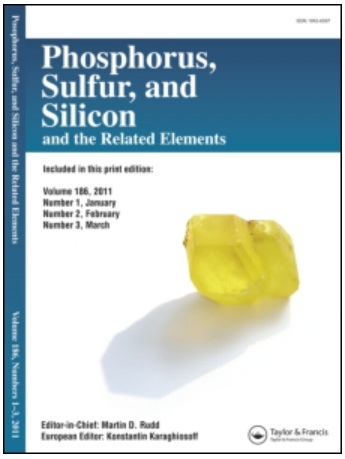

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Chemoselective Synthesis of Functionalized 2,5-Dihydro-2-thioxo-1*H*-imidazoles from 5,5-Diarylthiohydantoins and Activated Acetylenes

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CHEMOSELECTIVE SYNTHESIS OF FUNCTIONALIZED 2,5-DIHYDRO-2-THIOXO-1*H*-IMIDAZOLES FROM 5,5-DIARYLTHIOHYDANTOINS AND ACTIVATED ACETYLENES

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Stable crystalline phosphorus ylides are obtained in excellent yields from the 1:1:1 addition reaction between 5,5-diarylthiohydantoins and dialkyl acetylenedicarboxylates in the presence of triphenylphosphine. These phosphoranes undergo a smooth intramolecular Wittig reaction followed by an electrocyclic ring opening to produce dialkyl 2-(2,5-dihydro-5,5-diaryl-2-thioxo-1H-imidazol-4-yl)but-2-enedioates in good yields.

Keywords Acetylenic ester; 2,5-dihydro-2-thioxo-1*H*-imidazole; intramolecular Wittig reaction; thiohydantoin; triphenylphosphine

INTRODUCTION

Thiohydantoins represent an important class of biologically active molecules of broad medicinal and agrochemical applications. Furthermore, many thiohydantoins are responsible for inhibition of fatty acid hydrolases, glycogen phosphorylases, amylases, and serine proteases.[1–3]

As part of our study on the development of new routes to heterocyclic and carbocyclic systems,[4–10] we report in this article on the chemoselective synthesis of functionalized 2,5-dihydro-5,5-diaryl-2-thioxo-1*H*-imidazoles **4**. Thus, the reaction of diarylthiohydantoins **1** (5,5-diaryl-2-thioxoimidazolidin-4-one) with activated acetylenes **2** in the presence of triphenylphosphine (Ph_3P) leads to the phosphoranes **3**. These phosphoranes undergo intramolecular Wittig reaction[7–11] in boiling toluene to produce dialkyl 2-(2,5-dihydro-5,5-diaryl-2-thioxo-1*H*-imidazol-4-yl)but-2-enedioates **4** in good yields (Scheme 1).

RESULTS AND DISCUSSION

The reaction of 5,5-diarylthiohydantoins **1** with dialkyl acetylenedicarboxylates **2** in the presence of Ph_3P proceeded at room temperature in CH_2Cl_2, and was completed

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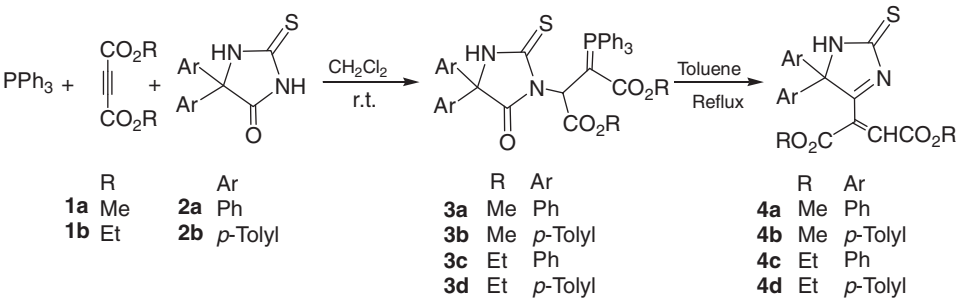


	R	Ar
1a	Me	
1b	Et	
2a		Ph
2b		*p*-Tolyl

	R	Ar
3a	Me	Ph
3b	Me	*p*-Tolyl
3c	Et	Ph
3d	Et	*p*-Tolyl

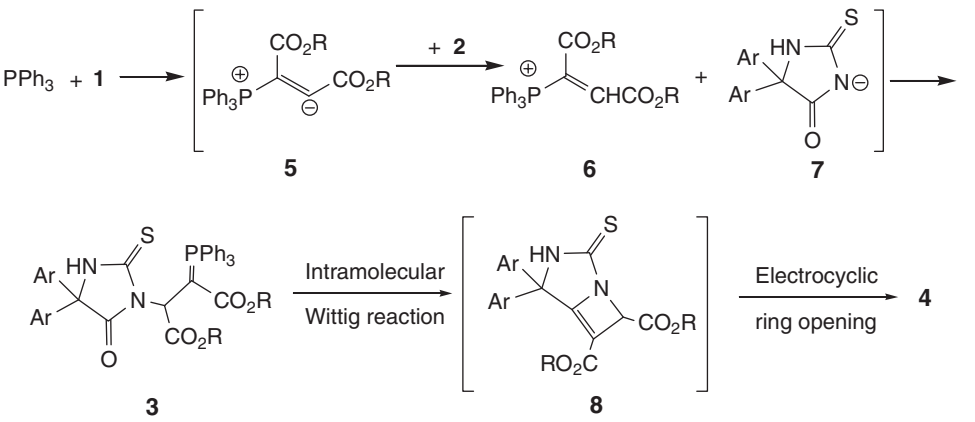
	R	Ar
4a	Me	Ph
4b	Me	*p*-Tolyl
4c	Et	Ph
4d	Et	*p*-Tolyl

Scheme 1 Synthesis of compounds **3** and **4**.

within a few hours. ^{1}H and ^{13}C NMR spectra of the crude products clearly indicated the formation of dialkyl 2-(5,5-diphenyl-2-thioxoimidazolidin-4-one)-3-(triphenylphosphanylidene)succinates **3** (Scheme 1). No products other than **3** could be detected in the reaction mixture. The structure of compounds **3a–3d** was deduced from their IR, ^{1}H, and ^{13}C NMR spectra. The mass spectra of these stable phosphoranes displayed molecular ion peaks at appropriate *m/z* values. Any initial fragmentation involved loss from, or complete loss of, the side chains and scission of the heterocyclic ring system.

Phosphorus ylides **3** undergo a smooth intramolecular Wittig reaction followed by an electrocyclic ring opening reaction in boiling toluene to produce dialkyl 2-(2,5-dihydro-5,5-diaryl-2-thioxo-1*H*-imidazol-4-yl)but-2-enedioates **4** (Scheme 1). Structure **4** was assigned to the isolated products on the basis of their elemental analyses and IR, ^{1}H, and ^{13}C NMR and mass spectral data. Thus, the ^{1}H NMR spectra of **4a–4d** exhibited the C=CH signals at 7.1–7.2 ppm, which is in agreement with the (*E*) configuration[12] for the vinyl moiety of **4**. Further evidence was obtained from the ^{13}C NMR spectra, which displayed C=CH carbon resonances at about 129–131 ppm and a C=S carbon signal at about 183 ppm.

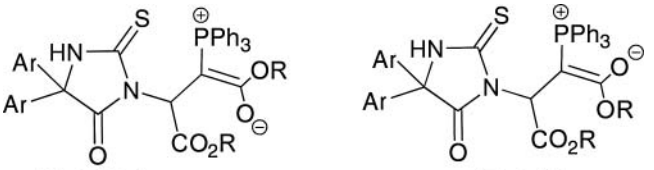
Although we have not yet established experimental proof for the mechanism of the formation of compounds **3** and **4**, a plausible mechanism was proposed as shown in Scheme 2. It is reasonable to assume that phosphorus ylide **3** results from the initial addition of Ph_3P to the acetylenic ester and subsequent protonation of the 1:1 adduct **5**, followed by



Scheme 2 A plausible mechanism for the formation of compounds **3** and **4**.

attack of the anionic nitrogen of **7**, formed by deprotonation of the acidic N-H hydrogen of compound **2**, at the vinylphosphonium cation **6** to form the phosphoranes **3**. Ylides **3** undergo a chemoselective intramolecular Witting reaction[7–11] to produce the fused bicyclic intermediates **8**, which apparently undergo an electrocyclic ring opening reaction under the reaction conditions employed to produce the final products **4**.

The ^{1}H and ^{13}C NMR spectra of the ylides **3a–3d** are consisted with the presence of two diastereoisomers. The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group, and rotation about the partial double bond in the (*E*)-**3** and (*Z*)-**3** geometrical isomers (Scheme 3) is slow on the NMR time scale at ambient temperature. The free-energy of activation for interconversion of the geometrical isomers in similar phosphoranes has been determined by dynamic NMR spectroscopy to be about 65–70 kJ mol^{-1}.[4–6]



Scheme 3 (*E*)- and (*Z*)-stereoisomers of compound **3**.

The ^{1}H and ^{13}C NMR spectra of compounds **4** showed two different aryl groups, and the ^{1}H NMR spectra of compounds **4b** and **4d** exhibited characteristic $(AB)X_3$ patterns for the diastereotopic methylene protons. The Ar-CH_3 region of the ^{1}H NMR spectrum of **4d** in $CDCl_3$ at ambient temperature displayed two sharp singlets for the Ar-CH_3 groups. The ^{1}H NMR of **4d** in 1,2-dichlorobenzene at 25°C is similar to that measured in $CDCl_3$. Increasing the temperature results in coalescence of the Ar-CH_3 resonances. At 90°C, a relatively broad singlet was observed for the Ar-CH_3 groups. This dynamic NMR effect is attributed to restricted rotation around the single bond attaching the vinyl substituent to the 2-thioxo-1*H*-imidazole ring system.

Although an extensive line shape analysis in relation to the dynamic NMR effect observed for **4d** was not undertaken in the present work, the variable temperature spectra are sufficient to calculate the free-energy barrier for the restricted rotation around C=C bond. From the coalescence of the Ar-CH_3 protons and by using the expression $k = \pi\Delta\nu/1.42$, the first-order rate constant (k) was calculated. Application of the absolute rate theory with a transmission coefficient of 1 gives a free-energy of activation ($\Delta G^{\neq}$) of 71 ± 2 kJ mol^{-1} for **4d**, where all known sources of error are estimated and included.[12]

In summary, we have prepared novel thioxohydantoin-containing phosphorus ylides via one-pot reaction between Ph_3P and dialkyl acetylenedicarboxylates in the presence of strong NH-acidic 5,5-diarylthioxohydantoins. These phosphorans are converted to functionalized 2,5-dihydro-2-thioxo-1*H*-imidazoles. The procedure described here provides an acceptable method for the preparation of phosphoranes bearing a thioxohydantoin moiety, which can be employed for the synthesis of 2-thioxo-1*H*-imidazoles.

EXPERIMENTAL

Acetylenic esters **1** and Ph_3P were obtained from Fluka and were used without further purification. 5,5-Diarylthiohydantoins **2** were prepared by known methods.[13] Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, N, and S were performed using a Heraeus CHN-O-Rapid analyzer. The experimental data were in good agreement with the calculated values. The ^1H and ^{13}C NMR spectra ($CDCl_3$) were measured with a Bruker DRX-300 Avance spectrometer. IR spectra were recorded on a Shimadzu IR-460 spectrometer. Chromatography columns were prepared from Aldrich silica gel 70–230 mesh.

General Procedure for the Preparation of Phosphorus Ylides 3

To a stirred solution of 2 mmol of **1** and 2 mmol of **2** in CH_2Cl_2 (5 mL), a solution of 0.52 g of Ph_3P (2 mmol) in CH_2Cl_2 (2 mL) was added dropwise at 5°C over 10 min. After 3 h stirring at r.t., the product was filtered and washed with cold AcOEt.

Dimethyl 2-(5,5-diphenyl-2-thioxoimidazolidin-4-one)-3-(triphenylphosphanylidene)succinate (3a). Yellow powder; mp: 184–186°C; yield: 0.97 g (72%). IR (KBr) (ν_{max}/cm^{-1}): 3440 (NH), 1743 (C=O), 1437 (C=C). Anal. Calcd (%) for $C_{39}H_{33}N_2O_5PS$ (672.73): C, 69.63; H, 4.94; N, 4.16; S, 4.77. Found: C, 70.10; H, 5.06; N, 4.25; S, 4.61. EI-MS: *m/z* (%): 672 (M^+, 4), 595 (16), 266 (17), 224 (100), 166 (78), 77 (43), 59 (11), 31 (59).

Major isomer (*Z*)-**3a** (55%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.12$ (3 H, s, MeO), 3.83 (3 H, s, MeO), 5.31 (1 H, d, $^3J_{PC} = 15.5$, CH), 7.33–7.72 (25 H, m, 5 C_6H_5), 8.34 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 37.1$ (d, $^1J_{PC} = 130.2$, P=C), 49.3 (MeO), 50.4 (MeO), 57.0 (d, $^2J_{PC} = 17.1$, CH), 71.0 (C), 127.3 (d, $^1J_{PC} = 91.3$, P–C_{ipso}), 127.4 (CH), 128.2 (CH), 128.9 (d, $^3J_{PC} = 12.2$, C_{meta}), 129.4 (CH), 132.1 (d, $^4J_{PC} = 2.0$, C_{para}), 134.0 (d, $^2J_{PC} = 11.1$, C_{ortho}), 139.1 (C_{ipso}), 165.6 (COO), 170.1 (d, $^2J_{pc} = 14.0$, COO), 172.2 (C=O), 182.1 (C=S).

Minor isomer (*E*)-**3a** (45%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.52$ (3 H, s, MeO), 3.79 (3 H, s, MeO), 5.31 (1 H, d, $^3J_{pc} = 17.5$, CH), 7.33–7.72 (25 H, m, 5 C_6H_5), 8.34 (1 H, s, NH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 38.5$ (d, $^1J_{PC} = 140.0$, P–C), 49.4 (MeO), 53.2 (MeO), 56.5 (d, $^2J_{PC} = 17.2$, CH), 71.0 (C), 126.5 (d, $^1J_{PC} = 93.3$, P–C_{ipso}), 127.4 (CH), 128.3 (CH), 129.2 (d, $^3J_{PC} = 12.2$, C_{meta}), 129.4 (CH), 132.3 (d, $^4J_{PC} = 1.9$, C_{para}), 134.1 (d, $^2J_{PC} = 11.2$, C_{ortho}), 139.2 (C_{ipso}), 165.7 (COO), 170.1 (d, $^2J_{PC} = 14.1$, COO), 172.3 (C=O), 182.2 (C=S).

Dimethyl 2-(5,5-di-*p*-tolyl-2-thioxoimidazolidin-4-one)-3-(triphenylphosphanylidene)succinate (3b). Yellow powder; mp: 180–183°C; yield: 0.86 g (62%). IR (KBr) (ν_{max}/cm^{-1}): 3478 (NH), 1747 (C=O), 1493 (C=C). Anal. Calcd (%) for $C_{41}H_{37}N_2O_5PS$ (700.78): C, 70.27; H, 5.32; N, 4.00; S, 4.58. Found: C, 70.01; H, 5.26; N, 3.90; S, 4.41. EI-MS: *m/z* (%):700 (M^+, 2), 623 (12), 294 (18), 252 (100), 194 (69), 91 (35), 77 (23), 59 (8), 31 (65).

Major isomer (*Z*)-**3b** (54%): ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.34$ (3 H, s, Me), 2.35 (3 H, s, Me), 3.10 (3 H, s, MeO), 3.83 (3 H, s, MeO), 5.28 (1 H, d, $^3J_{PC} = 15.5$, CH), 7.05–7.98 (23 H, m, 3 C_6H_5, 2 C_6H_4), 8.62 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.5$ (Me), 21.6 (Me), 37.1 (d, $^1J_{PC} = 130$, P=C), 49.4 (MeO), 52.7 (MeO), 57.0 (d, $^2J_{PC} = 17.0$, CH), 71.5 (C), 127.1 (CH), 127.3 (d, $^1J_{PC} = 91$, P–C_{ipso}), 128.3 (CH), 128.9 (d, $^3J_{PC} = 12.1$, C_{meta}), 129.4 (CH), 132.1 (d, $^4J_{PC} = 2.0$, C_{para}), 134.0

(d, $^2J_{PC}$ = 11.1, C_{ortho}), 139.0 (C_{ipso}), 165.7 (COO), 170.1 (d, $^2J_{pc}$ = 14.2, COO), 172.1 (C=O), 183.2 (C=S).

Minor isomer (*E*)-**3b** (46%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.34 (3 H, s, Me), 2.35 (3 H, s, Me), 3.53 (3 H, s, MeO), 3.78 (3 H, s, MeO), 5.28 (1 H, d, $^3J_{PC}$ = 17.5, CH), 7.35–7.98 (23 H, m, 3 C_6H_5, 2 C_6H_4), 8.62 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (Me), 21.6 (Me), 38.5 (d, $^1J_{PC}$ = 140.1, P=C), 49.4 (MeO), 53.3 (MeO), 56.5 (d, $^2J_{PC}$ = 17.0, CH), 71.5 (C), 126.5 (d, $^1J_{PC}$ = 93.2, P–C_{ipso}), 127.1 (CH), 128.3 (CH), 129.2 (d, $^3J_{PC}$ = 12.0, C_{meta}), 129.4 (CH), 132.3 (d, $^4J_{PC}$ = 1.9, C_{para}), 134.1 (d, $^2J_{PC}$ = 11.2, C_{ortho}), 139.1 (C_{ipso}), 165.8 (COO), 170.1 (d, $^2J_{PC}$ = 14.0, COO), 172.2 (C=O), 183.3 (C=S).

Diethyl 2-(5,5-diphenyl-2-thioxoimidazolidin-4-one)-3-(triphenylphosphanylidene)succinate (3c). Yellow powder; mp: 170–172°C; yield: 0.89 g (64%). IR (KBr) (ν_{max}/cm^{-1}): 3468 (NH), 1729 (C=O), 1489 (C=C). Anal. Calcd (%) for $C_{41}H_{37}N_2O_5PS$ (700.78): C, 70.27; H, 5.32; N, 4.00; S, 4.58. Found: C, 70.05; H, 5.26; N, 3.89; S, 4.50. EI-MS: *m/z* (%):700 (M^+, 3), 623 (16), 266 (20), 225 (100), 166 (82), 77 (39), 73 (15), 45 (71).

Major isomer (*Z*)-**3c** (60%): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.38 (3 H, t, $^3J_{HH}$ = 7.2, Me), 1.27 (3 H, t, $^3J_{HH}$ = 7.0, Me), 3.64–3.82 (2 H, complex (AB)X_3 system, CH_2O), 4.00 (2 H, q, $^3J_{HH}$ = 7.2, CH_2O), 5.31 (1 H, d, $^3J_{PC}$ = 15.5, CH), 7.33–7.72 (25 H, m, 5 C_6H_5), 8.34 (1 H, s, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.9 (Me), 14.2 (Me), 36.7 (d, $^1J_{PC}$ = 130.0, P=C), 57.6 (CH_2O), 60.0 (d, $^2J_{PC}$ = 18.0, CH), 60.3 (CH_2O), 71.3 (C), 127.1 (d, $^1J_{PC}$ = 89.2, P–C_{ipso}), 127.0 (CH), 127.9 (CH), 128.4 (d, $^3J_{PC}$ = 12.1, C_{meta}), 131.7 (CH), 131.8 (d, $^4J_{PC}$ = 1.9, C_{para}), 132.2 (d, $^2J_{PC}$ = 10.3, C_{ortho}), 139.0 (C_{ipso}), 168.4 (COO), 170.1 (d, $^2J_{pc}$ = 14.0, COO), 171.3 (C=O), 183.2 (C=S).

Minor isomer (*E*)-**3c** (40%): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.11 (3 H, t, $^3J_{HH}$ = 7.2, Me), 1.34 (3 H, t, $^3J_{HH}$ = 7.2, Me), 4.07–4.21 (2 H, complex (AB)X_3 system, CH_2O), 4.28 (2 H, q, $^3J_{HH}$ = 7.2, CH_2O), 5.31 (1 H, d, $^3J_{PC}$ = 17.5, CH), 7.33–7.72 (25 H, m, 5 C_6H_5), 8.34 (1 H, s, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1 (Me), 14.7 (Me), 38.5 (d, $^1J_{PC}$ = 140, P=C), 58.7 (CH_2O), 59.3 (d, $^2J_{PC}$ = 18.0, CH), 60.4 (CH_2O), 71.3 (C), 126.5 (d, $^1J_{PC}$ = 91, P–C_{ipso}), 127.1 (CH), 128.1 (CH), 128.7 (d, $^3J_{PC}$ = 12.2, C_{meta}), 131.8 (CH), 131.9 (d, $^4J_{PC}$ = 1.8, C_{para}), 133.7 (d, $^2J_{PC}$ = 10.1, C_{ortho}), 139.1 (C_{ipso}), 168.5 (COO), 170.1 (d, $^2J_{PC}$ = 14.1, COO), 172.3 (C=O), 183.3 (C=S).

Diethyl 2-(5,5-di-*p*-tolyl-2-thioxoimidazolidin-4-one)-3-(triphenylphosphanylidene)succinate (3d). Yellow powder; mp: 174–176°C; yield: 0.80 g (55%). IR (KBr) (ν_{max}/cm^{-1}): 3420 (NH), 1665 (C=O), 1430 (C=C). Anal. Calcd (%) for $C_{43}H_{41}N_2O_5PS$ (728.83): C, 70.86; H, 5.67; N, 3.84; S, 4.40. Found: C, 69.98; H, 5.56; N, 3.96; S, 4.62. EI-MS: *m/z* (%):728 (M^+, 2), 651 (15), 294 (24), 252 (100), 194 (75), 91 (41), 77 (22), 73 (9), 45 (62).

Major isomer (*Z*)-**3d** (57%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.38 (3 H, t, $^3J_{HH}$ = 7.2, Me), 1.27 (3 H, t, $^3J_{HH}$ = 7.2, Me), 2.34 (3 H, s Me), 2.35 (3 H, s, Me), 3.64–3.82 (2 H, complex (AB)X_3 system, CH_2O), 4.00 (2 H, q, $^3J_{HH}$ = 7.2, CH_2O), 5.30 (1 H, d, $^3J_{PC}$ = 15.5, CH), 7.33–7.72 (23 H, m, 3 C_6H_5, 2 C_6H_4), 8.34 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (Me), 14.2 (Me), 21.5 (Me), 21.6 (Me), 36.7 (d, $^1J_{PC}$ = 131.2, P=C), 58.8 (CH_2O), 61.8 (CH_2O), 57.0 (d, $^2J_{PC}$ = 17.0, CH), 71.3 (C), 127.1 (d, $^1J_{PC}$ = 89.3, P–C_{ipso}), 127.0 (CH), 127.9 (CH), 128.4 (d, $^3J_{PC}$ = 12.2, C_{meta}), 131.7 (CH), 131.9 (d, $^4J_{PC}$ = 1.8, C_{para}), 132.3 (d, $^2J_{PC}$ = 10.7, C_{ortho}), 139.1 (C_{ipso}), 165.4 (C=O), 171.9 (COO), 170.1 (d, $^2J_{PC}$ = 14.1, COO), 183.2 (C=S).

Minor isomer (*E*)-**3d** (43%): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.11$ (3 H, t, $^3J_{HH} = 7.0$, Me), 1.34 (3 H, t, $^3J_{HH} = 7.0$, Me), 2.34 (3 H, s, Me), 2.35 (3 H, s, Me), 4.07–4.21 (2 H, complex (AB)X_3 system, CH_2O), 4.28 (2 H, q, $^3J_{HH} = 7.2$, CH_2O), 5.31 (1 H, d, $^3J_{PC} = 17.5$, CH), 7.33–7.72 (23 H, m, 3 C_6H_5, 2 C_6H_4), 8.34 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.1$ (Me), 14.7 (Me), 21.5 (Me), 21.6 (Me), 38.5 (d, $^1J_{PC} = 140.2$, P=C), 58.7 (CH_2O), 61.7 (CH_2O), 56.7 (d, $^2J_{PC} = 17.1$, CH), 71.3 (C), 126.5 (d, $^1J_{PC} = 91.2$, P–C_{ipso}), 127.2 (CH), 128.1 (CH), 128.7 (d, $^3J_{PC} = 12.2$, C_{meta}), 131.8 (CH), 131.9 (d, $^4J_{PC} = 2.0$, C_{para}), 133.7 (d, $^2J_{PC} = 10.4$, C_{ortho}), 139.2 (C_{ipso}), 165.8 (COO), 170.1 (d, $^2J_{PC} = 14.1$, COO), 172.3 (C=O), 183.3 (C=S).

General Procedure for Conversion of 3 to 4

A solution of 1.2 mmol of **3** in toluene (20 mL) was refluxed for 12 h. The solvent was removed under reduced pressure, and the yellowish oil was extracted using cold Et_2O. Then, the ether layer was evaporated under reduced pressure, and the residue was separated by silica column chromatography (Merck 230–400 mesh) using hexane/AcOEt as eluent to afford pure imidazoles **4**.

Dimethyl 2-(2,5-dihydro-5,5-diphenyl-2-thioxo-1*H*-imidazol-4-yl)but-2-enedioate (4a). Colorless crystals; mp: 155–157°C; yield: 0.38 g (81%). IR (KBr) (ν_{max}/cm^{-1}): 3478 (NH), 1765 and 1720 (C=O). Anal. Calcd (%) for $C_{21}H_{18}N_2O_4S$ (394.44): C, 63.94; H, 4.60; N, 7.10; S, 8.13. Found: C, 63.90; H, 4.46; N, 6.91; S, 8.21. EIMS: *m/z* (%): 394 (M^+, 15), 316 (25), 225 (30), 166 (100), 77 (28), 59 (12), 31 (21). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.50$ (3 H, s, MeO), 3.85 (3 H, s, MeO), 7.20 (1 H, s, CH), 7.41–7.50 (10 H, m, 10 CH), 8.02 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 52.7$ (MeO), 53.9 (MeO), 74.3 (C), 127.7 (2 CH), 127.8 (2 CH), 129.3 (2 CH), 129.5 (2 CH), 129.6 (CH), 131.0 (CH), 132.4 (CH), 131.2 (C), 137.3 (C), 138.4 (C), 162.2 (COO), 162.9 (COO), 171.8 (C=N), 180.3 (C=S).

Dimethyl 2-(2,5-dihydro-2-thioxo-5,5-di-*p*-tolyl-1*H*-imidazol-4-yl)but-2-enedioate (4b). Colorless crystals; mp: 162–164°C; yield: 0.43 g (85%). IR (KBr) (ν_{max}/cm^{-1}): 3344 (NH), 1760 and 1714 (C=O). Anal. Calcd (%) for $C_{23}H_{22}N_2O_4S$ (422.50): C, 65.38; H, 5.25; N, 6.63; S, 7.59. Found: C, 65.70; H, 5.16; N, 6.59; S, 7.51. EI-MS: *m/z* (%): 422 (M^+, 14), 330 (21), 252 (44), 194 (100), 91 (76), 59 (18), 31 (24). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.37$ (3 H, s, Me), 2.39 (3 H, s, Me), 3.53 (3 H, s, MeO), 3.85 (3 H, s, MeO), 7.21 (1 H, s, CH), 7.34–7.72 (8 H, m, CH), 7.83 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.5$ (Me), 23.0 (Me), 52.7 (MeO), 53.9 (MeO), 74.0 (C), 127.7 (2 CH), 127.8 (2 CH), 129.3 (2 CH), 129.5 (2 CH), 129.6 (CH), 131.0 (CH), 131.2 (C), 132.5 (CH), 137.3 (C), 138.4 (C), 162.3 (COO), 162.9 (COO), 171.8 (C=N), 180.3 (C=S).

Diethyl 2-(2,5-dihydro-5,5-diphenyl-2-thioxo-1*H*-imidazol-4-yl)but-2-enedioate (4c). Colorless crystals; mp: 151–153°C; yield: 0.38 g (75%). IR (KBr) (ν_{max}/cm^{-1}): 3468 (NH), 1765 and 1703 (C=O). Anal. Calcd (%) for $C_{23}H_{22}N_2O_4S$ (422.50): C, 65.38; H, 5.25; N, 6.63; S, 7.59. Found: C, 65.78; H, 5.18; N, 6.56; S, 7.54. EI-MS: *m/z* (%): 422 (M^+, 17), 344 (28), 225 (36), 166 (100), 77 (25), 73 (13), 45 (23).^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.91$ (3 H, t, $^3J_{HH} = 7.2$, Me), 1.13 (3 H, t, $^3J_{HH} = 7.2$, Me), 3.97–4.13 (2 H, m, (AB)X_3 system, $^3J_{AX} = 7.2$, $^3J_{BX} = 7.2$, $^2J_{AB} = 12.1$, CH_2O), 4.28 (2 H, q, $^3J_{HH} = 7.2$, CH_2O), 7.16 (1 H, s, CH), 7.30–7.73 (10 H, m, 10 CH), 8.29 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.2$ (Me), 14.3 (Me), 62.0 (CH_2O), 63.3

(CH_2O), 74.2 (C), 127.7 (2 CH), 127.9 (2 CH), 129.3(2 CH), 129.4 (2 CH), 129.5 (CH), 131.3 (CH), 132.5 (CH), 131.4 (C), 137.4 (C), 138.5 (C), 161.8 (COO), 162.6 (COO), 171.8 (C=N), 180.5 (C=S).

Diethyl 2-(2,5-dihydro-2-thioxo-5,5-di-*p*-tolyl-1*H*-imidazol-4-yl)but-2-enedioate (4d). Colorless crystals; mp: 156–158°C; yield: 0.34 g (63%). IR (KBr) (ν_{max}/cm^{-1}): 3338 (NH), 1762 and 1725 (C=O). Anal. Calcd (%) for $C_{25}H_{26}N_2O_4S$ (450.55): C, 66.64; H, 5.82; N, 6.22; S, 7.12. Found: C, 66.90; H, 5.70; N, 6.11; S, 7.21. EI-MS: *m/z* (%): 450 (M^+, 12), 358 (26), 252 (51), 194 (100), 91 (63), 73 (21), 31 (30). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.91$ (3H, t, $^3J_{HH} = 7.2$, Me), 1.13 (3 H, t, $^3J_{HH} = 7.2$, Me), 2.37 (3 H, s, Me), 2.40 (3 H, s, Me), 3.97–4.13 (2H, (AB)X_3 system, $^3J_{AX} = 7.2$, $^3J_{BX} = 7.2$, $^2J_{AB} = 12.2$, CH_2O), 4.28 (2H, q, $^3J_{HH} = 7.2$, CH_2O), 7.16 (1 H, s, CH), 7.30–7.73 (8 H, m, 8 CH), 8.29 (1 H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.2$ (Me), 14.3 (Me), 21.5 (Me), 21.6 (Me), 62.0 (CH_2O), 63.3 (CH_2O), 74.2 (C), 127.7 (2 CH), 127.9 (2 CH), 129.3 (2 CH), 129.4 (2 CH), 129.5 (CH), 131.3 (CH), 131.4 (C), 132.5 (CH), 137.4 (C), 138.5 (C), 161.8 (COO), 162.6 (COO), 171.8 (C=N), 180.5 (C=S).

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