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Base-Induced Addition-Elimination Reactions of Electron-Deficient Vinylarenes Containing a Carbonyl or Ester Group Utilizing 4-Phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (PTAD)

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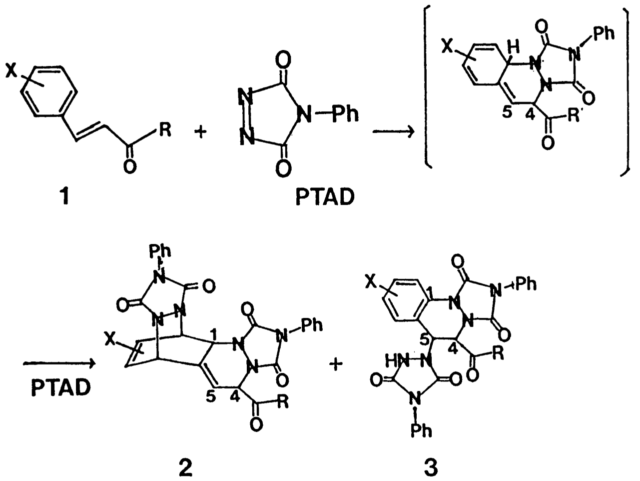
Synopsis. The reaction of electron-deficient vinylarenes such as styrylketones and cinnamate with PTAD afforded double Diels–Alder products and Diels–Alder ene products; the latter underwent novel base-induced elimination of 4-phenyl-1,2,4-triazolidine-3,5-dione via a stable carbanion.

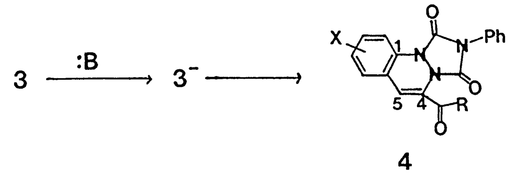
The reactions of 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (PTAD) have been used extensively in organic syntheses, and a diversity of reactions with alkenes have been documented, such as [4+2],[1] [2+2],[2] ene,[3] and dipolar reactions.[4,5] In particular, the reactions of PTAD with electron-rich vinylarenes exemplified by styrene,[1b] vinylpyridines,[6] and benzylidenebicyclic compounds,[2,5] resulted in 1 : 2 adducts. However, no studies have described that the 3,5-dioxo-4-phenyl-1,2,4-triazolidin-1-yl group (PTAD·H) is a latent leaving group. We have found that PTAD·H served as a good leaving group in the reaction products of PTAD with styrylketones or cinnamate.

Results and Discussion

The reaction of 1-phenyl-1-penten-3-one **1a** with PTAD in dichloromethane at 25 °C afforded the double Diels–Alder product **2a** and the Diels–Alder ene product **3a** through a 1 : 1 adduct as depicted in Scheme 1 in isolated yields of 27% and 24%, respectively. Pursuit of the reaction by ^{1}H NMR spectroscopy in $CDCl_3$ at appropriate intervals failed to detect the 1 : 1 adduct because of the higher reactivity of the diene. The Diels–Alder ene product decomposed partially during purification procedures (silica-gel chromatography and recrystallization). Careful recrystallization from acetonitrile gave pure **3a** as a white powder. The spectral data and the elemental analyses supported the proposed structure. The ^{1}H NMR showed two doublet signals at δ=5.33 and 6.02 corresponding to 4-H and 5-H, respectively. The ^{13}C NMR also showed two doublet signals at δ=52.7 and 63.9. A molecular ion peak (*m*/*z* 510) was observed on the mass spectrum. When a catalytic amount of triethanolamine was added to an acetonitrile solution of **3a** at 25 °C, the solution turned yellow after a few minutes to afford yellow crystals of **4a** in 94% yield after conventional purifications. This structure was again assigned on the basis of spectral and elemental analyses. The ^{1}H NMR showed a singlet proton signal at a lower field (δ=6.21) in addition to an ethyl signal (δ=1.25 and 2.32) and a phenyl signal (δ=7.03—8.35). Compound **4a** resulted from the novel base-induced elimination of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD·H_2). This elimination reaction could be carried out in situ without isolation of **3a**.



Scheme 1.



Scheme 2.

Thus, the in situ reaction was extended to a series of electron-deficient vinylarenes such as styrylketones, cinnamate, and cinnamonitrile.[7] As shown in Table 1, similar successive addition–elimination reactions took place in all cases except for **1h** and **1j**. Concerning **1h**, unidentified products were obtained. **1j** was inert to

Table 1. Product Yields of **4** by Addition–Elimination Reaction in situ

	Starting compound		Yield (%) of **4**[a)]
	X	R	
1a	H	Et	34 (94)
1b	H	Me	27 (90)
1c	H	Ph	16 (87)
1d	*p*-OMe	Me	52
1e	*p*-OMe	Ph	61 (92)
1f	*p*-Cl	Me	26 (70)
1g	*o*-Cl	Me	33 (68)
1h	*p*-NO_2	Me	0 (30)[b)]
1i	*p*-OMe	OEt	27
1j	Cinnamonitrile		0 (78)[b)]

a) Yield based on **1**. The values in parentheses show yields based on isolated crude **3**. b) The values in parentheses show recovered yields of starting materials.

PTAD possibly because of the lower electron-density of the diene.

In order to elucidate the elimination mechanism in particular, the deuterium exchange reaction of **3a** was investigated by ^{1}H NMR ($CDCl_3$) spectroscopy in the presence of deuterium oxide and a catalytic amount of sodium carbonate. Addition of sodium carbonate caused the immediate exchange at C-4 more rapidly than the formation of **4a**. Furthermore, the recovered starting material was completely deuterated at C-4. These findings suggest that the elimination reaction may proceed via a carbanion as shown in Scheme 2. Presumably, the electron-withdrawing carbonyl or ester group and amide groups each stabilize the conjugate base of **3**. In summary, the PTAD·H group is a good leaving group in the elimination reaction via a carbanion.

Experimental

Materials and Instruments. Substituted styrylketones, cinnamate, and cinnamonitrile **1a**—**j** were synthesized according to the reported procedures or obtained from a commercial source. PTAD was freshly prepared by Cookson's method.[8] The ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ solution using Me_4Si as an internal standard on a Hitachi R-600 or a JEOL FX-200 spectrometer. The mass spectra were recorded on a JEOL JMS DX-303 spectrometer, operating at an ionizing potential of 70 eV. The IR spectra were taken as KBr disks using a Shimadzu R-460 spectrometer. The elemental analyses were performed using a Yanagimoto Model MT-3 CHN analyzer.

Reaction of 1a with PTAD. PTAD (13.8 mmol) was added portionwise over 2 h in the dark at 25 °C to a solution of **1a** (6.59 mmol) in dichloromethane (10 ml) and the mixture was stirred overnight. The solvent was removed and the residue was flash-chromatographed on silica gel (Wakogel C-200) with dichloromethane as an eluent. **3a** from the first eluate and **2a** from the second eluate were obtained in yields of 24% and 27%, respectively.

2a; Mp 184 °C (acetone); ^{1}H NMR δ=0.99 (t, 3H), 2.52 (q, 2H), 4.10 (bs, 1H), 5.08—5.30 (m, 1H), 5.30—5.51 (m, 1H), 6.28—6.50 (m, 2H), 6.65—6.90 (m, 2H), and 7.45—7.68 (m, 10H); ^{13}C NMR δ=7.0 (q), 32.1 (t), 52.9 (d), 54.1 (d), 60.0 (d), 62.1 (d), 118.6 (d), 125.4 (d), 125.6 (d), 128.3 (d), 128.4 (d), 129.0 (d), 129.1 (d), 129.3 (d), 130.1 (s), 130.9 (s), 131.0 (d), 131.2 (d), 151.7 (s), 154.8 (s), 154.9 (s), and 200.8 (s); IR 1782, 1776, and 1709 cm^{-1}; MS *m/z* (%) 510 (6, M$^+$) and 333 (100, M$^+$−$PTADH_2$). Found: C, 63.70; H, 4.22; N, 16.44%. Calcd for $C_{27}H_{22}N_6O_5$: C, 63.50; H, 4.35; N, 16.47%.

3a; Mp 139—140 °C (acetonitrile); ^{1}H NMR δ=1.06 (t, 3H), 2.62 (q, 2H), 5.33 (d, 1H, *J*=2 Hz), 6.02 (d, 1H, *J*=2 Hz), 7.16—7.38 (m, 14H), and 8.40 (bs, 1H); ^{13}C NMR δ=7.1 (q), 32.2 (t), 52.7 (d), 63.9 (d), 114.6 (s), 116.4 (d), 124.7 (d), 125.3 (d), 126.2 (d), 128.4 (d), 128.6 (d), 129.2 (d), 129.7 (d), 130.8 (d), 131.4 (d), 133.2 (s), 146.8 (s), 151.8 (s), 153.8 (s), and 201.5 (s); IR 3160, 1764, and 1708 cm^{-1}; MS *m/z* (%) 510 (0.4, M$^+$) and 333 (100, M$^+$−$PTADH_2$). Found: C, 63.33; H, 4.27; N, 16.42%. Calcd for $C_{27}H_{22}N_6O_5$: C, 63.50; H, 4.35; N, 16.47%.

General Procedure of in situ Addition-Elimination Reaction. PTAD (13.8 mmol) was added portionwise to the stirred acetonitrile solution (10 ml) of **1** (6.59 mmol) as described above. The mixture was stirred at 25 °C overnight and then a drop of triethanolamine was added to the reaction mixture. The solution turned yellow in a few minutes. After 1 h, conventional purification procedures (concentration by a rotary evaporator, silica-gel column chromatography, and recrystallization) gave yellow crystals.

4a; Mp 202—203 °C (benzene); ^{1}H NMR δ=1.25 (t, 3H), 2.32 (q, 2H), 6.21 (s, 1H), and 7.03—8.35 (m, 9H); ^{13}C NMR δ=8.1 (q), 34.4 (t), 113.3 (d), 115.4 (d), 119.7 (s), 125.7 (d), 125.9 (d), 128.1 (d), 128.7 (d), 129.2 (d), 130.6 (s), 131.1 (d), 133.2 (s), 134.6 (s), 143.9 (s), 146.2 (s), and 194.6 (s); IR 1746 and 1638 cm^{-1}; MS *m/z*(%) 333 (100, M$^+$). Found: C, 68.56; H, 4.41; N, 12.56%. Calcd for $C_{19}H_{15}N_3O_3$: C, 68.44; H, 4.54; N, 12.61%.

4b; Mp 201—202 °C (benzene-hexane); ^{1}H NMR δ=2.48 (s, 3H), 6.31 (s, 1H), and 7.09—8.25 (m, 9H); ^{13}C NMR δ=28.1 (q), 114.7 (d), 115.4 (d), 119.6 (s), 125.7 (d), 125.9 (d), 128.4 (d), 128.7 (d), 129.2 (d), 130.6 (s), 131.4 (d), 133.4 (s), 134.8 (s), 144.1 (s), 146.4 (s), and 190.7 (s); IR 1746 and 1690 cm^{-1}; MS *m/z* (%) 319 (100, M$^+$). Found: C, 67.74; H, 3.98; N, 13.01%. Calcd for $C_{18}H_{13}N_3O_2$: C, 67.69; H, 4.11; N, 13.17%.

4c; Mp 174—175 °C (benzene-hexane); ^{1}H NMR δ=6.12 (s, 1H), and 6.99—8.38 (m, 14H); ^{13}C NMR δ=114.2 (d), 115.4 (d), 120.0 (s), 125.8 (d), 127.9 (d), 127.5 (d), 128.8 (d), 129.1 (d), 129.4 (d), 127.9 (s), 130.6 (s), 131.1 (d), 131.6 (s), 133.9 (d), 134.4 (s), 143.1 (s), 145.7 (s), and 185.5 (s); IR 1752 and 1692 cm^{-1}; MS *m/z* (%) 381 (100, M$^+$). Found: C, 72.52; H, 3.77; N, 10.92%. Calcd for $C_{23}H_{15}N_3O_3$: C, 72.42; H, 3.97; N, 11.06%.

4d; Mp 202—203 °C (benzene); ^{1}H NMR δ=2.48 (s, 3H), 3.85 (s, 3H), 6.44 (s, 1H), and 6.61—7.90 (m, 8H); ^{13}C NMR δ=27.7 (q), 55.7 (q), 101.5 (d), 111.7 (s), 112.1 (d), 117.0 (d), 125.1 (d), 128.8 (d), 129.3 (d), 129.9 (d), 130.7 (s), 130.8 (s), 136.6 (s), 144.0 (s), 146.8 (s), 162.5 (s), and 190.2 (s); IR 1743 and 1706 cm^{-1}; MS *m/z* (%) 349 (100, M$^+$). Found: C, 65.50; H, 4.24; N, 11.92%. Calcd for $C_{19}H_{15}N_3O_3$: C, 65.30; H, 4.33; N, 12.04%.

4e; Mp 209 °C (benzene-hexane); ^{1}H NMR δ=3.86 (s, 3H), 6.25 (s, 1H), and 7.33—8.10 (m, 13H); ^{13}C NMR δ=55.7 (q), 101.6 (d), 111.5 (d), 112.5 (d), 116.6 (s), 125.8 (d), 128.5 (d), 128.7 (d), 129.1 (d), 129.4 (d), 130.7 (s), 133.7 (d), 135.8 (s), 136.1 (s), 143.0 (s), 146.1 (s), 162.2 (s), and 185.3 (s); IR 1758, 1709, and 1653 cm^{-1}; MS *m/z* (%) 411 (100, M$^+$). Found: C, 69.81; H, 4.03; N, 10.45%. Calcd for $C_{24}H_{17}N_3O_4$: C, 70.05; H, 4.17; N, 10.22%.

4f; Mp 241—243 °C (ethanol); ^{1}H NMR δ=2.51 (s, 3H), 6.78 (s, 1H), and 7.02—7.58 (m, 8H); ^{13}C NMR δ=28.2 (q), 113.8 (d), 115.8 (d), 118.2 (s), 125.8 (d), 125.9 (d), 128.9 (d), 129.1 (d), 129.4 (d), 130.4 (s), 133.5 (s), 135.5 (s), 137.3 (s), 143.9 (s), 146.3 (s), and 190.4 (s); IR 1762, 1712, and 1682 cm^{-1}; MS *m/z* (%) 355 (39, M$^+$+2) and 353 (100, M$^+$). Found: C, 61.17; H, 3.47; N, 11.67%. Calcd for $C_{18}H_{12}N_3O_3Cl$: C, 61.09; H, 3.42; N, 11.89%.

4g; Mp 216—217 °C (ethanol); ^{1}H NMR δ=2.55 (s, 3H), 6.79 (s, 1H), and 7.38—7.58 (m, 8H); ^{13}C NMR δ=28.2 (q), 110.5 (d), 113.7 (d), 118.5 (s), 125.9 (d), 126.5 (d), 128.9 (d), 129.3 (d), 130.5 (s), 131.6 (d), 133.0 (s), 134.4 (s), 143.7 (s), 146.2 (s), and 190.4 (s); IR 1757, 1717, and 1690 cm^{-1}; MS *m/z* (%) 355 (41, M$^+$+2) and 353 (100, M$^+$). Found: C, 61.89; H, 3.40; N, 11.60%. Calcd for $C_{18}H_{12}N_3O_3Cl$: C, 61.09; H, 3.42; N, 11.89%.

4i; Mp 182 °C (ethanol); ^{1}H NMR δ=1.37 (t, 3H), 3.84 (s, 3H), 4.37 (q, 2H), 7.07 (s, 1H), and 7.09—7.59 (m, 8H); ^{13}C NMR δ=14.1 (q), 55.7 (q), 62.3 (t), 101.3 (d), 111.4 (d), 112.3 (d), 118.2 (d), 123.0 (s), 125.9 (d), 128.6 (d), 129.2 (d), 129.5 (d), 130.8 (s), 136.9 (s), 143.3 (s), 146.7 (s), 160.2 (s), and 162.3 (s); IR 1780, 1773, 1711, and 1707 cm^{-1}; MS *m/z* (%) 379 (100, M$^+$). Found: C, 63.07; H, 4.42; N, 11.05%. Calcd for $C_{20}H_{17}N_3O_5$: C, 63.30; H, 4.52; N, 11.08%.

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