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Full Paper

Synthesis and Photoreaction of 2-Amino-3-cyano-4-aryl-4*H*-pyrans

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A series of 2-amino-3-cyano-4-aryl-4*H*-pyrans (**1**) were synthesised by reacting malononitrile, ethyl acetoacetate, and aromatic aldehydes under ultrasound irradiation. The photochemical properties, including the photostability and photoreaction of **1**, were investigated in conventional solvents. The results indicated that compounds **1** were unstable and underwent a photoreaction to the 1,3-butadienes under irradiation with UV light. A mechanism for the photoreaction is proposed and investigated using electron spin resonance spectroscopic techniques. The 1,3-butadiene structures were determined by ^{1}H and ^{13}C NMR spectra, high-resolution mass spectrometry, and single crystal X-ray diffraction analysis.

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Introduction

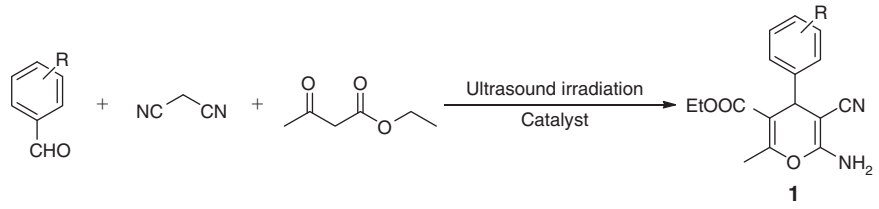
4*H*-Pyrans are very important heterocyclic compounds that frequently exhibit a variety of biological activities.[1] In addition, 4*H*-pyrans are useful intermediates for the synthesis of various compounds, such as pyranopyridine derivatives, polyazanaphthalenes, and pyridin-2-ones.[2] However, the preparations of 4*H*-pyrans have many drawbacks, such as longer reaction times, unsatisfactory yields, harsh reaction conditions, and excessive use of reagents and catalysts.[3] Therefore, a more convenient method of preparing 4*H*-pyrans is essential. Ultrasound has become a highly useful method for performing a wide range of chemical reactions and processes. The application of ultrasound irradiation in organic reactions is also rapidly increasing, and a large number of organic reactions can be performed with a higher yield, shorter reaction time, and milder conditions.[4] To expand the application of ultrasound in the synthesis of organic compounds, we report a novel and efficient method for the synthesis of **1** by use of malononitrile, ethyl acetoacetate, and aromatic aldehydes using a sodium ethoxide catalyst under ultrasound irradiation (Scheme 1).

Although the photochemical properties of heterocyclic compounds have been studied,[5] **1** has received very little attention. To evaluate the photochemical properties, the photostability, photoreaction, and reaction mechanism of **1** have been investigated. The photoreaction products were determined by ^{1}H and ^{13}C NMR spectroscopy, high-resolution mass spectrometry, and single crystal X-ray diffraction analysis.

Results and Discussion

*Synthesis of 2-Amino-3-cyano-4-aryl-4*H*-pyrans*

To achieve suitable conditions for the synthesis of 2-amino-3-cyano-4-aryl-4*H*-pyrans (**1**), the reactions have been investigated for the preparation of **1a**. The effects of the catalyst, solvent, reaction temperature, and intensity power of ultrasound were examined. Initially, to search for the optimal catalyst, the reaction was examined using triethylamine, piperidine, sodium hydroxide, and sodium ethoxide as the catalysts. Under ultrasound irradiation in ethanol at 50°C and 150 W, 10 mol % sodium ethoxide in ethanol resulted in the best yield (i.e. 85 %) (Table 1). The reaction was then performed in ethanol, dichloromethane, acetonitrile, and dimethylformamide, and the desired product was obtained in 85, 37, 65, and 80 % yield, respectively. Therefore, ethanol was chosen as the solvent for the reaction. Next, the optimal reaction temperature and ultrasound intensity power were evaluated at 30, 50, and 80°C with 80, 150, and 250 W of power. When the reaction was performed at 50°C and 150 W, the best yield of the desired product was



Scheme 1. Synthesis of 2-amino-3-cyano-4-aryl-4*H*-pyrans.

Table 1. Yields of 1a under different reaction conditions

Entry[A]	Cat. (conc. [mol %])	Solvent	Temp. [°C]	Power [W]	Time [min]	Yield [%][B]
1	Triethylamine (10)	Ethanol	80	150	30	60
2	Piperidine (10)	Ethanol	80	150	15	78
3	Sodium hydroxide (10)	Ethanol	80	150	10	82
4	Sodium ethoxide (10)	Ethanol	80	150	10	85
5	Sodium ethoxide (5)	Ethanol	80	150	30	30
6	Sodium ethoxide (15)	Ethanol	80	150	10	83
7	Sodium ethoxide (10)	CH_2Cl_2	80	150	60	37
8	Sodium ethoxide (10)	CH_3CN	80	150	60	65
9	Sodium ethoxide (10)	DMF	80	150	15	80
10	Sodium ethoxide (10)	Ethanol	30	150	10	34
11	Sodium ethoxide (10)	Ethanol	50	150	10	86
12	Sodium ethoxide (10)	Ethanol	50	50	10	80
13	Sodium ethoxide (10)	Ethanol	50	250	10	77

[A]Reaction conditions: malononitrile (10 mmol), ethyl acetoacetate (10 mmol), and benzaldehyde (10 mmol), solvent (15 mL), and catalyst under ultrasound irradiation.
[B]Isolated yield.

Table 2. Yields of 2-amino-3-cyano-4-aryl-4*H*-pyrans

Entry	R	Time [min]	Yield [%][A]
1a	H	10	86
1b	*p*-CH_3	10	86
1c	*p*-F	5	87
1d	*m*-Cl	10	89
1e	*p*-Br	5	92
1f	*3,4*-diF	10	90
1g	*3,5*-diCF_3	10	89
1h	*p*-NO_2	5	91
1i	*p*-OCH_3	30	65

[A]Isolated yield.

obtained (i.e. 86 %). As shown in Table 1, the best reaction conditions involved the presence of sodium ethoxide (10 mol %) in ethanol as the solvent at 50°C and 150 W. Under the optimised conditions, a series of **1** was obtained, and the results are shown in Table 2.

As shown in Table 2, all of the reactions proceeded efficiently, and the desired products were obtained in good to excellent yields (65–92 %). For example, **1a** was obtained in 86 % yield after 10 min of ultrasound irradiation, whereas **1a** was isolated in 80 % yield after 3 h with a traditional heating method.[6]

*Photochemical Properties of the 2-Amino-3-cyano-4-aryl-4*H*-pyrans*

*Photostability of 2-Amino-3-cyano-4-aryl-4*H*-pyrans*

The UV-vis absorption spectra of **1a**, **1b**, **1c**, **1d**, and **1e** in THF at a concentration of 5×10^{-5} M are shown in Fig. 1. Several absorption peaks were observed in the linear absorption spectra for all of the molecules in the wavelength range of 220 to 450 nm, while almost no linear absorption was observed beyond 370 nm. The shapes of the spectra are similar because these compounds have the same stem nuclei of the 2-amino-3-cyano-4-aryl-4*H*-pyran structure. The maximum absorptions range from 224 to 234 and 284 to 296 nm and are similar to the UV-vis absorption spectra of **1a**.

According to the absorption spectroscopic characteristics, **1a** was chosen as a representative compound to investigate the

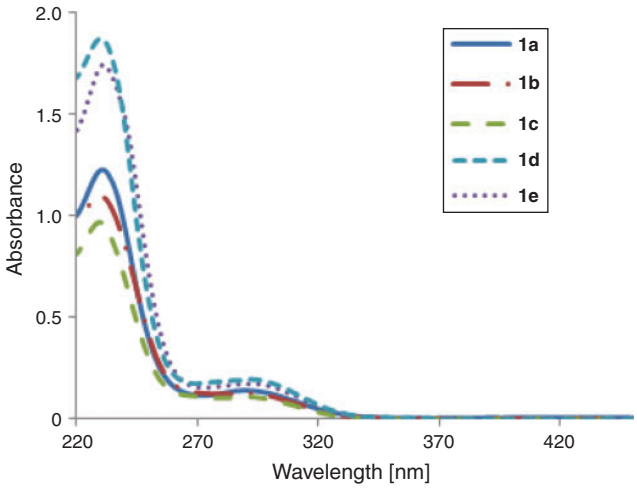
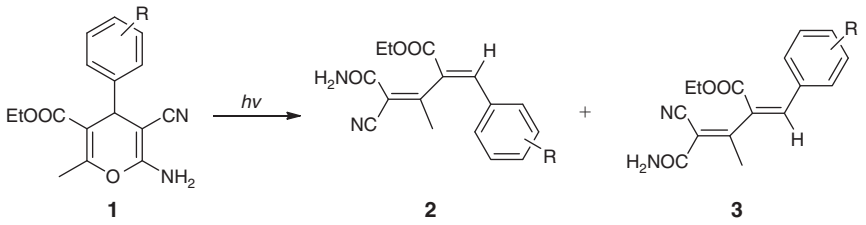


Fig. 1. The UV-vis absorption spectra in THF at a concentration of 5×10^{-5} M.

photostability of the 2-amino-3-cyano-4-aryl-4*H*-pyrans and was irradiated at different wavelengths (i.e. 256, 280–300, 300–320, 320–350, 350–360, and 360–370 nm) in THF for the same time (40 h). Compound **1a** was unstable and yielded polymers with UV irradiation at <300 nm (i.e. 256 and 280–300 nm). At 300–370 nm, **1a** yields products **2a** and **3a** (Scheme 2), the yields of which increase at 300–320 nm. The photostability was investigated by the changes of UV-vis absorption spectrum irradiated under UV (300–320 nm) irradiation in THF at a concentration of 5×10^{-5} M (Fig. 2). After irradiation for 40 h, the two wavelength maxima of **1a** (224–234 and 284–296 nm) changed dramatically from those taken before the irradiation. In particular, the wavelength maximum at 224–234 nm decreased in magnitude, and new peaks appeared at 258–266 and 322–332 nm. The changes in the UV-vis absorption spectra may be caused by the fragmenting of the pyran ring and the formation of conjugated dienes during irradiation.

*Photoreaction of the 2-Amino-3-cyano-4-aryl-4*H*-pyrans*

Because the photoreaction of **1a** yielded products **2a** and **3a**, it is necessary to explore the photoreaction conditions of **1a**.



Scheme 2. Photoreaction of 2-amino-3-cyano-4-aryl-4*H*-pyrans.

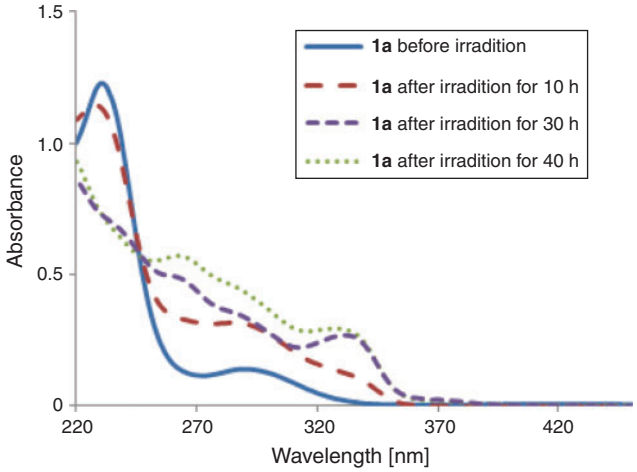


Fig. 2. The UV-vis absorption spectra of **1a** before and after irradiation.

Table 3. Yields of products 2 and 3

Entry	R	Yield of **2** [%][A]	Yield of **3** [%][A]
1a	H	41.0	26.0
1b	*p*-CH_3	46.0	24.4
1c	*p*-F	45.1	–
1d	*m*-Cl	29.3	31.4
1e	*p*-Br	21.5	29.4
1f	3,4-diF	30.2	36.1
1g	3,5-diCF_3	–	48.2
1h	*p*-NO_2	–	–
1i	*p*-OCH_3	18.8	–

[A]Isolated yield.

The primary factor affecting the photoreaction is the solvents. Conventional solvents, such as dichloromethane, THF, acetone, and methanol, were evaluated in the photoreaction of **1a** under UV (300–320 nm) irradiation for 50 h. Different solvents produced **2a** and **3a** in different yields (**2a**: 15.0–41.0 %, **3a**: 11.0–26.0 %). The best results were obtained in THF with a 41.0 % yield for **2a** and a 26.0 % yield for **3a**.

Compounds **1b**–**1i** were irradiated in THF under the UV (300–320 nm) irradiation for 50 h, and the results are shown in Table 3. Like **1a** (R = H), **1b** (R = *p*-CH_3), **1d** (R = *m*-Cl), **1e** (R = *p*-Br), and **1f** (R = *3,4*-diF) also yielded **2** and **3** with different yields (**2**: 21.5–46.0 %, **3**: 24.4–36.1 %). It is important to note that **1c** (R = *p*-F) and **1i** (R = *p*-OCH_3) only yielded **2** with 18.8 and 45.1 % yields and **1g** (R = *3,5*-diCF_3) only yielded **3g** with a 48.2 % yield. The differences of the yields of **2** and **3** may be related to the steric hindrance of the substituents on the benzene ring. When the steric hindrance of the substituents on the benzene ring was small, the yield of **2** was higher (i.e. for **1a** (R = H) and **1b** (R = *p*-CH_3)), and in some cases **3** could not be obtained (i.e. for **1c** (R = *p*-F) and **1i** (R = *p*-OCH_3)). When the steric hindrance was large, the yield of **3** was better (i.e. for **1d** (R = *m*-Cl) **1e** (R = *p*-Br), and **1f** (R = 3,4-diF)) and **2** was not obtained (i.e. for **1g** (R = 3,5-diCF_3)). In addition, **1h** (R = *p*-NO_2) produced none of the desired products, which is most likely a result of the nitro group being sensitive to UV light resulting in a nitroso free radical.[7]

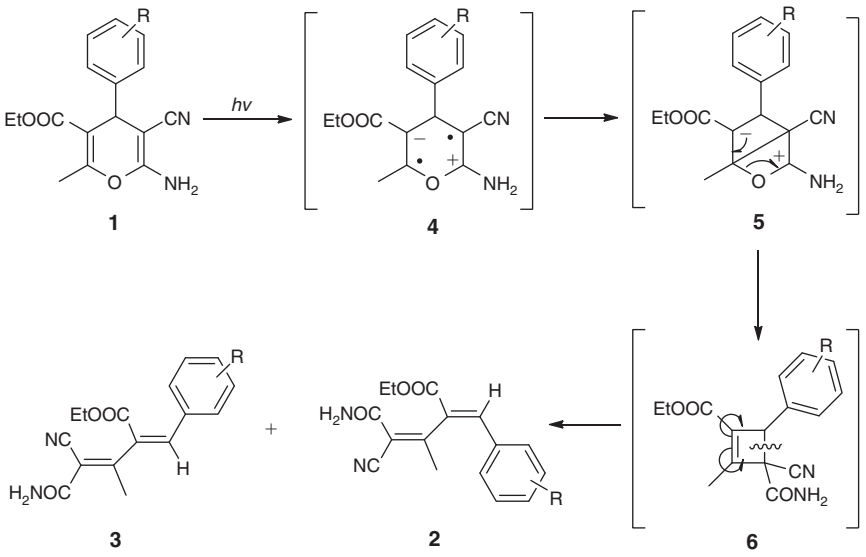
Photoreaction Mechanism of the 2-Amino-3-cyano-4-aryl-4H-pyrans

To the best of our knowledge, the pyran ring transformation to 1,3-butadiene is novel. The mechanism outlined in Scheme 3 was proposed to account for the formation of products **2** and **3**. It involves intramolecular single-electron transfer from the enamino moiety to the ester within the resulting zwitterion-biradical **4**, followed by transannular bond formation to afford the zwitterion **5**, which collapses to cyclobutene **6** by the cleavage of the carbon–oxygen bond. Cyclobutene **6**, which is a four-membered ring, is destabilised under irradiation to yield **2** and **3**. The existence of cyclobutene **6** was accepted based on the work of Armesto et al.,[8] which examined the photoreaction of 2-amino-3,5-dicyano-4-alkyl-4*H*-pyrans to cyclobutenes. The main difference between the two photoreactions is the substituent on the reactant at C-4 of the pyran ring. The reactant used by Armesto et al. had an alkyl substituent, while **1** had an aryl substituent. The aryl substituent may make cyclobutene **6** more unstable than the alkyl and result in the formation of **2** and **3** by cleavage of the carbon–carbon bond.

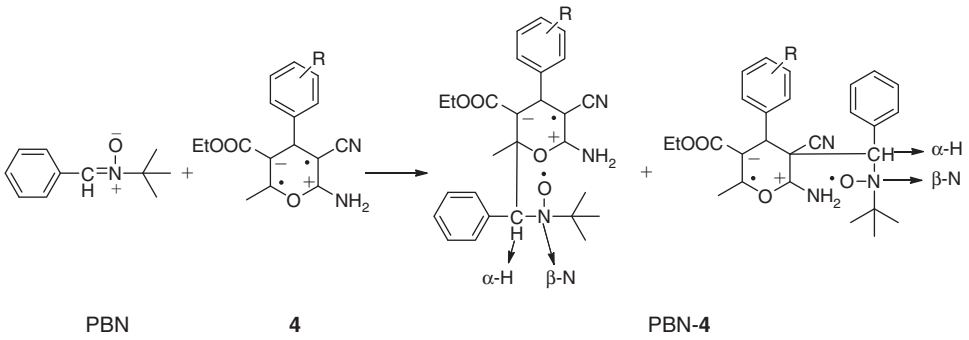
Electron spin resonance (ESR) spectroscopic techniques can be used to investigate the characteristics of radical generation. It is difficult to observe radical **4** because the lifetime of this radical is extremely short. Radical **4** was confirmed using a combination of spin trapping reagents and ESR with phenyl-*tert*-butyl nitrone (PBN) as the trapping agent.[9] The reaction of radical **4** with PBN generated PBN adduct PBN-**4** (Scheme 4). The obtained ESR signals involved a six-line spectrum with **1a**/PBN (Fig. 3). No signals were observed with **1a** or PBN alone. These results demonstrated that radical **4** was generated in the photoreaction. The ESR signals correspond to a triplet from the α-nitrogen that is further split into a doublet by the β-proton.

Structure Determination of Products 2 and 3

The structures of products **2** and **3** were verified by ^{1}H and ^{13}C NMR spectroscopy, and high-resolution mass spectrometry (HRMS). Products **2a** and **3a** will be used as representative examples for discussing structural details. In the ^{1}H NMR spectrum of **2a**, there were signals corresponding to the five protons on the benzene ring in the range of 7.281–7.411 ppm, a signal from the alkene at 7.660 ppm, a signal from the methyl at 2.294 ppm, signals from the ethoxy group at 1.322



Scheme 3. Proposed mechanism for the formation of products **2** and **3**.



Scheme 4. Reaction of **4** with phenyl-*tert*-butyl nitrone (PBN).

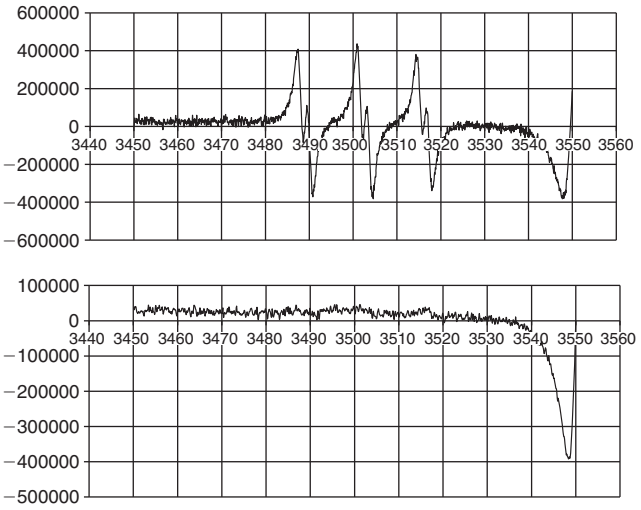


Fig. 3. ESR spectrum of **1a**/phenyl-*tert*-butyl nitrone (PBN) and **1a** or PBN alone.

and 4.280 ppm, and signals from the amino group at 5.739 and 6.160 ppm. In the ^{13}C NMR spectra of **2a**, only 14 signals were observed as a result of the symmetry of the benzene ring. The carbonyl carbons resided at 164.45 and 161.25 ppm, the cyano carbon resided at 116.34 ppm, the signal corresponding to the methyl appeared at 14.18 ppm, the two signals attributable to the ethoxy group appeared at 24.64 and 61.53 ppm, and the signals from the benzene ring were observed at 129.61–133.72 ppm. The remaining signals were attributed to the alkene carbons (109.81, 131.49, 138.03, and 165.92 ppm). HRMS (ESI$^+$) of **2a** showed a molecular ion peak at *m*/*z* 285.1235, which is consistent with the calculated value (i.e. *m*/*z* 285.1239) for **2a** $[M+H]^+$.

The NMR and HRMS data for **3a** was similar to the data for **2a**. In the ^{1}H NMR spectrum of **3a**, there were signals corresponding to the five protons on the benzene ring in the range of 7.266–7.393 ppm, a signal from the alkene at 7.169 ppm, a signal from the methyl at 2.507 ppm, signals from the ethoxy group at 1.180 and 4.221 ppm, and signals from the amino group at 5.723 and 6.290 ppm. In the ^{13}C NMR spectra of **3a**, only 14 signals were observed because of the symmetry of the benzene ring. The carbonyl carbons resided at 164.43 and 156.35 ppm, the cyano carbon resided at 115.44 ppm, the signal of the methyl appeared at 14.08 ppm, the two signals attributable to the ethoxy group appeared at 21.64 and 61.33 ppm, and the signals from the benzene ring were observed at 128.76–133.92 ppm. The remaining signals were attributed to the alkene carbons (109.68, 131.69, 138.02, and 166.88 ppm). HRMS (ESI$^+$) of **3a** showed a molecular ion peak at *m*/*z* 285.1228, which is consistent with the calculated value (i.e. *m*/*z* 285.1239) for **3a** $[M+H]^+$.

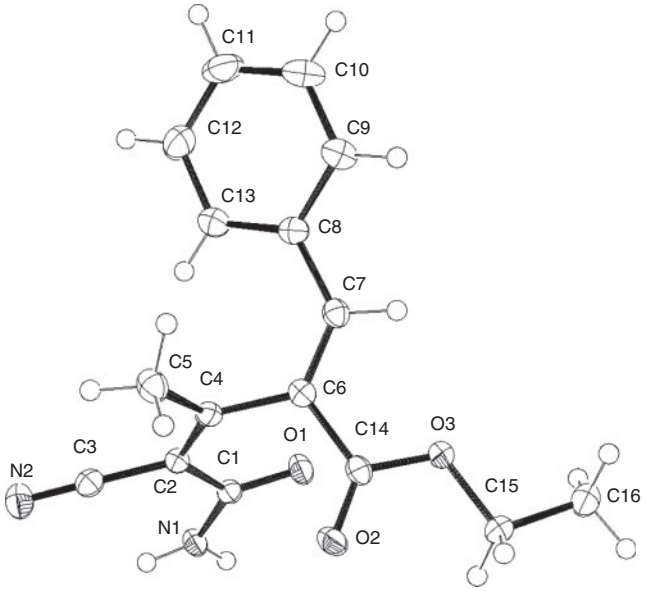


Fig. 4. *ORTEP* diagram of the crystal structure of **2a** (drawn at 50 % thermal ellipsoids).

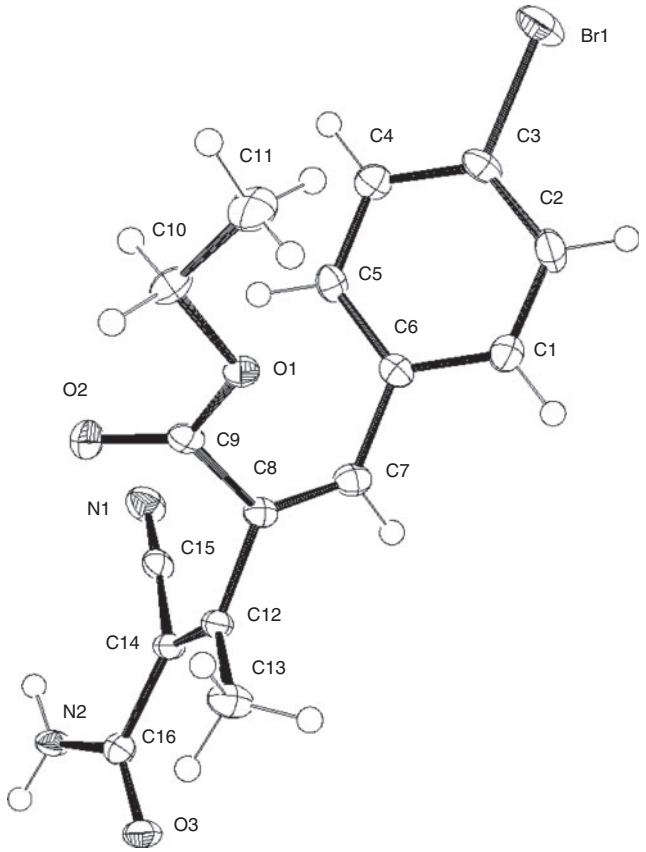


Fig. 5. *ORTEP* diagram of the crystal structure of **3e** (drawn at 50 % thermal ellipsoids).

The 3D structures of **2** and **3** were confirmed by single crystal X-ray diffraction. The single crystal X-ray diffraction data for **2a** (CCDC number 958698) confirmed that **2a** was (2*Z*,4*E*)-2-cyano-4-ethylformyl-3-methyl-5-phenyl-2,4-dienamide (Fig. 4). The single crystal X-ray diffraction data for **3e** (CCDC number 958794) confirmed that it was (2*E*,4*Z*)-2-cyano-4-ethylformyl-3-methyl-5-(4-bromophenyl)-2,4-dienamide (Fig. 5). Based on these results, **2** and **3** were geometric isomers with (2*Z*,4*E*) and (2*E*,4*Z*) at the double bond positions. However, only two geometric isomers were obtained in this reaction among the possible conformers. This may be correlated with the mechanism of this reaction. In the photoreaction, the cyclobutene **6** is formed in the more stabilised spatial structure. Cyclobutenes **6** undergo ring-opening reactions under irradiation conditions to yield 1,3-butadienes. The ring-opening activation enthalpies and barrier for **2** (2*Z*,4*E*) and **3** (2*E*,4*Z*) are presumably lower than other conformers, which may be the reason why only **2** (2*Z*,4*E*) and **3** (2*E*,4*Z*) are obtained in this reaction.

Conclusion

A series of 2-amino-3-cyano-4-aryl-4*H*-pyrans were synthesised by reaction of malononitrile, ethyl acetoacetate, and aromatic aldehydes in the presence of sodium ethoxide in ethanol at 50°C and 150 W under ultrasound irradiation. The photostability of the 2-amino-3-cyano-4-aryl-4*H*-pyrans was investigated with a variety of wavelengths, and the 2-amino-3-cyano-4-aryl-4*H*-pyrans were determined to be unstable under irradiation at 300–320 nm. The photoreaction conditions were investigated in different conventional solvents, and better yields were obtained in THF for ~50 h. The main products (i.e. 1,3-butadienes) were isolated, and their structures were determined by ^{1}H and ^{13}C NMR spectra and HRMS. The single crystal X-ray diffraction analysis indicated that the 1,3-butadienes had (2*Z*,4*E*) and (2*E*,4*Z*) conformations. The proposed reaction mechanism involved a photoinduced free radical reaction and the decomposition of the unstable intermediate cyclobutene to 1,3-butadienes. The radical was observed using ESR spectroscopy using the spin-trapping method with PBN as the trapping agent.

Experimental

All of the chemicals were purchased from commercial sources and were used without further purification. Ultrasound irradiation was performed in a GEX750-5C ultrasonic instrument (ACE GLASS Inc., Vineland N.J., USA). Thin-layer chromatography (TLC) was conducted on silica gel 60 F254 plates (Merck KGaA). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400 and 100 MHz, respectively, using $CDCl_3$ or DMSO-d_6 as the solvent and tetramethylsilane (TMS) as the internal standard. The melting points were determined on a XT-5A digital melting point apparatus and are uncorrected. HRMS was performed using an Agilent G3250AA LC/MSD TOF mass spectrometer. The ESR spin-trapping experiment was conducted using a Bruker A300 X-band spectrometer with a 100 kHz magnetic field modulation. Irradiation for the photochemical properties and photoreactions was conducted using a PHILIPS PL-S 11W/10/2P mercury lamp.

*Procedure for the Synthesis of 2-Amino-3-cyano-4-aryl-4*H*-pyrans (**1a**–**1i**)*

In a 100 mL flask, malononitrile (10 mmol), ethyl acetoacetate (10 mmol), an aromatic aldehyde (10 mmol), and ethanol (15 mL) were thoroughly mixed with a catalytic amount of sodium ethoxide (1 mmol). The reaction mixture was sonicated at 50°C and at 150 W. After the completion of the reaction (monitored by TLC), the reaction was allowed to cool to room temperature, and the generated solid was filtered and recrystallised from ethanol to yield pure products **1a**–**1i**.

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-phenyl-4H-pyran (**1a**)*

Yield 2.44 g (86 %); white solid; mp 176.4–177.2°C (Lit.[3] 176.0°C). δ_H (400 MHz, DMSO-d_6) 1.026 (m, 3H, CH_2CH_3), 2.314 (s, 3H, CH_3), 3.966 (m, 2H, CH_2CH_3), 4.296 (s, 1H, Ar-CH), 6.902 (s, 2H, NH_2), 7.138–7.233 (m, 3H, Ar-H), 7.293–7.330 (t, 2H, Ar-H).

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(4-methylphenyl)-4H-pyran (**1b**)*

Yield 2.56 g (86 %); pale yellow solid; mp 176.1–177.1°C (Lit.[10] 177.0–179.0°C). δ_H (400 MHz, DMSO-d_6) 1.052 (m, 3H, CH_2CH_3), 2.258 (s, 3H, Ar-CH_3), 2.304 (s, 3H, CH_3), 3.961 (m, 2H, CH_2CH_3), 4.265 (s, 1H, Ar-CH), 6.893 (s, 2H, NH_2), 7.024–7.043 (d, 2H, Ar-H), 7.102–7.121 (d, 2H, Ar-H).

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(4-fluorophenyl)-4H-pyran (**1c**)*

Yield 2.63 g (87 %); white solid; mp 166.6–167.2°C (Lit.[11] 168.0°C). δ_H (400 MHz, DMSO-d_6) 1.028 (m, 3H, CH_2CH_3), 2.306 (s, 3H, CH_3), 3.964 (m, 2H, CH_2CH_3), 4.315 (s, Ar-CH), 6.952 (s, 2H, NH_2), 7.109–7.199 (m, 4H, Ar-H).

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(3-chlorophenyl)-4H-pyran (**1d**)*

Yield 2.83 g (89 %); white solid; mp 177.9–178.7°C (Lit.[12] 177.0–178.0°C). δ_H (400 MHz, DMSO-d_6) 1.028 (m, 3H, CH_2CH_3), 2.322 (s, 3H, CH_3), 3.981 (m, 2H, CH_2CH_3), 4.332 (s, Ar-CH), 7.020 (s, 2H, NH_2), 7.119–7.373 (m, 4H, Ar-H).

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(4-bromophenyl)-4H-pyran (**1e**)*

Yield 3.34 g (92 %); pale yellow solid; mp 172.8–173.2°C (Lit.[13] 172.0–174.0°C). δ_H (400 MHz, DMSO-d_6) 1.038 (m, 3H, CH_2CH_3), 2.315 (s, 3H, CH_3), 3.971 (m, 2H, CH_2CH_3), 4.036 (s, 1H, Ar-CH), 6.961 (s, 2H, NH_2), 7.109–7.128 (d, 2H, Ar-H), 7.496–7.517 (d, 2H, Ar-H).

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(3,4-difluorophenyl)-4H-pyran (**1f**)*

Yield 2.88 g (90 %); white solid; mp 171.6–172.3°C. δ_H (400 MHz, DMSO-d_6) 1.030 (m, 3H, CH_2CH_3), 2.320 (s, 3H, CH_3), 3.969 (m, 2H, CH_2CH_3), 4.364 (s, 1H, Ar-CH), 7.023 (s, 2H, NH_2), 7.179–7.412 (m, 3H, Ar-H). δ_C (100 MHz, DMSO-d_6) 14.14, 18.68, 38.60, 57.15, 60.67, 106.87, 116.51, 117.80, 119.89, 124.38, 143.31, 147.48, 149.91, 157.78, 158.92, 165.68. *m/z* 321.1045. HRMS Anal. Calc. for $C_{16}H_{15}F_2N_2O_3$: 321.1051.

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-[3,5-bis(trifluoromethyl)phenyl]-4H-pyran (**1g**)*

Yield 3.74 g (89 %); white solid; mp 167.8–168.2°C. δ_H (400 MHz, DMSO-d_6) 0.955 (m, 3H, CH_2CH_3), 2.346 (s, 3H, CH_3), 3.933 (m, 2H, CH_3CH_2), 4.659 (s, 1H, Ar-CH), 7.161 (s, 2H, NH_2), 7.814 (s, 2H, Ar-H), 8.009 (s, 1H, Ar-H). δ_C (100 MHz, DMSO-d_6) 13.79, 18.75, 38.91, 56.46, 60.69, 106.01, 119.61, 125.06, 128.58, 130.70, 131.02, 149.14, 158.76, 159.05, 165.42. *m/z* 421.0980. HRMS Anal. Calc. for $C_{18}H_{15}N_2O_3F_6$: 421.0987.

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-4H-pyran (**1h**)*

Yield 2.99 g (91 %); yellow solid; mp 181.4–182.2°C (Lit.[13] 180.0–182.0°C). δ_H (400 MHz, DMSO-d_6) 1.034 (m, 3H, CH_2CH_3), 2.350 (s, 3H, CH_3), 3.958 (m, 2H, CH_2CH_3), 4.474 (s, 1H, Ar-CH), 7.111 (s, 2H, NH_2), 7.433–7.455 (d, 2H, Ar-H), 8.187–8.209 (d, 2H, Ar-H).

*2-Amino-3-cyano-5-ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-4H-pyran (**1i**)*

Yield 2.04 g (65 %); pale yellow solid; mp 110.8–111.4°C (Lit.[3] 110.0°C). δ_H (400 MHz, DMSO-d_6) 1.061 (m, 3H, CH_2CH_3), 2.287 (s, 3H, CH_3), 3.719 (s, 3H, OCH_3), 3.956 (m, 2H, CH_2CH_3), 4.239 (s, 1H, Ar-CH), 6.853 (s, 2H, NH_2), 6.870–6.873 (d, 2H, Ar-H), 7.042–7.063 (d, 2H, Ar-H).

Procedure for Determining Photochemical Stability

Different wavelengths of light (i.e. 256, 300–320, 320–350, 350–360, 360–370, 370–380, 380–390, 390–400, and 400–410 nm) were produced by PHILIPS PL-S 11W/10/2P mercury lamps. The samples were dissolved in THF and were irradiated in quartz cuvettes.

Procedure for the Photoreaction of 2-Amino-3-cyano-4-aryl-4H-pyrans

2-Amino-3-cyano-4-aryl-4*H*-pyrans (**1**) (1 mmol) were dissolved in THF (100 mL) and irradiated with UV light (300–320 nm) for 40 h. After completion of the reaction, the solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel to yield products **2** and **3**.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-phenyl-2,4-dienamide (**2a**)*

Yield 116 mg (41.0 %); mp 87.5–88.4°C. δ_H (400 MHz, $CDCl_3$) 1.322 (m, 3H, CH_2CH_3), 2.294 (s, 3H, CH_3), 4.280 (s, 2H, CH_2CH_3), 5.739, 6.160 (s, 2H, NH_2), 7.281–7.411 (m, 5H, Ar-H), 7.660 (s, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.18, 24.64, 61.53, 109.81, 116.34, 128.96, 129.61, 129.89, 131.49, 133.72, 138.03, 161.25, 164.45, 165.92. *m/z* 285.1235. HRMS Anal. Calc. for $C_{16}H_{17}N_2O_3$: 285.1239. X-Ray diffraction analysis (Fig. 2). The CCDC number for this product is 958698.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-(4-methylphenyl)-2,4-dienamide (**2b**)*

Yield 137 mg (46.0 %); mp 85.5–86.2°C. δ_H (400 MHz, $CDCl_3$) 1.304 (m, 3H, CH_2CH_3), 2.297 (s, 3H, CH_3), 2.380 (s, 3H, CH_3), 4.259 (m, 2H, CH_3CH_2), 5.989, 6.147 (s, 2H, NH_2), 7.178–7.279 (m, 4H, Ar-H), 7.621 (s, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.16, 21.42, 24.52, 61.42, 110.00, 116.33, 129.72, 129.74, 130.36, 130.84, 138.17, 140.42, 161.77, 164.64, 165.64. *m/z* 299.1392. HRMS Anal. Calc. for $C_{17}H_{19}N_2O_3$: 299.1396.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-(4-fluorophenyl)-2,4-dienamide (**2c**)*

Yield 136 mg (45.1 %); mp 132.4–133.2°C. δ_H (400 MHz, $CDCl_3$) 1.313 (m, 3H, CH_2CH_3), 2.284 (s, 3H, CH_3), 4.270 (t, 2H, CH_2CH_3), 5.813, 6.185 (s, 2H, NH_2), 7.069–7.388 (m, 4H, Ar-H), 7.611 (s, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.15, 24.52, 61.56, 110.06, 116.10, 129.93, 131.32, 131.52, 131.60,

136.70, 161.27, 162.18, 164.32, 165.48. *m/z* 303.1139. HRMS Anal. Calc. for $C_{16}H_{16}FN_2O_3$: 303.1145.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-(3-chlorophenyl)-2,4-dienamide (**2d**)*

Yield 93 mg (29.3 %); mp 125.5–126.2°C. δ_H (400 MHz, $CDCl_3$) 1.347 (m, 3H, CH_2CH_3), 2.599 (s, 3H, CH_3), 4.353 (m, 2H, CH_2CH_3), 5.678, 6.123 (s, 2H, NH_2), 7.267–7.402 (m, 4H, Ar-H), 7.738 (s, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.14, 24.64, 61.67, 109.99, 116.06, 127.16, 129.51, 129.74, 130.19, 133.11, 134.92, 135.61, 136.07, 161.10, 164.09, 165.27. *m/z* 319.0851. HRMS Anal. Calc. for $C_{16}H_{16}N_2O_3Cl$: 319.0850.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-(4-bromophenyl)-2,4-dienamide (**2e**)*

Yield 78 mg (21.5 %); mp 69.2–70.1°C. δ_H (400 MHz, $CDCl_3$) 1.311 (m, 3H, CH_2CH_3), 2.273 (s, 3H, CH_3), 4.270 (s, 2H, CH_2CH_3), 5.837, 6.188 (s, 2H, NH_2), 7.175–7.536 (m, 4H, Ar-H), 7.567 (d, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.14, 24.54, 61.63, 110.08, 116.11, 124.31, 130.92, 132.24, 132.31, 132.66, 136.43, 161.42, 164.26, 165.23. *m/z* 363.0333. HRMS Anal. Calc. for $C_{16}H_{16}BrN_2O_3$: 363.0344.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-(3,4-difluorophenyl)-2,4-dienamide (**2f**)*

Yield 96 mg (30.2 %); mp 71.0–71.9°C. δ_H (400 MHz, $CDCl_3$) 1.313 (m, 3H, CH_2CH_3), 2.282 (s, 3H, CH_3), 4.356 (m, 2H, CH_2CH_3), 5.821, 6.207 (s, 2H, NH_2), 7.085–7.278 (m, 3H, Ar-H), 7.533 (s, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.16, 24.54, 61.72, 109.23, 115.97, 117.95, 118.54, 125.97, 130.87, 135.25, 139.19, 149.11, 151.60, 162.03, 164.04, 166.14. *m/z* 321.1042. HRMS Anal. Calc. for $C_{16}H_{15}F_2N_2O_3$: 321.1051.

*(2Z,4E)-2-Cyano-4-ethylformyl-3-methyl-5-(4-methoxyphenyl)-2,4-dienamide (**2i**)*

Yield 59 mg (18.8 %); mp 267.5–268.4°C. δ_H (400 MHz, $CDCl_3$) 1.305 (m, 3H, CH_2CH_3), 2.320 (s, 3H, CH_3), 3.850 (s, 3H, OCH_3), 4.257 (m, 2H, CH_2CH_3), 5.878, 6.163 (s, 2H, NH_2), 6.893–7.300 (m, 4H, Ar-H), 7.61 (s, 1H, CH). δ_C (100 MHz, $CDCl_3$) 14.20, 24.49, 55.38, 61.39, 109.98, 114.51, 116.40, 126.14, 128.71, 131.63, 138.08, 161.06, 161.51, 164.69, 165.79. *m/z* 315.1352. HRMS Anal. Calc. for $C_{17}H_{19}N_2O_4$: 315.1345.

*(2E,4Z)-2-Cyano-4-ethylformyl-3-methyl-5-phenyl-2,4-dienamide (**3a**)*

Yield 73 mg (26.0 %); mp 141.6–142.4°C. δ_H (400 MHz, $CDCl_3$) 1.180 (m, 3H, CH_2CH_3), 2.507 (s, 3H, CH_3), 4.221 (m, 2H, CH_2CH_3), 5.723, 6.290 (s, 2H, NH_2), 7.169 (s, 1H, CH), 7.266–7.393 (m, 5H, Ar-H). δ_C (100 MHz, $CDCl_3$) 14.08, 21.64, 61.33, 109.68, 115.44, 128.76, 129.66, 129.89, 131.69, 133.92, 138.02, 156.35, 164.43, 166.88. *m/z* 285.1228. HRMS Anal. Calc. for $C_{16}H_{17}N_2O_3$: 285.1239.

*(2E,4Z)-2-Cyano-4-ethylformyl-3-methyl-5-(4-methylphenyl)-2,4-dienamide (**3b**)*

Yield 72 mg (24.4 %); mp 122.6–123.5°C. δ_H (400 MHz, $CDCl_3$) 1.232 (m, 3H, CH_2CH_3), 2.388 (s, 3H, Ar-CH_3), 2.507 (s, 3H, CH_3), 4.255 (m, 2H, CH_2CH_3), 5.720, 6.293 (s, 2H, NH_2), 7.135 (s, 1H, CH), 7.181–7.343 (m, 4H, Ar-H). δ_C (100 MHz, $CDCl_3$) 12.16, 18.52, 21.42, 61.72, 110.03, 116.33, 129.72, 129.72, 129.78, 130.36, 130.83, 140.17, 142.42, 155.77, 164.74, 167.67. *m/z* 299.1391. HRMS Anal. Calc. for $C_{17}H_{19}N_2O_3$: 299.1396.

*(2E,4Z)-2-Cyano-4-ethylformyl-3-methyl-5-(3-chlorophenyl)-2,4-dienamide (**3d**)*

Yield 100 mg (31.4 %); mp 140.6–141.3°C. δ_H (400 MHz, $CDCl_3$) 1.324 (m, 3H, CH_2CH_3), 2.277 (s, 3H, CH_3), 4.284 (m, 2H, CH_2CH_3), 5.662, 6.163 (s, 2H, NH_2), 7.203 (s, 1H, CH), 7.280–7.572 (m, 4H, Ar-H). δ_C (100 MHz, $CDCl_3$) 13.71, 20.56, 61.93, 107.46, 116.77, 127.11, 128.83, 129.50, 129.60, 134.31, 135.42, 135.76, 138.76, 162.51, 164.91, 166.56. *m/z* 319.0850. HRMS Anal. Calc. for $C_{16}H_{16}N_2O_3Cl$: 319.0850.

*(2E,4Z)-2-Cyano-4-ethylformyl-3-methyl-5-(4-bromophenyl)-2,4-dienamide (**3e**)*

Yield 106 mg (29.4 %); mp 126.8–127.6°C. δ_H (400 MHz, $CDCl_3$) 1.223 (m, 3H, CH_2CH_3), 2.516 (s, 3H, Ar-CH_3), 4.241 (m, 2H, CH_2CH_3), 5.667, 6.273 (s, 2H, NH_2), 7.076 (s, 1H, CH), 7.279–7.535 (m, 4H, Ar-H). δ_C (100 MHz, DMSO-d_6) 13.97, 19.96, 61.94, 110.50, 116.43, 123.36, 131.26, 131.98, 133.75, 133.83, 138.12, 156.50, 163.38, 166.11. *m/z* 363.0334. HRMS Anal. Calc. for $C_{16}H_{16}BrN_2O_3$: 363.0344. X-Ray diffraction analysis (Fig. 3). The CCDC number for this product is 958794.

*(2E,4Z)-2-Cyano-4-ethylformyl-3-methyl-5-(3,4-difluorophenyl)-2,4-dienamide (**3f**)*

Yield 115 mg (36.1 %); mp 107.7–108.7°C. δ_H (400 MHz, $CDCl_3$) 1.246 (m, 3H, CH_2CH_3), 2.515 (s, 3H, Ar-CH_3), 4.262 (q, 2H, CH_2CH_3), 5.702, 6.271 (s, 2H, NH_2), 7.033 (s, 1H, CH), 7.165–7.353 (m, 3H, Ar-H). δ_C (100 MHz, $CDCl_3$) 13.77, 20.58, 61.95, 107.51, 116.75, 117.24, 118.03, 125.97, 130.83, 135.00, 138.19, 148.73, 151.21, 162.50, 164.68, 166.62. *m/z* 321.1039. HRMS Anal. Calc. for $C_{16}H_{15}F_2N_2O_3$: 321.1051.

*(2E,4Z)-2-Cyano-4-ethylformyl-3-methyl-5-(3,5-bis(trifluoromethyl)phenyl)-2,4-dienamide (**3g**)*

Yield 202 mg (48.2 %); mp 117.9–118.9°C. δ_H (400 MHz, $CDCl_3$) 1.186 (m, 3H, CH_2CH_3), 2.551 (s, 3H, Ar-CH_3), 4.228 (m, 2H, CH_2CH_3), 5.874, 6.307 (s, 2H, NH_2), 7.166 (s, 1H, CH), 7.822–7.896 (m, 3H, Ar-H). δ_C (100 MHz, $CDCl_3$) 13.55, 20.64, 62.26, 108.18., 116.47, 127.06, 12128.30, 128.84, 131.33, 130.22, 136.11, 137.01, 162.37, 164.01, 165.80. *m/z* 421.0976. HRMS Anal. Calc. for $C_{18}H_{15}N_2O_3F_6$: 421.0987.

ESR Spin-Trapping Experiment

THF solutions containing 5×10^{-4} mol L^{-1} **1a** and 5×10^{-4} mol L^{-1} PBN were added to quartz, cylindrical ESR tubes and were deoxygenated with N_2 for 15 min. Each sample was irradiated with UV light (300–320 nm) for 10 min and immediately subjected to ESR analysis. The magnetic parameters were measured by reference to the signals of tetracyanoquinodimethane lithium salt (TCNQ-Li, $g = 2.00252$) and Mn^{2+}/MgO. The experiment was conducted at room temperature.

*X-Ray Diffraction Analysis for **2a** (Fig. 4 and Table 4) and **3e** (Fig. 5 and Table 5)*

Crystals of **2a** and **3e** suitable for X-ray diffraction analysis were obtained by the slow evaporation of an ethyl acetate solution of **2a** and **3e** at room temperature. The single crystal X-ray

Table 4. Crystal data and structure refinement for 2a

Parameter	**2a**
Empirical formula	$C_{16}H_{17}N_2O_3$
Formula weight	284.31
Temperature	113 K
Wavelength	0.71073
Crystal system, space group	Triclinic, *P*-1
Unit cell dimensions	*a* 5.8653(13) Å
	b 9.968(2) Å
	c 13.817(3) Å
	α 72.367(15)°
	β 88.41(3)°
	γ 81.50(2)°
Volume	761.2(3) Å^3
Z	2
Calculated density	1.240 Mg m^{-3}
Absorption coefficient	0.087 mm^{-1}
F(000)	300.0
Crystal size	0.30 × 0.18 × 0.16 mm^{-3}
θ range for data collection	1.5°–27.9°
Index ranges	$-7 \le h \le 6$, $-13 \le k \le 13$, $-16 \le l \le 18$
Reflections collected/unique	7860/3569 [$R_{int} = 0.0423$]
Data/restraints/parameters	3569/0/200
Goodness-of-fit on F^2	0.894
R indices (all data)	$R^1 = 0.0590$, w$R^2 = 0.0777$
Largest diff. peak and hole	0.233 and −0.233 e Å^{-3}

Table 5. Crystal data and structure refinement for 3e

Parameter	**3e**
Empirical formula	$C_{16}H_{15}BrN_2O_3$
Formula weight	363.21
Temperature	113 K
Wavelength	0.71073
Crystal system, space group	Triclinic, *P*-1
Unit cell dimensions	*a* 7.478(3) (13) Å
	b 8.842(3) Å
	c 12.389(5) Å
	α 107.386(9)°
	β 93.652(5)°
	γ 90.037(6)°
Volume	779.9(5) Å^3
Z	2
Calculated density	1.547 Mg m^{-3}
Absorption coefficient	2.649 mm^{-1}
F(000)	368.0
Crystal size	0.20 × 0.18 × 0.12 mm^{-3}
θ range for data collection	1.7°–27.9°
Index ranges	$-9 \le h \le 9$, $-11 \le k \le 11$, $-16 \le l \le 16$
Reflections collected/unique	8250/3689 [$R_{int} = 0.0333$]
Data/restraints/parameters	3689/3/209
Goodness-of-fit on F^2	1.002
R indices (all data)	$R^1 = 0.0383$, w$R^2 = 0.0542$
Largest diff. peak and hole	0.377 and −0.650 e Å^{-3}

diffraction measurements were conducted on a Rigaku Saturn CCD area-detector diffractometer at 113(2) K using graphite monochromated $Mo_{K\alpha}$ radiation (λ 0.71073 Å) in the ω and φ scanning mode. An empirical absorption correction was applied using the *ABSCOR* program.[14] All structures were solved by direct methods using the *SHELXS-97* program[15] and refined by full matrix least-squares on F^2 using the *SHELXL-97* program.[16] All of the hydrogen atoms were geometrically fixed using the riding model. Details, including the crystal data, data collection, and structure refinements, are summarised in Table 4 and Table 5. CCDC-958698 and CCDC-958794 contain the supplementary crystallographic data for this paper. These data can be obtained, free of charge, from www.ccdc.cam.ac.uk/conts/retrieving.html.

Supplementary Material

^{1}H and ^{13}C NMR spectra of all new compounds and ^{1}H NMR spectra of all known compounds are available on the Journal's website.

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