Rearrangement of Some Allylic Sulphinate Esters to Allylic Sulphones. Ion-pair and Sigmatropic Shift Mechanisms

Derek J. Knight, Gordon H. Whitham,* and Jonathan G. Williams
The Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY

The mechanism of rearrangement of a number of allylic sulphinate esters to the corresponding allylic sulphones on heating in formamide has been investigated as a function of substrate structure. Simple systems such as crotyl and α-methylallyl sulphinate appear to follow a [2,3]-sigmatropic shift pathway, while others, particularly cyclohex-2-enyl sulphinates, show the characteristics of an ion-pair mechanism.

A need for allylic sulphones in connection with some recent investigations of ours,[1] led us to look into their preparation by rearrangement of allylic sulphinates. The literature[2] on this process is a bit confusing. Despite the important and authoritative contribution of Braverman [2c] which showed, for example, that α-methylallyl and crotyl arenesulphinates rearranged on ethanolysis in the presence of base to give crotyl and α-methylallyl sulphones respectively, a recent review [2b] still quotes only an older reference [2a] to the effect that the same mixture of the two sulphones is obtained from either starting material. More recent workers [2d–f] have however substantiated and extended Braverman's observations, and the generality of allylic inversion, reasonably attributed to a [2,3]-sigmatropic mechanism, seems to be established. Braverman has also made other important contributions in the area of sulphinate–sulphone rearrangements.[3]

When we investigated the rearrangement of six-membered alicyclic allylic sulphinates (see below) we found, under our conditions, results which seemed at variance with the [2,3]-sigmatropic shift mechanism. We therefore undertook a limited study of some acyclic and cyclic allylic sulphinates in an attempt to understand the apparent differences. It should be noted that only two esters (**1**) and (**2**) are the same as those studied by Braverman.[2c] They were chosen to provide a reference point for comparison since, as will be seen, our rearrangement conditions were rather different to those used by Braverman. A further point arises out of our work on the 1,3-rearrangement of allylic sulphones,[1] which indicated the need to be aware of the possibility of such rearrangements occurring under the conditions used for the sulphinate to sulphone isomerisation.

Results

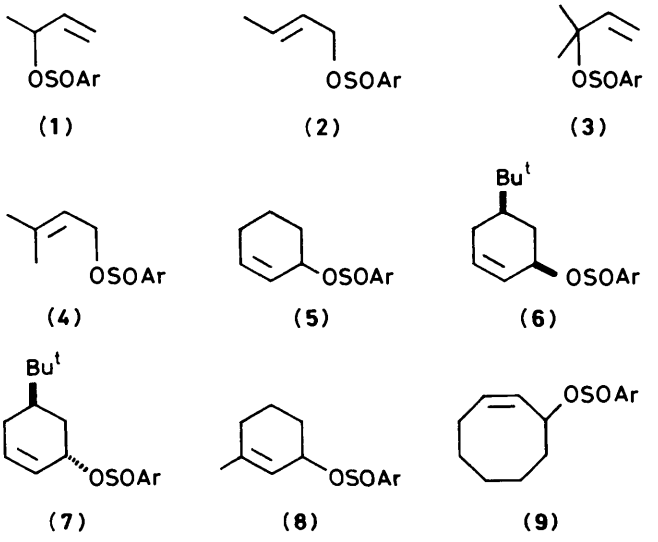
In preliminary experiments we found that the choice of solvent for the thermal rearrangement of allylic sulphinates was important. We did not use hydroxylic solvents owing to the intrusion of S–O cleavage which we experienced, although we have recently been informed by Professor Braverman[4] that ethanol is a suitable solvent provided an appropriate base, *e.g.* 2,6-dimethylpyridine, is present to preclude acid-catalysed transesterification. Relatively non-polar non-hydroxylic solvents such as chloroform, carbon tetrachloride and toluene, and neat material lead to unreproducible erratic results. In agreement with Hiroi [2d] we found that certain dipolar aprotic solvents were satisfactory. In our experience, formamide with the higher E_T[5] (56.6) gave more consistent results than dimethylformamide (DMF), E_T 43.8, which sometimes required addition of 2,4,6-trimethylpyridine to prevent side reactions. We therefore chose formamide as the standard solvent for the work described in this paper.

The allylic sulphinates shown in Scheme 1 (Ar = *p*-MeC_6H_4

Table. Rearrangement of allylic sulphinates on heating in formamide

	Sulphinate	Time	Temperature (°C)	Product(s)[a]
1	(**1**)[b]	6 h[c]	100	(**10**)[d]
2	(**1**)[b]	40 min[c]	100	(**10**):(**1**),[e] 1:1
3	(**2**)	6 h[c]	100	(**11**)[f]
4	(**3**)	1 h	100	(**12**)[g]
5	(**4**)	1 h	100	(**12**) 30%, (**13**) 70%[h]
6	(**4**)	1 h[i]	100	(**12**) 20%, (**12**; Ar = Ph) 30%, (**13**) 45%, (**13**; Ar = Ph) 5%
7	[1-^{2}H]-(**5**)[b]	5 h	75	[1-^{2}H]-(**14**):[3-^{2}H]-(**14**), 1:1[j,k]
8	(**5**)	3 h[i]	105	(**14**):(**14**; Ar = Ph), 2:1
9	(**6**)	5 h	80	(**15**) 70%, (**16**) 30%[l]
10	(**7**)	5 h	80	(**15**) 25%, (**16**) 75%[l]
11	(**8**)	4 h	55	(**17**) 85%, (**18**) 15%[h]
12	(**9**)[b]	24 h	100	(**19**)
13	[1-^{2}H]-(**9**)	24 h[c]	100	[3-^{2}H]-(**19**)[j]

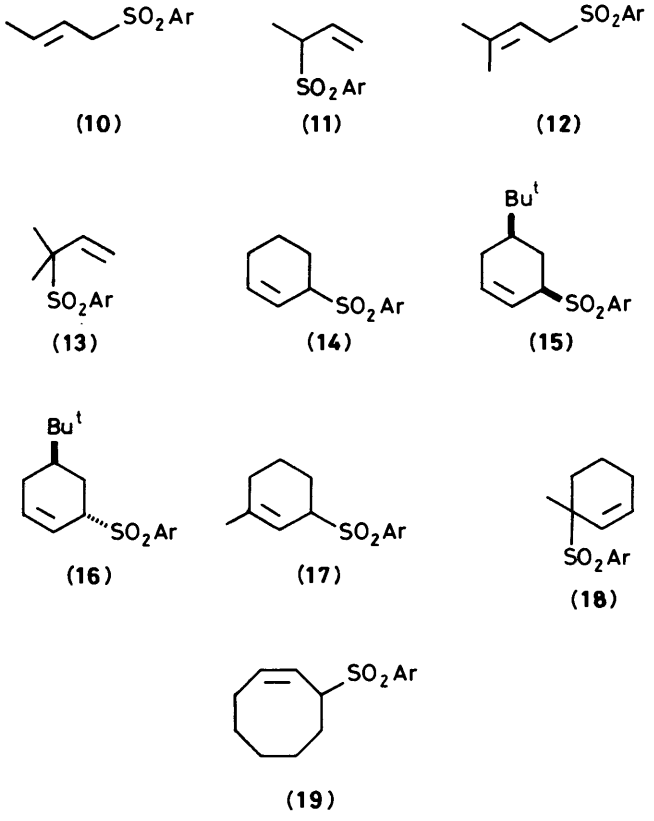
[a] Analysis by n.m.r. of crude product, composition given for reactions in which the products quoted are the only significant ones present. Unless otherwise stated Ar = *p*-$CH_3C_6H_4$. [b] 1:1 Mixture of the two diastereoisomers. [c] Hydroquinone (5 mol%) added. [d] <1% (*Z*)-Sulphone; (**11**) not detected. [e] Compound (**2**) absent, recovered (**1**) now 3:2 mixture of diastereoisomers. [f] Compound (**10**) not detected. [g] Compound (**13**) not detected. [h] Ratio unaffected in run with hydroquinone (5 mol%) present. [i] $PhSO_2Na$ (1 equiv.) present. [j] Recovered allylic sulphinate after shorter reaction time showed no scrambling of ^{2}H. [k] Ratio of diastereoisomers in recovered sulphinate still 1:1. [l] Product sulphones stable to reaction conditions.



Scheme 1. Allylic sulphinates

unless otherwise stated) were prepared from the known alcohols by standard procedures. In the case of sulphinates (**5**) and (**9**) the C-1 (^{2}H) substituted analogues were also prepared *via* reduction of the corresponding αβ-unsaturated ketones with lithium aluminium deuteride.

Results of the thermal rearrangement of the allylic sulphinates are summarised in the Table. Product sulphone structures are cited in Scheme 2. They were identified by

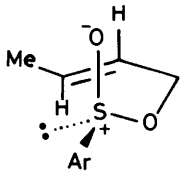


Scheme 2. Allylic sulphones

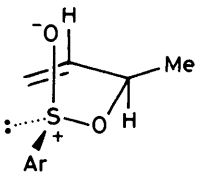
comparison with authentic materials. In some cases it was necessary to add hydroquinone to the reaction mixture to prevent radical-initiated isomerisation [1] of product sulphones.

Discussion

The results obtained on rearrangement of 1-methylallyl sulphinate (**1**) to *trans*-crotyl sulphone (**10**) and crotyl sulphinate (**2**) to 1-methylallyl sulphone (**11**) demonstrate clear allylic 'inversion' in each case and show that there can be no intermediate(s) in common to the two reactions. Noteworthy is the highly stereospecific formation of sulphone (**10**), especially as it is known that the equilibrium ratio of (*E*)-(**10**) to (*Z*)-(**10**) is about 3:1.[1b] Apparently a fairly tight transition state structure is involved and this is supported by the observation that of the two diastereoisomers of compound (**1**), one rearranges appreciably faster than the other. We therefore fully corroborate Braverman's report[2c] and disagree with the statement in the review literature.[2b] Taken together with the observation of Hiroi *et al.*[2d] that the (*S*)-(−)-isomer of sulphinate (**2**) underwent rearrangement to the (*S*)-(+)-isomer of sulphone (**11**) with 87% stereospecificity on heating in DMF, it seems likely that a [2,3]-sigmatropic shift mechanism is involved in the rearrangement of the sulphinates (**1**) and (**2**). Thus a 'boat-like' transition state with a quasi-equatorial aryl-group (**20**) is proposed for the (**2**) ⟶ (**11**) process. As a corollary, the



(**20**)



(**21**)

preferred transition state for (**1**) ⟶ (**10**) should be as shown in structure (**21**), indicating that it is the (*RS*,*SR*)-diastereoisomer of the sulphinate (**1**) which rearranges more rapidly.

In the case of the rearrangement of the more heavily substituted allylic sulphinates (**3**) and (**4**), only the former shows clean allylic inversion to give sulphone (**12**) while the latter gives a mixture of sulphones (**12**) and (**13**). Although it is known that sulphone (**13**) can undergo isomerisation to compound (**12**) under conditions of free-radical catalysis,[1b] it is unlikely that such an isomerisation is obtruding here since the same ratio of sulphones (**12**) to (**13**) was obtained in the presence of hydroquinone. We consider that whereas the rearrangement of sulphinate (**3**), where migration occurs from a tertiary to a primary position, probably involves a [2,3]-sigmatropic shift mechanism, the rearrangement of sulphinate (**4**) occurs partly by a [2,3]-shift, to give the sulphone (**13**), and partly by an ion-pair mechanism. The latter view is supported by the finding that rearrangement of the *p*-tolyl sulphonate (**4**) in the presence of sodium benzenesulphinate gives the mixture of *p*-tolyl and phenyl sulphones shown in the Table (entry 6). Apparently the ion-pair collapses to give predominantly (6:1) primary allyl sulphone so that in the rearrangement of sulphinate (**4**), *ca.* 65% of reaction occurs by a [2,3]-shift to give compound (**13**) and 35% by an ion-pair. Not surprisingly, the proportion of reaction *via* the ion-pair process is increased by addition of sodium benzenesulphinate.

In the case of cyclohex-2-enyl sulphinate (**5**), allylic inversion can only be detected by labelling. We used the deuteriated substrate [1-^{2}H]-(**5**) for our investigation and showed that thermal rearrangement gave a mixture (1:1) of the two sulphones [1-^{2}H]-(**14**) and [3-^{2}H]-(**14**). Furthermore, recovered starting material after partial rearrangement showed no deuterium scrambling, thereby excluding a [3,3]-sigmatropic shift leading to interconversion of allylic sulphinates for this substrate under the conditions of reaction. In addition, sulphinate (**5**) is a mixture (1:1) of diastereoisomers and the recovered material was still a 1:1 mixture showing that the diastereoisomers do not isomerise at different rates as in the case of sulphinate (**1**). We therefore consider that isomerisation of compound (**5**) involves an allylic carbonium ion-sulphinate ion pair, lack of scrambling in recovered starting material shows that ionisation is not reversible under our conditions, recombination occurring at sulphur only. Consistent with the ion-pair hypothesis is the crossover experiment in the presence of sodium phenylsulphinate (Table, entry 8).

An ion pair mechanism also provides the most satisfactory explanation of the low stereospecificity in the isomerisation of the conformationally biased sulphinates (**6**) and (**7**) to the sulphones (**15**) and (**16**) (Table, entries 9 and 10). That some stereospecificity is maintained, however, implies that the ion-pairs involved must be fairly intimate.

Isomerisation of the methyl-substituted cyclohexenyl sulphinate (**8**) (Table, entry 11) also has the hallmarks of an ion-pair process.

Apparently all the six-membered ring allylic sulphinates we have studied rearrange to sulphones by an ionisation-recombination mechanism. It may be that the steric and stereoelectronic demands of the [2,3]-sigmatropic shift mechanism are too stringent in the six-membered ring, either because of non-

bonded interactions between S=O and ring hydrogens or because of partial bridgehead double-bond character in a bicyclic transition state, or both. However the corresponding allylic sulphenates do rearrange by a [2,3]-shift mechanism,[6] and although steric interactions (absence of S=O) would be less important in this instance, an allylic carbonium–sulphenate ion pair would be expected to be less stable than an allylic carbonium–sulphinate ion pair, simply on account of anion stabilities.

In an attempt to evaluate stereoelectronic constraints we looked at rearrangement of the cyclo-octenyl sulphinate [1-^{2}H]-(**9**) (Table, entries 12 and 13). Provided competing radical processes are inhibited, clean allylic inversion was found in formation of sulphone [3-^{2}H]-(**19**). It appears that rearrangement by a [2,3]-shift pathway is once again dominant, though whether this is due to relaxation of stereoelectronic constraints (eight-membered *versus* a six-membered ring) or to the lower stability of an allylic carbonium ion in an eight membered ring,[7] is uncertain.

In conclusion, the mechanism of rearrangement of allylic sulphinates to allylic sulphones in formamide appears to be crucially dependent on the structure of the particular compound in question. For relatively lightly substituted systems where steric effects are not very important and where the allylic carbonium ions which would be involved in a possible ion-pair process are not particularly stable, the [2,3]-shift mechanism predominates. More sterically demanding systems, particularly those where the corresponding allylic carbonium ion is relatively stable, *e.g.* cyclohex-2-enyl, prefer an ion-pair mechanism. It is relevant to point out that Braverman[2c] has already envisaged the possibility of the contribution of an ionic structure to the transition state for rearrangement of allylic sulphinates, although he had not found evidence for it at that time under his conditions.

Experimental

N.m.r. spectra were recorded on Perkin-Elmer R24 (60 MHz) or Bruker WH300 (300 MHz) instruments using Me_4Si as internal standard. Analytical g.l.c. was carried out using a Pye Unicam 104 instrument with OV17 or Carbowax 20M columns at 195 °C.

Preparation of Allylic Sulphinates.—Method A. Allylic alcohol (19 mmol) was added during 15 min to a stirred solution of undistilled toluene-*p*-sulphinyl chloride[8] (4.5 g, 25 mmol) in dry pyridine (6 ml) in an acetone–solid CO_2 bath. The mixture was stirred for 30 min with cooling, then for 30 min at 20 °C. Ether (70 ml) was added, the ether layer was washed with dilute HCl, aqueous Na_2CO_3, water and brine, dried (K_2CO_3) and evaporated giving the sulphinate as an orange or yellow oil.

Method B. A solution of allylic alcohol (10 mmol) in dichloromethane (7 ml) was added dropwise to the sulphinyl chloride (2 g, 11 mmol) and pyridine (0.98 g, 12.4 mmol) in dichloromethane (10 ml) at −78 °C. The mixture was stirred for 15 min at low temperature and for 30 min at 20 °C. The organic layer was washed with aqueous HCl, aqueous Na_2CO_3, water and brine, dried ($CaCl_2$) and evaporated to give the sulphinate as an oil.

The following were prepared: but-3-en-2-yl toluene-*p*-sulphinate (**1**) (Method A) (69%), δ ($CDCl_3$; 300 MHz) 1.32 (3 H, d, *J* 7 Hz, CH_3CH, one isomer), 1.41 (3 H, d, *J* 7 Hz, CH_3CH, other isomer), 2.40 (3 H, s, CH_3Ar, both isomers), 4.77—4.93 (1 H, m, 2-H, both isomers), 5.05—5.35 (2 H, m, 4-H, both isomers), 5.7—5.97 (1 H, m, 3-H, both isomers), 7.29 (2 H, m), and 7.51 (2 H, m, AA′BB′ Ar–H, both isomers); but-2-enyl toluene-*p*-sulphinate (**2**) (Method A) (81%), δ ($CDCl_3$; 60 MHz) 1.7 (3 H, d, *J* 5 Hz, CH_3CH), 2.4 (3 H, s, CH_3Ar), 3.9—4.7 (2 H, m, CH_2), 5.2—6.0 (2 H, m, 2-H and 3-H), 7.25 (2 H, d, ArH), and 7.55 (2 H, d, ArH); 2-methylbut-3-en-2-yl toluene-*p*-sulphinate (**3**) (Method B) (89%), δ ($CDCl_3$; 60 MHz) 1.55 (3 H, s, CH_3C), 1.6 (3 H, s, CH_3C), 2.38 (3 H, s, CH_3-Ar), 5.1—5.4 (2 H, m, 4-H), 5.9—6.35 (1 H, q, *J* 18 and 10 Hz, 3-H), 7.2 (2 H, d, ArH), and 7.55 (2 H, d, ArH); 3-methylbut-2-enyl toluene-*p*-sulphinate (**4**) (Method A) (93%), δ ($CDCl_3$; 60 MHz) 1.6 (3 H, s, CH_3C), 1.7 (3 H, s, CH_3C), 2.38 (3 H, s, CH_3Ar), 3.9—4.7 (2 H, m, 1-H), 5.3 (1 H, bt, *J* 7 Hz, 2-H), 7.3 (2 H, d, ArH), and 7.6 (2 H, d, ArH); cyclohex-2-enyl toluene-*p*-sulphinate (**5**) (Method A) (85%); δ ($CDCl_3$; 300 MHz) 1.5—2.1 (6 H, m), 2.4 (3 H, s, CH_3Ar), 4.75—4.85 (1 H, m, 1-H), 5.45 (dd, *J* 10 and 5 Hz, 2-H of one diastereoisomer), 5.8 (dd, *J* 10 and 5 Hz, 2-H of other diastereoisomer), 5.9 (dt, *J* 10 and 5 Hz, which collapsed on irradiation at 5.45, 3-H of one diastereoisomer), 5.95 (dt, *J* 10 and 5 Hz, 3-H of other diastereoisomer), 7.3 (2 H, d, ArH), and 7.6 (2 H, ArH); [1-^{2}H]cyclohex-2-enyl toluene-*p*-sulphinate had a similar n.m.r. spectrum except for the absence of the multiplet at 4.75—4.85 and the appearance of the multiplets at 5.45 and 5.8 as broad doublets (*J* 10 Hz); *cis*-5-t-butylcyclohex-2-enyl toluene-*p*-sulphinate (**6**) (Method A) (95%); δ ($CDCl_3$; 300 MHz) 0.8 and 0.9 (9 H, both s, Bu^t of both diastereoisomers), 1.3—2.1 (5 H, m), 2.4 (3 H, s, CH_3Ar), 4.95—5.05 (1 H, m, 1-H), 5.45—5.5 (m, 2-H of one diastereoisomer), 5.7—5.75 (m, 2-H of other diastereoisomer), 5.75—5.95 (1 H, m, 3-H of both diastereoisomers), 7.3 (2 H, d, ArH), and 7.6 (2 H, d, ArH); *trans*-5-t-butylcyclohex-2-enyl toluene-*p*-sulphinate (**7**) (Method A) (95%); δ ($CDCl_3$; 300 MHz), 0.8 and 0.9 (9 H, both s, Bu^t of both diastereoisomers), 1.2—2.2 (5 H, m), 2.4 (3 H, s, CH_3Ar), 4.85 (1 H, br s, 1-H), 5.4—5.45 (m, 2-H of one diastereoisomer), 5.8—5.9 (m, 2-H of other diastereoisomer), 5.95—6.15 (1 H, m, 3-H of both diastereoisomers), 7.3 (2 H, d, ArH), and 7.6 (2 H, d, ArH); 3-methylcyclohex-2-enyl toluene-*p*-sulphinate (**8**) (Method A) (92%); δ ($CDCl_3$; 300 MHz) 1.5—2.05 (9 H, m, CH_3-C and ring methylenes), 2.4 (3 H, s, CH_3Ar), 4.75—4.9 (1 H, m, 1-H), 5.25 (br s, 2-H of one diastereoisomer, 5.6 (br s, 2-H of other diastereoisomer), 7.3 (2 H, d, ArH), and 7.6 (2 H, d, ArH); cyclo-oct-2-enyl toluene-*p*-sulphinate (**9**) (Method B) (96%); δ ($CDCl_3$; 300 MHz) 1.25—2.3 (10 H, m, ring methylenes), 2.45 (3 H, s, CH_3Ar), 5.2—5.3 (1 H, m, 1-H), 5.43 (dd, *J* 11, 6 Hz, 2-H one isomer), 5.48—5.57 (m, 3-H, one isomer), 5.48—5.57 (m, 3-H, one isomer), 5.6 (dd, *J* 12 and 7 Hz, 2-H, one isomer), 5.7—5.8 (m, 3-H one isomer), 7.3 (2 H, ArH), and 7.6 (2 H, ArH). [1-^{2}H]Cyclo-oct-2-enyl toluene-*p*-sulphinate had a similar n.m.r. spectrum except for the absence of the multiplet at δ 5.2—5.3 and the appearance of the multiplets at 5.43 and 5.6 as broad doublets.

Rearrangement of Allylic Sulphinates.—A solution of the sulphinate in formamide was set aside under the conditions and for the time specified in the Table. After cooling, water was added and the mixture was extracted with ether. The ethereal layer was washed with dilute HCl, aqueous Na_2CO_3, water, dried (K_2CO_3), and evaporated. Reaction mixtures were analysed by n.m.r. and/or by g.l.c. by comparison with authentic samples of product sulphones prepared by known procedures with the exception of 3-(*p*-tolylsulphonyl)cyclo-octene.

3-(p-*Tolylsulphonyl)cyclo-octene.*—*p*-Thiocresol (2.7 g, 22 mmol) was added to a stirred solution of sodium methoxide from sodium (0.5 g, 22 mmol) in methanol (13 ml) at 18 °C. 3-Bromocyclo-octene (4.0 g, 21 mmol) was added and the solution was heated at reflux for 1 h. After cooling the solution was extracted with light petroleum (200 ml) and the latter was evaporated *in vacuo* to give 3-(*p*-tolylthio)cyclo-octene as a crude oil (4.4 g, 90%), δ($CDCl_3$) 0.9—2.4 (10 H, m, ring methylenes), 2.3 (3 H, s, CH_3), 4.1 (1 H, m, 3-H), 5.3—5.9 (2 H, m, 1-H and 2-H), 7.05 (2 H, d, ArH), and 7.3 (2 H, d, ArH).

The crude allylic sulphide (1.0 g, 4.2 mmol) in acetic acid (12 ml) containing sodium acetate (1.9 g, 0.023 mol) was stirred with hydrogen peroxide (30%; 1.3 ml, 10.4 mmol) at 50 °C for 16 h. Water was added, the mixture was extracted with ether and the ethereal layer washed with aqueous NaOH. After drying (Na_2SO_4), the solution was evaporated under reduced pressure to give a solid (1.0 g). Recrystallisation from n-pentane gave the *sulphone*, m.p. 81—82 °C (Found: C, 67.9; H, 7.7; S, 12.2. $C_{15}H_{20}O_2S$ requires C, 68.1; H, 7.6;, S, 12.1%); δ ($CDCl_3$; 300 MHz) 1.23—2.27 (10 H, m, ring methylenes), 2.45 (3 H, s, CH_3), 4.03 (1 H, m, 3-H), 5.63 (1 H, t, 2-H), 5.88 (1 H, q, 1-H), 7.33 (2 H, d, ArH), and 7.77 (2 H, d, ArH).

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