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Reaction of functionalized maleimides with versatile nucleophiles. Synthesis, electronic spectra and molecular orbital study

Yasuhiro Shigemitsu [a,*], Kaori Komiya [b], Naoko Mizuyama [b], Yoshinori Tominaga [b]

[a] *Industrial Technology Center of Nagasaki, 2-1303-8, Ikeda, Omura, Nagasaki 856-0026, Japan*
[b] *Faculty of Environmental studies, Nagasaki University, 1-14, Bunkyo-machi, Nagasaki 852-8521, Japan*

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Abstract

This article comprehensively describes the condensation reactions of functionalized maleimides (3-methylthio-2,5-dioxo-1*H*-pyrroles) with some nucleophilic reagents to afford a series of novel heterocycles, as briefly reported in a previous communication [Tominaga Y, Komiya K, Itonaga S, Yoshioka N, Kataoka S, Sasaki K, et al. Heterocycles 1997;46:41]. The reactions of the functionalized maleimides (**5a**–**c**) with *N*,*N*-dialkylanilines (**6a**–**d**) smoothly proceeded to give the corresponding 3-(4-dialkylamino)phenyl-1-methyl-1*H*-pyrrole-2,5-diones (**7a**–**i**). Cyclic products, the 2*H*,4*H*-[1]benzopyrano[3,4-*c*]pyrrole-1,3,4-triones (**10a**–**c**, **12**, **13**) were also obtained within the same reaction framework, using 3-dialkylaminophenols (**6g**–**j**) and resorcinol (**6k**) as the nucleophilic reagents. Further treatments of (**7a**,**b**,**h**) with Lawesson's reagent afforded the brilliant blue mono-thiocarbonyls, 4-(4-dialkylamino)phenyl-3-cyano-1-methyl-5-oxo-pyrrole-2-thiones (**9a**–**c**). The UV/vis spectral characteristics of the new heterocycles, particularly of the controversial aromatic mono-thiocarbonyl compounds (**9a**–**c**), were computationally analyzed by means of semi-empirical and Time Dependent Density Functional Theory (TDDFT) quantum chemistry calculations.

Keywords: Maleimides; Thiocarbonyl compounds; Electronic spectra; Molecular orbital calculations

1. Introduction

Fused or functionalized maleimides are synthetically useful intermediates for the preparation of polycyclic and fused pyridazine derivatives [1,2]. They are also known as active dienophiles in Diels–Alder reactions or as 1,3-dipolar reagents [3].

During the course of our studies, ketene dithioacetals (**1a**,**b**) were found to be useful building blocks to synthesize a variety of fused [4] as well as simple heterocycles [5]. The efficient synthesis of 2-hydroxyimino-4-methoxycarbonyl-3-methylthiomaleimide derivatives (**3a**,**b**) was developed through the cyclization reaction of (**1a**,**b**) with methyl cyanoacetate [6]. Unfortunately the hydroxyimino species were insufficiently soluble and unreactable. We solved this problem by converting (**3a**) into 3-methylthio-4-methoxy-2,5-dioxo-1*H*-pyrroles (**5a**) via the hydrolysis of the intermediate (**4a**) [7].

Specifically, the methylation of (**3a**) with dimethyl sulfate in the presence of sodium hydroxide in dimethyl sulfoxide (DMSO) gave the corresponding dimethyl product (**4a**) which smoothly undergoes hydrolysis with hydrochloric acid to give the desired product (**5a**). This method is also applicable for the synthesis of (**5b**), as illustrated in Fig. 1. We furthermore explored the wider utility of the functionalized maleimides (**5a**,**b**) which serve as active electrophilic reagents to afford fused pyridazine derivatives [7] and polymethine dyes [8].

In order to exploit their further potential as key building blocks, we herein describe the reaction of (**5a**,**b**) with versatile nucleophiles, including *N*,*N*-dialkylanilines, julolidine (**6e**) and *N*-phenylaza-15-crown-5-ether (**6f**) to afford 3-(4-dialkylamino)phenyl-1-methyl-1*H*-pyrrole-2,5-diones (**7a**–**i**) and their thioimidized derivatives (**9a**–**c**) via the treatment with Lawesson's reagent [9]. The cyclic products, 7-dialkylamino-2*H*,4*H*-[1]benzopyrano[3,4-*c*]pyrrole-1,3,4-triones (**10a**–**c**, **12**, **13**), were also obtained within the same synthetic framework (Fig. 2).

* Corresponding author. Tel./fax: +81 957 52 1133.
E-mail address: shige@tc.nagasaki.go.jp (Y. Shigemitsu).

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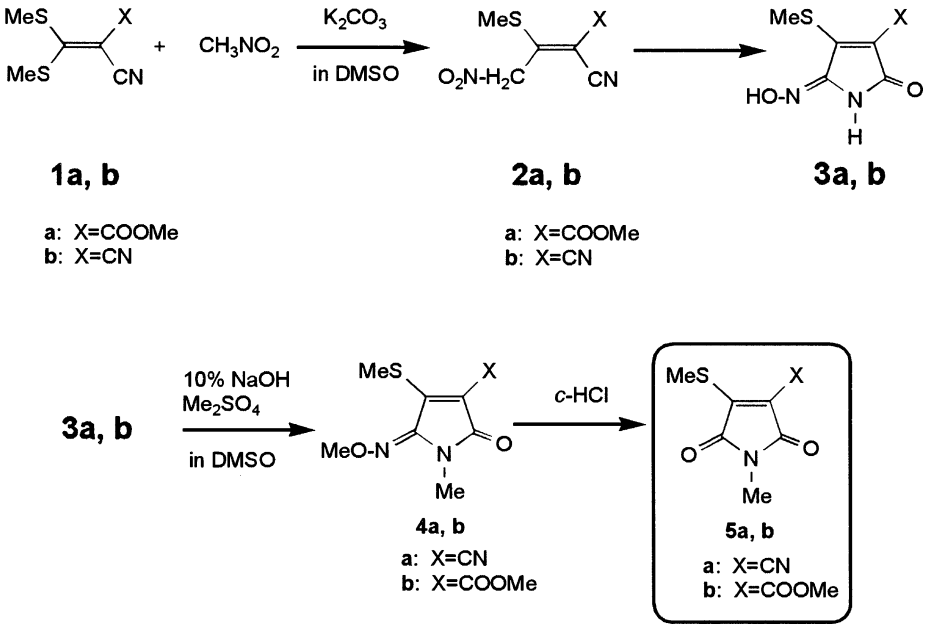


Fig. 1. Synthetic route to 3-methylthio-2,5-dioxo-1*H*-pyrroles (**5a**–**c**).

A further objective of this study is to establish the structure–color relationships of the newly obtained heterocycles. Among a variety of quantum chemistry techniques, TDDFT [10] has been rapidly emerging for the transition energy predictions in the UV/vis region of electronic spectra. TDDFT shows good performance in the prediction of valence excitation energies for many molecules [11,12], as well as its simple formulation with modest computational burden, its theoretical simplicity and independence from empirical parameters. Excluding some difficult cases such as multi-configuration character excitations [13] or Rydberg excitations, which require asymptotic correction of the exchange-correlation functionals for quantitative accuracy [14], TDDFT is of universal use for small to medium sized dyes, with careful considerations to the functional characteristics and basis set selections.

This paper is organized as follows. In the next section, the synthesis and the experimental characterizations of the novel heterocycles are described. Next, the computational procedure is outlined, followed by the calculation results of the first intense λ_{max} of the target compounds. In particular, we focused on the prediction of the controversial bathochromic shift of the novel mono-thiocarbonyls (**9a**–**c**) from the viewpoint of their industrial applications, because the existing brilliant blue dyes such as disperse polymethine derivatives suffer from chemical instability and poor light fastness [15]. The final section summarizes this article.

2. Synthesis and electronic spectra

Compound (**5a**) reacted with *N*,*N*-dimethylaniline (**6a**) under reflux in acetic acid to give (**7a**). Reaction of (**5a**) with other *N*,*N*-dialkylanilines (**6b**–**d**) occured under the same reaction conditions to afford the corresponding 3-(4-dialkylamino)phenylmaleimides (**7b**–**d**). The methyl ester (**7e**) was also readily obtained by the reaction of (**5b**) with (**6a**). The relative low yield of (**7g**) indicates that the reactivity of (**5b**) was reduced by demethylation of the *N*-position. Compounds (**7f**–**g**) were synthesized via the reactions of (**5b**) and (**5c**) with the corresponding *N*,*N*-dialkylanilines (**6a**,**b**). The demethoxycarbonylated compound, 3-(4-dimethylaminophenyl)maleimide (**8**), was prepared by the treatment of (**7e**) with polyphosphoric acid (PPA). Julolidine (**6e**) also reacted with (**5a**) to yield the corresponding product (**7h**). The reaction of the crown ether (**6f**) with (**5a**) in acetic acid afforded (**7i**).

The reaction mechanism may be explained as shown in Fig. 3. Following the loose π complex formation, the nucleophilic attack of the dialkylanilines occurred at 2-position of the counterpart maleimides in Michael addition fashion to give the products, associated with the leaving of methylthio group as a methylmercaptane.

The thioimidation reactions of (**7a**,**b**,**h**) with Lawesson's reagent under reflux resulted in the corresponding mono-thiocarbonyls (**9a**–**c**) (Fig. 4). The comparison of (**7a**) and (**9a**) ^{1}H NMR spectra indicates that this thioimidation selectively occurred at a distant carbonyl group due to the structural hindrance between the phenyl group of *N*,*N*-dialkylaniline and the reagent [16]. Actually, the chemical shifts of the aryl protons with doublet coupling were assigned to δ 6.75 and δ 8.46 for (**7a**), respectively, whereas δ 66.78 and δ 68.49 for (**9a**), respectively. This slight change means no drastic influence was introduced on the environment of the aryl protons by the thioimidation, indicating that the distant carbonyl group was selectively converted to the thiocarbonyl group, as in the case of the conversion from carbonyl group to dicyano-methylene group [17]. No further thioimidation adducts were obtained by reflux time extension or excess Lawesson's reagent.

A variety of coumarin derivatives such as 7-dimethylaminocoumarines are in wide industrial use as laser dyes [18].

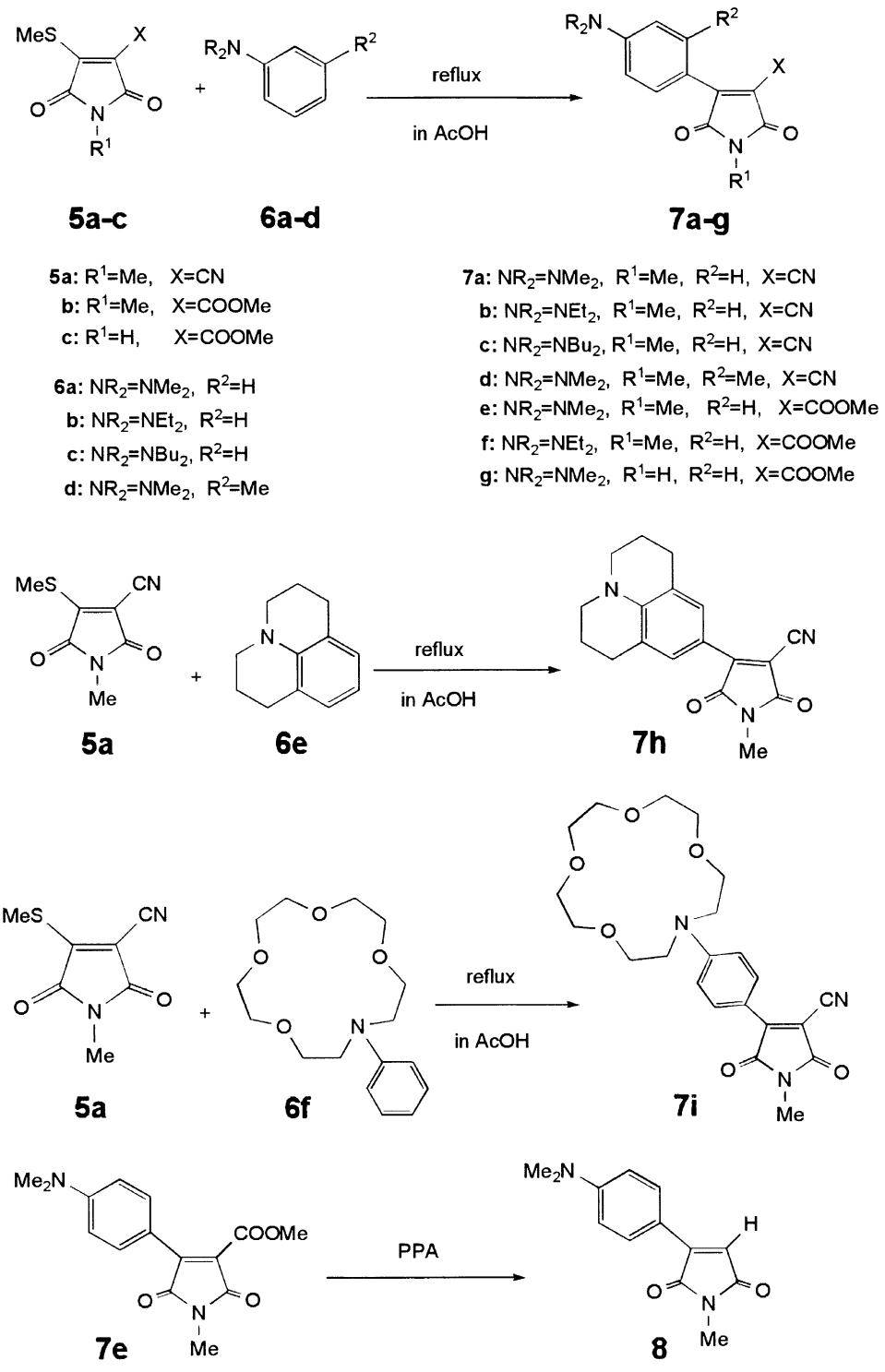


Fig. 2. Synthesis of (**7a–i**, **8**).

The pyrrolocoumarin dye, 7-dimethylamino-2-methyl-2*H*,4*H*-[1]benzopyrano[3,4-*c*]pyrrole-1,3,4-trione (**10a**), was obtained via the reaction of 3-dimethylaminophenol (**6g**) with (**5a**) under reflux in acetic acid as shown in Fig. 5. The diethylamino and dibutylamino compounds (**10b**,**c**) were readily derived from (**5a**) and the dialkylaminophenols (**6h**,**i**) in the same manner. That is, (**5a**) reacted with (**6i**) under reflux in acetic acid to finally produce (**10c**) via an intermediate imino compound (**11**), which was not isolated in this reaction. The reaction of (**5a**) with 8-hydroxyjulolidine (**6j**) also occurred to give 1,2,5,6,7-pentahydro-10-methyl-3*H*,10*H*,12*H*-pyrrolo-[3′,4′:3,4][1]benzopyrano[6,7,8-*ij*]quinolizine-9,11,12-trione (**12**). When resorcinol (**6k**) was used to react with (**5a**) under the reaction similar to that described above, the product (**13**)

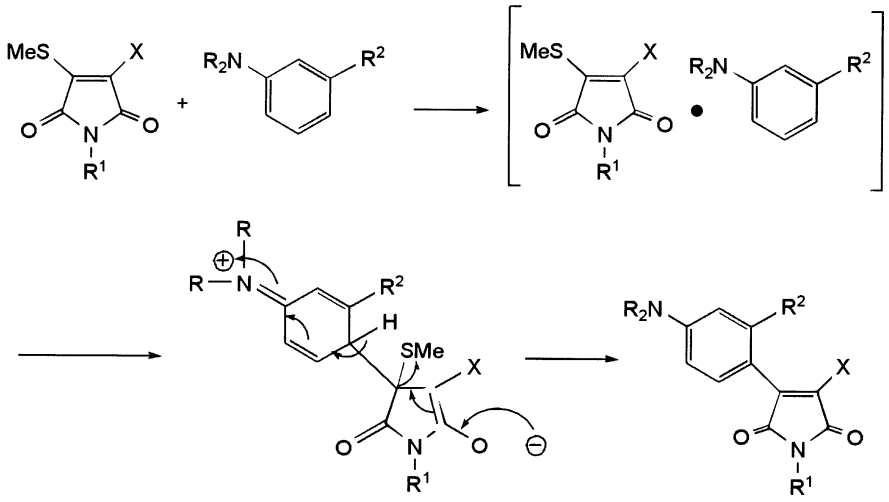


Fig. 3. Reaction mechanism.

was obtained in a quite low yield. It had been already found that resorcinol reacts with the ketene dithioacetals under the basic conditions to give the 1-methylthio-2-cyano-6-hydroxycoumarin in a good yield [19]. We therefore investigated the reaction of resorcinol (**6k**) with (**5a**) under basic condition. Actually, the reaction of (**5a**) with (**6k**) under reflux in the presence of sodium hydride in tetrahydrofuran (THF) gave the desired product (**13**) in a significantly improved yield.

The UV/vis spectra were measured in ethanol at room temperature. The most hypsochromic dye is the demethoxycarbonylated compound (**8**), followed by the methyl ester derivatives (**7e–g**), and then by the cyano analogues (**3a–d**), leading to (**7h**) with a remarkably bathochromic shift by 117 nm relative to (**8**), due to the strong donating character of the julolidine ring [20]. The fused polycyclic compounds (**10a–c**, **12**, **13**) showed the absorption maxima ranging 517–552 nm. The noteworthy red shift of the mono-thiocarbonyl peaks was observed (81 nm of (**7a** → **9a**) for example) because of the enhanced molecular polarizability by the substitution of an oxygen atom to a sulfur atom. The molar absorption coefficients ($\log \varepsilon$) increased in the order of (**8**) → (**7a**) → (**7h**) → (**9c**), as the push–pull character was enhanced. The second intense band in the UV region shows the bathochromic shift in the same order of the first band. The weak n–π* absorption peaks derived from the carbonyl oxygen or thiocarbonyl sulfur lone pair were expected to appear in the longer wavelength region than the intense π–π* band but they were overlapped with the main π–π* band and hidden in the spectrum. In the following section, the first intense π–π* absorption peaks are investigated computationally in detail.

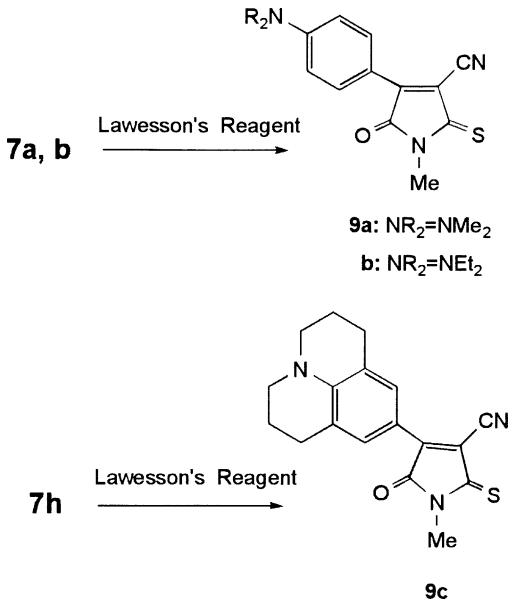


Fig. 4. Thioimidation conversion to (**9a–c**).

3. Quantum chemical calculations

3.1. Computational details

The semi-empirical molecular orbital calculations were performed employing CAChe software package [21] and all DFT and TDDFT calculations by means of GAUSSIAN98 suite of program [22]. The full geometry optimizations for (**7a–h**, **9a–c**) were carried out both by AM1 [23] and by Density Functional Theory (DFT) with Dunning's correlation-consistent polarized valence double-zeta (cc-pVDZ) [24] basis set in conjunction with the combined Becke three-parameter hybrid exchange/Lee–Yang–Parr correlation functional (B3LYP) [25], using the default convergence criterion on force and displacement. ZINDO [26] calculations were carried out with INDO/1 preset parameters in order to obtain the intense π–π* lowest vertical excitation energies along with their associated oscillator strengths for the AM1- and DFT-optimized geometries, respectively. The default SECI (Single Excited Configuration Interaction) method distributes 28 electrons among the highest 14 occupied MOs and the lowest

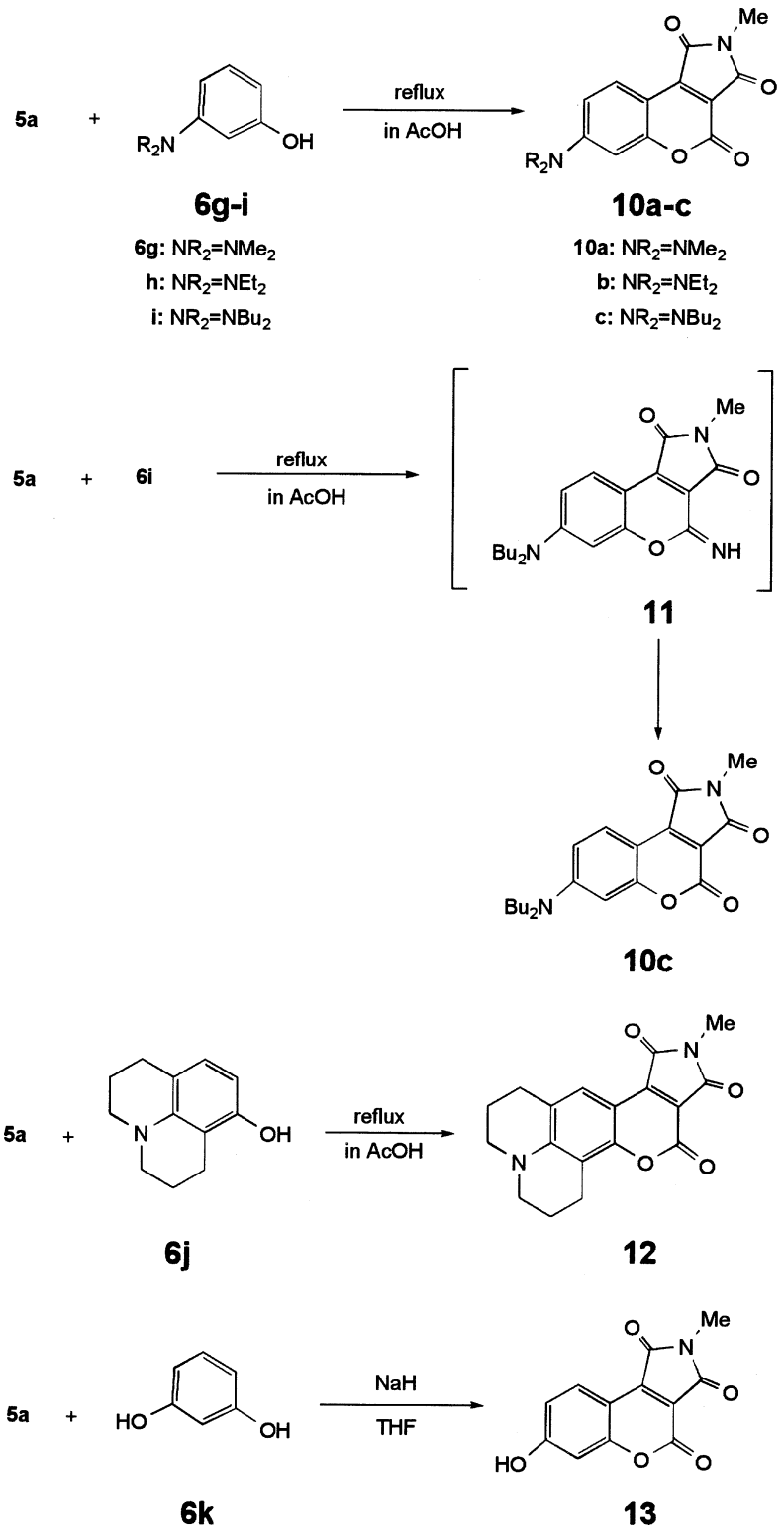


Fig. 5. Synthesis of coumarin derivatives (**10a–c**, **12**, **13**) using (**5a**).

unoccupied 14 MOs designed to generate the single excited configurations. A series of TDDFT calculations with three different types of exchange-correlation functionals, i.e., SVWN [27], PW91 [28] and B3LYP, were performed on the DFT-optimized geometries to calculate the intense $\pi-\pi^*$ lowest vertical excitation energies with a compact 6-31+G* basis set, in consideration for the established conception that TDDFT is less dependent on a basis set selection compared to other conventional ab initio methods. Since the theoretical vertical excitation energies approximately correspond to

band maxima in the experimental spectra, 0.1–0.2 eV uncertainties are expected for small to medium sized molecules. No zero point correction was considered. Solvent effects were taken into consideration with the PCM method [29] combined with TDDFT/6-31+G*. The TICT (Twisted Intermolecular Charge Transfer) states of *N*,*N*-dialkyl group were not taken into consideration, with the group being fixed to the optimized geometry. This hypothesis is based on the minor contribution of the TICT states to the potential energy landscape, as demonstrated for coumarin120/151 [30].

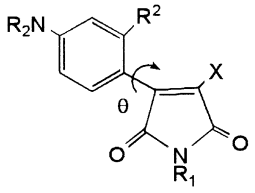
Two distinctive conformers of (**7h**) would exist in solution, depending on the *syn*/*anti* conformation of the julolidyl ring. However, the electronic properties including the excitation energy, the dipole moment and the ionization potential were reported to remain unchanged regardless of the conformation [31]. Therefore we adopted only the stable *anti*-conformer.

3.2. Calculation results

3.2.1. The lowest π–π* transitions of sulfur-free compounds (*7a–i*)

Two series of ZINDO calculations were performed on the basis of different geometry optimization schemes, i.e., using MOPAC AM1 and DFT (B3LYP)/cc-pVDZ. The ZINDO//DFT λ_{max} agreement with the experimental λ_{max} was better than that of the ZINDO//AM1, reflecting the significance of the geometrical accuracy. Actually, there were considerable deviations in the optimized twist angles between the AM1- and DFT-optimized structures, with the former giving somewhat distorted geometries whereas the latter giving almost the flat geometries excluding (**7d**) that has the steric hindrances between the maleimide ring and the counterpart moiety (Fig. 6). We have already reported the same AM1 and DFT geometrical tendencies elsewhere [8].

The highly accurate optimized geometries of a maleimide molecule have been reported using DFT (B3LYP)/6-311+G* [32] and π-CASSCF/ANO optimization [33], respectively, in which the carbonyl double bond length (C=O) embedded within the ring was examined in detail. The DFT length (1.206 Å) is perfectly consistent with the experimental one obtained by the electron diffraction study in the gas phase [34] whereas CASSCF (1.193 Å) slightly underestimated probably due to the lack of dynamical electron correlations. The DFT technique, therefore, assumed to be reliable in the C=O bond length prediction. The DFT-optimized C=O bond lengths of our maleimide derivatives were somewhat stretched than that of a maleimide molecule (for example, 1.217 and 1.212 Å for (**7a**), respectively). The bond elongation can be attributed to the intramolecular π-conjugation merocyanine chromic system of (**7a–i**), extending from the *N*,*N*-dialkylaniline moiety to the maleimide ring.



Entry	AM1	DFT[a]
7a	-38.8	0.0
7b	-39.6	1.4
7c	37.2	0.0
7d	103	135
7e	32.2	23
7f	45.2	22
7g	31.2	24
7h	-140	0.5
7i	76.9	0.9
8	-33.8	0.0
9a	39.5	0.0
9b	39.2	1.8
9c	38.5	0.8

[a] DFT(B3LYP)/cc-pVDZ

Fig. 6. Optimized tortional angles of (**7a–i**, **8**, **9a–c**).

It is well known that ZINDO prediction errors are generally ca. 0.15–0.25 eV on average [26] and systematically overestimate the experimental vertical excitation energies as the π-conjugation length elongates due to the imbalance between one- and two-electron parts of the electronic transition energy [35]. Actually, both the ZINDO//DFT and the ZINDO//AM1 predictions severely underestimated the λ_{max} of (**7a–i**, **9a–c**) as shown in Table 1. The excitation characters can be dominantly described by the HOMO–LUMO transition consistently, with the overwhelming configuration weights of the single excitation state. Although the structurally hindered (**7d**) gave the abnormally small oscillator strength (0.03) using the ZINDO//AM1, the ZINDO//DFT removed the abnormality probably because of the geometrical refinement.

The combination of the exchange-correlation functionals and basis sets is well known to strongly affect on TDDFT excitation energies in no systematic way, also critically depending on the state characteristics of the target molecules. For example, polyenes and polymethines have been examined in detail. The 1^1B_{1u} and 2^1A_{1g} excitation energies of polyenes were underestimated using the Local Density Approximation (LDA) functionals and the Generalized Gradient Approximation (GGA) functionals, while they were overestimated with the hybrid functionals [36]. The diffuse function augmentation is also critical, leading to the significant energy lowering of both states. The HOMO–LUMO excitation energies of polymethines, corresponding to 1^1B_{1u} excitation energies of polyenes, were largely overestimated using the B3LYP hybrid functional, nearly 1 eV [37]. Bauernschmitt et al. reported that the accuracy of B3LYP functional outperformed the LDA and GGA functionals for several low-lying valence excitation energies of small molecules [38]. For larger systems such as benzene, porphin and C70, the B3LYP functional combined with 6-31+G* basis set gave much better valence excitation energies than using LDA functionals as well as other wavefunction-based conventional calculations [39]. Fabian et al. reported that TDDFT predictions are moderately sensitive to basis set magnitude, the variation from 3-21+G* to 6-31+G* gave no significant lowering of the valence excitation energies for both sulfur-free and sulfur-containing molecules [40]. Wiberg et al. reported that additional polarization functions beyond the (d,p) level have little effect on the calculated energies but that diffuse functions are essential in reproducing the experimental λ_{max} [41]. For coumarin C151

Table 1
ZINDO results for the first intense absorption of (**7a–i**, **8**, **9a–c**)

Entry	λ_{max} (nm)		Oscillator strengths		Weights of S_1 main configuration		HOMO[a] (eV)	LUMO[a] (eV)
	ZINDO//AM1	ZINDO//DFT	ZINDO//AM1	ZINDO//DFT	ZINDO//AM1	ZINDO//DFT		
7a	385	418	0.32	0.62	0.86(H → L)	0.96(H → L)	−8.76	−1.86
7b	385	424	0.42	0.65	0.94(H → L)	0.96(H → L)	−8.70	−1.83
7c	395	425	0.33	0.65	0.90(H → L)	0.96(H → L)	−8.67	−1.83
7d	396	423	0.03	0.34	0.83(H → L)	0.93(H → L)	−8.75	−1.74
7e	381	414	0.34	0.54	0.91(H → L)	0.95(H → L)	−8.63	−1.62
7f	375	420	0.17	0.57	0.79(H → L)	0.95(H → L)	−8.62	−1.49
7g	358	412	0.35	0.59	0.90(H → L)	0.95(H → L)	−8.73	−1.61
7h	391	435	0.41	0.65	0.96(H → L)	0.96(H → L)	−8.48	−1.79
7i	391	415	0.05	0.64	0.95(H → L)	0.96(H → L)	−8.82	−1.85
8	344	380	0.39	0.49	0.92(H → L)	0.93(H → L)	−8.62	−1.28
9a	379	481	0.35	0.70	0.87(H → L)	0.94(H → L)	−8.77	−2.46
9b	434	488	0.45	0.73	0.93(H → L)	0.94(H → L)	−8.69	−2.43
9c	442	500	0.44	0.74	0.94(H → L)	0.95(H → L)	−8.48	−2.40

[a] ZINDO//DFT.

molecules, the TDDFT excitation energies with the pure GGA functional PBE0 were shown to be smaller by ca. 0.5 eV than the values obtained using B3LYP [30,31], giving better agreement with experimental λ_{max}.

Our TDDFT results (Table 2) are summarized as follows.

1. Concerning the influence of exchange-correlation functionals on the λ_{max} prediction, SVWN and PW91 were superior to the widely used B3LYP to give better coincidence with experiment. TDDFT (B3LYP) combined with PCM scheme corrected the underestimated λ_{max} to the right direction. For (**7d**,**g**), however, the methods overshot the experimental λ_{max}. There have been controversial arguments over TDDFT performance for the inter- and intramolecular CT excitation energy. Tozer el al. reported a significant overestimation (ca. 1 eV) for intra-CT (Interresidual) excitation of oligopeptides [42]. In contrast, Fabian et al. reported excellent agreement of the intra-CT excitation energy between TDDFT and the experiment [43a] for aliphatic thiocarbonyl compounds. Our molecules have a typical intramolecular CT type excitation character and gave considerable discrepancies between TDDFT (B3LYP) and experimental peaks.
2. The cause of the bathochromic shift of (**7a–i**) with reference to (**8**) can be qualitatively attributed to the LUMO energy level lowering, caused by the introduction of the methyl ester and cyano group at 3-position of the maleimide ring.
3. For the sterically hindered (**7d**), neither significant peak shift (as small as 9 nm bathochromic shift from that of (**7a**)) nor variation in the molar absorption coefficient ($\log \varepsilon$) was observed by introduction of a methyl substituent at the 3-position of the maleimide ring which interferes with the molecular planarity. This seems to be inconsistent with a chemical intuition because the π plane distortion between two moieties generally leads to a hypsochromic shift owing to the collapse of the entire π conjugation. The TDDFT peaks are considerably different between

Table 2
TDDFT and experimental results for the first intense absorption of (**7a–i**, **8**, **9a–c**)

Entry	Theoretical λ_{max}/oscillator strength				Weights of main configuration[b]	HOMO[b] (eV)	LUMO[b] (eV)	λ_{max}/log ε (expl.)
	SVWN	BPW91	B3LYP	B3LYP[a]				
7a	540/0.36	530/0.37	472/0.44	501/0.50	0.61(H → L)	−6.013	−3.238	543/4.85[c]
7b	542/0.40	534/0.40	477/0.48	504/0.55	0.61(H → L)	−5.905	−3.184	544/4.51
7c	547/0.42	539/0.47[d]	481/0.51	507/0.58	0.61(H → L)	−0.215	−3.156	547/4.35
7d	617/0.23[d]	605/0.23[d]	532/0.28	578/0.32	0.63(H → L)	−5.905	−3.265	534/4.24
7e	536/0.32[d]	526/0.32[d]	469/0.41	508/0.44	0.62(H → L)	−5.850	−2.830	495/3.65
7f	550/0.37	541/0.37	473/0.46	508/0.49	0.62(H → L)	−5.632	−2.803	508/4.24
7g	552/0.33	541/0.33	470/0.42	507/0.44	0.63(H → L)	−5.741	−2.911	478/4.08
7h	553/0.39	544/0.39	492/0.48	520/0.55	0.60(H → L)	−5.687	−3.075	576/4.57
7i	560/0.35	547/0.36	476/0.52	504/0.58	0.61(H → L)	−6.068	−3.292	534/4.55
8	534/0.30	522/0.30	450/0.36	494/0.38	0.63(H → L)	−5.605	−2.612	459/4.24
9a	605/0.37	597/0.37	532/0.46	559/0.54	0.59(H → L)	−5.959	−3.510	624/4.31
9b	607/0.40	600/0.41	538/0.50	562/0.58	0.59(H → L)	−0.216	−0.127	614/4.50
9c	606/0.40[b]	610/0.41	553/0.51	577/0.59	0.59(H → L)	−0.208	−0.123	665/4.66

[a] Using PCM option with EtOH dielectronic constant (23.1).
[b] Using B3LYP.
[c] Measured in DMSO because of insolubility in ethanol.
[d] Using 6-31G*.

(**7a**) and (**7d**), giving 77 nm (B3LYP) bathchromic shift from (**7a**) to (**7d**). The relatively small TDDFT oscillator strength of (**7d**) (0.23) indicates the artificial intrusions of other higher states or the limitation of the multi-configuration character description of TDDFT.

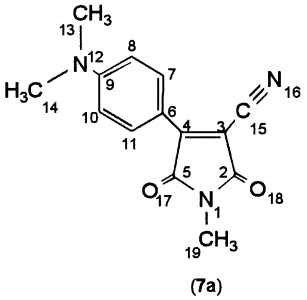
4. Demethylation at the ring nitrogen led to a 17 nm bathochromic shift of (**7e** → **7g**), due to the vanishing hyperconjugation of the methyl group. The shift was reproduced qualitatively with all types of the TDDFT calculations.

3.2.2. *The lowest π−π* transitions of the mono-thiocarbonyl compounds (**9a−c**)*

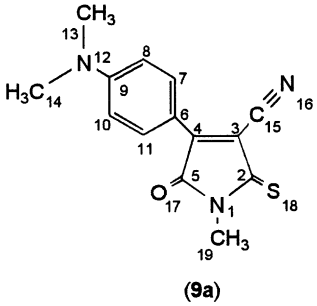
The significant red shift of the π−π* absorption peaks accompanied by thioimidation has been a controversial subject and stimulated extensive quantum chemical studies [43,44]. In general, the errors of TDDFT for sulfur-containing compounds have proved to be smaller than those of sulfur-free compounds [40]. The systematic studies have been reported with TDDFT and CASPT2 for thiocarbonyl compounds, including aliphatic thiocarbonyl compounds [43a] and aliphatic/conjugated sulphines [43b]. Both reports demonstrated an excellent performance of TDDFT, comparable with the highly accurate CASPT2 predictions or experimental data.

For the conjugate thiocarbonyl aromatics, on the other hand, no systematic calculations have been reported with the exception of the semi-empirical MO investigations [45]. This study is the pioneering TDDFT calculations for the compounds whose C═S moiety resonates with a five-membered aromatic ring. The electronic resonance between aromatic ring and thiocarbonyl group is expected to influence the electronic spectra and it is also interesting how TDDFT works for aromatic thiocarbonyls with a push−pull intra-CT character [42].

The optimization performance on the C═S bond length of sulphines (thione S-oxides) was systematically examined at DFT (B3LYP) and MP2 level of theory using a 6-31G series of basis set [43b], in which the DFT (B3LYP) optimization was proved to slightly overestimated the length (by 0.01 Å) even with a sufficiently large basis set (6-311++G(3df,3pd)) and that the valence transition energies were sensitive to the optimized C═S bond length. In contrast, the valence excitation energies proved to be insensitive to the C═S bond length for the aliphatic thiocarbonyl compounds [43a]. In the present study, the DFT-optimized C−N bond lengths in the maleimide ring of (**7a**) and (**9a**) were calculated to be quite shorter, whereas the DFT-optimized C═S lengths of the thiocarbonyl moiety of (**9a**) were longer than those optimized with AM1 level of theory, as illustrated in Fig. 7. The geometrical change associated with the thioimidation seems to be local, without a significant influence on the bond length of the dimethylaniline moiety of (**9a**). A compact cc-pVDZ set we employed because of the computational limitation would be problematic



(**7a**)



(**9a**)

Bond length/A	7a		9a	
	AM1	DFT[a]	AM1	DFT[a]
N_1-C_2	1.447	1.402	1.421	1.380
N_1-C_5	1.443	1.384	1.458	1.399
N_1-C_{19}	1.520	1.451	1.467	1.452
C_2-C_3	1.451	1.492	1.495	1.474
C_2-$O(S)_{18}$	1.209	1.212	1.591	1.652
C_3-C_4	1.360	1.378	1.361	1.383
C_3-C_{15}	1.411	1.418	1.415	1.420
C_4-C_5	1.515	1.531	1.507	1.520
C_4-C_6	1.448	1.445	1.447	1.445
C_5-O_{17}	1.210	1.217	1.208	1.217
C_6-C_7	1.401	1.420	1.401	1.420
C_6-C_{11}	1.401	1.420	1.401	1.420
C_7-C_8	1.384	1.382	1.384	1.382
C_8-C_9	1.406	1.424	1.406	1.423
C_9-C_{10}	1.406	1.421	1.406	1.422
C_9-C_{12}	1.437	1.370	1.437	1.370
C_{10}-C_{11}	1.384	1.384	1.384	1.383
C_{12}-C_{13}	1.481	1.455	1.481	1.456
C_{12}-C_{14}	1.481	1.455	1.481	1.455

[a] DFT(B3LPY)/cc-pVDZ

Fig. 7. Optimized key bond lengths of (**7a**) and (**9a**).

and further sophisticated C=S length optimization would be required with more extensive basis sets.

The λ_{max} of the mono-thiocarbonyl compounds (**9a–c**) exhibited considerable red shifts in comparison with the corresponding parent sulfur-free compounds (**7a**,**b**,**h**) in the experiment. The shifts were not reproduced with the ZINDO// AM1 probably derived from the unsatisfactory geometrical accuracies and both the ZINDO//DFT and the ZINDO//AM1 considerably overestimated the λ_{max}, as in the case of the previous sulfur-free compounds. Although some deviations exist between TDDFT and experimental λ_{max}, the bathochromic shifts caused by the thioimidation were qualitatively reproduced in a systemtic manner using all types of the functionals. However, even including the solvent effect could not reproduce quantitatively agreement with the experimental λ_{max}. For instance, the TDDFT λ_{max} of (**9c**) using TDDFT (B3LYP)/6-31+G* combined with PCM option appeared in the shorter wavelength region by 88 nm than the corresponding experimental peak. There were neither significant differences between (**7h**) and (**9c**) in the HOMO/LUMO special distribution nor the excitation characters which were overwhelmingly dominated with HOMO→LUMO transition. The red shift, therefore, would be qualitatively explainable by the LUMO energy level lowering of (**7h**) relative to the LUMO lowering of (**9c**).

4. Conclusions

In this study, the 3-methylthio-2,5-dioxo-1*H*-pyrroles (**5a–c**) were found to be useful in synthesizing 3-(4-dialkylamino)-phenyl-1-methyl-1*H*-pyrrole-2,5-diones (**7a–i**). The reaction scheme also provided an efficient route to the pyrrolocoumarin derivatives, i.e., the 4*H*-[1]benzopyrano[3,4-*c*]pyrrole-1,3,4-triones (**10a–c**, **12**, **13**). The obtained compounds (**7a**,**b**,**h**) were converted to the corresponding mono-thiocarbonyl blue dyes (**9a–c**) by treatment of Lawesson's reagent. The absorption maxima of (**9a–c**) exhibited the significant red shifts compared to the parent compounds (**7a**,**b**,**h**), which are quite interesting from the industrial viewpoints because thiocarbonyl compounds are generally known to be thermally and photochemically stable [46].

We computationally analyzed the $S_1 \leftarrow S_0$ vertical transition energies of the newly synthesized dyes possessing the intramolecular push–pull chromophoric system. As a whole, TDDFT demonstrated a qualitatively satisfactory performance in predicting the peaks, with a relative exchange-correlation functional dependency as well as systematically slight overestimations of the energies. We pioneeringly established TDDFT performance in the prediction of the peaks of the novel aromatic mono-thiocarbonyl compounds (**9a–c**). The agreement between the TDDFT (B3LYP) and the experimental λ_{max} was not satisfactory, in contrast to the TDDFT (B3LYP) excellent performance for the aliphatic thiocarbonyl compounds [43a].

Further studies on the potential availability of the functionalized maleimides (**5a–c**) are now in progress and will be presented along with quantum chemistry calculations in our future articles.

5. Experimental

5.1. General

All melting points were determined in a capillary tube and are uncorrected. The infrared (IR) spectra were recorded in potassium bromide pellets using a JASCO 810 spectrometer and ultraviolet (UV) absorption spectra were determined in 95% ethanol using a Shimadzu UV3100pc spectrometer. Nuclear magnetic resonance (NMR) spectra were obtained using Gemini 300NMR (300 MHz) and JEOL-GX-400 (400 MHz) spectrometers with tetramethylsilane as the internal standard. Mass (MS) spectra were recorded on JEOL MS-DX303 mass spectrometer. Elemental analyses were performed at the Microanalytical Laboratory of the Center for Instrumental Analysis in Nagasaki University.

5.2. 3-Cyano-4-(4-*N*,*N*-dimethylamino)phenyl-1-methyl-1*H*-pyrrole-2,5-dione (*7a*)

A solution of 1.82 g (15 mmol) of *N*,*N*-dimethylaniline (**6a**) and 1.83 g (10 mmol) of (**5a**) in 20 ml of acetic acid was refluxed for 9 h. The color of the reaction mixture soon changed to red solution. After cooling, the precipitate that appeared was collected by filtration and recrystallized from methanol to give 1.52 g (6.0 mmol, 60%) of greenish needles, mp 222–226 °C. IR (KBr) ν_{max} cm^{-1}: 2920, 2200 (CN), 1750, 1685 (C=O), 1605, 1560, 1515, 1430, 1375, 1355, 1215, 1070, 985, 825, 740. UV (DMSO) λ_{max} nm (log ε): 543 (4.85), 271 (4.78). ^{1}H NMR ($CDCl_3$) δ: 3.10 (3H, s, NMe), 3.17 (6H, s, NMe_2), 6.75 (2H, d, J = 9.4 Hz, 3′,5′-H), 8.46 (2H, d, J = 9.4 Hz, 2′,6′-H). EI-MS *m*/*z*: 256 (M^+ + 1, 16), 255 (M^+, 100), 254 (72), 239 (3), 169 (9), 126 (4), 85 (16). Anal. Calcd. for $C_{14}H_{13}N_3O_2$ = 255.279: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.72; H, 5.23; N, 16.37.

5.3. 3-Cyano-4-(4-*N*,*N*-diethylamino)phenyl-1-methyl-1*H*-pyrrole-2,5-dione (*7b*)

A solution of 0.45 g (3.0 mmol) of *N*,*N*-diethylaniline (**6b**) and 0.36 g (2.0 mmol) of (**5a**) in 10 ml of acetic acid was refluxed for 5 h. The color of reaction mixture was changed to red and then red violet. After cooling, the precipitate that appeared was collected by filtration and recrystallized from a mixture of methanol and toluene to give 0.30 g (1.06 mmol) of dark brown needles, mp 184–187 °C, in 53% yield. IR (KBr) ν_{max} cm^{-1}: 2980, 2935, 2875, 2202 (CN), 1750, 1700 (C=O), 1605, 1565, 1510, 1475, 1420, 1370, 1350, 1275, 1195, 1165, 1075, 1000, 985, 920, 860, 825, 740, 720, 620, 575, 500. UV (EtOH) λ_{max} nm (log ε): 544 (4.51), 353 (3.17), 282 (4.22). ^{1}H NMR ($CDCl_3$) δ: 1.23 (6H, t, J = 7.1 Hz, CH_2CH_3), 3.09 (3H, s, NMe), 3.51 (4H, q, J = 7.1 Hz, CH_2CH_3), 6.74 (2H, d, J = 9.5 Hz, 3′,5′-H), 8.44 (2H, d, J = 9.5 Hz, 2′,6′-H); EI-MS *m*/*z*: 283 (M^+, 42),

269 (17), 268 (100), 240 (18), 155 (7), 126 (5), 99 (7). Anal. Calcd. for $C_{16}H_{17}N_3O_2 = 283.333$: C, 67.82; H, 6.05; N,14.83. Found: C, 67.74; H, 6.10; N, 14.74.

5.4. 3-Cyano-4-(4-N,N-dibutylaminophenyl)-1-methyl-1H-pyrrole-2,5-dione (**7c**)

A solution of 0.62 g (3.0 mmol) of *N*,*N*-dibutylaniline (**6c**) and 0.36 g (2.0 mmol) of (**5a**) in 10 ml of acetic acid was refluxed for 16 h. After removal of the solvent, the residue was chromatographed on a silica gel column using toluene as an the eluent to give 0.24 g (0.71 mmol) of dark greenish needles, mp 121–124 °C, in 35% yield. IR (KBr) ν_{max} cm^{-1}: 2950, 2925, 2855, 2205 (CN), 1750, 1705 (C=O), 1605, 1560, 1510, 1435–1445 (br), 1410, 1385, 1355, 1285, 1260, 1240, 1215, 1075, 1020. UV (EtOH) λ_{max} nm (log ε): 547 (4.35), 363 (3.52), 280 (4.21). ^{1}H NMR ($CDCl_3$) δ: 0.92 (3H, t, $J = 7.5$ Hz,$-CH_2CH_3$), 1.29–1.37 (2H, m, CH_2), 1.53–1.57 (2H, m, CH_2), 2.87 (3H, s, NMe), 3.34 (2H, t, $J = 7.5$ Hz, CH_2), 6.64 (2H, d, $J = 9.3$ Hz, 3′,5′-H), 8.37 (2H, d, $J = 9.3$ Hz, 2′,6′-H). EI-MS *m/z*: 340 ($M^+ + 1$, 6), 339 (M^+, 16), 296 (31), 279 (31), 240 (11), 182 (33), 167 (28), 149 (58), 138 (11), 113 (11), 110 (11), 97 (25), 71 (14), 70 (12), 57 (23), 55 (11), 44 (100), 43 (16). HRMS: Calcd. for $C_{20}H_{25}N_3O_2 = 339.1946$. Found: 339.1939.

5.5. 3-Cyano-1-methyl-4-(4-N,N-dimethylamino-2-methylphenyl)-1H-pyrrole-2,5-dione (**7d**)

A solution of 0.68 g (5.0 mmol) of 3-methyl-*N*.*N*-dimethylaniline (**6d**) and 0.91 g (5.0 mmol) of (**5a**) in 15 ml of acetic acid was refluxed for 9 h. After evaporation of the solvent, the residue was chromatographed on a column of silica gel using toluene as the eluent to give 0.51 g (1.9 mmol) of black needles in 38% yield. An analytical sample was recrystallized from methanol to give black needles, mp 206–210 °C. IR (KBr) ν_{max} cm^{-1}: 2920, 2210 (CN), 1760, 1702 (C=O), 1615, 1575, 1525, 1435, 1370, 1280, 1205, 1065, 995, 890, 840, 815, 745, 600. UV (EtOH) λ_{max} nm (log ε): 534 (4.24), 267 (4.30), 206 (4.46). ^{1}H NMR ($CDCl_3$) δ: 2.46 (3H, s, CH_3), 3.10 (6H, s, NMe_2), 3.14 (3H, s, NMe), 6.61 (1H, d, $J = 2.7$ Hz, 3-H), 6.63 (1H, dd, $J = 9.6$, 2.7 Hz, 5-H), 7.53 (1H, d, $J = 9.6$ Hz, 6-H). EI-MS *m/z*: 270 ($M^+ + 1$, 18), 269 (M^+, 100), 268 (49), 183 (10), 168 (4), 140 (6), 92 (10), 69 (11). Anal. Calcd. for $C_{15}H_{15}N_3O_2 = 269.306$: C, 66.90; H, 5.61; N,15.60. Found: C, 66.94; H, 5.63; N, 15.51.

5.6. 1-Methyl-4-(4-N,N-dimethylamino)phenyl-3-methoxycarbonyl-1H-pyrrole-2,5-dione (**7e**)

A solution of 2.43 g (20 mmol) of *N*,*N*-dimethylaniline (**6a**) and 2.15 g (10 mmol) of 1-methyl-3-methylthio-4-methoxycarbonylmaleimide (**5b**) in 40 ml of acetic acid was refluxed for 7 h. The color of reaction solution changed from yellow to orange and then to dark red. After removal of the solvent, the residue was chromatographed on silica gel with toluene as the eluent to give 1.3 g (4.5 mmol, 49% yield) reddish brown needles, mp 87–91 °C. IR (KBr) ν_{max} cm^{-1}: 3005, 2950, 1770, 1705 (C=O), 1690 (C=O), 1615, 1590, 1435, 1378, 1330, 1315, 1235, 1205, 1170, 1075, 1015, 1000. UV (EtOH) λ_{max} nm (log ε): 495 (3.81), 387 (3.60), 270 (4.07). ^{1}H NMR ($CDCl_3$) δ: 2.88 (3H, s, NMe), 3.05 (3H, s, NMe), 3.09 (3H, s, NMe), 3.91 (3H, s, OMe), 6.70 (2H, d, $J = 9.3$ Hz, 3′,5′-H), 7.82 (2H, d, $J = 9.3$ Hz, 2′,6′-H). EI-MS *m/z*: 288 (M^+, 12), 215 (29), 185 (10), 184 (24), 183 (100), 158 (10), 143 (14), 139 (11), 127 (11), 126 (11), 101 (12), 99 (40), 85 (11), 84 (18), 73 (12), 69 (11), 59 (31), 45 (23). HRMS: Calcd. for $C_{15}H_{16}N_2O_4 = 288.1110$. Found: 288.1120.

5.7. 4-(4-N,N-Diethylamino)phenyl-1-methyl-3-methoxycarbonyl-1H-pyrrole-2,5-dione (**7f**)

A solution of 0.45 g (3.0 mmol) of *N*,*N*-diethylaniline (**6b**) and 0.43 g (2.0 mmol) of 1-methyl-3-methylthio-4-methoxycarbonylmaleimide (**5b**) in 15 ml of acetic acid was refluxed for 20 h. The color of reaction solution was changed from yellow to orange and then to dark red. After removal of the solvent, the residue was purified by preparative thin layer chromatography (TLC) (silica gel using a mixture of toluene and ethyl acetate 6:1 as an eluent) to give 0.23 g (0.73 mmol, 36% yield) of reddish brown oil, IR (KBr) ν_{max} cm^{-1}: 2980, 2950, 2900, 2375, 1755, 1720 (C=O), 1705 (C=O), 1690 (C=O), 1590, 1525, 1460, 1435, 1405, 1375, 1350, 1270, 1240, 1200, 1160, 1135, 1075, 1005. UV (EtOH) λ_{max} nm (log ε): 508 (4.24), 272 (4.24). ^{1}H NMR ($CDCl_3$) δ: 1.22 (3H, t, $J = 7.1$ Hz, $-CH_2-$), 3.08 (3H, s, NMe), 3.44 (2H, q, $J = 7.1$ Hz, Me), 3.90 (3H, s, OMe), 6.67 (2H, d, $J = 9.3$ Hz, 3′,5′-H), 7.83 (2H, d, $J = 9.3$ Hz, 2′,6′-H). EI-MS *m/z*: 317 ($M^+ + 1$, 11), 316 (M+, 58), 302 (18), 301 (100), 259 (20), 215 (18), 184 (11), 183 (44), 156 (12), 99 (18), 84 (11), 59 (10). HRMS: Calcd. for $C_{17}H_{12}N_2O_4 = 316.1422$. Found: 316.1412.

5.8. 4-(4-N,N-Dimethylamino)phenyl-3-methoxycarbonyl-1H-pyrrole-2,5-dione (**7g**)

A solution of 0.36 g (3.0 mmol) of *N*,*N*-dimethylaniline (**6a**) and 0.40 g (2.0 mmol) of **5c** in 10 ml of acetic acid was refluxed for 9 h. The color of the reaction mixture changed from yellow to red. After the reaction, the reaction mixture was poured into 80 ml of ice-water. The resulting precipitate was collected by filtration to give 78 mg (0.28 mmol) of black needles in 14% yield. An analytical sample was recrystallized from methanol to give black needles, mp 180–183 °C. IR (KBr) ν_{max} cm^{-1}: 3060, 2950, 2925, 1760, 1720 (C=O), 1710 (C=O), 1610, 1590, 1525, 1435, 1375, 1330, 1245, 1235, 1200, 1170, 1065, 950, 825, 805, 650. UV (EtOH) λ_{max} nm (log ε): 478 (4.08), 264 (4.24). ^{1}H NMR ($CDCl_3$) δ: 3.09 (6H, s, NMe_2), 3.90 (3H, s, OMe), 6.70 (2H, d, $J = 8.5$ Hz, 3′,5′-H), 7.81 (2H, d, $J = 8.5$ Hz, 2′, 6′-H). EI-MS *m/z*: 275 ($M^+ + 1$, 17), 274 (M^+, 100), 273 (15), 243 (12), 217 (23), 216 (55), 215 (16), 145 (11). HRMS Calcd. for $C_{14}H_{14}N_2O_4 = 274.0953$. Found: 274.0954.

5.9. 4-(4-N,N-Dimethylaminophenyl)-1-methyl-1H-pyrrole-2,5-dione (**8**)

A mixture of 0.64 g (2.2 mmol) of **7e** and 40 ml of polyphosphoric acid was heated and stirred on hot-stirrer at 150–160 °C for 6 h. After reaction, the reaction mixture was poured into 50 ml of ice-water and neutralized with 10% sodium hydroxy solution. The mixture was extracted with two 50 ml portions of dichloromethane. The combined organic layer and extracts were washed once with aqueous saturated sodium chloride, dried over magnesium sulfate, filtered into a 200 ml round-bottomed flask and concentrated with a rotary evaporator. The residue was chromatographed on a silica gel column with a toluene as the eluent to give 0.12 g (0.52 mmol) of **8** as orange needles in 13% yield. An analytical sample was recrystallized from methanol to give orange needles, mp 218–220 °C. IR (KBr) ν_{max} cm^{-1}: 3100, 2895–2925 (br), 2820, 1740 (C=O), 1690 (C=O), 1605, 1585, 1520, 1450, 1430, 1380, 1365, 1330, 1200, 1125, 1065, 815. UV (EtOH) λ_{max} nm (log ε): 459 (4.24), 265 (4.27). ^{1}H NMR ($CDCl_3$) δ: 3.05 (3H, s, N–Me), 3.06 (6H, s, NMe_2), 6.44 (1H, s,=C–H), 6.70 (2H, d, J = 9.2 Hz, 3′,5′-H), 7.92 (2H, d, J = 9.2 Hz, 2′,6′-H). EI-MS *m/z*: 231 (M^+ + 1, 15), 230 (M^+, 100), 229 (55), 145 (15), 144 (14), 129 (8), 101 (4), 72 (10), 43 (12). Anal. Calcd. for $C_{13}H_{14}N_2O_2$ = 230.269: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.59; H, 6.16; N, 12.09.

5.10. 3-Cyano-4-(4,6,9,10-tetrahydro-6H,8H-benzo-[ij]quinolizin-2-yl)-1-methyl-1H-pyrrol-2,5-dione (**7h**)

A solution of 1.04 g (6.0 mmol) of julolidine (**6e**) and 0.73 g (4.0 mmol) of (**5a**) in 10 ml of acetic acid was refluxed for 2 h. The color of reaction mixture soon changed to dark red and then to dark violet. After cooling, the resulting precipitate was collected by filtration and recrystallized from a mixture of toluene and methanol to give 1.05 g (3.4 mmol) of dark green needles, mp 236–238 °C, in 85% yield. IR (KBr) ν_{max} cm^{-1}: 2952, 2845, 2202 (CN), 1750 (C=O), 1698 (C=O), 1615, 1565, 1522, 1438, 1382, 1360, 1315, 1280, 1212, 1183, 1100, 1063, 1002, 940, 741, 605. UV (EtOH) λ_{max} nm (log ε): 862 (2.09), 576 (4.57), 360 (3.03), 292 (4.15), 211 (4.47). ^{1}H NMR ($CDCl_3$) δ: 1.99 (4H, dd, J = 6.3, 5.8 Hz, 2,6-H), 2.77 (4H, t, J = 6.3 Hz, 1,7-H), 3.07 (3H, s, NMe), 3.40 (4H, t, J = 5.8 Hz, 3,5-H), 8.07 (2H, s, 8′,10′-H). EI-MS *m/z*: 308 (M^+ + 1, 3), 307 (M^+, 16), 256 (3), 230 (2), 149 (5), 97 (3), 83 (3), 71 (3), 69 (4), 57 (6), 55 (8), 43 (100). Anal. Calcd. for $C_{18}H_{17}N_3O_2$ = 307.355: C, 70.34; H, 5.58; N, 13.76. Found: C, 70.35; H, 5.59; N, 13.60.

5.11. N-4-(3-Cyano-1-methyl-2,5-dioxo-1H-pyrrol-3-yl)-phenylaza-15-crown-5-ether (**7i**)

A solution of 0.89 g (3.0 mmol) of *N*-phenylaza-15 crown-5-ether (**6f**) and 0.36 g (2.0 mmol) of (**5a**) in 10 ml of acetic acid was refluxed for 26 h. The color of the reaction mixture was soon changed to red and then to dark red for 20 min. After the removal of the solvent, the residue was crystallized by the addition of 1 ml of ethanol. The crystallized product was collected by filtration and recrystallized from methanol to give 0.25 g (0.58 mmol) of dark greenish needles, mp 182–183 °C, in 29% yield. IR (KBr) ν_{max} cm^{-1}: 2860, 2202 (CN), 1755 (C=O), 1698 (C=O), 1610, 1560, 1510, 1435, 1405, 1340, 1218, 1123, 1075, 995, 823. UV (EtOH) λ_{max} nm (log ε): 534 (4.55), 348 (3.15), 279 (4.26). ^{1}H NMR ($CDCl_3$) δ: 1.61 (H_2O), 3.10 (3H, s, NMe), 3.63 (4H, br s, OCH_2), 3.67 (8H, br s, OCH_2), 3.75 (4H, d, J = 5.5 Hz, NCH_2 or OCH_2), 3.80 (4H, d, J = 5.5 Hz, NCH_2 or OCH_2), 6.77 (2H, d, J = 9.4 Hz, 3′,5′-H), 8.43 (2H, d, J = 9.4 Hz, 2′,6′-H). EI-MS *m/z*: 430 (M^+ + 1, 28), 429 (M^+, 92), 296 (12), 284 (15), 278 (10), 266 (12), 254 (16), 253 (16), 240 (19), 225 (17), 120 (39), 105 (52), 97 (20), 69 (42), 57 (48), 43 (100). Anal. Calcd. for $C_{22}H_{27}N_3O_6$ = 429.477: C, 61.53; H, 6.34; N, 9.78. Found: C, 61.08; H, 6.34; N, 9.65.

5.12. 3-Cyano-4-(4-N,N-dimethylamino)phenyl-1-methyl-5-oxo-1H-pyrrole-2-thione (**9a**)

A mixture of 1.50 g (3.7 mmol) of Lawesson's reagent and 0.25 g (1.0 mmol) of (**7a**) and 10 ml of toluene was refluxed for 4 h. The color of reaction mixture changed to red, violet and then blue. After cooling, the reaction mixture was chromatographed on silica gel column using toluene as the eluent to give 0.19 g (0.72 mmol) of green needles, mp 231–235 °C, in 72% yield. IR (KBr) ν_{max} cm^{-1}: 2920, 2205 (CN), 1710 (C=O), 1605, 1525, 1510 (C=S), 1425, 1385, 1360, 1330 (C=S), 1302, 1210, 1135, 1075, 970, 825. UV (EtOH) λ_{max} nm (log ε): 624 (4.31). ^{1}H NMR ($CDCl_3$) δ: 3.17 (6H, s, NMe_2), 3.37 (3H, s, NMe), 6.78 (2H, d, J = 9.4 Hz, 3′,5′-H), 8.49 (2H, d, J = 9.4 Hz, 2′,6′-H). EI-MS *m/z*: 272 (M^+ + 1, 18), 271 (M^+, 100), 270 (34), 242 (7), 210 (6), 169 (7), 136 (4), 107 (6), 91 (15). Anal. Calcd. for $C_{14}H_{13}N_3OS$ = 271.339: C, 61.97; H, 4.83; N, 15.49; S, 11.82. Found: C, 61.75; H, 4.83; N, 15.41; S, 11.72.

5.13. 3-Cyano-4-(4-N,N-diethylamino)phenyl-1-methyl-5-oxo-1H-pyrrole-2-thione (**9b**)

This compound (0.29 g, 0.98 mmol) was prepared from (**7b**) (0.56 g, 2.0 mmol) and Lawesson's reagent (2.43 g, 6.0 mmol) in 49% yield in a manner similar to that described for the preparation of (**9a**). An analytical sample was recrystallized from methanol to give green prisms, mp 189–190 °C. IR (KBr) ν_{max} cm^{-1}: 2980, 2925, 2375, 2345, 2205 (CN), 1715 (C=O), 1600, 1555, 1505, 1475, 1458, 1422, 1365, 1350, 1330 (C=S), 1305, 1275, 1215, 1160, 1135, 1070, 1005, 965, 910, 825. UV (EtOH) λ_{max} nm (log ε): 615 (4.50), 380 (3.93), 270 (4.01). ^{1}H NMR ($CDCl_3$) δ: 1.27 (6H, t, J = 7.1 Hz, CH_3), 3.36 (3H, s, NMe), 3.51 (4H, q, J = 7.1 Hz, NCH_2), 6.77 (2H, d, J = 9.5 Hz, 3′,5′-H), 8.48 (2H, d, J = 9.5 Hz, 2′,6′-H). EI-MS *m/z*: 300 (M^+ + 1, 11), 299 (M^+, 54), 285 (19), 284 (100), 256 (19), 201 (6), 155 (8). Anal. Calcd. for $C_{14}H_{13}N_3OS$ = 299.393: C, 64.19;

H, 5.72; N, 14.04; S, 10.71. Found: C, 64.16; H, 5.74; N, 14.03; S, 10.47.

5.14. 3-Cyano-4-(4,6,9,10-tetrahydro-6H,8H-benzo-[ij]quinolizin-2-yl)-1-methyl-5-oxo-1H-pyrrole-2-thione (**9c**)

This compound (0.19 g, 0.59 mmol) was prepared from (**7i**) (0.31 g, 1.0 mmol) and Lawesson's reagent (1.61 g, 4.0 mmol) in 49% yield in a manner similar to that described for the preparation of (**9a**). An analytical sample was recrystallized from a mixture of toluene and methanol to give dark red needles, mp 261–264 °C. IR (KBr) ν_{max} cm^{-1}: 2940, 2835–2850 (br), 2200 (CN), 1703 (C=O), 1610, 1510, 1440, 1415, 1353, 1300, 1202, 1190, 1130, 1098, 1063, 1040, 1023, 995, 940, 915, 735. UV (EtOH) λ_{max} nm (log ε): 665 (4.66), 377 (4.00), 312 (3.87), 278 (3.93), 249 (3.89). ^{1}H NMR ($CDCl_3$) δ: 2.00 (4H, dt, $J = 6.3$, 5.8 Hz, 2,6-H), 2.79 (4H, t, $J = 6.3$ Hz, 1,7-H), 3.34 (3H, s, NMe), 3.39 (4H, t, $J = 5.8$ Hz, 3,5-H), 8.12 (2H, s, 8,10-H). EI-MS *m/z*: 324 ($M^+ + 1$, 23), 323 (M^+, 100), 322 (36), 307 (3), 294 (3), 105 (5), 43 (8). Anal. Calcd. for $C_{18}H_{17}N_3OS = 323.416$: C, 66.85; H, 5.30; N, 12.99; S, 9.91. Found: C, 66.58; H, 5.32; N, 12.78; S, 9.82.

5.15. 2-Methyl-7-dimethylamino-2H,4H-[1]benzopyrano[3,4-c]pyrrole-1,3,4-trione (**10a**)

A mixture of 2.06 g (15 mmol) of *N*,*N*-dimethyl-3-aminophenol (**6g**) and 2.15 g (10 mmol) of (**5a**) and 40 ml of acetic acid was refluxed 2 h. After cooling, the precipitate was collected by filtration to give 2.35 g (8.6 mmol) of dark red crystals in 86% yield. An analytical sample was recrystallized from a mixture of toluene and methanol to give dark red crystals, mp 326–329 °C. IR (KBr) ν_{max} cm^{-1}: 3110, 3070, 2940, 1765, 1720 (C=O), 1630, 1600, 1540, 1515, 1425, 1375, 1305, 1260, 1235, 1080. UV (EtOH) λ_{max} nm (log ε): 517 (4.41). ^{1}H NMR ($CDCl_3 + CF_3COOH$) δ: 3.15 (3H, s, NMe), 3.25 (6H, s, NMe_2), 6.60 (1H, br s, 6-H), 6.87 (1H, br s, 8-H), 8.27 (1H, br s, 9-H). EI-MS *m/z*: 273 ($M^+ + 1$, 15), 272 (M^+, 100), 271 (54), 243 (2), 215 (3), 187 (2), 159 (8), 131 (5), 122 (4), 116 (4), 79 (12). Anal. Calcd. for $C_{14}H_{12}N_2O_4 = 272.263$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.65; H, 4.44; N, 10.34.

5.16. 7-Diethylamino-2-methyl-2H,4H-[1]benzopyrano[3,4-c]pyrrole-1,3,4-trione (**10b**)

This compound (0.548 g, 1.8 mmol) was prepared from (**6h**) (0.50 g, 3.0 mmol) and (**5a**) (0.43 g, 2.0 mmol) in 91% yield in a manner similar to that described for the preparation of (**10a**). An analytical sample was recrystallized from methanol to give red needles, mp 258–261 °C. IR (KBr) ν_{max} cm^{-1}: 3105, 2980, 2940, 2700, 2365, 2345, 1765 (C=O), 1735 (C=O), 1695, 1605, 1505, 1460, 1430, 1375, 1345, 1270, 1075. UV (EtOH) λ_{max} nm (log ε): 525 (4.47), 332 (3.39), 269 (4.40). ^{1}H NMR ($CDCl_3$) δ: 1.28 (6H, t, $J = 7.2$ Hz, CH_2CH_3), 3.14 (3H, s, NMe), 3.51 (4H, q, $J = 7.2$ Hz, CH_2CH_3), 6.54 (1H, s, 6-H), 6.74 (1H, d, $J = 9.3$ Hz, 8-H), 8.24 (1H, d, $J = 9.3$ Hz, 9-H). EI-MS *m/z*: 301 ($M^+ + 1$, 9), 300 (M^+, 47), 286 (18), 285 (100), 257 (17), 172 (4), 143 (3). Anal. Calcd. for $C_{16}H_{16}N_2O_4 = 300.317$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.92; H, 5.40; N, 9.28.

5.17. 7-Dibutylamino-2-methyl-2H,4H-[1]benzopyrano[3,4-c]pyrrole-1,3,4-trione (**10c**)

This compound (0.69 g, 1.95 mmol) was prepared from (**6i**) (0.66 g, 3.0 mmol) and (**5a**) (0.43g, 2.0 mmol) in 97% yield in a manner similar to that described for the preparation of (**10a**). An analytical sample was recrystallized from methanol to give red needles, mp 213–216 °C. This compound was also obtained by the reaction of (**6i**) with (**5b**) under the same reaction condition in 28.4% yield. IR (KBr) ν_{max} cm^{-1}: 2960, 2930, 2865, 1765 (C=O), 1730 (C=O), 1730 (C=O), 1695 (C=O), 1600, 1510, 1470, 1435, 1380, 1365, 1350, 1280, 1260, 1185, 1080, 1005. UV (EtOH) λ_{max} nm (log ε): 526 (4.40), 409 (3.89), 269 (4.36). ^{1}H NMR ($CDCl_3$) δ: 0.99 (6H, t, $J = 7.5$ Hz, CH_3), 1.40 (4H, q, $J = 7.5$ Hz, CH_2), 1.59–1.67 (4H, m, CH_2), 3.14 (3H, s, NMe), 3.39–3.44 (2H, m, CH_2), 6.52 (1H, d, $J = 2.5$ Hz, 6-H), 6.72 (1H, dd, $J = 9.3$, 2.5 Hz, 7-H), 8.25 (1H, d, $J = 9.3$ Hz, 8-H). EI-MS *m/z*: 357 ($M^+ + 1$, 9), 356 (M^+, 42), 314 (20), 313 (100), 271 (28), 257 (39), 83 (11), 71 (10), 69 (21), 57 (27), 55 (21), 44 (14). Anal. Calcd. for $C_{20}H_{24}N_2O_4 = 356.425$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.00; H, 6.72; N, 7.79.

5.18. 1,2,5,6,7-Pentahydro-10-methyl-3H,10H,12H-pyrrolo[3′,4′:3,4][1]-benzopyrano[6,7,8-ij]quinolizine-9,11,12-trione (**12**)

This compound (0.31 g, 0.96 mmol) was prepared from 8-hydroxyjulolidine (**6j**) (0.28 g, 1.5 mmol) and (**5a**) (0.22 g, 1.0 mmol) in 96% yield in a manner similar to that described for the preparation of (**10a**). An analytical sample was recrystallized from a mixture of toluene and methanol to give black needles, mp 315–319 °C. IR (KBr) ν_{max} cm^{-1}: 2935, 2855, 2370, 2345, 1760 (C=O), 1720 (C=O), 1695 (C=O), 1615, 1595, 1520, 1430, 1370, 1310, 1215, 1190, 1150, 1120. UV (EtOH) λ_{max} nm (log ε): 552 (4.47), 350 (3.13), 280 (4.28), 209 (4.49). ^{1}H NMR ($CDCl_3$) δ: 2.06 (4H, m, 2,6-H), 2.77–2.87 (4H, m, 1,7-H), 3.12 (3H, s, NMe), 3.40 (4H, m, 3,5-H), 7.80 (1H, s, 8-H); EI-MS *m/z*: 325 ($M^+ + 1$, 20), 324 (M^+, 100), 323 (40), 295 (3), 211 (4), 182 (3), 162 (4), 119 (3), 91 (3), 77 (3), 44 (6). Anal. Calcd. for $C_{18}H_{16}N_2O_4 = 324.339$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.71; H, 5.05; N, 8.62.

5.19. 7-Hydroxy-2-methyl-2H,4H-[1]benzopyrano-[3,4-c]pyrrole-1,3,4-trione (**13**)

5.19.1. Method A

A mixture of 0.33 g (3.0 mmol) of resorcinol (**6k**), 0.43 g (2.0 mmol) of (**5a**), and 10 ml of acetic acid was refluxed for

20 h. After removal of the solvent, the residue was crystallized by the addition of methanol. The resulting crystallized product was collected by filtration and recrystallized from methanol to give 9 mg (0.037 mmol) of yellow crystals in 1.8% yield.

5.19.2. Method B

Sodium hydride (50% dispersion in mineral oil, 0.48 g, 10 mmol) was placed in dry tetrahydrofuran (30 ml) and used after being washed twice with hexane (30 ml). The slurry was cooled to 20 °C and resorcinol (**6k**) (0.55 g, 5.0 mmol) was added with stirring under stream nitrogen. After the addition the solution was stirred at room temperature for 15 min. Compound (**5a**) (1.07 g, 5.0 mmol) was added in one portion. The mixture was refluxed 2 h. After the solvent was removed, the residue was added 200 ml of ice-water and then this solution was acidified with 10% hydrochloric acid. The mixture was stored overnight. The resulting precipitate was collected by filtration and recrystallized from methanol to give 0.73 g (3.0 mmol) of yellow crystals in 60% yield. An analytical sample was recrystallized from methanol to give yellow needles, mp > 340 °C. IR (KBr) ν_{max} cm^{-1}: 3470, 1780, 1720 (C═O), 100 (C═O), 1610, 1450, 1380, 1270, 1070, 1020. UV (EtOH) λ_{max} nm (log ε): 516 (4.12), 263 (4.09). ^{1}H NMR (DMSO) δ: 3.00 (3H, s, NMe), 6.87 (1H, d, J = 1.7 Hz, 6-H), 6.99 (1H, dd, J = 8.8, 1.7 Hz, 8-H), 8.25 (1H, d, J = 8.8 Hz, 9-H), 11.47 (1H, s, OH). EI-MS *m/z*: 246 (M^+ + 1, 6), 245 (M^+, 100), 188 (32), 173 (9), 160 (17), 151 (15), 57 (10). Anal. Calcd. for $C_{12}H_7NO_5$ = 245.193: C, 58.78; H, 2.88; N, 5.71. Found: C, 58.77; H, 2.89; N, 5.57.

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