Addition Reactions of Lithium Ester Enolates, α-Lithionitriles, and Sodium Amides to Dimethyl(vinyl)sulphonium Salts

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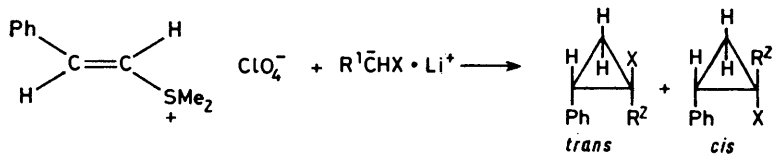
Reactions of dimethyl(vinyl)sulphonium salts (1) with some lithium ester enolates and α-lithionitriles (2) give cyclopropanes (3). However, when the α-carbon atoms of the lithium salt are tertiary [compounds (4)] butene derivatives (5) are formed. With α-lithiopropio- and α-lithiobutyro-nitriles (8), moreover, pyrrolines (11) are obtained. Sodium *N*-methylacetamide adds to dimethylstyrylsulphonium perchlorate (1a) to yield *N*-methyl-*N*-(1-phenylvinyl)acetamide (16).

VINYLSULPHONIUM salts are useful reagents as good Michael acceptors in reactions with nucleophiles such as hydroxide ion,[1] phenoxide ion,[2] active methylene compounds,[3] and sulphonium ylides.[4] In addition, we have recently shown that the salts react with ketone enolate anions to yield cyclopropanes, oxirans, and thiadecalins depending upon the substituents of the nucleophiles.[5] We now report addition reactions of lithium ester enolates, α-lithionitriles, and sodium amides to the salts.



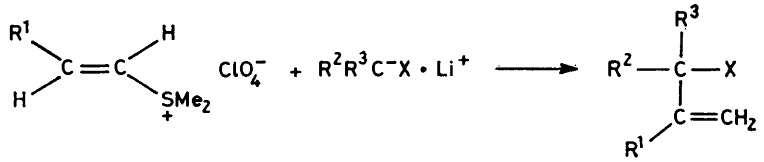
(1a) (2) a; R^1 = H, X = CO_2Et; b; R^1 = Bu^n, X = CO_2Et; c; R^1 = H, X = CN

(3) a; R^2 = H, X = CO_2Et; b; R^2 = Bu^n, X = CO_2Et; c; R^2 = C(Ph)=CH_2, X = CN

SCHEME 1

When dimethylstyrylsulphonium perchlorate (1a) was heated with ethyl lithioacetate (2a), generated by the treatment of ethyl acetate with lithium di-isopropylamide, at 50 °C in THF–DMF (1 : 1), *trans*-1-ethoxycarbonyl-2-phenylcyclopropane (3a) was obtained in 42% yield. Similarly the cyclopropanes (3b and c) were formed by reaction of the salt (1a) with lithium ester enolate (2b) or α-lithionitrile (2c), respectively (Scheme 1). ^{1}H N.m.r. spectra of the cyclopropanes (3b and c) showed the product (3b) to be a mixture of *trans*- and *cis*-isomers in the ratio 3 : 7 whilst (3c) was the pure *cis*-isomer. The product (3c) was presumably formed from further reaction of the expected initially formed 1-cyano-2-phenylcyclopropane (which was not isolated) with a further quantity of the salt (1a).

On the other hand, lithium ester enolates or α-lithionitriles (4), whose α-carbons were tertiary, reacted with the salts (1) to give butene derivatives (5) in good yields (Scheme 2). In the reaction of (1a) with (4a), a by-product formulated as $C_{14}H_{18}OS$ was obtained in 20% yield; structural assignment, however was unsuccessful. Formation of cyclopropanes (3) and butene derivatives (5) is explained as follows. While the nucleophiles (2) add to the salts (1) to give betaines (6), followed by the elimination of dimethyl sulphide, addition reactions of (4) to (1) afford ylides (7) which are easily changed to the alkenes (5) *via* a Hofmann-type elimination.[6]



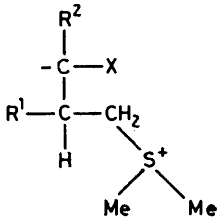
(1) a; R^1 = Ph; b; R^1 = Pr^i

(4) a; R^2 = R^3 = Me, X = CO_2Et; b; R^2 = Me, R^3 = Ph, X = CO_2Et; c; R^2 = R^3 = Me, X = CN

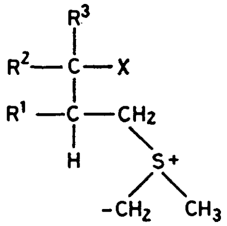
(5) a; R^1 = Ph, R^2 = R^3 = Me, X = CO_2Et; b; R^1 = R^3 = Ph, R^2 = Me, X = CO_2Et; c; R^1 = Ph, R^2 = R^3 = Me, X = CN; d; R^1 = Pr^i, R^2 = R^3 = Me, X = CN

SCHEME 2

Furthermore, the reactions of (1a) with α-lithiopropionitrile (8a) and α-lithiobutyronitrile (8b) under conditions identical to those described above gave the pyrrolines (11) together with trace amounts of the β-aminoacrylonitriles (10) but none of the expected cyclopropanes. The lithium salts (9), were presumed as intermediates in these reactions, which took place at an appreciably faster rate than that of addition reactions of



(6)



(7)

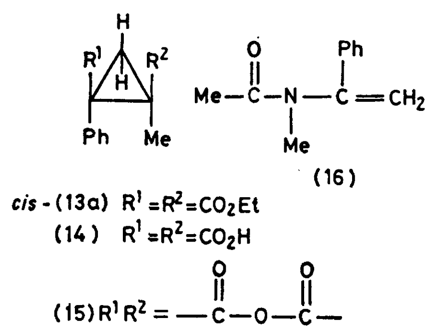
(8) to (1a) (Scheme 3). In fact, β-aminoacrylonitriles (10) prepared independently from corresponding nitriles and lithium di-isopropylamide,[7] reacted with (1a) to give the pyrrolines (11) in good yields.

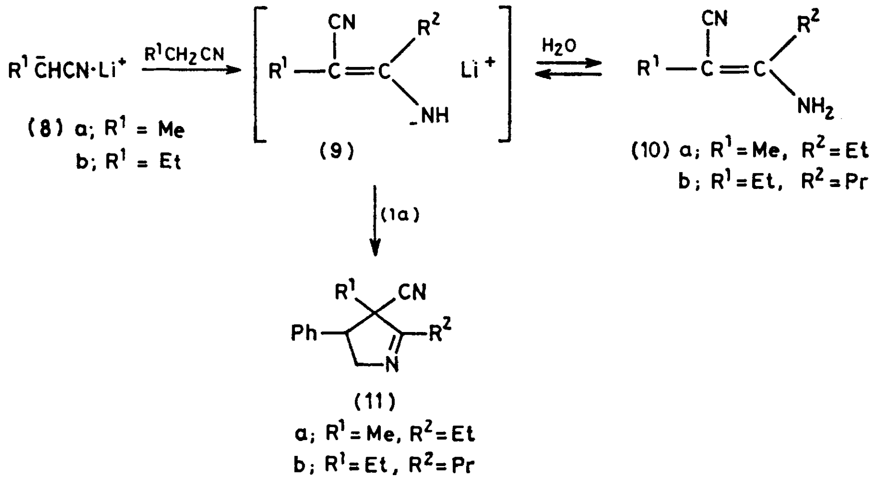
Although many reactions of vinylsulphonium salts with active methylene compounds have been reported to yield cyclopropanes, α-monoalkylated ones would be expected to afford olefins corresponding to (5) on the basis of the results described above. The salt (1a), however, reacted with ethyl lithiomethylmalonate (12a) to unexpectedly give 1,2-diethoxycarbonyl-2-methyl-1-phenylcyclopropane (13a) in 64% yield. Similar results were obtained in the reactions of (1a) with other enolates (12b and c) (Scheme 4).

While the cyclopropane (13c) was obtained as the *cis*-isomer alone, (13a and b) were obtained as mixtures of *cis*- and *trans*-isomers in the ratios 10 : 1 and 9 : 1, respectively.* The structures of (13) were determined by spectral data and elemental analyses (see Experimental section); *trans*-(13a) was identified by comparison (i.r., g.l.c.) with an authentic sample prepared from 1,2-diethoxycarbonyl-1-phenylprop-1-ene (*cis* : *trans* 1 : 1) and dimethyloxosulphonium methylide. Alkaline hydrolysis of *cis*-(13a) and subsequent thermolysis at 180 °C gave the acid anhydride (15) in 62% yield. It has been reported that thermal treatment of cyclopropane-1,2-dicarboxylic acid leads to an acid anhydride whilst cyclopropane-1,1-dicarboxylic acid decarboxylates to form the monocarboxylic acid.[8]

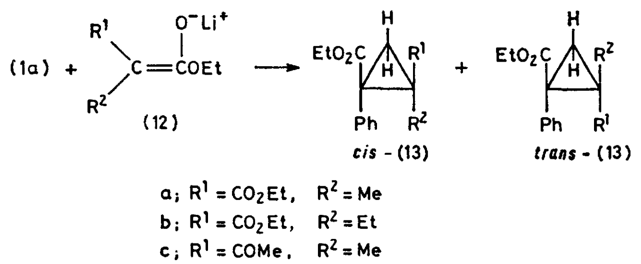
Although further work will be necessary to clarify the reaction mechanism, migration of an ethoxycarbonyl group is of interest in the synthesis of cyclopropane-1,2-dicarboxylic acid derivatives.

The vinylsulphonium salt (1a) reacted with sodium *N*-methylacetamide at 150 °C to yield *N*-methyl-*N*-(1-phenylvinyl)acetamide (16) in 69% yield. Attempts at similar reactions with other amides such as *N*-phenylacetamide and isatin were unsuccessful. The reaction unfortunately lacks generality since the decomposition of (1) takes place faster than the addition reaction at elevated temperatures.





SCHEME 3



SCHEME 4

* The ratios were determined by g.l.c. but only *cis*-isomers were isolated and characterized as pure samples.

Finally, the addition reactions of lithium ester enolates and α-lithionitriles to vinylsulphonium salts provide a convenient method for the synthesis of cyclopropanes, olefins, and pyrrolines, thus showing the versatility of these salts in organic synthesis.

EXPERIMENTAL

M.p.s were determined with a Yanagimoto micro-apparatus. ^{1}H N.m.r. spectra were recorded for solutions in $CDCl_3$ (Me_4Si as internal reference) with a JEOL JNM-PMX-60 spectrometer, i.r. spectra with a JASCO IR-E spectrophotometer, and mass spectra with a Hitachi RMU-6E instrument.

The preparations of *trans*-dimethylstyrylsulphonium perchlorate (1a) and trans-dimethylisobutenylsulphonium perchlorate (1b) were described previously.[5] 3-Amino-2-cyanopent-2-ene (10a) and 4-amino-3-cyanohept-3-ene (10b) were prepared from the corresponding nitriles in the presence of lithium di-isopropylamide:[7] (10a), m.p. 45—47 °C; (10b), b.p. 93—95 °C at 1 mmHg.

General Procedure for the Reaction of Vinylsulphonium Salts (1) *with Lithium Ester Enolates and α-Lithionitriles.*—To a stirred solution of lithium di-isopropylamide (12 mmol) in dry THF (40 ml) at −78 °C was added an equimolar amount of nitrile or ester under N_2 and stirring continued for 3 h. A solution of vinylsulphonium salt (10 mmol) in dry DMF (40 ml) was added to the mixture dropwise at −78 °C. The resulting yellow-orange solution was stirred at 50 °C for 6—15 h. After cooling, the mixture was poured into water (100 ml) and extracted with 80-ml portions of chloroform. The combined extracts were washed with water (100 ml) and saturated brine (100 ml) and dried (Na_2SO_4). After removal of the solvent, the residue was distilled *in vacuo*. Details of the reactions are shown in the Table.

Reactions of vinylsulphonium salts (1) with lithium ester enolates and α-lithionitriles

Sulphonium salts	Nucleophiles	Reaction time (h)	Products	Yield [a] (%)
(1a)	(2a)	12	(3a)	42
(1a)	(2b)	11.5	(3b)	41
(1a)	(2c)	6	(3c)	82 [b]
(1a)	(4a)	7	(5a)	30
(1a)	(4b)	9	(5b)	48
(1a)	(4c)	15	(5c)	73
(1b)	(4c)	8	(5d)	88
(1a)	(8a)	8	(11a)	84 [c]
(1a)	(8b)	8	(11b)	88 [c]
(1a)	(12a)	7	(13a)	64
(1a)	(12b)	9	(13b)	24
(1a)	(12c)	11	(13c)	35

[a] Unchanged vinylsulphonium salts were recovered as methyl vinyl sulphides. [b] Based on (1a). [c] Based on (8).

trans-1-*Ethoxycarbonyl*-2-*phenylcyclopropane* (3a) had b.p. 90—92 °C at 0.5 mmHg (lit.,[9] 93—94 °C at 0.1 mmHg); $\nu_{max.}$ (neat) 1 715, 1 605, and 1 040 cm^{-1}; *m/e* (70 eV) 190 (M^+); δ 1.13—1.36 (4 H, t, and m, *J* 7.0 Hz, Me and CH), 1.44—1.68 (1 H, m, CH), 1.76—2.00 (1 H, m, CH), 2.36—2.60 (1 H, m, CH), 4.13 (2 H, q, *J* 7.0 Hz, C*H*$_2$Me), and 6.95—7.32 (5 H, m, aromatic) (Found; C, 76.1; H, 7.65. $C_{12}H_{14}O_2$ requires C, 75.76; H, 7.42%).

1-*Butyl*-1-*ethoxycarbonyl*-2-*phenylcyclopropane* (3b) had b.p. 100—104 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 710, 1 600, and 1 025 cm^{-1}; *m/e* (70 eV) 246 (M^+); δ 0.64—2.16 (14 H, m), 2.44 (0.7 H, m), 2.76 (0.3 H, m), 4.24 (2 H, q, *J* 7.1 Hz, C*H*$_2$Me), and 7.02—7.44 (5 H, m, aromatic) (Found: C, 77.75; H, 9.0. $C_{16}H_{22}O_2$ requires C, 78.01; H, 9.00%).

trans-1-*Cyano*-2-*phenyl*-1-(β-*styryl*)*cyclopropane* (3c) had b.p. 155—158 °C at 1 mmHg; $\nu_{max.}$ (neat) 2 230, 1 620, 1 600, 1 020, and 900 cm^{-1}; *m/e* (70 eV) 245 (M^+); δ 1.79 (1 H, d of d, *J* 9.1 and 4.5 Hz), 2.00 (1 H, d of d, *J* 6.1 and 4.5 Hz), 2.33 (1 H, d of d, *J* 9.1 and 6.1 Hz), 5.37 (1 H, s, C=C*H*H), 5.55 (1 H, s, C=CH*H*), and 7.20—7.52 (10 H, m, aromatic) (Found: C, 88.1; H, 6.0; N, 5.8. $C_{18}H_{15}N$ requires C, 88.13; H, 6.16; N, 5.71%).

3-*Ethoxycarbonyl*-3-*methyl*-2-*phenylbut*-1-*ene* (5a) had b.p. 65—66 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 720, 1 600, and 910 cm^{-1}; *m/e* (70 eV) 218 (M^+); δ 1.16 (3 H, t, *J* 7.6 Hz, Me), 1.39 (6 H, s, 2 × Me), 4.10 (2 H, q, *J* 7.6 Hz, C*H*$_2$Me), 5.12 (1 H, s, C=C*H*H), 5.28 (1 H, s, C=CH*H*), and 7.08—7.32 (5 H, m, aromatic) (Found: C, 76.7; H, 8.55. $C_{14}H_{18}O_2$ requires C, 77.03; H, 8.31%).

3-*Ethoxycarbonyl*-2,3-*diphenylbut*-1-*ene* (5b) had b.p. 114—116 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 720, 1 620, 1 600, and 905 cm^{-1}; *m/e* (70 eV) 280 (M^+); δ 1.10 (3 H, t, *J* 7.0 Hz, Me), 1.73 (3 H, s, Me), 4.10 (2 H, q, *J* 7.0 Hz, C*H*$_2$Me), 5.17 (1 H, s, C=C*H*H), 5.40 (1 H, s, C=CH*H*), and 7.07—7.63 (10 H, m, aromatic) (Found: C, 81.25; H, 7.25. $C_{19}H_{20}O_2$ requires C, 81.39; H, 7.19%).

3-*Cyano*-3-*methyl*-2-*phenylbut*-1-*ene* (5c) had b.p. 103—105 °C at 5 mmHg; $\nu_{max.}$ (neat) 2 240, 1 620, and 915 cm^{-1}; *m/e* (70 eV) 171 (M^+); δ 1.52 (6 H, s, 2 × Me), 5.12 (1 H, s, C=C*H*H), 5.53 (1 H, s, C=CH*H*), and 7.20—7.36 (5 H, m, aromatic) (Found: C, 84.4; H, 7.45; N, 8.3. $C_{12}H_{13}N$ requires C, 84.17; H, 7.65; N, 8.18%).

3-*Cyano*-2-*isopropyl*-3-*methylbut*-1-*ene* (5d) had b.p. 89—90 °C at 55 mmHg; $\nu_{max.}$ (neat) 2 240, 1 630, and 905 cm^{-1}; *m/e* (70 eV) 137 (M^+); δ 1.13 (6 H, d, *J* 6.4 Hz, 2 × Me), 1.48 (6 H, s, 2 × Me), 2.43 (1 H, m, *J* 6.4 Hz), 4.98 (1 H, s, C=C*H*H), and 5.15 (1 H, s, C=CH*H*) (Found: C, 78,55; H, 11.2; N, 10.25. $C_9H_{15}N$ requires C, 78.77; H, 11.02; N, 10.21%).

3-*Cyano*-2-*ethyl*-3-*methyl*-4-*phenyl*-1-*pyrroline* (11a) had b.p. 140—141 °C at 1 mmHg; $\nu_{max.}$ (neat) 2 200 and 1 600 cm^{-1}; *m/e* (70 eV) 212 (M^+); δ 1.18 (3 H, t, *J* 7.6 Hz, Me), 1.77 (3 H, s, Me), 2.32 (2 H, m, CH_2), 2.49 (2 H, q, *J* 7.6 Hz, C*H*$_2$Me), 3.10 (1 H, m, CH), and 7.26—7.40 (5 H, m, aromatic) (Found: C, 79.1; H, 7.55; N, 13.3. $C_{14}H_{16}N_2$ requires C, 79.21; H, 7.60; N, 13.20%). To a solution of lithium di-isopropylamide (18 mmol) in dry THF (50 ml) at −78 °C was added 2.0 g (18 mmol) of (10a) under N_2 and stirring was continued for 1.5 h. A solution of (1a) (4.0 g, 15 mmol) in dry DMF (50 ml) was added to the reaction mixture at −78 °C. The resulting yellow solution was allowed to stir at 50 °C for 9 h. After similar work-up to above, 2.2 g (69%) of (11a) was obtained.

3-*Cyano*-3-*ethyl*-4-*phenyl*-2-*propyl*-1-*pyrroline* (11b) had b.p. 145—147 °C at 1 mmHg; $\nu_{max.}$ (neat) 2 220 and 1 605 cm^{-1}; *m/e* (70 eV) 240 (M^+); δ 1.09 (6 H, 2 t, *J* 7.0 Hz, 2 × Me), 1.66 (2 H, ses, *J* 7.0 Hz, CH_2C*H*$_2$Me), 2.15 (2 H, q, *J* 7.0 Hz, C*H*$_2$Me), 2.26—2.66 (4 H, m), 3.10 (1 H, m), and 7.15—7.42 (5 H, m, aromatic) (Found: C, 79.7; H, 8.4; N, 11.45. $C_{16}H_{20}N_2$ requires C, 79.95; H, 8.39; N, 11.66%). Similar treatment of (1a) (4.0 g, 15 mmol) with (10b) (2.5 g, 18 mmol) gave 2.0 g (56%) of (11b).

cis-1,2-*Diethoxycarbonyl*-2-*methyl*-1-*phenylcyclopropane* (13a) had b.p. 110—113 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 710, 1 600, and 1 020 cm^{-1}; *m/e* (70 eV) 276 (M^+); δ 1.10 (3 H, s, Me), 1.24 (6 H, t, *J* 7.6 Hz, 2 × Me), 2.20 (1 H, d, *J* 6.1 Hz), 3.34 (1 H, d, *J* 6.1 Hz), 4.14 (4 H, q, *J* 7.6 Hz, 2 ×

CH_2Me), and 7.08—7.40 (5 H, m, aromatic) (Found: C, 69.25; H, 7.55. $C_{16}H_{20}O_4$ requires C, 69.54; H, 7.30%).

cis-1,2-*Diethoxycarbonyl-2-ethyl-1-phenylcyclopropane* (13b) had b.p. 120—125 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 715, 1 600, and 1 020 cm^{-1}; *m/e* (70 eV) 290 (M^+); δ 0.79 (3 H, t, *J* 7.6 Hz, Me), 1.28 (6 H, t, *J* 7.6 Hz, 2 × Me), 1.64 (2 H, q, *J* 7.6 Hz, CH_2Me), 2.46 (1 H, d, *J* 6.1 Hz), 3.40 (1 H, d, *J* 6.1 Hz), 4.16 (4 H, q, *J* 7.6 Hz, 2 × OCH_2Me), and 7.15—7.26 (5 H, m, aromatic) (Found: C, 70.1; H, 7.95. $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64%).

cis-1-*Acetyl-2-ethoxycarbonyl-1-methyl-2-phenylcyclopropane* (13c) had b.p. 98—101 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 720, 1 600, and 1 020 cm^{-1}; *m/e* (70 eV) 246 (M^+); δ 1.12 (3 H, s, Me), 1.24 (3 H, t, *J* 7.0 Hz, CH_2*Me*), 2.30 (3 H, s, Me), 2.39 (1 H, d, *J* 6.2 Hz), 3.42 (1 H, d, *J* 6.2 Hz), 4.18 (2 H, q, *J* 7.0 Hz, OCH_2Me), and 7.09—7.75 (5 H, m, aromatic) (Found: C, 73.1; H, 7.4. $C_{15}H_{18}O_3$ requires C, 73.14; H, 7.37%).

2-*Methyl-1-phenylcyclopropane-1,2-dicarboxylic Anhydride* (15).—A solution of *cis*-(13a) (2.6 g, 9.4 mmol) in aqueous ethanol containing sodium hydroxide (0.8 g) was refluxed for 15 h. To the cooled reaction mixture was added dilute hydrochloric acid until pH 7—8. The resulting mixture was extracted with chloroform and dried (Na_2SO_4). Upon removal of the solvent, 2.2 g of the crude dicarboxylic acid (14) was obtained. The crude (14) (1.4 g) was heated at 180 °C without solvent for 15 h. After cooling, the mixture was distilled *in vacuo* to give 0.8 g (62%) of (15). The distillate solidified on standing overnight and was recrystallized from benzene-hexane to give the pure *anhydride* (15), m.p. 99—100 °C; $\nu_{max.}$ (Nujol) 1 850, 1 760, and 1 000 cm^{-1}; *m/e* (70 eV) 202 (M^+); δ 1.30 (3 H, s, Me), 3.03 (1 H, d, *J* 3.8 Hz), 3.12 (1 H, d, *J* 3.8 Hz), and 7.06—7.87 (5 H, m, aromatic) (Found: C, 71.0; H, 4.95. $C_{12}H_{10}O_3$ requires C, 71.28; H, 4.99%).

N-*Methyl*-N-(1-*phenylvinyl*)*acetamide* (16).—A solution of (1a) (4.0 g, 15 mmol) and sodium *N*-methylacetamide, [from *N*-methylacetamide (1.3 g, 18 mmol) and sodium hydride (0.43 g, 18 mmol)] in dry THF–DMF (1 : 1, 60 ml) was heated at 150 °C for 15 h in a sealed tube. The normal work-up gave the *amide* (16) (1.8 g, 69%), b.p. 92—94 °C at 1 mmHg; $\nu_{max.}$ (neat) 1 650, 1 620, and 900 cm^{-1}; *m/e* (70 eV) 175 (M^+); δ 2.01 (3 H, s, Me), 3.08 (3 H, s, Me), 5.21 (1 H, s, C=C*H*H), 5.63 (1 H, s, C=CH*H*), and 7.18—7.50 (5 H, m, aromatic) (Found: C, 75.2; H, 7.6; N, 8.0. $C_{11}H_{13}NO$ requires C, 75.40; H, 7.48; N, 7.99%).

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