise with stirring 6.13 g (0.04 mol) of $POCl_3$. The reaction mixture was stirred at 65–70°C for 5 h, cooled to room temperature, and poured into 200 ml of water, after which the product was extracted with methylene chloride. The organic layers were combined and washed with water and aqueous $NaHCO_3$ solution. The solvent was evaporated, and the viscous residue was washed with hexane and recrystallized from ethanol. White crystals. Yield 73%, mp 86–88°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 1.42 t (2H, CH_3, *J* 7.2); 4.31 q (3H, CH_2, *J* 7.2); 7.29 t (1H, carbazole, *J* 8.1); 7.40, 7.43 d (1H, carbazole, *J* 8.1); 7.5 t (1H, carbazole-C6, *J* 8.1); 7.95, 7.98 dd (1H, carbazole, *J* 8.4); 8.10 , 8.11 d (1H, carbazole, *J* 8.4); 8.55 s (1H, carbazole); 10.05 s (1H, CHO).

3,4-Ethylenedioxythiophene-2-carbaldehyde IV was prepared by the procedure similar to that described in [15]. To a solution of 7.1 g (0.05 mol) of 3,4-ethylenedioxythiophene in 50 ml of dry 1,2-dichloroethane we added dropwise with stirring and cooling with cold water 3.7 g (0.05 mol) of dry dimethylformamide and then (over a period of 0.5 h) 7.67 g (0.05 mol) of $POCl_3$. After adding the reactants, the mixture was stirred for 15 min at room temperature and then for 5–6 h at approximately 80°C, after which it was cooled with ice-cold water, 10 ml of H_2O was added dropwise, and the mixture was stirred for 30 min and poured into cold water; the layers were separated. The organic layer was washed with water and evaporated; a small amount of the target product was obtained. To the aqueous layer, ~50 ml of concentrated HCl was added, and the mixture was left overnight. The product precipitated in the form of slightly colored needles. It was filtered off, and the filtrate was treated with an additional ~15-ml portion of HCl and allowed to stand for 3 h, after which an additional crop of the aldehyde was filtered off. Yield about 90%, mp 155°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm): 4.25–4.28 m (2H, CH_2O), 4.34–4.37 m (2H, CH_2O), 6.79 s (1H, thiophene), 9.90 (1H, CHO).

1-Ferrocenyl-3-(thiophen-2-yl)propenone V. A mixture of 0.74 g (0.0066 mol) of thiophene-2-carbaldehyde and 1.5 g (0.0066 mol) of acetylferrocene in 150 ml of a 2% NaOH solution was refluxed for 2 h. The precipitate formed on cooling was filtered off and washed with a large amount of cold water. The product purity was checked by TLC (eluent methylene chloride). If necessary, the product was purified by column chromatography on silica gel (eluent CH_2Cl_2). Red-violet crystals, yield about 67%, mp 75–76°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 4.20 s (5H, ferrocene), 4.57 br.s (2H, ferrocene), 4.89 br.s (2H, ferrocene), 6.93 and 6.88 d (1H, CH=, *J* 15.0), 7.08 t (1H, thiophene, *J* 3.6), 7.33 d (1H, thiophene, *J* 3.6), 7.39 d (1H, thiophene, *J* 4.5), 7.86 and 7.91 d (1H, CH=, *J* 15.0).

3-(3,4-Ethylenedioxythiophen-2-yl)-1-ferrocenylpropenone VII was prepared by the procedure similar to that for **V**. Red-orange crystals, yield 75%, mp 178–180°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 4.2 br.s (5H, Fc), 4.25 m (2H, CH_2O), 4.35 m (2H, CH_2O), 4.54 t (2H, Fc, *J* 1.8), 4.87 t (2H, Fc, *J* 1.8), 6.45 s (1H, thiophene), 6.87 and 6.92 d (1H, CH=, *J* 15.3), 7.78 and 7.83 d (1H, CH=, *J* 15.6). Mass spectrum, *m*/*z*: M^+ 380 (100%). $C_{19}H_{16}FeO_3S$. *M* 380.23.

3-(*N*-Ethylcarbazol-3-yl)-1-ferrocenylpropenone VI. A mixture of 0.558 g (0.0025 mol) of *N*-ethyl-3-carbaxolecarbaldehyde and 0.62 g (0.0027 mol) of acetylferrocene was stirred in 20 ml of refluxing methanol containing 0.7 g (0.0125 mol) of KOH for 3 h. After cooling, a half of the solvent was removed, the residue was poured into water, the mixture was extracted with CH_2Cl_2, the combined organic layers were washed with water, the solvent was removed, and the solid residue was separated on a column packed with silica gel (eluent hexane : acetone = 4 : 1). Red crystalline substance, yield 68%, mp 197–199°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 1.46 t (3H, CH_3, *J* 6.9), 4.23 s (3H, Fc), 4.36–4.43 q (2H, CH_2, *J* 6.9), 4.58 br.s (2H, Fc), 4.97 br.s (2H, Fc), 7.16 and 7.21 d (1H, CH=, *J* 15.9), 7.25–7.31 m (3H, carbazole), 7.41 and 7.44 d (1H, carbazole, *J* 8.4), 7.50 t (1H, carbazole, *J* 8.4), 7.77 and 7.80 d (1H, carbazole, *J* 9.6), 8.00 and 8.05 d (1H, CH=, *J* 15.9), 8.15 and 8.17 d (H, carbazole, *J* 7.2), 8.36 s (1H, carbazole).

1,1'-Di[3-(thiophen-2-yl)prop-2-enoyl]ferrocene IX. A mixture of 2.7 g (0.01 mol) of diacetylferrocene and 2.24 g (0.02 mol) of 2-thiophenecarbaldehyde in 500 ml of a 2% NaOH solution was refluxed for 2 h. After the reaction completion and cooling, the precipitate that formed was filtered off, washed with a large amount of water, and recrystallized from chlorobenzene. Decomposes at temperatures higher than 200°C. ^{1}H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 4.57 br.s (4H, ferrocene), 4.86 br.s (4H, 2 thiophene), 6.84 t (2H, 2 thiophene, *J* 3.6), 6.96–7.36 m (6H, 4H thiophene + 2H =CH), 7.84 and 7.89 d (2H, 2=CH, *J* 14.8).

2-Amino-4-ferrocenyl-6-(thiophen-2-yl)

pyrimidine X. A mixture of 2.1 g of 1-ferrocenyl-3-(thiophen-2-yl)propenone (0.0062 mol), 1.53 g of guanidine sulfate, and 5 ml of a 50% aqueous KOH solution in 50 ml of ethanol was stirred and then refluxed for 1 h. Then, under the same conditions, 3 ml of H_2O_2 was added in small portions over a period of 1 h. After that, the reaction mixture was poured into cold water. The precipitate was filtered off, dried, and purified by column chromatography (eluent CH_2Cl_2), with collection of the last fraction. Red-violet crystals. Yield 55%, mp 199–200°C. ^1H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 4.09 br.s (5H, ferrocene), 4.45 t (2H, ferrocene, *J* 1.8), 4.94 t (2H, ferrocene, *J* 1.8), 5.06 br.s (2H, NH_2), 7.02 s (1H, pyrimidine), 7.14 t (1H, thiophene, *J* 3.6), 7.45 and 7.47 dd (1H, thiophene, *J* 5.1), 7.73 and 7.74 dd (1H, thiophene, *J* 3.6). Mass spectrum, *m*/*z*: M^+ 361.1 (100.0%). $C_{18}H_{15}FeN_3S_2$. *M* 361.1.

6-Ferrocenyl-2-pyrrolo-4-(thiophen-2-yl) pyrimidine XI. A 0.54-g portion of 2-amino-4-ferrocenyl-6-(thiophen-2-yl)pyrimidine **X** (0.0015 mol) was dissolved in a minimal amount of CH_3COOH. To the resulting solution, 0.204 g (0.00154 mol) of 2,5-dimethoxytetrahydrofuran was added. The mixture was refluxed for 2 h, cooled, and poured into 150 ml of cold water. The precipitate was filtered off and washed with ethanol. The product was purified by column chromatography (eluent CH_2Cl_2). ^1H NMR spectrum ($CDCl_3$, δ, ppm, *J*, Hz): 4.20 br.s (5H, ferrocene), 4.57 t (2H, ferrocene, *J* 1.8), 4.88 t (2H, ferrocene, *J* 1.8), 6.35 t (2H, pyrrole, *J* 2.1), 7.08 t (1H, thiophene, *J* 3.9), 7.30 s (1H, pyrimidine), 7.33 and 7.34 d (2H, thjiophene, *J* 3.6), 7.38 and 7.39 d (1H, thiophene, *J* 4.8), 7.92 d (2H, pyrrole, *J* 2.1).

CONCLUSION

New ferrocene-containing pyrimidines were synthesized from a series of ferrocene-containing chalcone derivatives, and their electrochemical constants were determined.

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REFERENCES

1. Shvekhgeimer, M.A., *Usp. Khim.*, 1996, vol. 65, no. 1, pp. 43–83.
2. Lemenovskii, D.A., *Soros. Obraz. Zh.*, 1997, no. 2, pp. 64–69.
3. Maynadié, J., Delavaux-Nicot, B., Lavabre, D., and Fery-Forgues, S., *J. Organomet. Chem.*, 2006, vol. 691, no. 6, pp. 1101–1109.
4. Delavaux-Nicot. B., Manadié. J., Lavabre. D., and Fery-Forgues, S., *J. Organomet. Chem.,* 2007, vol. 692, no. 4, pp. 874–886.
5. Dombrowski, K.E., Baldwin, W., and Sheats, J.E., *J. Organomet. Chem.*, 1986, vol. 302, no. 3, pp. 281–306.
6. *Handbook of Conducting Polymers*, Skotheim, T.A., Elsenbaumer, R.L., and Reynolds, J.R., Eds., New York: Dekker, 1998.
7. Abashev, G.G., Bushueva, A.Yu., Kudryavtsev, P.G., et al., *in Materialy mezhdunarodnoi konferentsii “Tekhnicheskaya khimiya. Ot teorii k praktike”* (Proc. Int. Conf. “Technical Chemistry. From Theory to Practice”), Perm, 2008, pp. 72–77.
8. Son, K.-I., Kang, S.-Y., and Noh, D.-Y., *Bull. Korean Chem. Soc.*, 2009, vol. 30, no. 2, pp. 513–516.
9. Varga, L., Nagy, T., Kövesdi, I., et al., *Tetrahedron*, 2003, vol. 59, no. 5, pp. 655–662.
10. Solankee, A., Lad, S., Solankee, S., and Patel, G., *Indian J. Chem.*, 2009, vol. 48B, no. 10, pp. 1442–1446.
11. Adib, A., Tahermansouri, H., Kologami, S.A., et al., *Tetrahedron Lett.,* 2006, vol. 47, no. 33, pp. 5957–5960.
12. Tsierkezos, N.G., *J. Solution Chem.*, 2007, vol. 36, no. 3, pp. 289–302.
13. Rozenblum, M. and Santer, J.O*., J. Am. Chem. Soc.*, 1959, vol. 81, pp. 5517–5518.
14. Bai, G., Li, J., Li, D., et al., *Dyes. Pigments*, 2007, vol. 75, no. 1, pp. 93–98.
15. Maruyama, S., Tao, X.-T., Hokari, H., et al., *J. Mater. Chem.*, 1999, vol. 9, no. 4, pp. 893–898.