

Aza-Michael Addition Reactions of Hydrazones with Activated Alkynes Catalyzed by Nitrogen-Containing Organic Bases

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Several highly efficient DABCO (1,4-diazabicyclo[2.2.2]octane)-catalyzed Michael-type reactions of hydrazones with activated alkynes are described in this paper. This aza-Michael addition reaction can be applied to different types of hydrazones, such as hydrazones **1** and hydroxy-bearing

hydrazones **5**. The corresponding adducts are achieved in high yields under mild reaction conditions. DABCO-promoted aza-Michael addition reactions were successfully applied to a series of hydrazones with activated alkynes to afford the corresponding adducts in moderate to good yields.

Introduction

The Michael addition reaction,^[1] which is one of the most important reactions in organic synthesis, has been well studied thus far. In addition, the Morita–Baylis–Hillman (MBH) reaction, which is also one of the most fundamental reactions in organic chemistry consisting of a Michael addition, an aldol reaction and a proton transfer in the presence of catalytic amounts of nucleophilic Lewis bases, has made great progress recently.^[2] Furthermore, in the base-catalyzed Michael addition,^[3] many interesting findings have been disclosed when using inorganic^[4] or organic bases^[5,6] during recent years. It should also be noted that besides classical Michael addition, oxo-^[7] and aza-Michael^[8] additions, which are of great importance in both pharmacology and biosynthesis,^[9] have been well investigated with regards to their developments in asymmetric induction.^[10] On the basis of these previously reported results, it was found that, in some cases, nitrogen-containing organic bases can act as a Brønsted base instead of a Lewis base. For example, Nemoto has reported a novel modified MBH reaction of propiolate with different aldehydes promoted by a catalytic amount of 1,4-diazabicyclo[2.2.2]octane (DABCO) in 2002.^[11] Earlier, a DABCO-catalyzed self- and cross-condensation of acetylenic ketones was reported by Ramachandran and his co-workers.^[12] In 2005, Shi and co-workers reported DABCO-catalyzed Michael additions of hydrazones with activated olefins, such as methyl vinyl ketone (MVK), methyl acrylate, acrylonitrile

and phenyl vinyl ketone (PVK),^[13] affording the corresponding adducts in good yields under mild conditions. Since the activated alkynes, such as diethyl acetylenedicarboxylate, dimethyl acetylenedicarboxylate (DMAD) and propiolate have been widely used as important building blocks in organic synthesis^[14] and have a similar nature as activated olefins, we envisaged to utilize activated alkynes as substrates in the reaction system described above instead of activated olefins. During our ongoing investigation on the development of this reaction, we were pleased to find this nitrogen-containing organic-base-promoted Michael-type reaction system can be applied to the reactions of different hydrazones **1** (R–CH=N–NH–Bz and R–CH=N–NH–Ts) and hydroxy-containing hydrazones **5** with activated alkynes, such as diethyl acetylenedicarboxylate, DMAD and propiolate. The reactions proceeded smoothly and the corresponding adducts were achieved in moderate to excellent yields. In this paper, we wish to report the details of this finding.

Results and Discussion

We initially examined the reaction of hydrazone **1a** (0.20 mmol) and diethyl acetylenedicarboxylate (**2a**) (0.50 mmol) in the presence of various bases in CH₂Cl₂ (2.0 mL) at room temperature (25 °C) and the results of these experiments are summarized in Table 1. It was found that the reaction could not be promoted without the addition of base (Table 1, Entry 1), and none of the corresponding aza-Michael addition product (**Z**)-**3a** was obtained if using phosphorus-containing bases, such as PPh₃ and PnBu₃, as the catalysts (Table 1, Entries 11 and 12). In the presence of 100, 50 or 10 mol-% of Et₃N, the reaction proceeded inefficiently to give the addition product (**Z**)-**3a** in up to 36% yield after 24 h (Table 1, Entries 2–4). Its ¹H NMR spectrum has been indicated in Figure S1 (Support-

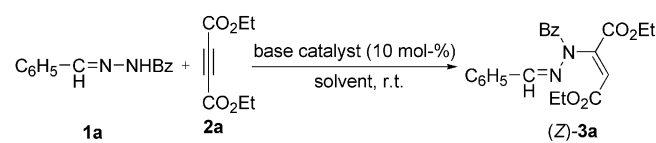
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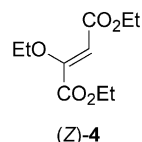
ing Information). When we employed commonly used tertiary amine catalyst DABCO, the reaction proceeded smoothly to give the adduct (Z)-**3a** in 77% yield after only 6 h (Table 1, Entry 5). The use of 10 mol-% of DABCO in CH₂Cl₂ also promoted the reaction efficiently to give (Z)-**3a** in 71% yield, unless the lower catalyst loading was used (Table 1, Entries 6 and 7). Other nitrogen-containing bases, for instance DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), DMAP [4-(*N,N*-dimethylamino)pyridine] and pyridine, are not as effective as DABCO under identical conditions (Table 1, Entries 8–10). It was found that when using K₂CO₃, an inorganic base, as the catalyst the reaction could not be promoted even after a prolonged reaction time (Table 1, Entry 13).

Table 1. Survey of base catalysts and solvent effects of the reaction of hydrazone **1a** (1.0 equiv.) with **2a** (2.5 equiv.) at room temperature.^[a]



Entry	Base catalyst	Solvent	Time [h]	Yield [%] ^[b] (Z)- 3a
1	–	CH ₂ Cl ₂	24	0
2 ^[c]	Et ₃ N	CH ₂ Cl ₂	24	36
3 ^[d]	Et ₃ N	CH ₂ Cl ₂	24	13
4	Et ₃ N	CH ₂ Cl ₂	24	trace
5 ^[e]	DABCO	CH ₂ Cl ₂	6	77
6	DABCO	CH ₂ Cl ₂	6	71
7 ^[f]	DABCO	CH ₂ Cl ₂	6	53
8	DBU	CH ₂ Cl ₂	6	43
9	DMAP	CH ₂ Cl ₂	6	55
10	pyridine	CH ₂ Cl ₂	6	26
11	PPh ₃	CH ₂ Cl ₂	24	0
12	<i>n</i> -Bu ₃	CH ₂ Cl ₂	24	0
13 ^[g]	K ₂ CO ₃	CH ₂ Cl ₂	24	0
14	DABCO	THF	6	93
15	DABCO	EtOAc	6	88
16	DABCO	toluene	24	76
17	DABCO	MeCN	24	65
18	DABCO	DMF	6	86
19	DABCO	H ₂ O	24	0
20 ^[h]	DABCO	EtOH	24	39

[a] The reaction was carried out with 0.20 mmol of **1a**, 0.50 mmol of **2a** and 10 mol-% of base catalysts in CH₂Cl₂ (2.0 mL) under an ambient atmosphere. [b] Isolated yield. [c] 100 mol-% of Et₃N was used. [d] 50 mol-% of Et₃N was used. [e] 20 mol-% of DABCO was used. [f] 5 mol-% of DABCO was used. [g] 100 mol-% of K₂CO₃ was used. [h] Ethanol adduct (Z)-**4** was obtained in 32% yield.



Subsequently, the solvent effects have been examined by using DABCO (10 mol-%) as a catalyst. The reaction proceeded efficiently to give the corresponding adduct (Z)-**3a** in good yields in THF, EtOAc and DMF (Table 1, En-

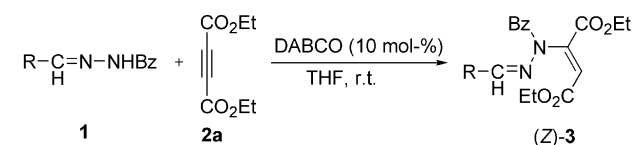
tries 14, 15 and 18). It should also be noted that when using 10 mol-% of DABCO in THF, the starting materials disappeared after stirring for 6 h at room temperature (the conversion of **1a** > 99%), and the isolated yield of **3a** can be improved to 93% (Table 1, Entry 14). The yields of (Z)-**3a** decreased when we utilized toluene and MeCN as the solvents and no reaction occurred in H₂O even after a prolonged reaction time, presumably due to the very low solubility of hydrazone **1a** in toluene, MeCN and H₂O since the starting materials **1a** and **2a** still remained in the reaction system (Table 1, Entries 16, 17 and 19).

Interestingly, when the reaction took place in EtOH, not only the Michael addition product (Z)-**3a** was formed in 39% yield, but the ethanol adduct **4** was also obtained in 32% yield. This is because the solvent EtOH could also participate in a Michael addition with **2a** in the presence of DABCO (Table 1, Entry 20).

When these aza-Michael reactions proceeded very well and the isolated yields of the products were over 80%, all of the starting materials disappeared and the conversions were over 96%. When the reaction afforded the products in poor isolated yields, the starting materials still remained in the reaction system and the conversions were low. The remaining starting materials could be isolated as well and did not decompose during the reaction.

With these optimized reaction conditions in hand, we next turned our interest to the reaction scope by using a variety of hydrazones **1** with diethyl acetylenedicarboxylate (**2a**) under the standard conditions. As summarized in Table 2, the corresponding adducts (Z)-**3** were obtained in high yields in the presence of 10 mol-% of DABCO (Table 2, Entries 1–11). For aromatic hydrazones **1b–j**, the reaction proceeded smoothly to produce adducts (Z)-**3b–j** in high yields in most cases whether electron-withdrawing

Table 2. Survey of hydrazone **1** (1.0 equiv.) with **2a** (2.5 equiv.) in the presence of DABCO (10 mol-%) at room temperature.^[a]

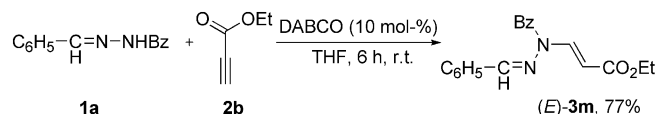


Entry	R	Time [h]	Yield [%] ^[b] (Z)- 3
1	2-ClC ₆ H ₄ 1b	6	85 3b
2	3-ClC ₆ H ₄ 1c	6	76 3c
3	4-ClC ₆ H ₄ 1d	6	87 3d
4	4-BrC ₆ H ₄ 1e	6	92 3e
5	4-MeC ₆ H ₄ 1f	6	90 3f
6	2-MeOC ₆ H ₄ 1g	6	95 3g
7	4-MeOC ₆ H ₄ 1h	6	93 3h
8	1-naph 1i	6	89 3i
9	2-furan 1j	6	87 3j
10	C ₆ H ₅ (CH ₂) ₂ 1k	6	90 3k
11	CH ₃ (CH ₂) ₂ 1l	6	87 3l

[a] The reaction was carried out with 0.20 mmol of **1**, 0.50 mmol of **2a** and 10 mol-% of DABCO in THF (2.0 mL) under an ambient atmosphere. [b] Isolated yield.

or -donating groups were present on the benzene ring of hydrazones **1** or not (Table 2, Entries 1 and 3–9), with the exception of 3-chlorobenzaldehyde **1c**. The use of this 3-substituted hydrazone **1c** as a reactant under the optimized reaction conditions afforded the corresponding product (*Z*)-**3c** in 76% yield, a lower yield than with other aromatic hydrazones (Table 2, Entry 2). With aliphatic hydrazones, such as **1k** and **1l**, the reaction also proceeded smoothly to give the corresponding adducts (*Z*)-**3k** and (*Z*)-**3l** in high yields of up to 90% (Table 2, Entries 10 and 11).

Furthermore, the reaction between hydrazone **1a** with ethyl propiolate (**2b**) was investigated under the optimized reaction conditions. To our delight, it did take place, affording the corresponding adduct (*E*)-**3m** in 77% yield (Scheme 1).



Scheme 1. The reaction of hydrazone **1a** (1.0 equiv.) with propiolate (**2b**) (2.5 equiv.) in the presence of DABCO (10 mol-%) at room temperature in THF (2.0 mL).

The substrate scope of this reaction was examined further with hydrazone **1n** bearing a *N*-Tos protecting group and DMAD (**2c**). The results are summarized in Table 3. We observed that hydrazones bearing a *N*-Bz protecting group produced the corresponding adduct as a single isomer (Table 1), but hydrazones with a *N*-Tos protecting group led to the adduct as mixtures of *Z* and *E* isomers, presumably due to the fact that the *N*-Tos protecting group is a sterically more bulky substituent than the *N*-Bz group and this steric effect affects the stereochemical outcome. The reaction of hydrazone **1n** with **2c** proceeded smoothly under the optimized reaction conditions to give adduct **3n** as a couple of *Z/E* (2.5:1) isomers in 90% yield (Table 3, Entry 1). The *Z/E* isomers of **3n** can be separated by a preparative TLC and the difference between the major (*Z*)-**3n** and minor product (*E*)-**3n** can be clearly observed from the

Table 3. Survey of hydrazone **1** with **2a** in the presence of base catalyst at room temperature.^[a]

Entry	R ¹ /R ²	Base catalyst	Time [h]	Yield [%] ^[b] 3	Z/E ^[c]
1	C ₆ H ₅ /Ts, 1n	DABCO	6	90 3n	2.5:1
2	C ₆ H ₅ /Ts, 1n	DMAP	24	49 3n	1:1
3	C ₆ H ₅ /Ts, 1n	DBU	24	35 3n	99:1
4	CO ₂ Et/Bz, 1o	DABCO	6	77 3o	10:1
5	CF ₃ /Bz, 1p	DABCO	6	83 3p	10:1

[a] The reaction was carried out with 1.0 equiv. of **1**, 2.5 equiv. of **2c** and 10 mol-% of base catalyst in THF (2.0 mL) under an ambient atmosphere. [b] Isolated yield. [c] Determined by analysis of the 400 MHz ¹H NMR spectra.

¹H NMR spectra as shown in Figures°S2 and S3 (Supporting Information). From Figures°S2 and S3, it can be seen that the exact chemical shifts of CH₃ and OCH₃ in the ¹H NMR spectrum of major product (*Z*)-**3n** are at δ = 2.41, 3.61 and 3.72 ppm, which differ from its corresponding minor product at δ = 2.45, 3.71 and 3.83 ppm. Moreover, the exact chemical shifts of the olefinic proton and CH=N in the ¹H NMR spectrum of (*E*)-**3n** at δ = 5.97 and 8.46 ppm were completely different from those of (*Z*)-**3n** at δ = 7.31 to 7.35 ppm. The stereochemical outcome of (*Z*)-**3n** has been unambiguously assigned by single-crystal X-ray diffraction (Figure 1).^[15] Therefore, the major products in Table 3 should have a *Z* configuration.

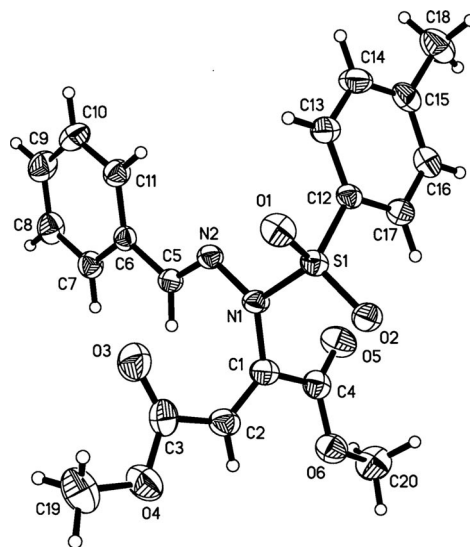
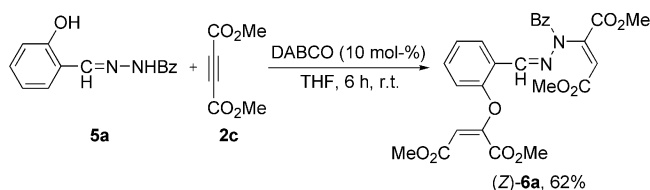


Figure 1. X-ray crystal structure of (*Z*)-**3n**.

By comparison of the ¹H NMR spectra of (*Z*)-**3n** and **3a**, we could further confirm that adducts **3a–j** in Tables 1 and 2 have a *Z* configuration (Figures°S1 and S2, Supporting Information).

Treatment of **1n** with **2c** in the presence of 10 mol-% DMAP in THF for 24 h afforded **3n** as a couple of *Z/E* (1:1) isomers in only 49% yield (Table 3, Entry 2) and a single isomer of adduct **3n** (*Z/E*, 99:1) was obtained in 35% yield with 10 mol-% DBU as a promoter (Table 3, Entry 3). Hydrazones **1o** and **1p**, synthesized by ethyl glyoxalate and trifluoroacetaldehyde ethyl hemiacetal, could also be applied in this reaction under the optimized conditions, giving the corresponding Michael addition products **3o** and **3p** in 77 and 83% yield, respectively, as two isomers in a 10:1 (*Z/E*) ratio (Table 3, Entries 4 and 5).

After having established the aza-Michael addition catalyzed by DABCO, we turned our attention to the investigation this Michael addition reaction with respect to hydrazone **5a**, which bears a phenolic hydroxy group. We assumed that the hydroxy group may also participate in the Michael reaction with DMAD (**2c**) in the presence of DABCO and we were pleased to find that hydrazone **5a** indeed reacted with **2c** in the presence of 10 mol-% DABCO in THF for 6 h, giving the corresponding multi-addition product (*Z*)-**6a** in 62% yield as a single isomer (Scheme 2).

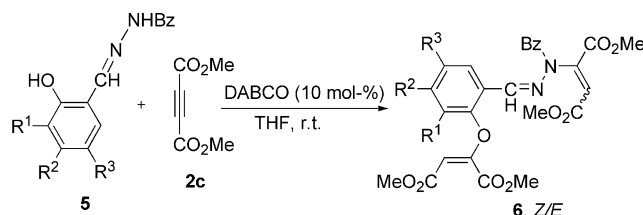


Scheme 2. Reaction of hydrazone **5a** (1.0 equiv.) with **2c** (2.5 equiv.) in the presence of DABCO (10 mol-%) at room temperature in THF (2.0 mL).

Moreover, the further survey of hydrazone **5** (1.0 equiv.) with **2c** (3.0 equiv.) was also performed and the results of these experiments are summarized in Table 4 and Scheme 3. Under the optimized reaction conditions and prolonged reaction time (12 to 24 h), the reaction proceeded efficiently to give the addition product **6** in up to 92% yield. But the substituted groups on the benzene ring may exert steric effects and the corresponding multi-adduct was obtained as a couple of *Z/E* isomers. When the benzene ring of **5** bears a 3-methoxy group ($R^1 = \text{OMe}$), the corresponding adduct (*Z*)-**6b** was obtained in 73% yield and the ratio of isomers was 84:16 (*Z/E*) (Table 4, Entry 1).

By using 4-substituted hydrazone **5c** ($R^2 = \text{OMe}$) as a reactant under the optimized reaction conditions product (*Z*)-**6c** was formed in a higher yield (83%) and as a moderate ratio of isomers (*Z/E*, 91:9; Table 4, Entry 2). When bearing a strongly electron-withdrawing group, such as a 5-nitro group ($R^3 = \text{NO}_2$), however, the reaction proceeded slowly to give the adduct (*Z*)-**6d** in 63% yield, even though the reaction time was prolonged, with a 83:17 (*Z/E*) ratio of isomers (Table 4, Entry 3). Hydrazone **5e**, containing a naphthalene group, could also react with **2c**, affording the

Table 4. Survey of hydrazone **5** (1.0 equiv.) with dimethyl acetylenedicarboxylate **2c** (3.0 equiv.) in the presence of base catalyst (10 mol-%) at room temperature.^[a]

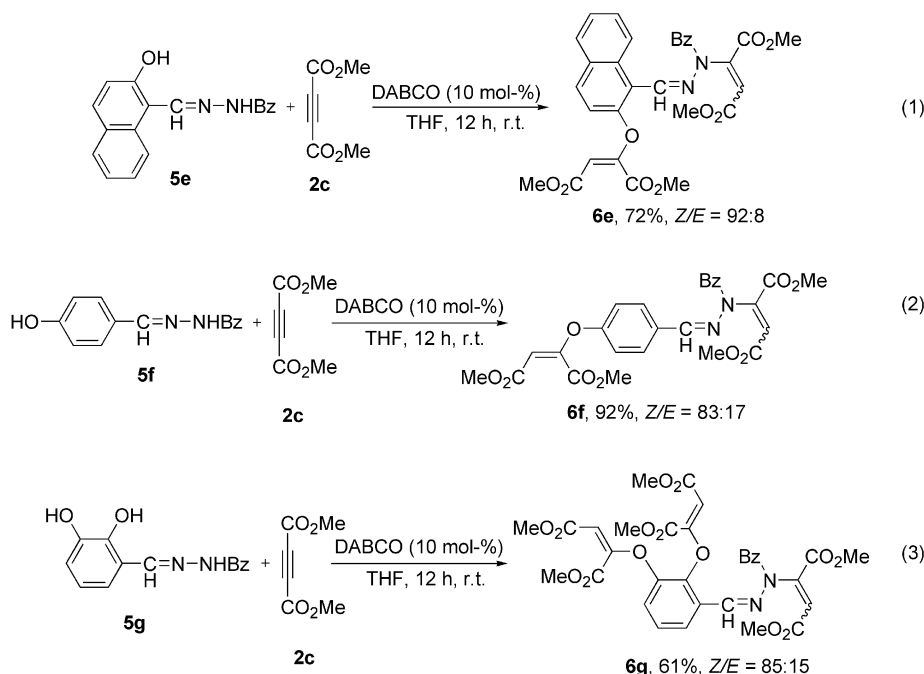


Entry	Base catalyst	Hydrazone 5 ($R^1/R^2/R^3$)	Time [h]	Yield [%] ^[b]	<i>Z/E</i> ^[c]
1	DABCO	5b (OMe/H/H)	12	77 6b	84:16
2	DABCO	5c (H/OMe/H)	12	83 6c	91:9
3	DABCO	5d (H/H/NO ₂)	24	63 6d	83:17

[a] The reaction was carried out with 0.20 mmol of **5**, 0.60 mmol of **2c** and 10 mol-% of DABCO in THF (2.0 mL) under an ambient atmosphere. [b] Isolated yield. [c] Determined by analysis of the 400 MHz ¹H NMR spectra.

adduct (*Z*)-**6e** in 73% yield along with a high ratio of isomers (*Z/E*, 92:8) (Scheme 3, Equation^o1). When using a 4-hydroxy-substituted hydrazone **5f**, the corresponding adduct (*Z*)-**6f** was obtained in the highest yield (92%) and the ratio of isomers was moderate (*Z/E*, 83:17; Scheme 3, Equation^o2).

It should be noted that unlike adduct (*Z*)-**3n**, *Z* and *E* isomers of multi-adduct **6b** could not be separated by preparative TLC. The difference between multi-adduct **6a**, which is obtained as a single isomer, and **6b**, which is formed as a couple of *Z/E* isomers, was clear from their ¹H NMR spectra, as shown in Figures^oS4 and S5 (Supporting



Scheme 3. Reaction of hydrazones **5e**, **5f** and **5g** (1.0 equiv.) with **2c** (3.0 equiv.) in the presence of DABCO (10 mol-%) at room temperature in THF (2.0 mL).

Information). From Figure S5, it can be seen that the signals of the methoxy group (OCH_3) in the ^1H NMR spectrum of the minor multi-adduct **6b** appeared at $\delta = 3.62$, 3.73, 3.74 and 3.84 ppm and the major multi-adduct **6b** appeared at $\delta = 3.63$, 3.71, 3.81 and 3.95 ppm, respectively. Moreover, the exact chemical shifts of the olefinic proton and $\text{CH}=\text{N}$ in the ^1H NMR spectrum of the couple of *Z/E* isomers were completely different. The olefinic proton and $\text{CH}=\text{N}$ signals of the minor multi-adduct **6b** appeared at $\delta = 6.22$ and 7.92 ppm and these signals in the major multi-adduct **6b** appeared at $\delta = 7.37$ to 7.66 ppm, respectively. Since the stereochemical outcome of (*Z*)-**6e** has been unambiguously assigned by single-crystal X-ray diffraction (Figure 2),^[16] by comparison with the ^1H NMR spectra of **6a**, **6b** and **6e** (Figure S6, Supporting Information), we confirmed that the stereochemical outcomes of major multi-adducts **6a–g** in Table 4 and Scheme 3 are *Z* isomers.

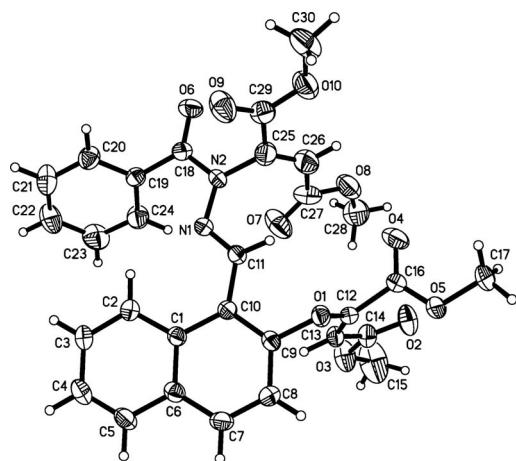
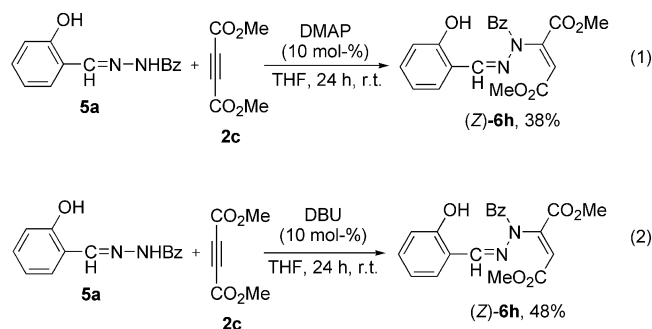


Figure 2. X-ray crystal structure of **6e**.

Under the same conditions, we next examined the reaction of hydrazone **5g**, bearing a 2,3-dihydroxybenzaldehyde, with **2c** (Scheme 3, Equation 3). The corresponding adduct (*Z*)-**6g**, which was formed by using one equivalent of hydrazone **5g** with three equivalents of **2c**, was achieved in 63% yield and the ratio of isomers 85:15 (*Z/E*).

Replacing base catalyst DABCO with other nitrogen-containing organic bases, such as DMAP and DBU afforded different results in the reaction of hydroxy-bearing substrate **5a** with **2c** under the optimized reaction conditions (Scheme 4, Equations 1 and 2). Hydrazone **5a** reacted with only one equivalent of **2c**, even with a prolonged reaction time, with DMAP and DBU as the catalysts respectively, to afford the corresponding adduct (*Z*)-**6h** in 38 and 48% yield as a single isomer.

To clarify whether a phenolic hydroxy-bearing substrate is essential to react with more than one equivalent of **2a** resulting the multi-addition product, the control experiments with the addition of one, two and three equivalents of phenol into the reaction system of hydrazone **1a** with **2a** were carried out under the standard conditions and the results are outlined in Table 5. It was found that the reactions of hydrazone **1a** with **2a** proceeded smoothly to afford ad-



Scheme 4. Reaction of hydrazones **5a** (1.0 equiv.) with **2c** (3.0 equiv.) in the presence of base catalysts (10 mol-%) at room temperature in THF (2.0 mL).

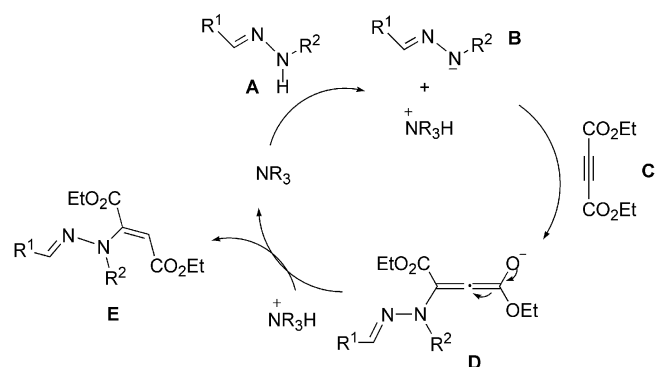
duct (*Z*)-**3a** in excellent yields (up to 99%) within 12 h and none of the phenol addition product was formed (Table 5, Entries 1 to 3). These results suggest that a substrate bearing a hydroxy group is essential to form the corresponding multi-addition products **6** during the reaction.

Table 5. Survey of hydrazone **1a** (1.0 equiv.) with **2a** (3.0 equiv.) in the presence of DABCO (10 mol-%) and phenol (*x*-equiv.) at room temperature.^[a]

Entry	Phenol (<i>x</i> equiv.)	Time [h]	Yield [%] ^[b] (<i>Z</i>)- 3a
1	1.0	12	98
2	2.0	12	99
3	3.0	12	96

[a] The reaction was carried out with 0.20 mmol of **1a**, 0.60 mmol of **2a**, *x*-equiv. phenol and 10 mol-% of DABCO in THF (2.0 mL) under an ambient atmosphere. [b] Isolated yield.

A plausible mechanism for this reaction is shown in Scheme 5. On the basis of the control experiments, we believe that DABCO acts as a Brønsted base in this reaction. After a proton has been abstracted by DABCO (NR_3), the hydrazone **A** is then transformed into a nucleophilic intermediate **B** that subsequently reacts with activated alkyne **C**



Scheme 5. A plausible reaction mechanism.

and generates allenic enolate **D**. Then, deprotonation of allenic enolate **D** produces the corresponding product **E** and regenerates DABCO to complete the catalytic cycle.

Conclusions

In conclusion, we have developed a Michael-type addition reaction of different hydrazones with activated alkynes. Through this synthesis route, we can achieve the corresponding interesting adducts in good to excellent yields.^[17] The advantages of this method are the use of simple and cheap starting materials and mild reaction conditions. In addition, several interesting results were obtained when using hydroxyl-substituted substrates, affording unexpected products in which both the NH and OH groups have reacted with the acetylenic bond.

Experimental Section

General Remarks: ¹H and ¹³C NMR spectra were recorded with a Bruker AM-400 spectrometer for solutions in CDCl₃ with tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded by EI methods, and HRMS was measured with a Finnigan MA⁺ mass spectrometer. THF and toluene were distilled from sodium (Na) under an argon atmosphere. CH₃CN and dichloromethane were distilled from CaH₂ under an argon atmosphere. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF₂₅₄ silica-gel coated plates. Flash column chromatography was carried out by using 300–400 mesh silica gel at increased pressure.

General Procedure for the Reactions of Hydrazones with Activated Alkynes Promoted by DABCO: Diethyl acetylenedicarboxylate (**2a**) (85 mg, 0.5 mmol) was added dropwise into a reaction vessel containing a solution of hydrazone **1a** (45.4 mg, 0.20 mmol) and DABCO (2.2 mg, 0.02 mmol) in THF (2.0 mL) at room temperature. After the resulting mixture had been stirred for 6 h, the corresponding adduct **3a** was purified by flash column chromatography (SiO₂).

Diethyl 2-[(E)-1-Benzoyl-2-benzylidenehydrazinyl]fumarate (3a): Pale-yellow oil (93%, 73 mg). IR (acetone): $\tilde{\nu}$ = 3065, 2983, 2938, 2905, 1729, 1673, 1609, 1489, 1447, 1393, 1321, 1259, 1206, 1158, 1097, 1070, 1055, 1028, 1010, 907 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.21 (t, *J* = 6.8 Hz, 3 H, CH₃), 1.28 (t, *J* = 6.8 Hz, 3 H, CH₃), 4.18 (q, *J* = 6.8 Hz, 2 H, CH₂), 4.30 (q, *J* = 6.8 Hz, 2 H, CH₂), 7.31–7.33 (m, 3 H, ArH), 7.39 (s, 1 H, CH), 7.43–7.51 (m, 5 H, ArH), 7.53 (s, 1 H, CH), 7.87 (dd, *J* = 2.8, 1.2 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.9, 13.9, 61.6, 62.6, 127.3, 127.4, 128.6, 129.9, 130.0, 130.9, 131.2, 133.9, 134.2, 136.1, 141.5, 161.8, 162.4, 170.2 ppm. MS (EI): *m/z* (%) = 394 (1.4) [M]⁺, 349 (2.0), 321 (3.7), 288 (12.8), 218 (8.7), 105 (100), 77 (27.6). 51 (3.3). C₂₂H₂₂N₂O₅ (394.15): calcd. C 66.99, H 5.62, N 7.10; found C 66.91, H 5.56, N 7.06.

Diethyl 2-[(E)-1-Benzoyl-2-(2-chlorobenzylidene)hydrazinyl]fumarate (3b): Pale-yellow oil (85%, 73 mg). IR (acetone): $\tilde{\nu}$ = 3066, 2983, 2938, 1729, 1677, 1601, 1473, 1447, 1390, 1319, 1259, 1206, 1158, 1052, 1030, 907 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.23 (t, *J* = 7.2 Hz, 3 H, CH₃), 1.30 (t, *J* = 7.2 Hz, 3 H, CH₃), 4.20 (q, *J* = 7.2 Hz, 2 H, CH₂), 4.32 (q, *J* = 7.2 Hz, 2 H, CH₂), 7.15–7.33 (m, 3 H, ArH), 7.40 (s, 1 H, CH), 7.43–7.53 (m, 3 H,

ArH), 7.68 (dd, *J* = 8.0, 2.0 Hz, 1 H, ArH), 7.85 (dd, *J* = 8.0, 1.6 Hz, 2 H, ArH), 7.94 (s, 1 H, CH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.9, 61.6, 62.7, 126.9, 127.2, 127.5, 129.6, 129.8, 130.8, 131.0, 131.1, 131.2, 134.0, 134.3, 136.1, 138.1, 161.5, 162.2, 170.3 ppm. MS (EI): *m/z* (%) = 428 (0.7) [M]⁺, 393 (1.6), 355 (1.7), 315 (1.5), 288 (6.9), 218 (7.1), 105 (100), 77 (22.0), 51 (2.1). HRMS (EI): calcd. for C₂₂H₂₁ClN₂O₅ [M + H]⁺ 428.1139; found 428.1140.

Diethyl 2-[(E)-1-Benzoyl-2-(3-chlorobenzylidene)hydrazinyl]fumarate (3c): Pale-yellow oil (76%, 65 mg). IR (acetone): $\tilde{\nu}$ = 3065, 2983, 2938, 2906, 1729, 1601, 1564, 1474, 1447, 1391, 1312, 1261, 1206, 1158, 1096, 1076, 1055, 1028, 915 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.22 (t, *J* = 7.2 Hz, 3 H, CH₃), 1.29 (t, *J* = 7.2 Hz, 3 H, CH₃), 4.19 (q, *J* = 7.2 Hz, 2 H, CH₂), 4.30 (q, *J* = 7.2 Hz, 2 H, CH₂), 7.22–7.35 (m, 2 H, ArH), 7.36–7.39 (m, 2 H, ArH and CH), 7.44–7.55 (m, 5 H, ArH and CH), 7.85 (dd, *J* = 8.4, 1.6 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.9, 13.9, 61.6, 62.7, 125.4, 127.1, 127.5, 129.7, 129.8, 131.1, 131.3, 133.9, 134.6, 135.7, 135.9, 139.7, 161.6, 162.3, 170.2 ppm. MS (EI): *m/z* (%) = 428 (0.8) [M]⁺, 383 (1.0), 355 (1.4), 288 (9.5), 218 (2.6), 105 (100), 89 (1.8), 77 (18.9), 51 (2.3). HRMS (EI): calcd. for C₂₂H₂₁ClN₂O₅ [M + H]⁺ 428.1139; found 428.1133.

Diethyl 2-[(E)-1-Benzoyl-2-(4-chlorobenzylidene)hydrazinyl]fumarate (3d): Pale-yellow oil (87%, 75 mg). IR (acetone): $\tilde{\nu}$ = 3066, 2983, 2938, 2906, 1728, 1673, 1610, 1491, 1447, 1395, 1322, 1263, 1206, 1159, 1088, 1070, 1054, 1028, 1014, 908 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.21 (t, *J* = 7.2 Hz, 3 H, CH₃), 1.28 (t, *J* = 7.2 Hz, 3 H, CH₃), 4.18 (q, *J* = 7.2 Hz, 2 H, CH₂), 4.30 (q, *J* = 7.2 Hz, 2 H, CH₂), 7.27–7.30 (m, 3 H, ArH), 7.39–7.53 (m, 6 H, ArH and CH), 7.87 (dd, *J* = 8.4, 1.2 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.9, 61.6, 62.7, 127.4, 128.5, 128.8, 129.8, 131.0, 131.3, 132.4, 134.0, 135.8, 136.0, 140.0, 161.6, 162.3, 170.2 ppm. MS (EI): *m/z* (%) = 428 (0.8) [M]⁺, 383 (0.8), 355 (1.3), 315 (1.5), 288 (7.6), 218 (3.4), 105 (100), 77 (22.8), 41 (0.6). HRMS (EI): calcd. for C₂₂H₂₁ClN₂O₅ [M + H]⁺ 428.1139; found 428.1138.

Diethyl 2-[(E)-1-Benzoyl-2-(4-bromobenzylidene)hydrazinyl]fumarate (3e): Pale-yellow solid (92%, 87 mg). M.p. 105–109 °C. IR (acetone): $\tilde{\nu}$ = 3065, 2983, 2938, 2905, 1728, 1673, 16109, 1489, 1447, 1393, 1368, 1321, 1259, 1206, 1158, 1097, 1070, 1055, 1028, 10140, 907 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.21 (t, *J* = 7.2 Hz, 3 H, CH₃), 1.27 (t, *J* = 7.2 Hz, 3 H, CH₃), 4.18 (q, *J* = 7.2 Hz, 2 H, CH₂), 4.30 (q, *J* = 7.2 Hz, 2 H, CH₂), 7.34–7.36 (m, 2 H, ArH), 7.39 (s, 1 H, CH), 7.43 (s, 1 H, CH), 7.43–7.53 (m, 5 H, ArH), 7.84 (dd, *J* = 8.4, 1.6 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.9, 61.5, 62.6, 124.1, 125.4, 127.4, 128.6, 129.8, 130.9, 131.2, 131.7, 132.8, 134.0, 135.9, 140.0, 161.6, 162.2, 170.1 ppm. MS (EI): *m/z* (%) = 474 (0.8) [M]⁺, 472 (0.8) [M]⁺, 401 (1.4), 399 (1.4), 346 (18.7), 315 (24.7), 288 (11.1), 226 (4.7), 218 (4.2), 105 (100), 89 (3.8), 77 (23.2), 43 (4.3). HRMS (EI): calcd. for C₂₂H₂₁BrN₂O₅ [M + H]⁺ 472.0634; found 472.0637.

Diethyl 2-[(E)-1-Benzoyl-2-(4-methylbenzylidene)hydrazinyl]fumarate (3f): Pale-yellow oil (90%, 73 mg). IR (acetone): $\tilde{\nu}$ = 3059, 2983, 2938, 1729, 1668, 1613, 1579, 1493, 1447, 1397, 1324, 1259, 1206, 1178, 1155, 1095, 1054, 1029, 908 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.19 (t, *J* = 7.2 Hz, 3 H, CH₃), 1.26 (t, *J* = 7.2 Hz, 3 H, CH₃), 2.31 (s, 3 H, CH₃), 4.17 (q, *J* = 7.2 Hz, 2 H, CH₂), 4.28 (q, *J* = 7.2 Hz, 2 H, CH₂), 7.12 (d, *J* = 6.8 Hz, 2 H, ArH), 7.32–7.51 (m, 6 H, ArH and CH), 7.53 (s, 1 H, CH), 7.87 (d, *J* = 6.8 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.8, 21.2, 61.4, 62.5, 127.2, 127.3, 129.2, 129.8, 130.8, 131.0, 131.1, 134.2, 136.1, 140.2, 141.7, 161.8, 162.3, 170.0 ppm.

MS (EI): m/z (%) = 408 (0.8) [M]⁺, 363 (0.8), 335 (1.5), 288 (4.2), 218 (5.0), 105 (100), 91 (4.9), 77 (19.4), 51 (2.6). HRMS (EI): calcd. for C₂₃H₂₄N₂O₅ [M + H]⁺ 408.1685; found 408.1686.

Diethyl 2-[(E)-1-Benzoyl-2-(2-methoxybenzylidene)hydrazinyl]fumarate (3g): Pale-yellow oil (95%, 80 mg). IR (acetone): $\tilde{\nu}$ = 3072, 2982, 2939, 2906, 2840, 1728, 1668, 1606, 1577, 1489, 1466, 1447, 1394, 1368, 1322, 1289, 1206, 1157, 1106, 1049, 1026, 909 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.21 (t, J = 7.2 Hz, 3 H, CH₃), 1.27 (t, J = 7.2 Hz, 3 H, CH₃), 3.79 (s, 3 H, OCH₃), 4.18 (q, J = 7.2 Hz, 2 H, CH₂), 4.29 (q, J = 7.2 Hz, 2 H, CH₂), 6.83–6.88 (m, 2 H, ArH), 7.26–7.31 (m, 1 H, ArH), 7.37 (s, 1 H, CH), 7.41–7.51 (m, 3 H, ArH), 7.62 (dd, J = 7.6, 2.0 Hz, 1 H, ArH), 7.86 (dd, J = 8.4, 2.0 Hz, 2 H, ArH), 7.95 (s, 1 H, CH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.8, 55.3, 61.4, 62.5, 110.8, 120.6, 122.2, 126.2, 127.3, 129.9, 130.7, 130.9, 131.2, 134.3, 136.4, 137.4, 158.0, 161.9, 162.4, 170.2 ppm. MS (EI): m/z (%) = 424 (1.2) [M]⁺, 379 (1.2), 351 (1.5), 288 (4.4), 218 (14.8), 105 (100), 91 (3.9), 77 (24.7), 43 (14.3). HRMS (EI): calcd. for C₂₃H₂₄N₂O₆ [M + H]⁺ 424.1634; found 424.1636.

Diethyl 2-[(E)-1-Benzoyl-2-(4-methoxybenzylidene)hydrazinyl]fumarate (3h): Pale-yellow oil (93%, 78 mg). IR (acetone): $\tilde{\nu}$ = 3066, 2982, 2938, 2839, 1729, 1667, 1607, 1578, 1514, 1447, 1400, 1368, 1325, 1299, 1254, 1205, 1170, 1110, 1054, 1029, 909 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.20 (t, J = 7.2 Hz, 3 H, CH₃), 1.27 (t, J = 7.2 Hz, 3 H, CH₃), 3.77 (s, 3 H, OCH₃), 4.17 (q, J = 7.2 Hz, 2 H, CH₂), 4.28 (q, J = 7.2 Hz, 2 H, CH₂), 6.84 (dd, J = 6.8, 2.0 Hz, 2 H, ArH), 7.36 (s, 1 H, CH), 7.42–7.51 (m, 6 H, ArH and CH), 7.86 (dd, J = 8.8, 2.0 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.9, 55.2, 61.4, 62.5, 113.9, 126.5, 127.3, 128.8, 129.8, 130.7, 130.9, 134.3, 136.2, 141.5, 161.1, 161.9, 162.4, 170.0 ppm. MS (EI): m/z (%) = 424 (2.9) [M]⁺, 379 (1.4), 351 (2.0), 288 (3.6), 218 (9.6), 105 (100), 91 (2.5), 77 (24.2), 51 (2.6). HRMS (EI): calcd. for C₂₃H₂₄N₂O₆ [M + H]⁺ 424.1634; found 424.1636.

Diethyl 2-[(E)-1-Benzoyl-2-(naphthalen-1-ylmethylene)hydrazinyl]fumarate (3i): Pale-yellow oil (89%, 79 mg). IR (acetone): $\tilde{\nu}$ = 3058, 2982, 2937, 1729, 1672, 1601, 1579, 1510, 1447, 1408, 1368, 1312, 1259, 1206, 1152, 1086, 1053, 1028, 911 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.20 (t, J = 7.2 Hz, 3 H, CH₃), 1.27 (t, J = 7.2 Hz, 3 H, CH₃), 4.19 (q, J = 7.2 Hz, 2 H, CH₂), 4.31 (q, J = 7.2 Hz, 2 H, CH₂), 7.30–7.32 (m, 1 H, ArH), 7.34–7.56 (m, 6 H, ArH and CH), 7.63 (d, J = 8.4 Hz, 1 H, ArH), 7.80–7.83 (m, 2 H, ArH), 7.88 (dd, J = 8.4, 1.6 Hz, 2 H, ArH), 8.11 (s, 1 H, CH), 8.41 (d, J = 8.4 Hz, 1 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.9, 14.0, 61.6, 62.7, 124.6, 125.0, 126.0, 127.0, 127.6, 128.5, 129.0, 129.1, 129.4, 130.3, 130.6, 130.8, 131.6, 133.7, 134.6, 135.9, 142.1, 161.9, 162.5, 170.7 ppm. MS (EI): m/z (%) = 444 (1.6) [M]⁺, 399 (1.2), 339 (0.8), 293 (1.6), 218 (18.6), 105 (100), 91 (1.0), 77 (20.1), 51 (2.3). HRMS (EI): calcd. for C₂₆H₂₄N₂O₅ [M + H]⁺ 444.1685; found 444.1687.

Diethyl 2-[(E)-1-Benzoyl-2-(furan-2-ylmethylene)hydrazinyl]fumarate (3j): Yellow oil (87%, 67 mg). IR (acetone): $\tilde{\nu}$ = 3124, 3066, 2984, 2939, 2906, 1729, 1668, 1601, 1579, 1484, 1448, 1400, 1368, 1320, 1260, 1207, 1170, 1095, 1075, 1053, 1026, 938 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.22 (t, J = 7.2 Hz, 3 H, CH₃), 1.27 (t, J = 7.2 Hz, 3 H, CH₃), 4.19 (q, J = 7.2 Hz, 2 H, CH₂), 4.29 (q, J = 7.2 Hz, 2 H, CH₂), 6.41 (dd, J = 3.6, 1.6 Hz, 1 H, ArH), 6.61 (d, J = 3.6 Hz, 1 H, ArH), 7.27 (s, 1 H, CH), 7.35–7.51 (m, 5 H, ArH and CH), 7.87 (dd, J = 8.4, 1.6 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.8, 13.9, 61.6, 62.6, 111.7, 112.3, 127.4, 130.1, 131.0, 131.2, 132.0, 133.7, 136.0, 144.2, 149.4, 161.7, 162.3, 169.8 ppm. MS (EI): m/z (%) = 384 (2.4) [M]⁺, 339 (1.6), 311 (2.2), 288 (5.3), 218 (2.1), 105 (100), 94 (3.6), 77 (21.2), 51 (2.9).

HRMS (EI): calcd. for C₂₀H₂₀N₂O₆ [M + H]⁺ 384.1321; found 384.1327.

Diethyl 2-[(E)-1-Benzoyl-2-(3-phenylpropylidene)hydrazinyl]fumarate (3k): Pale-yellow oil (90%, 76 mg). IR (acetone): $\tilde{\nu}$ = 3061, 3027, 2983, 2983, 2937, 1729, 1671, 1602, 1579, 1495, 1448, 1399, 1368, 1322, 1259, 1206, 1095, 1054, 1029, 899 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.22 (t, J = 7.2 Hz, 3 H, CH₃), 1.26 (t, J = 7.2 Hz, 3 H, CH₃), 2.56 (dt, J = 8.0, 5.6 Hz, 2 H, CH₂), 2.77 (t, J = 8.0 Hz, 2 H, CH₂), 4.17 (q, J = 7.2 Hz, 2 H, CH₂), 4.25 (q, J = 7.2 Hz, 2 H, CH₂), 6.95–6.98 (m, 1 H, ArH), 7.10 (dd, J = 6.8, 1.6 Hz, 2 H, ArH), 7.16–7.20 (m, 2 H, ArH and CH), 7.23–7.27 (m, 2 H, ArH), 7.34–7.45 (m, 3 H, ArH and CH), 7.71 (dd, J = 8.0, 1.6 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.9, 32.2, 33.9, 61.4, 62.4, 125.9, 127.3, 128.2, 128.2, 128.3, 129.6, 130.6, 130.7, 134.2, 136.3, 140.5, 145.1, 161.7, 162.4, 169.9 ppm. MS (EI): m/z (%) = 422 (1.0) [M]⁺, 349 (1.7), 317 (6.5), 218 (4.7), 117 (3.6), 105 (100), 91 (7.7), 77 (19.5), 51 (2.3). HRMS (EI): calcd. for C₂₄H₂₆N₂O₅ [M + H]⁺ 422.1842; found 422.1839.

Diethyl 2-[(E)-1-Benzoyl-2-butylidenehydrazinyl]fumarate (3l): Pale-yellow oil (87%, 58 mg). IR (acetone): $\tilde{\nu}$ = 3052, 2958, 2874, 1732, 1667, 1602, 1448, 1436, 1400, 1326, 1266, 1213, 1173, 1147, 1059, 1015, 909 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 0.89 (t, J = 7.2 Hz, 3 H, CH₃), 1.47 (dt, J = 14.8, 7.2 Hz, 2 H, CH₃), 2.23 (dt, J = 7.2, 5.6 Hz, 2 H, CH₂), 3.74 (s, 3 H, CH₃), 3.82 (s, 3 H, CH₃), 6.94 (t, J = 5.2 Hz, 1 H, ArH), 7.25 (s, 1 H, CH), 7.37–7.48 (m, 3 H, ArH and CH), 7.77 (dd, J = 7.2, 1.6 Hz, 2 H, ArH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 13.3, 19.5, 34.2, 52.3, 53.2, 127.3, 129.6, 130.3, 130.7, 134.1, 136.6, 147.0, 162.4, 162.8, 170.0 ppm. MS (EI): m/z (%) = 332 (1.0) [M]⁺, 289 (5.8), 260 (1.9), 210 (1.9), 105 (100), 77 (37.3), 51 (4.7), 43 (3.3). HRMS (EI): calcd. for C₁₇H₂₀N₂O₅ [M + H]⁺ 332.1372; found 332.1371.

(E)-Ethyl 3-[(E)-1-Benzoyl-2-benzylidenehydrazinyl]acrylate (3m): Yellow solid (77%, 50 mg). M.p. 103–106 °C. IR (acetone): $\tilde{\nu}$ = 3063, 2980, 2904, 1709, 1681, 1622, 1574, 1491, 1448, 1369, 1272, 1236, 1152, 1076, 1157, 1042, 1001, 965, 927 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 1.26 (t, J = 7.2 Hz, 3 H, CH₃), 4.17 (q, J = 7.2 Hz, 2 H, CH₂), 5.73 (d, J = 13.6 Hz, 1 H, CH), 7.41–7.52 (m, 5 H, ArH), 7.64 (dd, J = 6.8, 1.6 Hz, 2 H, ArH), 7.76 (dd, J = 6.8, 1.2 Hz, 2 H, ArH), 8.19 (d, J = 13.6 Hz, 1 H, CH), 8.40 (s, 1 H, CH) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 14.2, 60.1, 102.0, 128.4, 128.5, 128.8, 129.1, 131.7, 132.2, 132.3, 132.8, 140.6, 165.9, 167.1, 167.4 ppm. MS (EI): m/z (%) = 322 (2.6) [M]⁺, 277 (1.9), 216 (4.4), 171 (1.1), 105 (100), 77 (32.5), 51 (6.1). C₁₉H₁₈N₂O₃ (322.13): calcd. C 70.79, H 5.63, N 8.69; found C 70.56, H 5.59, N 8.66.

Dimethyl 2-[(E)-2-Benzylidene-1-tosylhydrazinyl]fumarate (3n; Z/E, 2.5:1): Pale-yellow solid (90%, 101 mg). M.p. 109–112 °C. IR (acetone): $\tilde{\nu}$ = 3074, 2952, 2830, 1746, 1725, 1602, 1573, 1492, 1449, 1435, 1373, 1281, 1205, 1173, 1141, 1088, 1039, 844, 811 cm⁻¹. ¹H NMR (400 MHz, CDCl₃, TMS): δ = 2.41 (s, 3 H, CH₃, Z), 2.45 (s, 1.2 H, CH₃, E), 3.61 (s, 3 H, OCH₃, Z), 3.71 (s, 1.2 H, CH₃, E), 3.72 (s, 3 H, OCH₃, Z), 3.83 (s, 1.2 H, CH₃, E), 5.97 (s, 0.4 H, CH, E), 7.31–7.35 (m, 7 H, ArH and CH, Z), 7.56–7.59 (m, 2 H, ArH, Z), 7.91 (dd, J = 6.8, 2.0 Hz, 2 H, ArH, Z), 8.46 (s, 0.4 H, CH, E) ppm. ¹³C NMR (100 MHz, CDCl₃, TMS): δ = 21.5, 52.4, 53.1, 127.3, 128.5, 128.8, 129.0, 130.1, 133.0, 133.4, 134.3, 135.0, 142.9, 144.2, 162.4, 163.1 ppm. MS (EI): m/z (%) = 416 (7.5) [M]⁺, 385 (1.4), 352 (1.1), 261 (15.0), 245 (6.7), 229 (100), 201 (54.0), 133 (13.3), 104 (10.8), 91 (23.4), 77 (17.4), 65 (9.8), 51 (4.6). HRMS (EI): calcd. for C₂₀H₂₀N₂O₆S [M + H]⁺ 416.1049; found 416.1038.

Dimethyl 2-[(E)-1-Benzoyl-2-(2-ethoxy-2-oxoethylidene)hydrazinyl]fumarate (3o; Z/E, 10:1): Colourless oil (93%, 68 mg). IR (acetone):

$\tilde{\nu}$ = 3074, 2978, 2956, 2896, 1736, 1687, 1595, 1448, 1438, 1382, 1364, 1346, 1303, 1269, 1215, 1154, 1059, 1040, 908 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 1.29 (t, J = 7.2 Hz, 3 H, CH_3 , Z), 3.75 (s, 3 H, CH_3 , Z), 3.79 (s, 0.3 H, CH_3 , E), 3.85 (s, 3 H, CH_3 , Z), 3.90 (s, 0.3 H, CH_3 , E), 4.24 (q, J = 7.2 Hz, 2 H, CH_2 , Z), 6.52 (s, 0.1 H, CH, E), 6.85 (s, 1 H, CH, Z), 7.28 (s, 0.1 H, CHH, E), 7.36 (s, 1 H, CH, Z), 7.42–7.46 (m, 2 H, ArH, Z), 7.51–7.55 (m, 1 H, ArH, Z), 7.91–7.93 (m, 2 H, ArH, Z) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 13.9, 52.6, 53.6, 61.5, 127.0, 130.7, 130.8, 131.3, 131.9, 132.2, 135.7, 161.3, 162.2, 162.6, 170.0 ppm. MS (ESI): m/z (%) = 380 (100) $[\text{M} + 1]^+$. HRMS (MALDI): calcd. for $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_8 + 1$ $[\text{M} + 1]^+$ 380.1220; found 380.1215.

Dimethyl 2-[(E)-1-Benzoyl-2-(2,2,2-trifluoroethylidene)hydrazinyl]-fumarate (3p; Z/E, 10:1): Yellow oil (83%, 59 mg). IR (acetone): $\tilde{\nu}$ = 3072, 3007, 2958, 1737, 1692, 1633, 1601, 1581, 1493, 1449, 1438, 1402, 1308, 1274, 1222, 1146, 1059, 1013, 916 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 3.77 (s, 3 H, CH_3 , Z), 3.81 (s, 0.3 H, CH_3 , E), 3.86 (s, 3.3 H, CH_3 , Z and E), 6.54 (br., 0.1 H, CH, E), 6.80 (q, $J_{\text{H,F}}$ = 3.2 Hz, 1 H, CH, Z), 7.24 (q, $J_{\text{H,F}}$ = 3.2 Hz, 0.1 H, CH, E), 7.35 (s, 1 H, CH, Z), 7.44 (t, J = 7.2 Hz, 2 H, ArH, Z), 7.50–7.54 (m, 1 H, ArH, Z), 7.80 (dd, J = 7.2, 1.2 Hz, 2 H, ArH, Z) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 52.7, 53.6, 119.5 (q, $J_{\text{C,F}}$ = 270.3 Hz), 127.7, 127.8 (q, $J_{\text{C,F}}$ = 40.1 Hz), 129.0 (q, $J_{\text{C,F}}$ = 244.5 Hz), 130.1, 131.7, 131.9, 132.2, 135.2, 161.3, 162.2, 170.1 ppm. ^{19}F NMR (376 MHz, CDCl_3 , TMS): δ = –67.0 (d, J = 3.2 Hz, 0.1 F, minor), –66.8 (d, J = 3.2 Hz, 1 F, major) ppm. MS (EI): m/z (%) = 358 (0.4) $[\text{M}]^+$, 289 (1.8), 105 (100), 91 (0.5), 77 (29.6), 58 (2.8), 43 (9.6). HRMS (EI): calcd. for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_5\text{F}_3$ $[\text{M} + \text{H}]^+$ 358.0777; found 358.0773.

Dimethyl 2-[2-[(2-Benzoyl-2-[(Z)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl]hydrazono)methyl]phenoxy]maleate (6a): Yellow oil (62%, 65 mg). IR (acetone): $\tilde{\nu}$ = 3067, 2985, 2954, 2844, 1732, 1672, 1638, 1605, 1571, 1438, 1365, 1324, 1268, 1215, 1163, 1129, 1056, 1029, 913 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 3.64 (s, 3 H, CH_3), 3.72 (s, 3 H, CH_3), 3.83 (s, 3 H, CH_3), 3.95 (s, 3 H, CH_3), 4.90 (s, 1 H, CH), 7.08 (dd, J = 8.0, 0.8 Hz, 1 H, ArH), 7.23 (dt, J = 8.0, 0.4 Hz, 1 H, ArH), 7.37–7.41 (m, 1 H, ArH), 7.44 (s, 1 H, CH), 7.45–7.54 (m, 3 H, ArH), 7.65 (s, 1 H, CH), 7.75 (dd, J = 8.0, 1.6 Hz, 1 H, ArH), 7.86 (dd, J = 8.4, 1.6 Hz, 2 H, ArH) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 51.6, 52.3, 53.1, 53.3, 98.8, 121.5, 126.4, 127.1, 127.2, 127.5, 130.0, 131.1, 131.3, 131.4, 133.9, 134.9, 136.0, 151.3, 161.1, 161.8, 162.5, 162.9, 165.3, 170.5 ppm. MS (EI): m/z (%) = 524 (0.2) $[\text{M}]^+$, 493 (0.3), 416 (2.5), 261 (5.0), 229 (34.3), 201 (21.6), 105 (100), 91 (49.0), 77 (30.0), 65 (12.0), 51 (10.8). HRMS (EI): calcd. for $\text{C}_{26}\text{H}_{24}\text{N}_2\text{O}_{10}$ $[\text{M} + \text{H}]^+$ 524.1431; found 524.1432.

Dimethyl 2-[2-[(2-Benzoyl-2-[(Z)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl]hydrazono)methyl]-6-methoxyphenoxy]maleate (6b; Z/E, 84:16): Yellow oil (77%, 85 mg). IR (acetone): $\tilde{\nu}$ = 3072, 3006, 2955, 2845, 1735, 1676, 1641, 1610, 1577, 1479, 1460, 1438, 1396, 1364, 1302, 1267, 1215, 1163, 1128, 1068, 1028, 938 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 3.62 (s, 0.6 H, CH_3 , E), 3.63 (s, 3 H, CH_3 , Z), 3.71 (s, 3 H, CH_3 , Z), 3.73 (s, 0.6 H, CH_3 , E), 3.74 (s, 0.6 H, CH_3 , E), 3.81 (s, 3 H, CH_3 , Z), 3.82 (s, 3.6 H, CH_3 , Z and E), 3.84 (s, 0.6 H, CH_3 , E), 3.95 (s, 3 H, CH_3 , Z), 4.85 (s, 1 H, CH, Z), 6.22 (s, 0.2 H, CH, E), 6.97 (dd, J = 8.0, 1.2 Hz, 1 H, ArH, Z), 7.16 (t, J = 8.0 Hz, 1 H, ArH, Z), 7.29–7.34 (m, 1 H, ArH, Z), 7.44 (s, 1 H, CH, Z), 7.46–7.53 (m, 4 H, ArH), 7.65 (s, 1 H, CH, Z), 7.86 (dd, J = 8.4, 1.6 Hz, 2 H, ArH, Z), 7.92 (s, 0.2 H, CH, E) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 51.5, 52.2, 52.3, 52.7, 52.9, 53.2, 53.3, 55.9, 56.1, 97.5, 108.0, 113.6, 113.9, 117.9, 118.1, 124.4, 126.2, 127.3, 129.9, 130.9, 131.0, 131.2, 133.8, 134.1,

135.0, 135.9, 136.3, 140.0, 144.3, 149.6, 151.2, 152.0, 160.1, 161.7, 162.1, 162.4, 162.5, 162.7, 163.8, 165.4, 170.4 ppm. MS (EI): m/z (%) = 554 (0.5) $[\text{M}]^+$, 495 (5.6), 449 (2.5), 277 (4.3), 219 (2.3), 204 (4.4), 105 (100), 85 (6.7), 77 (28.8), 57 (10.1), 43 (6.5). HRMS (EI): calcd. for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{O}_{11}$ $[\text{M} + \text{H}]^+$ 554.1537; found 554.1540.

Dimethyl 2-[2-[(2-Benzoyl-2-[(Z)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl]hydrazono)methyl]-5-methoxyphenoxy]maleate (6c; Z/E, 91:9): Yellow oil (83%, 92 mg). IR (acetone): $\tilde{\nu}$ = 3067, 3005, 2955, 2845, 1735, 1671, 1640, 1612, 1567, 1503, 1438, 1400, 1364, 1267, 1211, 1153, 1129, 1098, 1055, 1028, 951 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 3.65 (s, 3 H, CH_3 , Z), 3.68 (s, 0.3 H, CH_3 , E), 3.71 (s, 3 H, CH_3 , Z), 3.75 (s, 0.3 H, CH_3 , E), 3.79 (s, 3 H, CH_3 , Z), 3.82 (s, 3 H, CH_3 , Z), 3.85 (s, 0.3 H, CH_3 , minor), 3.91 (s, 0.3 H, CH_3 , minor), 3.95 (s, 3 H, CH_3 , Z), 4.95 (s, 1 H, CH, Z), 6.59 (s, 0.1 H, CH, E), 6.59 (d, J = 2.8 Hz, 1 H, ArH, Z), 6.79 (dd, J = 8.8, 2.8 Hz, 1 H, ArH, Z), 7.42 (s, 1 H, CH, Z), 7.44–7.54 (m, 3 H, ArH, Z), 7.58 (s, 1 H, CH, Z), 7.68 (d, J = 8.0 Hz, 1 H, ArH, Z), 7.85 (dd, J = 8.0, 1.6 Hz, 1 H, ArH, Z), 8.01 (s, 0.1 H, CH, E) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 51.6, 52.3, 53.0, 55.6, 98.8, 106.4, 113.7, 118.4, 127.4, 128.1, 130.0, 131.2, 134.0, 135.2, 136.1, 152.3, 160.8, 161.9, 162.2, 162.5, 162.8, 165.3, 170.3 ppm. MS (EI): m/z (%) = 554 (0.6) $[\text{M}]^+$, 495 (6.6), 417 (1.3), 277 (6.0), 204 (9.3), 105 (100), 85 (12.9), 77 (31.3), 57 (20.2), 43 (12.8). HRMS (EI): calcd. for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{O}_{11}$ $[\text{M} + \text{H}]^+$ 554.1537; found 554.1542.

Dimethyl 2-[2-[(2-Benzoyl-2-[(Z)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl]hydrazono)methyl]-4-nitrophenoxy]maleate (6d; Z/E, 83:17): Yellow oil (63%, 71 mg). IR (acetone): $\tilde{\nu}$ = 3080, 3007, 2956, 1732, 1681, 1643, 1607, 1574, 1532, 1475, 1437, 1349, 1298, 1269, 1233, 1160, 1128, 1074, 1056, 1016, 961 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 3.70 (s, 3 H, CH_3 , Z), 3.73 (s, 0.6 H, CH_3 , E), 3.75 (s, 3 H, CH_3 , Z), 3.83 (s, 0.6 H, CH_3 , E), 3.85 (s, 0.6 H, CH_3 , E), 3.88 (s, 3 H, CH_3 , Z), 3.89 (s, 0.6 H, CH_3 , E), 3.92 (s, 3 H, CH_3 , Z), 5.16 (s, 1 H, CH, Z), 6.49 (s, 0.2 H, CH, E), 7.23 (d, J = 8.8 Hz, 1 H, ArH, Z), 7.45 (s, 1 H, CH, Z), 7.51–7.61 (m, 3 H, ArH, Z), 7.64 (s, 1 H, CH, Z), 7.84 (d, J = 8.0 Hz, 0.3 H, ArH, E), 7.87 (dd, J = 8.0, 1.2 Hz, 2 H, ArH, Z), 8.09 (s, 0.2 H, CH, E), 8.21 (dd, J = 8.0, 2.8 Hz, 1 H, ArH, Z), 8.60 (d, J = 2.8 Hz, 1 H, ArH, Z) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 52.0, 52.2, 52.5, 53.2, 53.3, 53.5, 103.0, 105.2, 121.8, 123.1, 125.7, 127.7, 127.9, 129.9, 131.5, 131.6, 132.4, 132.8, 133.4, 135.7, 145.9, 155.3, 157.9, 161.7, 162.1, 162.5, 164.4, 164.6, 170.5 ppm. MS (EI): m/z (%) = 569 (0.1) $[\text{M}]^+$, 510 (1.7), 448 (1.6), 260 (2.8), 204 (2.2), 201 (21.6), 105 (100), 85 (4.1), 77 (26.1), 57 (6.5), 53 (4.3). HRMS (EI): calcd. for $\text{C}_{26}\text{H}_{23}\text{N}_3\text{O}_{12}$ $[\text{M} + \text{H}]^+$ 569.1282; found 569.1286.

Dimethyl 2-[1-Benzoyl-2-[(2-[(E)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yloxy]naphthalen-1-yl)methylene]hydrazinyl]fumarate (6e; Z/E, 92:8): Yellow oil (72%, 81 mg). IR (acetone): $\tilde{\nu}$ = 3066, 2954, 2845, 1735, 1679, 1638, 1601, 1578, 1509, 1437, 1411, 1365, 1314, 1267, 1217, 1129, 1057, 1028, 909 cm^{-1} . ^1H NMR (400 MHz, CDCl_3 , TMS): δ = 3.63 (s, 3 H, CH_3 , Z), 3.65 (s, 0.3 H, CH_3 , E), 3.73 (s, 3 H, CH_3 , Z), 3.80 (s, 0.3 H, CH_3 , E), 3.85 (s, 3 H, CH_3 , Z), 3.88 (s, 0.3 H, CH_3 , E), 3.92 (s, 0.3 H, CH_3 , E), 3.98 (s, 3 H, CH_3 , Z), 4.90 (s, 1 H, CH, Z), 6.45 (s, 0.1 H, CH, E), 7.16–7.23 (m, 1 H, ArH, Z), 7.43–7.58 (m, 4 H, ArH, Z + CH), 7.77 (d, J = 8.0 Hz, 1 H, ArH, Z), 7.85–7.88 (m, 3 H, ArH, Z), 8.05 (s, 1 H, CH, Z), 8.72 (d, J = 8.0 Hz, 1 H, ArH, Z) ppm. ^{13}C NMR (100 MHz, CDCl_3 , TMS): δ = 51.6, 52.3, 53.1, 53.3, 98.8, 119.5, 120.1, 126.4, 127.1, 127.7, 128.0, 128.3, 129.0, 130.4, 130.5, 132.0, 132.1, 133.0, 134.7, 135.7, 137.1, 150.9, 160.8, 161.9, 162.5, 162.8, 165.3, 171.3 ppm. MS (EI): m/z (%) = 574 (0.3) $[\text{M}]^+$, 515 (2.8), 469 (1.2), 280 (3.9), 252 (5.4), 204 (12.9), 105 (100), 85 (5.9), 77 (33.9). 57

(12.0), 43 (8.8). HRMS (EI): calcd. for $C_{30}H_{26}N_2O_{10}$ [$M + H$]⁺ 574.1587; found 574.1587.

Dimethyl 2-[4-((2-Benzoyl-2-((Z)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)hydrazono)methyl)phenoxy]maleate (6f; Z/E, 83:17): Yellow oil (92%, 93 mg). IR (acetone): $\tilde{\nu}$ = 3066, 3004, 2955, 2847, 1730, 1671, 1601, 1579, 1504, 1437, 1497, 1363, 1324, 1268, 1211, 1162, 1130, 1057, 1015, 912 cm^{-1} . ¹H NMR (400 MHz, $CDCl_3$, TMS): δ = 3.67 (s, 3 H, CH_3 , Z), 3.69 (s, 0.6 H, CH_3 , E), 3.73 (s, 0.6 H, CH_3 , E), 3.75 (s, 3 H, CH_3 , Z), 3.84 (s, 0.6 H, CH_3 , E), 3.86 (s, 3 H, CH_3 , Z), 3.89 (s, 3 H, CH_3 , Z), 5.20 (s, 1 H, CH, Z), 5.28 (s, 0.2 H, CH, E), 6.65 (s, 0.2 H, ArH, E), 6.91 (d, J = 7.2 Hz, 0.4 H, ArH, E), 7.08 (dd, J = 7.2, 2.0 Hz, 2 H, ArH, Z), 7.41 (s, 1 H, CH, Z), 7.45–7.56 (m, 6 H, ArH and CH, Z), 7.85 (dd, J = 7.2, 0.8 Hz, 1 H, ArH, Z) ppm. ¹³C NMR (100 MHz, $CDCl_3$, TMS): δ = 51.6, 51.7, 52.3, 52.4, 52.8, 52.9, 53.3, 53.4, 100.1, 100.2, 115.8, 116.0, 120.7, 127.4, 127.7, 128.9, 129.2, 129.6, 129.7, 129.8, 131.0, 131.1, 131.9, 133.8, 134.0, 136.0, 136.2, 139.8, 149.0, 154.1, 157.9, 159.9, 162.1, 162.2, 162.6, 162.8, 163.4, 165.4, 169.4, 170.29 ppm. MS (EI): m/z (%) = 524 (1.2) [M]⁺, 493 (1.3), 380 (1.1), 260 (3.7), 204 (6.9), 105 (100), 85 (2.5), 77 (26.7), 57 (4.7), 43 (2.9). HRMS (EI): calcd. for $C_{26}H_{24}N_2O_{10}$ [$M + H$]⁺ 524.1431; found 524.1432.

(2'E)-Tetramethyl 2,2'-[3-((2-Benzoyl-2-((Z)-1,4-dimethoxy-1,4-dioxobut-2-en-2-yl)hydrazono)methyl)-1,2-phenylene]bis(oxy)dimaleate (6g; Z/E, 85:15): Yellow oil (61%, 78 mg). IR (acetone): $\tilde{\nu}$ = 3067, 3005, 2955, 2845, 1735, 1671, 1640, 1612, 1579, 1504, 1437, 1497, 1363, 1267, 1211, 1153, 1129, 1098, 1055, 1028, 951 cm^{-1} . ¹H NMR (400 MHz, $CDCl_3$, TMS): δ = 3.62 (s, 0.6 H, CH_3 , E), 3.65 (s, 3 H, CH_3 , Z), 3.69 (s, 0.6 H, CH_3 , E), 3.73 (s, 3 H, CH_3 , Z), 3.76 (s, 3.5 H, CH_3 , Z and E), 3.84 (s, 0.6 H, CH_3 , E), 3.87 (s, 3.6 H, CH_3 , Z and E), 3.88 (s, 3 H, CH_3 , Z), 3.90 (s, 0.6 H, CH_3 , E), 3.93 (s, 3 H, CH_3 , Z), 4.92 (s, 1 H, CH, Z), 5.10 (s, 0.2 H, CH, E), 5.23 (s, 1 H, CH, Z), 6.36 (s, 0.2 H, CH, E), 7.19 (dd, J = 8.0, 1.6 Hz, 1 H, ArH, Z), 7.27 (dt, J = 8.0, 2.0 Hz, 2 H, ArH, Z), 7.28 (s, 1 H, CH, Z), 7.45 (s, 1 H, CH, Z), 7.46–7.54 (m, 3 H, ArH, Z), 7.63 (s, 1 H, CH, Z), 7.64 (dd, J = 7.6, 1.6 Hz, 1 H, ArH, Z), 7.85 (dd, J = 8.0, 1.6 Hz, 1 H, ArH, Z) ppm. ¹³C NMR (100 MHz, $CDCl_3$, TMS): δ = 51.6, 51.7, 51.8, 52.3, 52.4, 52.9, 53.0, 53.1, 53.4, 99.3, 101.4, 110.9, 123.3, 124.5, 127.5, 127.8, 129.1, 129.9, 130.0, 131.0, 131.2, 131.6, 133.8, 135.8, 142.4, 145.0, 158.1, 159.4, 161.7, 162.2, 162.5, 165.0, 165.1, 170.5 ppm. MS (EI): m/z (%) = 682 (0.3) [M]⁺, 623 (3.1), 577 (2.1), 440 (90.2), 397 (65.1), 328 (93.2), 203 (41.8), 105 (100), 77 (27.4), 57 (87.8), 43 (73.2). HRMS (EI): calcd. for $C_{32}H_{30}N_2O_{15}$ [$M + H$]⁺ 682.1646; found 682.1643.

Dimethyl 2-[(E)-1-Benzoyl-2-(2-hydroxybenzylidene)hydrazinyl]-fumarate (6h): Red solid (48%, 38 mg). M.p. 118–120 °C. IR (acetone): $\tilde{\nu}$ = 3185, 3065, 2954, 1732, 1678, 1618, 1572, 1489, 1447, 1436, 1403, 1327, 1306, 1268, 1217, 1157, 1058, 1013, 919 cm^{-1} . ¹H NMR (400 MHz, $CDCl_3$, TMS): δ = 3.77 (s, 3 H, CH_3), 3.86 (s, 3 H, CH_3), 6.85 (t, J = 6.8 Hz, 2 H, ArH), 7.13 (dd, J = 8.0, 1.6 Hz, 1 H, ArH), 7.23 (dt, J = 6.8, 1.6 Hz, 1 H, ArH), 7.45 (s, 1 H, CH), 7.48–7.58 (m, 4 H, ArH), 7.61 (s, 1 H, CH), 7.73 (d, J = 6.8 Hz, 2 H, ArH), 9.61 (br., 1 H, OH) ppm. ¹³C NMR (100 MHz, $CDCl_3$, TMS): δ = 52.6, 53.6, 116.9, 117.1, 119.4, 128.2, 128.3, 128.4, 128.5, 128.7, 131.3, 131.4, 131.8, 133.7, 145.0, 157.3, 161.9, 162.5, 170.1 ppm. MS (EI): m/z (%) = 382 (3.1) [M]⁺, 217 (0.3), 132 (0.3), 105 (100), 91 (1.0), 77 (25.1), 65 (2.6), 51 (4.3), 43 (0.4). HRMS (EI): calcd. for $C_{20}H_{18}N_2O_6$ [$M + H$]⁺ 382.1165; found 382.1169.

Supporting Information (see footnote on the first page of this article): ¹H and ¹³C NMR spectroscopic data, X-ray crystal data of **3a** and **6e**, and detailed descriptions of experimental procedures.

Acknowledgments

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