New Features in the Intramolecular Capture of Nitrile Imines by the Sulphide Function

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o-Alkenylthio and *o*-alkynylthio substituted arylhydrazonyl chlorides (**2**) and (**9**) react with triethylamine in acetonitrile at room temperature to give 3*H*-4,1,2-benzothiadiazines (**6**) and (**13**) as a result of intramolecular attack of the sulphur on the intermediate nitrile imines (**3**) and (**10**) followed by a 2,3-sigmatropic shift in the resulting ylides (**5**) and (**12**). The reaction leading from the nitrile imine intermediates to benzothiadiazines is reversed on heating, allowing formation of intramolecular 1,3-dipolar cycloadducts (**4**) and (**11**) as the thermodynamic products. In one case, (**13b**), a novel diazetobenzothiazine (**14**) is formed.

In the course of our studies on functionalised 1,3-dipoles as precursors of heterocyclic systems, we found that *N*-aryl nitrile imines bearing a sulphide function in the *ortho* position can afford different cyclisation products, including 4,1,2-benzothiadiazines.[1] To shed light on the basic steps leading to the final products as well as on the factors governing the competitive modes of reaction, we have widened our investigation to take into account a greater variety of substituents on the sulphur and carbon atoms. Furthermore, reaction conditions other than those previously described were checked with the aim of facilitating the isolation of primary products. In the present paper, we report the behaviour of the nitrile imines (**3a—e**) and (**10a—d**) in acetonitrile (see Schemes 1 and 2).

Results

The nitrile imines under study were generated *in situ* from the hydrazonyl chlorides (**2a—e**) and (**9a—d**) which where, in turn, prepared by diazotisation of the appropriate *ortho*-substituted anilines and subsequent coupling with ethyl 2-chloroacetoacetate or 1-chloro-1-(4-nitrophenyl)propan-2-one. When compounds (**2a—e**) and (**9a—d**) were treated with an excess of triethylamine in acetonitrile at room temperature, a fast, clean reaction took place giving the products listed in Table 1. However, some of the isolated 3*H*-4,1,2-benzothiadiazines were found to be instable compounds which decomposed when heated as well as, partly at least, by chromatographic treatment on silica gel or alumina. In boiling benzene, both in the presence and in the absence of triethylamine, compounds (**6d, e**) and (**13a—d**) changed completely during periods of time in the range 15—170 h to give, beside some uncharacterisable material, the products indicated in Table 2. Under the same conditions, compounds (**6a—c**) were recovered unchanged after 3 days. It is worth noting that, when the reaction of the hydrazonyl chlorides (**2a—e**) and (**9a—d**) with triethylamine was carried out in benzene, the disappearance of the starting substrates was complete only after prolonging refluxing. Consequently, complex mixtures were usually obtained containing both benzothiadiazines and their conversion products; under these conditions, the isolation in the pure state of the benzothiadiazines was sometimes precluded.

Structural assignments to the products rely upon analytical and spectra data (see Table 3). The uncommon structure of 2-ethoxycarbonyl-3-methylene-2a-phenyl-2a,3-dihydro[1,2]diazeto[4,1-*c*][1,4]benzothiazine (**14**) was elucidated by *X*-ray diffraction analysis.[2]

Table 1. Reaction of the hydrazonyl chlorides (**2**) and (**9**) with triethylamine in acetonitrile at room temperature

Compound	Time (min)	Products[a]	Yields (%)	Isolation procedure[b,c]
(**2a**)	120	(**6a**)	72	A
		(**4a**)	5	[LP–Et_2O (2:1)]
(**2b**)	120	(**6b**)	69	A
		(**4b**)	4	[LP–Et_2O (2:1)]
(**2c**)	120	(**6c**)	82	A (toluene)
(**2d**)	40	(**6d**)	75	A
		(**4d**)	5	[LP–Et_2O (1:1)]
(**2e**)	40	(**6e**)	67	A
		(**4e**)	11	[LP–Et_2O (1:1)]
(**9a**)	30	(**13a**)	79	*d*
(**9b**)	40	(**13b**)	74	B
(**9c**)	20	(**13c**)	72	B
		(**11c**)	*e*	
(**9d**)	20	(**13d**)	81	B

[a] In order of elution. [b] A, Chromatography on silica gel column (eluant in parentheses); B, treatment of the crude product with di-isopropyl ether and filtration. [c] LP = light petroleum. [d] Crude product of *ca.* 95% purity. [e] This compound was evidenced in the crude product mixture, but not isolated; the ratio (**13c**):(**11c**) was approximately 85:15 (n.m.r.).

Table 2. Thermal reaction of 3*H*-4,1,2-benzothiadiazines (**6**) and (**13**) in boiling benzene[a]

Compound	Time (h)	Products[a]	Yields[b] (%)	Eluant[c]
(**6d**)	170	(**4d**)	33	LP–Et_2O (2:1)
(**6e**)	150	(**4a**)	51	LP–Et_2O (2:1)
(**13a**)	72	(**11a**)	59	LP–Et_2O (1:1)
(**13b**)	90	(**14**)	13	LP–Et_2O (2:1)
		(**11b**)	49	
(**13c**)	15	(**11c**)	53	CH_2Cl_2
(**13d**)	25	(**11d**)	62	CH_2Cl_2

[a] Compounds (**6a—c**) were recovered unchanged after 3 days. [b] After chromatography on silica gel column to remove some tarry material and uncharacterised by-products. [c] LP = light petroleum.

Discussion

The results now reported reveal that, under the conditions investigated, the hydrazonyl chlorides studied follow a general reaction course resulting exclusively or predominantly in 3*H*-

Table 3. Physical, spectral, and analytical data of new heterocyclic compounds[a,b,c]

Compound	M.p. (°C) (recrystallisation solvent)	$\nu_{max.}$ (Nujol)/ cm^{-1}	$\delta(CDCl_3)$[d]	Elemental analysis (%) Found (required) C	H	N
(4d)	145 (Pr^i_2O)		3.0—3.7 (4 H, m), 4.2—4.4 (1 H, m), 6.7—8.3 (8 H, m)	61.9 (61.7)	4.1 (4.2)	13.2 (13.5)
(4e)	157 (Toluene)		1.56 (3H, s), 2.95, 3.26 (2H, AB type, *J* 12), 3.29 (2 H, s), 6.6—7.3 (3 H, m), 7.5—8.3 (5 H, m)	62.5 (62.7)	4.8 (4.6)	12.7 (12.9)
(6c)	(B.p. 140—143 °C/ 0.2 mmHg)	1 730	1.04 (3 H, t), 1.43, 1.50 (3 H, two d), 3.2—3.8 (1 H, m), 4.03 (2 H, q), 5.0—5.4 (2 H, m), 5.8—6.5 (1 H, m), 7.2—7.5 (3 H, m), 7.9—8.1 (1 H, m)	60.9 (60.8)	5.8 (5.9)	10.0 (10.1)
(6d)[e]	95 (n-Hexane)		3.28 (2 H, d, *J* 7), 4.9—5.2 (2 H, m), 5.6—6.0 (1 H, m), 7.1—7.4 (3 H, m), 7.6—8.2 (5 H, m)	61.7 (61.7)	4.4 (4.2)	13.4 (13.5)
(6f)[f]	98 (Pr^i_2O)		1.61 (3 H, s), 3.28 (2 H, s), 4.6—4.9 (2 H, m), 7.1—7.4 (3 H, m), 7.6—8.2 (5 H, m)	62.5 (62.7)	4.8 (4.6)	12.7 (12.9)
(7)	58 (Pr^i_2O)	1 720	1.74 (3 H, s), 3.39 (2 H, s), 3.78 (3 H, s), 3.90 (3 H, s), 4.7—4.9 (2 H, s), 7.2—8.4 (8 H, m)	59.2 (59.1)	4.7 (4.5)	8.8 (9.0)
(11b)	117 (n-Hexane)	1 710	1.27 (3 H, t), 3.97 (2 H, s), 4.32 (2 H, q), 7.1—7.5 (8 H, m), 8.05—8.25 (1 H, m)	67.6 (67.8)	4.9 (4.9)	8.4 (8.3)
(11c)	206 (Toluene)		4.13 (2 H, s), 6.61 (1 H, s), 7.15—7.55 (3 H, m), 8.0—8.4 (5 H, m)	62.3 (62.1)	3.4 (3.6)	13.7 (13.6)
(11d)	160 (Pr^i_2O)		4.00 (2 H, s), 7.1—8.3 (13 H, m)	68.7 (68.6)	3.9 (3.9)	10.7 (10.9)
(13a)[g]	*h*	1 950 1 735	1.30 (3 H, t), 4.35 (2 H, q), 4.90 (2 H, d, *J* 6), 5.55 (1 H, t, *J* 6), 7.2—7.5 (3 H, m), 7.9—8.1 (1 H, m)			
(13b)[i]	82 (Pr^i_2O)	1 930 1 740	1.08 (3 H, t), 4.22 (2 H, q), 4.98, 5.15 (2 H, AB type, *J* 12), 7.1—7.7 (8 H, m), 7.8—8.1 (1 H, m)	67.5 (67.8)	4.8 (4.8)	8.1 (8.3)
(13c)	110 (Pr^i_2O)	1 945	4.78 (2 H, d, *J* 6), 5.53 (1 H, t, *J* 6), 7.2—7.5 (3 H, m), 7.9—8.5 (5 H, m)	61.9 (62.1)	3.8 (3.6)	13.8 (13.6)
(13d)	138 (Pr^i_2O)	1935	4.80, 5.18 (2 H, AB type, *J* 12), 7.0—7.5 (8 H, m), 7.9—8.4 (5 H, m)	68.6 (68.6)	4.1 (3.9)	10.7 (10.9)
(14)	92 (Pr^i_2O)	1 710	1.36 (3 H, t), 4.37 (2 H, q), 5.80 (1 H, s), 6.13 (1 H, s), 6.8—7.4 (6 H, m), 7.5—7.7 (3 H, m)	67.9 (67.8)	4.7 (4.8)	8.3 (8.3)

[a] Compounds (**4a, b**) and (**6a, b**) were described in ref. 1. [b] Compound (**11a**) was described in ref. 12. [c] All compounds listed gave correct molecular peaks in the mass spectra. [d] *J* in Hz. [e] ^{13}C N.m.r. ($CDCl_3$) δ 45.3 (t), 69.8 (s), 118.8—147.7 (set of signals). [f] ^{13}C N.m.r. ($CDCl_3$): δ 24.0 (q), 49.0 (t), 69.0 (s), 117.7—147.0 (set of signals). [g] ^{13}C N.m.r. ($CDCl_3$): δ 14.0 (q), 63.2 (t), 69.5 (s), 80.4 (t), 88.0 (d), 118.4 (s), 126.8 (d), 127.6 (d), 130.3 (d), 131.7 (d), 142.1 (s), 167.7 (s), and 209.2 (s). [h] Undistillable oil (purity >95%). [i] ^{13}C N.m.r. ($CDCl_3$) δ 13.7 (q), 63.2 (t), 73.0 (s), 80.8 (t), 102.0 (s), 118.5 (s), 126.7—133.0 (set of signals), 142.6 (s), 167.8 (s), and 210.4 (s).

4,1,2-benzothiadiazines. As shown in Schemes 1 and 2, a plausible pathway leading to these ring-closed products involves as the first stage the formation of the nitrile imines (**3**) and (**10**), the intervention of which is unquestionable because the hydrazonyl chlorides (**2**) and (**9**) did not change in the absence of triethylamine. These intermediates undergo ring closure owing to the nucleophilic participation of the sulphide function, thus forming the cyclic ylides (**5**) and (**12**) which, in turn, rearrange to the final products through the migration of the *S*-substituent to the α-carbon in accord with a known mode of evolution of sulphonium ylides.[3,4] The structures of the rearranged products demonstrate that this 1,2-migration is the consequence of a [2,3]-sigmatropic process involving a five-membered, cyclic transition state.

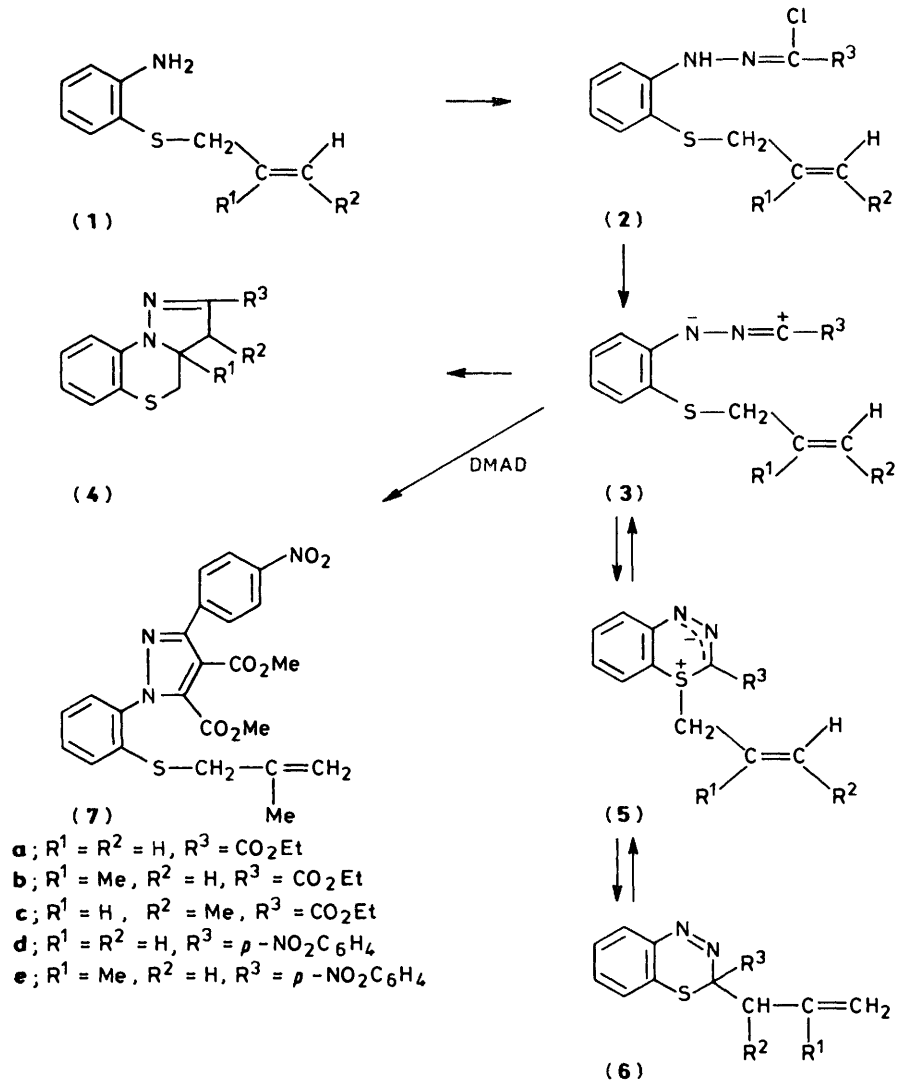
Although no example of intermolecular reaction between sulphides and nitrile imines has been hitherto reported, the ability of the divalent sulphur to capture the nitrile imine moiety is not surprising on considering (i) the potential carbenic nature of nitrile imines[5-7] and (ii) the documented reactivity of sulphides toward carbenes.[3,8] However, the most striking feature of the results here described is the observed reversibility of the pathway going from nitrile imines to 3*H*-4,1,2-benzothiadiazines. In several cases, this pathway was found to be kinetically, but not thermodynamically preferred over the alternative reaction of the nitrile imines (**3**) and (**10**), *i.e.* the intramolecular 1,3-dipolar cycloaddition to the carbon–carbon multiple bond giving fused-ring pyrazolines (**4**) or pyrazoles (**11**). That a nitrile imine is involved in the rearrangement of (**6**) and (**13**) to (**4**) and (**11**) was proven in one case by intercepting it with an external dipolarophile. In fact, when compound (**6e**) was heated in benzene in the presence of dimethyl acetylenedicarboxylate, the pyrazole derivative (**7**) was obtained along with (**4e**).

It should be noted that the cyclic ylides (**5**) and (**12**) could, in principle, evolve according to other pathways, *e.g.* either loss of the *S*-substituent or its 1,4-migration to the γ-nitrogen. This behaviour is similar to that recently found for sulphur–nitrogen ylides having the negative charge on a 1,3-diaza-allyl portion.[9] The observed preference for the 1,2-migration is perhaps due to a moderate enthalpy barrier determined by the concerted, pericyclic nature of the reaction itself.

As to the conversion of (**13**) into the novel tricyclic compound (**14**), little can be said at present, further work being needed to elucidate the driving force and the mechanism of this interesting rearrangement.

Experimental

M.p.s were determined with a Büchi apparatus and are uncorrected. I.r. spectra were taken with a Perkin-Elmer 377 spectrophotometer. ^1H and ^{13}C N.m.r. spectra were recorded with Varian EM-390 and Bruker WP 80 SY instruments,



Scheme 1.

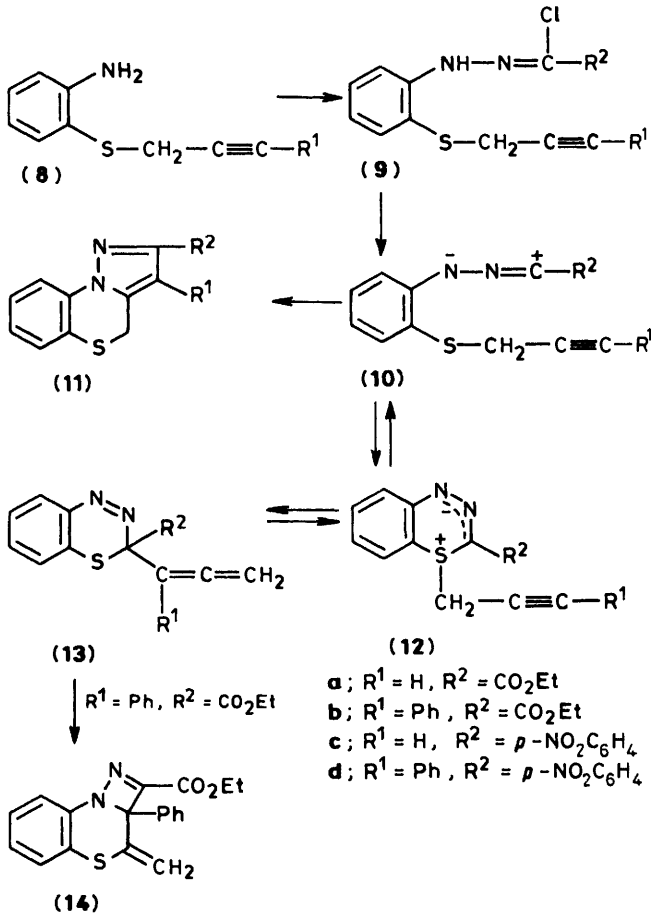
respectively; chemical shifts are given in p.p.m. from internal $SiMe_4$.

The amines (**1a**),[10] (**1b**),[11] (**8a**),[12] and (**8b**)[13] are known compounds. Preparations of the hydrazonyl chlorides (**2a, b**)[1] and (**9a**)[12] from (**1a, b**) and (**8a**) have been previously reported.

Preparation of the Amine (**1c**).—A solution of sodium 2-aminothiophenolate (0.124 mol) in ethanol (300 ml) was treated with *trans*-1-bromobut-2-ene (0.125 mol) and stirred at room temperature for 2 h. The solvent was partly removed under reduced pressure and the residue was taken up with chloroform and water. The organic layer was washed with aqueous sodium hydroxide, dried (Na_2SO_4), and evaporated. Fractional distillation of the residue under reduced pressure gave (**1c**) (79%), b.p. 96—99 °C/0.2 mmHg; δ($CDCl_3$) 1.6—1.7 (3 H, m), 3.2—3.4 (2 H, m) 4.3 (2 H, br s), 5.3—5.6 (2 H, m), 6.6—6.8 (1 H, m), and 7.0—7.5 (3 H, m).

Preparation of the Hydrazonyl Chloride (**2c**).—A solution of sodium nitrite (60 mmol) and ethyl 2-chloroacetoacetate (200 mmol) in 85% aqueous ethanol (180 ml) was cooled at −5 °C. A solution of (**1c**) (33 mmol) in 0.5 M-hydrochloric acid (200 ml) was added dropwise with vigorous stirring and ice cooling. The mixture was adjusted to pH 4 with sodium acetate and stirred at room temperature for 3 h. The solvent was partly removed under reduced pressure and the residue was extracted several times with ether. The organic solution was washed with aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. The excess of ethyl 2-chloroacetoacetate was removed under reduced pressure and the residue chromatographed on a silica gel column with toluene as eluant to afford (**2c**) (27%), m.p. 58—59 °C (from pentane); δ($CDCl_3$) 1.45 (3 H, t), 1.59 (3 H, d, *J* 6.5 Hz), 3.35 (2 H, d, *J* 6.5 Hz), 4.42 (2 H, q), 5.1—5.6 (2 H, m), 6.85—7.05 (1 H, m), 7.25—7.65 (3 H, m), and 9.7 (1 H, br s).

Preparation of Hydrazonyl Chlorides (**2d, e**) *and* (**9c, d**).—A solution of (**1a**) (9.0 mmol) in 1 M-hydrochloric acid (27 ml) was cooled at 0 °C and treated with sodium nitrite (11.0 mmol) in water (22 ml) with vigorous stirring. The mixture was filtered rapidly to remove some undissolved material and the cold filtrate was added dropwise to a solution of 1-chloro-1-(4-nitrophenyl)propan-2-one[14] (14.0 mmol) and sodium acetate (27 mmol) in 70% aqueous methanol (50 ml), with stirring and ice cooling. The resulting mixture was stirred at room temperature for 3 h and then extracted with diethyl ether. The organic layer was washed with water, dried (Na_2SO_4), and



Scheme 2.

evaporated. The residue was chromatographed on a silica gel column with light petroleum–diethyl ether (1:1) as eluant to give (**2d**) (34%), m.p. 84—85 °C (from di-isopropyl ether); δ($CDCl_3$) 3.45 (2 H, d, *J* 7 Hz), 4.8—5.2 (2 H, m), 5.5—6.2 (1 H, m), 6.7—8.4 (8 H, m), and 9.6 (1 H, br s).

Following the same procedure, the amines (**1b**), (**8a**), and (**8b**) were converted into (**2e**), (**9c**), and (**9d**), respectively. Yields, melting points, and n.m.r. data are as follows: (**2e**) (42%), m.p. 81—82 °C (from ethanol); δ($CDCl_3$) 1.93 (3 H, s), 3.40 (2 H, s), 4.5—4.8 (2 H, m), 6.7—8.4 (8 H, m), and 9.5 (1 H, br s); (**9c**) (30%), m.p. 141—142 °C (from ethanol); δ($CDCl_3$) 2.23 (1 H, t, *J* 2.5 Hz), 3.50 (2 H, d, *J* 2.5 Hz), 6.8—8.4 (8 H, m), and 9.6 (1 H, br s); (**9d**) (35%), m.p. 161—162 °C (from ethanol); δ($CDCl_3$) 3.73 (2 H, s), 6.9—8.3 (13 H, m), and 9.7 (1 H, br s).

Preparation of the Hydrazonyl Chloride (**9b**).—A mixture of (**8b**) (10 mmol), 1M-hydrochloric acid (30 ml), methanol (30 ml), and ethyl 2-chloroacetoacetate (20 mmol) was cooled at 0 °C. Sodium nitrite (12 mmol) in water (30 ml) was added with vigorous stirring and cooling. The mixture was adjusted to pH 4 with sodium acetate, stirred at room temperature for 3 h, and extracted with ether. The organic solution was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on a silica gel column with dichloromethane as eluant to give (**9b**) (55%), m.p. 70—71 °C (from pentane); δ($CDCl_3$) 1.38 (3 H, t), 3.70 (2 H, s), 4.34 (2 H, q), 6.8—7.8 (9 H, m), and 9.7 (1 H, br s).

Reaction of the Hydrazonyl Chlorides (**2a—e**) *and* (**9a—d**) *with Triethylamine.*—A solution of (**2**) or (**9**) (5 mmol) in acetonitrile (250 ml) was treated with triethylamine (25 mmol) and stirred at room temperature for the time given in Table 1. The solvent was removed under reduced pressure and the residue taken up with benzene and water. The organic solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was worked up as indicated in Table 1 to give the products listed therein.

Thermal Reaction of 3H-4,1,2-*Benzothiadiazines* (**6d, e**) *and* (**13a—d**).—A solution of (**6**) or (**13**) (2 mmol) in benzene (100 ml) was treated with triethylamine (10 mmol) and refluxed for the time given in Table 2. The solvent was removed under reduced pressure and the residue chromatographed on a silica gel column to afford the products indicated in Table 2.

Minor changes in times and yields were observed when the reaction was performed without addition of triethylamine.

Thermal Reaction of Compound (**6e**) *in the Presence of Dimethyl Acetylenedicarboxylate.*—A solution of (**6e**) (0.30 g) and dimethyl acetylenedicarboxylate (0.78 g) in benzene (50 ml) was refluxed for 7 days. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column. Elution with light petroleum–diethyl ether (8:1) gave (**4e**) (90 mg) followed by (**7**) (0.16 g).

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