Variable Regioselectivity in Reactions of *N*-Lithio-*N*-vinylaniline with Arenedicarboxylates and α,β-Unsaturated Esters

Alan R. Katritzky,* Daniela C. Oniciu, Balbino Mancheño and Richard A. Barcock
Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, Florida 32611-2046, USA

Regioselectivity patterns for the reactions of *N*-lithio-*N*-vinylaniline with several arenedicarboxylates and esters of α,β-unsaturated acids are reported. *N*-Lithio-*N*-vinylaniline reacted at both of its ambident anionic sites, to give β-enamino ketones and amide derivatives. A bridgehead compound resulting from cycloadditions involving *N*-lithio-*N*-vinylaniline was also formed in the reactions with ethyl cinnamate and ethyl phenylpropiolate. The structures of all compounds formed were fully characterised by NMR techniques.

Metallated imines are versatile nucleophiles capable of carbon–carbon bond formation,[1] and are especially useful for the introduction of a masked carbonyl function in the β-position with respect to an electrophilic carbon. The reactions of metallated imines with aldehydes and ketones have been widely studied.[2-6] Other important reactions of α-metallated imines are: (i) with esters to give β-enamino ketones;[7,8] (ii) with alkyl halides to give α-alkylated imines;[2,9] (iii) with α-halogeno ketones to give pyrroles;[10] (iv) with epoxides to yield 2-amino-tetrahydrofurans.[11]

There has also been interest in the reactions of α-metallated imines with α,β-unsaturated systems. Thus, Takabe *et al.* briefly described cycloalkenylations of *N*-isobutylidene-*tert*-butylamine with three different dienes (butadiene, isoprene, and myrcene) to afford cyclic and acyclic products in varying amounts as detected by GLC.[12] More recently, Würthwein allowed a polyfunctional α-metallated imine to react with simple dienes and an α,β-unsaturated carbonyl compound, paying close attention to the regio- and stereo-selectivity.[13] *N*-*tert*-Butyl-*N*-lithio-2-methylprop-1-enylamine and isoprene at low temperatures yielded two regioisomeric γ,δ-unsaturated imines, whereas at the temperature of refluxing THF a cyclic regioisomeric cyclohexene derivative was formed. The isolation of the acyclic γ,δ-unsaturated imines was the authors' main argument against a one-step cycloaddition mechanism (Diels–Alder type) for the generation of the cyclohexene derivative. 2,3-Dimethylbutadiene gave exclusively two regioisomeric γ,δ-unsaturated imines; methyl vinyl ketone produced a mixture of acyclic regioisomers *via* 1,2- and 1,4-attack.

We have previously reported a high yielding one-pot procedure for the generation of various β-enamino ketones by treating *N*-(1-anilinoethyl)benzotriazole **1** successively with 2 equiv. of lithium diisopropylamide, and then esters of aliphatic and aromatic acids.[8] We now report extensions of this reaction to arenedicarboxylates and esters of α,β-unsaturated acids which show interesting regioselectivity patterns.

Results and General Discussion

N-Lithio-*N*-vinylaniline (LVA) **2**, obtained by treating *N*-(1-anilinoethyl)benzotriazole **1** with lithium diisopropylamide (2.0 equiv.) in THF at −78 °C (Scheme 1), was treated *in situ* with an equimolar amount of an ester **3**. Ethyl cinnamate **3a** at −78 °C in THF thus afforded two compounds; the expected β-enamino ketone **4** (50%), resulting from a nucleophilic attack of the carbanion of the lithiated imine, and a bridged cyclic amide 5-anilino-2,7-diphenyl-2-azabicyclo[2.2.2]octan-3-one **5** (15%), the structure of which was deduced from the ^1H and ^{13}C NMR spectra, as explained later.

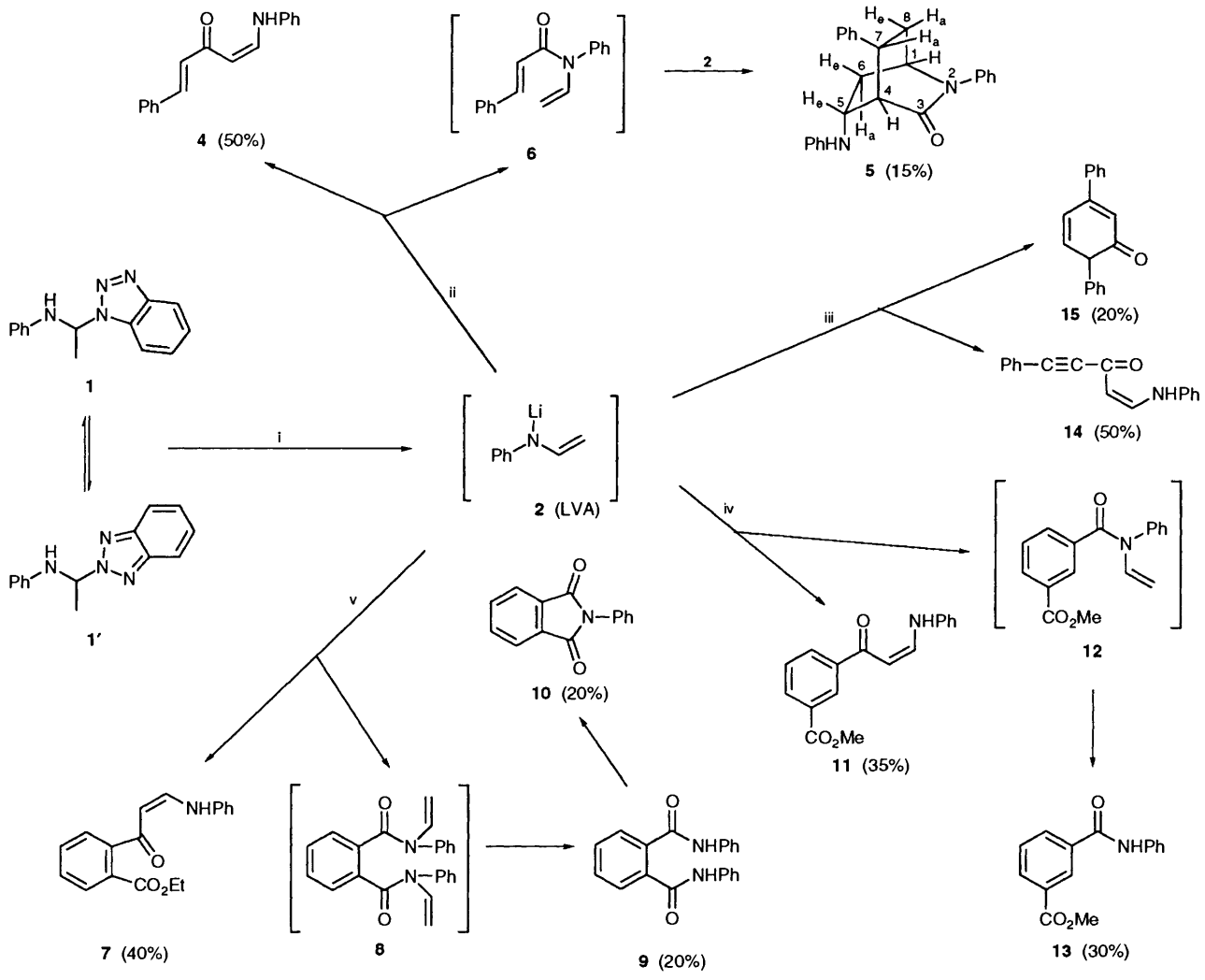
Reaction of the anion **2** with diethyl phthalate **3b** gave the β-enamino ketone **7** (40%), di-*N*-phenylphthalamide **9** (20%), and *N*-phenylphthalimide **10** (20%). The β-enamino ketone **7** results from an attack of the β-carbon of the anion **2** directly at the ester functionality. Nucleophilic attack by the nitrogen atom of LVA **2** on both ester functionalities should give bis(*N*-phenylvinyl)phthalamide **8**, which is expected to be unstable and readily convert into di-*N*-phenylphthalamide **9** which, in turn, gives *N*-phenylphthalimide **10** *via* an intramolecular cyclisation and subsequent elimination of aniline.

Treatment of LVA **2** with dimethyl isophthalate **3c** gave rise to the β-enamino ketone **11** (35%), and the corresponding *meta*-substituted benzamide **13** (30%). Ethyl phenylpropiolate **3d** showed behaviour similar to that of ethyl cinnamate. Three compounds were isolated; the corresponding β-enamino ketone **14** (50%), the bridged cyclic amide **5** (15%) and 1,4-diphenylpyridin-2(1*H*)-one **15** (20%).

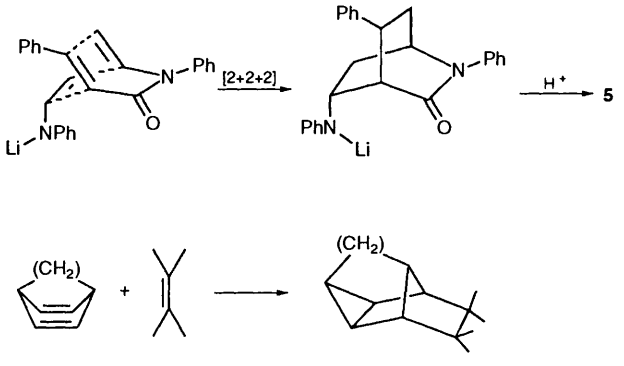
The molar ratios between the compounds formed in these reactions show that, while LVA **2** reacted at both ambident nucleophilic sites, the carbanion nucleophilicity generally predominates. The assumed *N*-vinyl secondary carboxamides **8** and **12**, directly formed from nucleophilic attack by the nitrogen atom of LVA **2**, would be expected to form the simple amides **9** and **13**, respectively, by hydrolysis and elimination of acetaldehyde. However, it is presumed that in the case of the *N*-vinyl amide **6**, an alternative reaction pathway involving the cycloaddition of a further molecule of LVA **2** (discussed below) is preferred. The reasons why the mono amide **13** only, is generated from dimethyl isophthalate **3c**, whereas the bis amide **9** is generated from diethyl phthalate **3b**, are not clear.

Formation of the bridgehead derivative **5** can be rationalised by a cycloaddition of the intermediate **6** and the LVA **2** (see Scheme 2). This type of cycloaddition is similar to those of the norbornadiene and might be effected by thermodynamic control,[14,15] resulting from the *trans*-configuration of the diene. Moreover, similar [2 + 2 + 2] cycloadditions have been already reported (*cf.* Scheme 2).[16,17] The intermediate **6** was not detected in the reaction mixture by GC/MS, but it could be expected to be formed by a nucleophilic attack of the nitrogen atom of **2** directly at the ester functionality. The reactive intermediate **6** is presumably completely consumed by further reaction with LVA **2**.

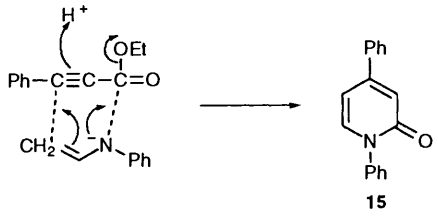
1,4-Diphenylpyridin-2(1*H*)-one **15** is formed by addition of LVA **2**, acting as a bi-nucleophile, to ethyl phenylpropiolate acting as a bi-electrophile (Scheme 3). Neither the order of the bond-forming steps nor the mechanism for the formation of a significant quantity of **5** (15%) from **3d** is clear, although in the



Scheme 1 *Reagents and conditions:* i, LDA (2 equiv.), THF, −78 °C, 0.5 h; ii, PhCH=CHCO$_2$Et **3a**; iii, CH≡CCO$_2$Et **3d**; iv, C$_6$H$_4$(CO$_2$Me)$_2$-*m* **3c**; v, C$_6$H$_4$(CO$_2$Et)$_2$-*o* **3b**



Scheme 2



Scheme 3

latter a reduction, possibly by unchanged LDA, is obviously implicated.

NMR Discussion

As shown by the coupling constants ($J_{CH=CH}$ 8.0 Hz) for the two vinyl hydrogens of the double bonds in the enamino moiety, the enaminones **4**, **7**, **11** and **14** all have a *cis* structure. The same *cis* structure was previously reported for other unsymmetrical enamino ketones obtained with LDA.[7,8,18]

Assignments for compound **5** in both the ^{1}H NMR (Fig. 1) and ^{13}C NMR spectra were based on ^{1}H–^{1}H COSY (Fig. 2), ^{13}C–^{1}H HETCOR (Fig. 3), 2DJ (Fig. 4) and APT-NMR experiments. The axial and equatorial (a and e) designations refer to the relative position of the protons or substituents in the amide ring, as shown in structure **5**. The signals in the ^{13}C NMR spectrum were in accordance with the expected chemical shifts[19] and their correlation with the signals of the attached protons in the ^{13}C–^{1}H HETCOR spectrum (Fig. 3, Table 1). The following features of the ^{1}H NMR spectrum (Fig. 1), support the assignment of structure **5**.

(i) Resonance of 4-H as a triplet, due to coupling with the two vicinal methine protons 5-H and 7-H. The protons 5-H and 7-H must have an equatorial-axial relationship, because of (i) no long range axial-axial coupling (observed in related systems)[20] was found, and (ii) the absence of any observed NOE, expected for an equatorial-equatorial relationship.

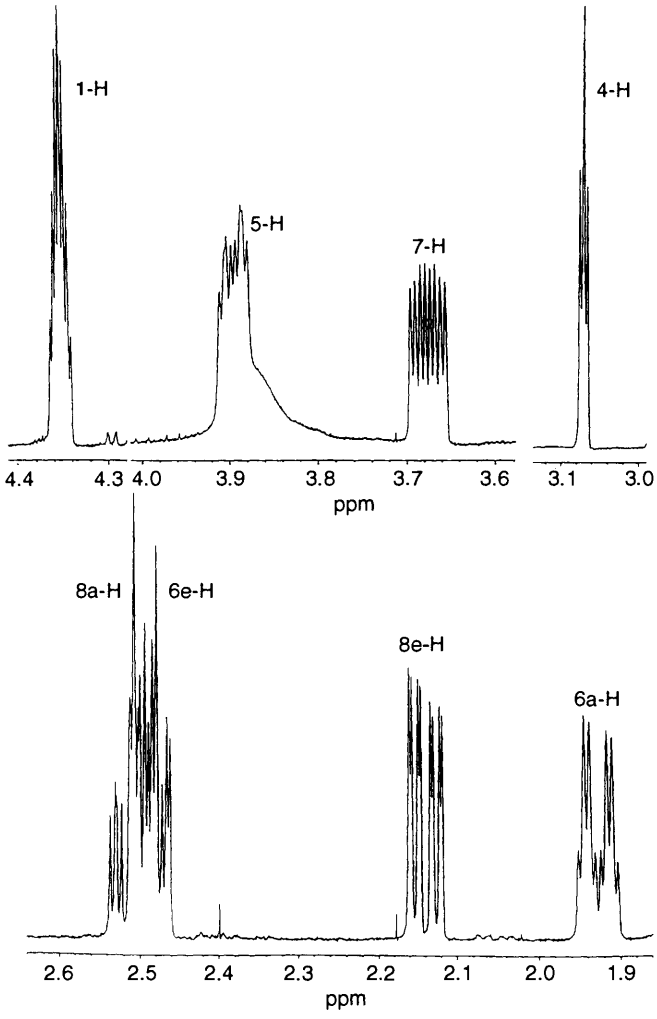


Fig. 1 Partial ^{1}H NMR spectrum of compound **5**

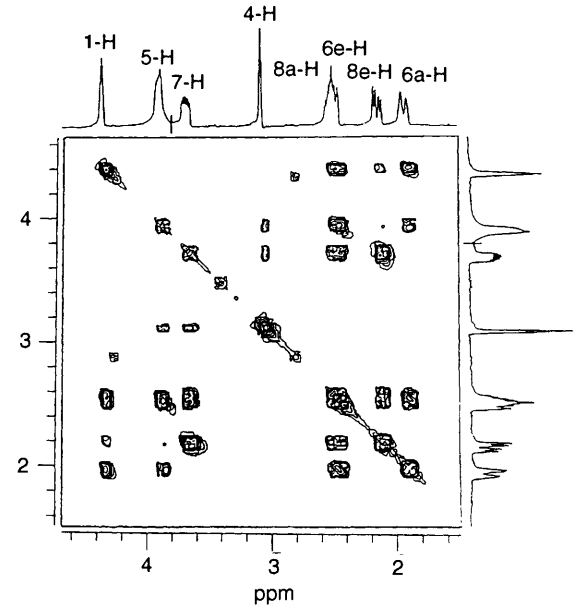


Fig. 2 Partial ^{1}H–^{1}H COSY for compound **5**

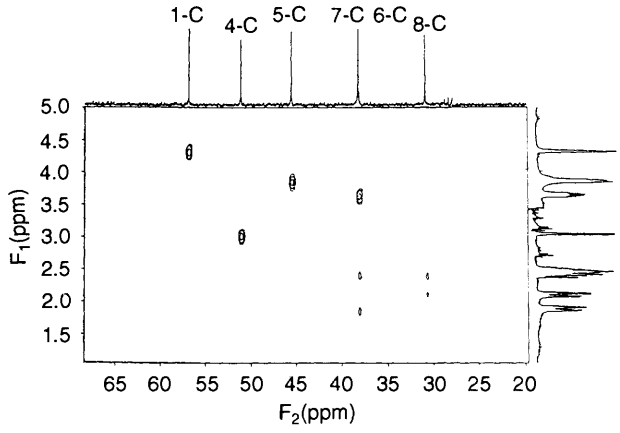


Fig. 3 Partial ^{13}C–^{1}H HETCOR for compound **5**

(ii) The signal for 5-H, overlapped with the NH signal, formed eight peaks, *i.e.* a double doublet of doublets (Fig. 1) due to coupling with 4-H (J 2.8 Hz) and the two protons of the adjacent methylene group 6e-H (J 9.0 Hz) and 6a-H (J 3.8 Hz). The axial position was assigned to the *N*-phenylamino substituent and the equatorial to 5-H, due to the large e-e coupling constant of 5-H with 6e-H, and the smaller e-a coupling constant with 6a-H.

(iii) 6a-H at δ 1.95 shows long-range W four-bond coupling with 8a-H.[20] 6a-H appears at the highest field probably because of shielding by the ring current of the *N*-phenyl group attached to 5-C. The signal for 6a-H should appear as a dddd with a large geminal coupling constant (J 13.9 Hz), two vicinal coupling constants with 5-H (J 3.8 Hz) and 1-H (J 3.5 Hz), and the long-range coupling with 8a-H (J 3.0 Hz). However, due to the similarity of the small coupling constants, the signal is not totally resolved. The values of the coupling constants were all determined from measurements of the hydrogens coupled with 6a-H, and confirmed using spin-decoupler experiments.

(iv) The axial 5-phenylamino group shows a positive NOE of the *ortho* hydrogens when 6a-H is irradiated. Assignment of the 7-phenyl group to the *exo* position relative to the amido group is supported by the values for the couplings of the adjacent geminal 7-H, which resonates as a double doublet of doublets (Table 1). The large coupling constant 7-H, 8a-H (J 11.5 Hz) is characteristic for an axial-axial relationship.[21]

(v) 6e-H appears as eight peaks: a double doublet of doublets, which are overlapped with the 8a-H signal. These signals were interpreted using a 2DJ spectroscopy experiment (Fig. 4).

(vi) 1-H appears as a seven lines multiplet (Fig. 1), due to coupling with the two adjacent methylene groups in positions 6 and 8 of the ring. The dddd is not totally resolved, but the values of the coupling constants in this signal were obtained from measurements of the hydrogens coupled with 1-H, and confirmed by spin-decoupler experiments.

The values for the coupling constants are related to the dihedral angles and conformation of the molecule by the Karplus function. We used the ALTONA (written in BASIC) PC program[22] for an empirically generalised Karplus-type equation,[23] which takes into account the electronegativity and orientation of the substituents attached to the considered CH–CH fragment. This particular Karplus-type equation,[23] assumes that when the number of substituents in a fragment is three, only the α-atoms need to be defined, because the β-atoms do not contribute to the electronegativity. The values of the observed coupling constants were in good general agreement with those calculated for an eclipsed conformation for this molecule (Table 2). However, it would be expected for this conformation that J(1-H, 6a-H) = J(1-H, 8a-H) and J(1-H, 6e-H) = J(1-H, 8e-H). In fact, the experimental 1-H, 8a-H (J 4.0 Hz) coupling constant is greater than that for 1-H, 6a-H (J 3.5 Hz) and the 1-H, 8e-H (J 1.7 Hz) coupling constant is less

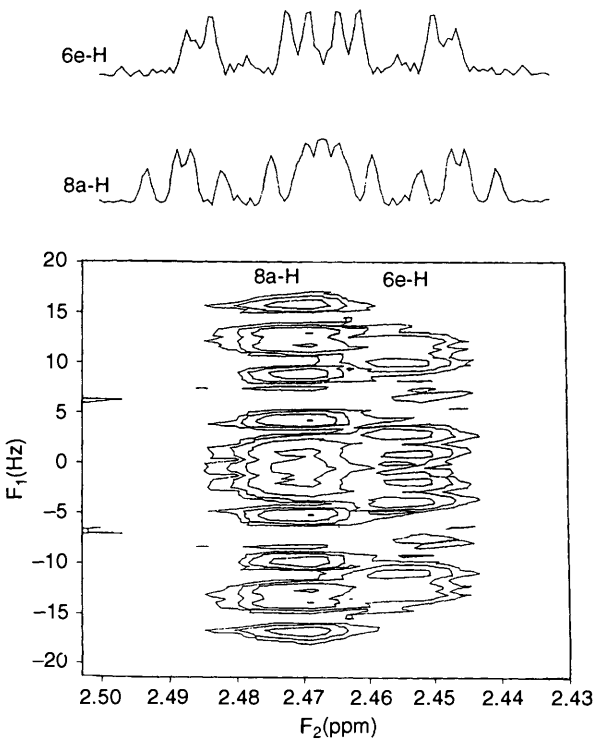


Fig. 4 Partial 2D *J* spectroscopy experiment for compound **5**

than that for 1-H, 6e-H (*J* 2.1 Hz), suggesting that there is a small deviation of 2–3° from the eclipsed conformation in **5**, with a reduction of the dihedral angle (1-H)–C–C–(8a-H) and a subsequent increase of the dihedral angle (1-H)–C–C–(6a-H). Similar findings have previously been reported for certain substituted bicyclo[2.2.2]oct-2-enes.[24]

The ^1H and ^{13}C NMR spectra temperature range (−60 to +30 °C) showed no significant change, suggesting no conformational equilibrium.

Experimental

Melting points were determined on a Kofler hot-stage microscope and are uncorrected. The ^1H and ^{13}C NMR spectra were obtained on either a Varian VXR 300 or a General Electric QE 300 spectrometer with tetramethylsilane as the internal standard. *J* Values are given in Hz. Signals marked † may be interchanged and those marked ‡ overlapped. The structures of the compounds **4**, **5**, **7**, **9**–**11**, and **13**–**15** were assigned by bidimensional NMR; the connectivities between protons were determined by COSY experiments and the connectivities between carbons and protons were determined by HETCOR. The *J* values for compound **5** were determined by ^1H NMR experiments using a Varian Unity 500 MHz spectrometer. High resolution mass spectra were recorded on a Kratos AEI MS 30 mass spectrometer. Thin layer chromatography (TLC) was carried out on pre-coated TLC plates (silica gel G60) obtained from Fisher. The esters **3a**–**d** were purchased from Aldrich and used without further purification. Lithium diisopropylamide (LDA) was purchased from Aldrich as a 1.5 mol dm^{-3} solution in cyclohexane. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under nitrogen prior to use. All moisture-sensitive reactions were carried out in a dry argon atmosphere.

1-(1-*Anilinoethyl*)*benzotriazole* **1**.—This compound was prepared according to the literature procedure.[25] The product obtained was triturated with Et_2O and then recrystallised from EtOH to give colourless crystals (70%), m.p. 124 °C (lit.,[25] 124–130 °C).

Preparation of N-*Lithio*-N-*vinylaniline* (*LVA*) **2** *from* N-(1-*Anilinoethyl*)*benzotriazole* **1**.—LDA (2.46 cm^3, 3.70 mmol) was added to the benzotriazole **1** (0.40 g, 1.68 mmol) in THF (30 cm^3) at −78 °C and the reaction mixture was left for 0.5 h. A yellow anion was formed which was assumed to be the title compound **2**. It was then allowed to react with various esters **3a**–**d**, as follows.

Reactions of the LVA **2**.—*With ethyl cinnamate* **3a**. A solution of ethyl cinnamate **3a** (0.30 g, 1.68 mmol) in THF (20 cm^3) was added to LVA **2** (1.68 mmol) in THF (20 cm^3) at −78 °C and the reaction mixture was left for 2 h. After this period of time, the reaction mixture was allowed to reach ambient temperature. The solvent was evaporated and the residue was suspended in distilled water (30 cm^3). The aqueous layer was extracted with Et_2O (3 × 30 cm^3). The combined extracts were then washed with water (20 cm^3), dried ($MgSO_4$) and evaporated to yield the crude product mixture as a yellow solid, which was fractionated by column chromatography [Al_2O_3 (neutral, activity, 1, 80–200 mesh) hexane–CH_2Cl_2 4:1]. Two compounds were isolated: (1Z,4E)-1-anilino-5-phenylpenta-1,4-dien-3-one **4**, as yellow crystals (0.21 g, 50%), m.p. 160–161 °C (from EtOH) (lit.,[26] 158 °C); R_f(CH_2Cl_2) 0.75; δ_H(300 MHz; $CDCl_3$) 5.50 (1 H, d, *J* 8.0, 2-H), 6.78 (1 H, d, *J* 18.0, 4-H), 7.08 (3 H, m, 2″-H, 4″-H), 7.35 (5 H, m, 3″-H, 2′-H, 4′-H), 7.42 (1 H, dd, *J* 8.0, 12.5, 1-H), 7.55 (2 H, m, 3′-H), 7.60 (1 H, d, *J* 18.0, 5-H) and 12.18 (1 H, br d, *J* 12.5, NH); δ_C(75 MHz; $CDCl_3$) 98.1 (C-2), 116.2 (C-2″), 123.7 (C-4″), 127.6 (C-4′), 128.0 (C-2′†), 128.8 (C-3′†), 129.6 (C-4), 129.7 (C-3″†), 135.4 (C-1′), 139.6 (C-5), 140.2 (C-1″), 144.51 (C-1) and 189.2 (C-3); *m*/*z* 249 (M^+, 5%), 172 (100), 146 (5), 117 (6), 92 (5) and 77 (7).

The second product isolated was 5-*anilino*-2,7-*diphenyl*-2-*azabicyclo*[2.2.2]*octan*-3-*one* **5** as a colourless solid (93 mg, 15%), m.p. 169–171 °C (from EtOH) (Found: C; 81.35; H, 6.8; N, 7.4. $C_{25}H_{24}N_2O$ requires C, 81.52; H, 6.52; N, 7.61%); R_f(CH_2Cl_2) 0.14; ^1H NMR ($CDCl_3$) and ^{13}C NMR ($CDCl_3$) are presented in Table 1; *m*/*z* 368 (M^+, 100%), 312 (5), 263 (31), 234 (24), 221 (60), 157 (12), 104 (93) and 77 (54) (Found: M^+, 368.189. $C_{25}H_{24}N_2O$ requires *M*, 368.188).

With diethyl phthalate **3b**. A solution of diethyl phthalate (0.19 g, 0.84 mmol) in THF (20 cm^3) was added to LVA **2** (1.68 mmol) in THF (20 cm^3) at −78 °C, and the reaction mixture was stirred for 2 h. After this period of time, it was allowed to warm to ambient temperature. The solvent was evaporated and the residue was suspended in water (30 cm^3). The aqueous layer was extracted with CH_2Cl_2 (3 × 25 cm^3). The combined extracts were washed with water (20 cm^3), dried ($MgSO_4$), and evaporated and the residue was fractionated by column chromatography [Al_2O_3 (neutral, activity 1, 80–200 mesh) hexane–CH_2Cl_2 4:1]. Three products were isolated. The first product eluted was *N*-phenylphthalimide **10** (75 mg, 20%), m.p. 207 °C (from EtOH) (lit.,[27] 207 °C); the second product isolated was (2Z)-3-*anilino*-1-(2′-*ethoxycarbonylphenyl*)*prop*-2-*en*-1-*one* **7**, as yellow crystals (0.21 g, 40%), m.p. 69 °C (decomp.) (from EtOH); R_f (CH_2Cl_2) 0.41; δ_H(300 MHz; $CDCl_3$) 1.36 (3 H, t, *J* 7.1, CH_3), 4.38 (2 H, q, *J* 7.1, OCH_2), 5.64 (1 H, d, *J* 8.1, 2-H), 7.08 (1 H, t‡, *J* 8.8, 4″-H), 7.09 (2 H, d‡, *J* 7.3, 2″-H), 7.36 (2 H, dd, *J* 7.3, 8.8, 3″-H), 7.46 (1 H, dd‡, *J* 8.1, 12.5, 3-H), 7.42–7.56 (3 H, m, 3′-H,‡† 4′-H,‡† 5′-H,‡†), 7.78 (1 H, m, 6′-H†) and 11.85 (1 H, br d, *J* 12.5, NH); δ_C(75 MHz; $CDCl_3$) 13.9 (CH_3), 61.4 (OCH_2), 96.6 (C-2), 116.4 (C-2″), 123.8 (C-4″), 127.3 (C-6′), 129.4 (C-4′†), 129.4 (C-5′†), 129.7 (C-3″), 130.6 (C-2′†), 131.0 (C-3′), 140.2 (C-1″), 142.4 (C-1′), 144.3 (C-3), 168.1 (–CO_2–) and 193.9 (C-1); *m*/*z* 294 (M^+, 23%), 257 (25), 248 (66), 222 (62), 149 (40), 146 (40), 104 (45) and 77 (64) (Found: M^+, 295.120. $C_{18}H_{17}NO_3$ requires *M*, 295.120). The third product isolated was confirmed by ^1H and ^{13}C NMR and CHN analysis to be

Table 1 ^1H and ^{13}C NMR chemical shifts (ppm) and coupling constants (Hz) of **5**

Position	δ_H(ppm)	J (Hz)	δ_C (ppm)
1	4.35 (m)	4.0 (1, 8a), 1.7 (1, 8e), 2.1 (1, 6e), ~ 3.5 (1, 6a)	56.7
3	—	—	171.7 (C=O)
4	3.08 (t)	2.8 (4, 5), 2.8 (4, 7)	51.0
5	3.89 (ddd)	2.8 (5, 4), 9.0 (5, 6e), 3.8 (5, 6a)	45.5
6a	1.94 (dddd)	3.8 (6a, 5), 3.5 (6a, 1), 13.9 (6a, 6e), 3.0 (6a, 8a)	38.1
6e	2.48 (ddd)	13.9 (6e, 6a), 2.1 (6e, 1), 9.0 (6e, 5)	
7	3.68 (ddd)	11.5 (7, 8a), 5.9 (7, 8e), 2.8 (7, 4)	38.1
8a	2.50 (dddd)	11.5 (8a, 7), 4.0 (8a, 1), 13.9 (8a, 8e), 3.0 (8a, 6a)	30.7
8e	2.14 (ddd)	13.9 (8a, 8e), 5.9 (8e, 7), 1.7 (8e, 1)	
2-*N*-Phenyl	7.25 (m, 1 H)		124.0 (2C)
	7.42 (m, 2 H)		126.0
	7.44 (m, 2 H)		129.0 (2C)
			139.9*
5-Anilino	6.36 (d, 2 H)	8.8	113.1 (2C)
	6.68 (t, 1 H)	7.3	117.7
	7.09 (dd, 2 H)	7.3, 8.8	129.2 (2C)
			146.1
7-Phenyl	7.33 (m, 1 H)		127.5 (2C)
	7.38 (m, 2 H)		127.1
	7.42 (m, 2 H)		128.8 (2C)
			140.1*
NH	3.89 (br)		—

* Assignments are interchangeable.

Table 2 Experimental and calculated vicinal coupling constants for compound **5**, in an eclipsed conformation (Φ° is the dihedral angle)

Coupling	J (exp)	Φ° (eclipsed)	J (calc)
1, 8a	4.0	60	3.4
1, 8e	1.7	60	2.6
1, 6a	~ 3.5	60	3.4
1, 6e	2.1	60	2.6
4, 5	2.8	60	3.0
4, 7	2.8	60	2.8
5, 6a	3.8	120	3.8
5, 6e	9.0	0	9.8
8a, 7	11.5	0	10.4
8e, 7	5.9	120	4.2

di-*N*-phenylphthalamide **9** (0.11 g, 20%), m.p. 255–256 °C (from EtOH) (lit.,[28] 255–260 °C).

With dimethyl isophthalate **3c**. A solution of dimethyl isophthalate (0.16 g, 0.84 mmol) in THF (20 cm^3) was added to LVA **2** (1.68 mmol) in THF (20 cm^3) at −78 °C and the reaction mixture was left for 2 h. It was then allowed to reach ambient temperature when it was evaporated and the residue was suspended in water (20 cm^3). The aqueous layer was extracted with CH_2Cl_2 (3 × 30 cm^3). The combined extracts were washed with water (20 cm^3), dried ($MgSO_4$) and evaporated and the residue was fractionated by column chromatography [Al_2O_3 (neutral, activity 1, 80–200 mesh) hexane–CH_2Cl_2 9:1]. Two products were isolated: (Z)-2-*anilino*-1-(3′-*methoxycarbonylphenyl*)*prop*-2-*en*-1-*one* **11** as a yellow solid (0.17 g, 35%), m.p. 110–111 °C (from EtOH) (Found: C, 70.9; H, 5.3; N, 5.0. $C_{17}H_{15}NO_3$ requires C, 71.23; H, 5.34; N, 4.98%); R_f(CH_2Cl_2) 0.57; δ_H(300 MHz; $CDCl_3$) 3.90 (3 H, s, OCH_3), 6.00 (1 H, d, J 7.8, 2-H), 7.00 (1 H, t‡, 4″-H), 7.01 (2 H, d, J 8.6, 2″-H), 7.29 (2 H, dd, J 7.3, 8.6, 3″-H), 7.47 (1 H, t, J 7.8, 5′-H), 7.50 (1 H, dd, J 7.8, 12.5, 3-H), 8.01 (2 H, m, 4′-H, 6′-H), 8.52 (1 H, m, 2′-H) and 12.05 (1 H, d, J 12.5, NH); δ_C(75 MHz; $CDCl_3$) 52.2 (OCH_3), 93.5 (C-2), 116.4 (C-2″), 124.0 (C-4″), 128.4 (C-2′), 128.7 (C-5′), 129.8 (C-3″), 130.4 (C-3′), 131.6 (C-4′†), 132.4 (C-6′†), 139.4 (C-1′), 140.0 (C-1″), 145.5 (C-3), 166.7 (CO_2) and 189.7 (C-1). The second product isolated was 3-*methoxycarbonyl*-N-*phenylbenzamide* **13** as a colourless solid (0.14 g, 30%), m.p. 139–140 °C (from EtOH) (Found: C, 70.5; H, 5.2; N, 5.5. $C_{15}H_{13}NO_3$ requires C, 70.59; H, 5.10; N, 5.49%); R_f (CH_2Cl_2) 0.32; δ_H(300 MHz; $CDCl_3$) 3.91 (3 H, s, OCH_3), 7.16 (1 H, t, J 8.0, 4′-H), 7.36 (2 H, t, J 8.0, 3′-H), 7.53 (1 H, t, J 7.8, 5-H), 7.66 (2 H, d, J 8.0, 2′-H), 8.10 (1 H, d, J 7.8, 4-H†), 8.17 (1 H, d, J 7.8, 6-H†) and 8.46 (1 H, s, 2-H); δ_C(75 MHz; $CDCl_3$) 52.2 (OCH_3), 120.1 (C-2′), 124.5 (C-4′), 127.4 (C-2), 128.7 (C-5, C-3′), 130.2 (C-3), 131.7 (C-4†), 132.3 (C-6†), 135.0 (C-1), 137.4 (C-1′), 164.6 (NC=O) and 166.0 (CO_2).

With ethyl phenylpropiolate **3d**. A solution of ethyl phenylpropiolate **3d** (0.30 g, 1.68 mmol) in THF (20 cm^3) was added to the anion **2** (1.68 mmol) in THF (20 cm^3) at −78 °C and the reaction mixture was left for 2 h. It was then allowed to reach ambient temperature when it was evaporated and the residue was suspended in distilled water (30 cm^3). The aqueous layer was extracted with diethyl ether (3 × 30 cm^3). The combined extracts were then washed with water (20 cm^3), dried ($MgSO_4$), and evaporated to yield the crude product mixture as a yellow solid, which was fractionated by column chromatography [Al_2O_3 (neutral, activity 1, 80–200 mesh) hexane–CH_2Cl_2 4:1]. Three compounds were isolated: (Z)-5-*anilino*-1-*phenylpent*-4-*en*-1-*yn*-3-*one* **14**, which upon further purification by preparative TLC [Al_2O_3 E60 F_{254} neutral (Merck) CH_2Cl_2 R_f 0.77], yielded yellow crystals* (0.21 g, 50%), m.p. 99–100 °C (decomp.) (from EtOH); δ_H(300 MHz; $CDCl_3$) 5.60 (1 H, d, J 7.7, 4-H), 7.08 (3 H, m, 2″-H, 4″-H), 7.30–7.43 (5 H, m, 3′-H, 4′-H, 3″-H), 7.42 (1 H, dd‡, J 7.7, 13.6, 5-H), 7.57 (2 H, m, 2′-H) and 11.75 (1 H, br d, J 13.6, NH); δ_C(75 MHz; $CDCl_3$) 88.2 (C-2), 89.6 (C-1), 100.45 (C-4), 116.6 (C-2″), 121.1 (C-1′); 124.3 (C-4″), 128.4 (C-3′); 129.75 (C-3″), 129.8 (C-4′), 132.65 (C-2′), 139.8 (C-1″), 144.80 (C-5) and 175.89 (C-3); m/z 247 (M^+, 100%), 219 (45), 217 (20), 180 (6), 115 (43), 102 (12) and 77 (17) (Found: M^+, 247.093. $C_{17}H_{13}NO$ requires M, 247.099). The second product isolated was confirmed to be compound **5**. The third product was determined to be 1,4-*diphenylpyridin*-2(1H)-*one* **15** and was purified further by preparative TLC [Al_2O_3 E60 F_{254} neutral (Merck) CH_2Cl_2; R_f 0.11] to give an orange solid* (83 mg, 20%), m.p. 198 °C (decomp.) (from Et_2O); ν_{max}(NaCl)/cm^{-1} 1663.4 (C=O) and 1260.9 (C–O); δ_H(300 MHz; $CDCl_3$) 6.48

* Slight decomposition observed on storage at 5 °C. High resolution mass spectrum obtained.

(1 H, m‡, 5-H), 6.55 (1 H, br s, 3-H), 7.03–7.31 (10 H, m, 2 × phenyl-H) and 7.56 (1 H, br d‡, *J* 7.6, 6-H); δ_C(75 MHz; $CDCl_3$) 117.4 (C-5), 119.8 (C-3), 126.4 (C-2′), 127.95 (C-2″), 128.15 (C-4′), 128.7 (C-3″, C-4″), 129.1 (C-3′), 134.05 (C-1″), 141.8 (C-6), 141.9 (C-1′), 150.9 (C-4) and 179.0 (C-2); *m*/*z* 247 (M^+, 17%), 219 (60), 116 (12), 109 (10), 86 (11), 84 (11), 77 (12) and 49 (100) (Found: M^+, 247.096. $C_{17}H_{13}NO$ requires *M*, 247.099).

Acknowledgements

Dr. Balbino Mancheño is indebted to the Dirección General de Investigación Científica y Técnica (CDGICYT) of Spain, for financial support during his stay at the University of Florida. We also acknowledge the assistance of Dr. R. W. King with the ^1H and ^{13}C NMR experiments.

References

1 J. K. Whitesell and M. A. Whitesell, *Synthesis*, 1983, 517.
2 G. Wittig and H. Reiff, *Angew. Chem.*, 1968, **80**, 8.
3 G. Büchi and H. Wüest, *J. Org. Chem.*, 1969, **34**, 1122.
4 M. S. Chattha and A. M. Aguiar, *J. Org. Chem.*, 1971, **36**, 2892.
5 W. G. Dauben, G. H. Beasley, M. D. Broadhurst, B. Muller, D. J. Peppard, P. Pesnelle and C. Suter, *J. Am. Chem. Soc.*, 1975, **97**, 4973.
6 E. J. Corey, D. Enders and M. G. Bock, *Tetrahedron Lett.*, 1976, 7.
7 G. Bartoli, C. Cimarelli, G. Palmieri, M. Bosco and R. Dalpozzo, *Synthesis*, 1990, 895.
8 A. R. Katritzky, R. A. Barcock, Q.-H. Long, M. Balasubramanian, N. Malhotra and J. V. Greenhill, *Synthesis*, 1993, 233.
9 G. Wittig and H.-D. Frommeld, *Chem. Ber.*, 1964, **97**, 3548.
10 G. Wittig, R. Röderer and S. Fischer, *Tetrahedron Lett.*, 1973, 3517.
11 J.-F. Le Borgne, *J. Organomet. Chem.*, 1976, **122**, 139.
12 K. Takabe, H. Fujiwara, T. Katagiri and J. Tanaka, *Tetrahedron Lett.*, 1975, 1239.
13 S. Wegmann and E.-U. Würthwein, *Tetrahedron Lett.*, 1993, 307.
14 S. J. Cristol and R. L. Snell, *J. Am. Chem. Soc.*, 1958, **80**, 1950.
15 W. G. Dauben and R. L. Cargill, *Tetrahedron*, 1961, **15**, 197.
16 S. J. Cristol and R. L. Snell, *J. Am. Chem. Soc.*, 1954, **76**, 5000.
17 G. N. Fickes and T. E. Metz, *J. Org. Chem.*, 1978, **43**, 4057.
18 G. Bartoli, M. Bosco, C. Cimarelli, F. Dalpozzo and G. Palmieri, *Synlett*, 1991, 229.
19 E. Pretsch, T. Clerc, J. Seibl and W. Simon, *Tables of Spectral Data for Structure Determination of Organic Compounds* (trans. K. Biemann), Springer-Verlag, Berlin and Heidelberg, 1989.
20 A. P. Marchand, *Stereochemical Applications of NMR Studies in Rigid Bicyclic systems*, Verlag Chemie International, Deerfield Beach, Florida, 1982.
21 L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, Pergamon Press, Oxford, 1969, p. 280.
22 C. M. Cerda-García-Rojas, L. G. Zepeda and P. Joseph-Nathan, *Tetrahedron Computer Methodology*, 1990, **3**, 113.
23 C. A. G. Haasnoot, F. A. A. M. de Leeuw and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
24 D. B. Roll, B. J. Nist and A. C. Huitric, *Tetrahedron*, 1964, **20**, 2851.
25 A. R. Katritzky, B. Pilarski and L. Urogdi, *Org. Prep. and Proced. Int.*, 1989, **21**, 135.
26 L. M. Roch, *Ann. Chim. (Paris)*, 1961, **55**, 105.
27 M. L. Sherrill, F. L. Schaeffer and E. P. Shoyer, *J. Am. Chem. Soc.*, 1928, **50**, 474.
28 A. T. Dann, W. Davies, A. N. Hambly, R. E. Paul and G. C. S. Semmens, *J. Chem. Soc.*, 1933, 15.

Paper 3/04093C
Received 13*th July* 1993
Accepted 1*st September* 1993