Elimination–Addition. Part XIV.[1] Addition of Carboxylate Ions to Allenes and Acetylenes and Use of the Adducts in Acylation

By **G. D. Appleyard** and **C. J. M. Stirling**, King's College, Strand, London W.C.2

Base-catalysed additions of acetic, benzoic, and hippuric acids to propadienyl, prop-1-ynyl, and prop-2-ynyl *p*-tolyl sulphones and to ethynyl phenyl ketone occur readily under mild conditions. The products are 1-(arylsulphonylmethyl)vinyl or β-benzoylvinyl esters of the acids and as such are very reactive towards nucleophiles in acylation reactions.

Reactions of amines with the sulphonyl esters yield amides. Reactions of the keto-esters, however, involve either acylation or addition to the carbon–carbon double bond. The latter process regenerates the acid and occurs to an extent which depends upon the amine and upon the acid used. The adduct from benzoic acid and ethynyl phenyl ketone does not benzoylate amines but the acetate gives good yields of acetamides with primary amines although with secondary amines, mixtures of acid and amide or acid alone are obtained. Some acylamides are formed in good yield by addition of acid and triethylamine and then the amine to an acetylenic sulphone in dimethyl sulphoxide.

Reactions of the adducts with other nucleophiles have been briefly investigated. Acylations of phenol and methanol can be achieved; the latter reaction is carboxylate-ion catalysed, probably owing to the formation of an intermediate anhydride. Thiols give low yields of thiolesters.

EARLIER Parts have described additions of sulphur nucleophiles,[2] methoxide ions,[3] and amines [3-6] to allenes and acetylenes. We now report the formation of esters (IV) and (VII) by similar nucleophilic addition of carboxylate ions. The esters produced are very reactive towards nucleophiles and we have examined their behaviour with a variety of reagents.

Additions.—Reactions of three isomeric sulphones (I—III) have been studied. Two principal sets of reaction conditions were used; the free acid together with the sulphone in benzene is treated with triethylamine, or the acid and its sodium salt are allowed to react with the sulphone in dimethyl sulphoxide. The free

[1] Part XIII, A. C. Knipe and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1967 808.
[2] C. J. M. Stirling, *J. Chem. Soc.*, 1964, 5856.
[3] C. J. M. Stirling, *J. Chem. Soc.*, 1964, 5863.
[4] C. H. McMullen and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1966, 1217.
[5] C. H. McMullen and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1966, 1221.
[6] S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1967, 351.

acid acts as a proton source and prevents re-elimination of the acid. Acetic, benzoic, and hippuric acids have been added to one or more of the sulphones; yields and reaction conditions are summarised in Table 1. The

TABLE 1

Carboxylate adducts

Acetylene or allene	Acid	Conditions	Adduct	Time (hr.)	Yield (%)
p-Tolyl·SO_2·C:C·Me	BzOH	(*a*)	(IVb)	4·5	53
		(*b*)	(IVb)	2·5	60
p-Tolyl·SO_2·CH:C:CH_2	BzOH	(*a*)	(IVb)	4·25	65
		(*b*)	(IVb)	3	66
p-Tolyl·SO_2·CH_2·C:CH	BzOH	(*a*)	(IVb)	4·5	54
		(*b*)	(IVb)	2·75	80
p-Tolyl·SO_2·CH:C:CH_2	H	(*c*)	(IVc)	67	67
		(*a*)	(IVc)	4·5	33
p-Tolyl·SO_2·CH_2·C:CH	H	(*c*)	(IVc)	70·5	76
	AcOH	(*a*)	(IVa)	5·5	64
		(*b*)	(IVa)	4·25	47
p-Tolyl·SO_2·CH:C:CH_2	AcOH	(*b*)	(IVa)	4·25	33
PhCO·C:CH	AcOH	(*d*)	(VIIa)	0·75	91
	BzOH	(*e*)	(VIIb)	0·25	77

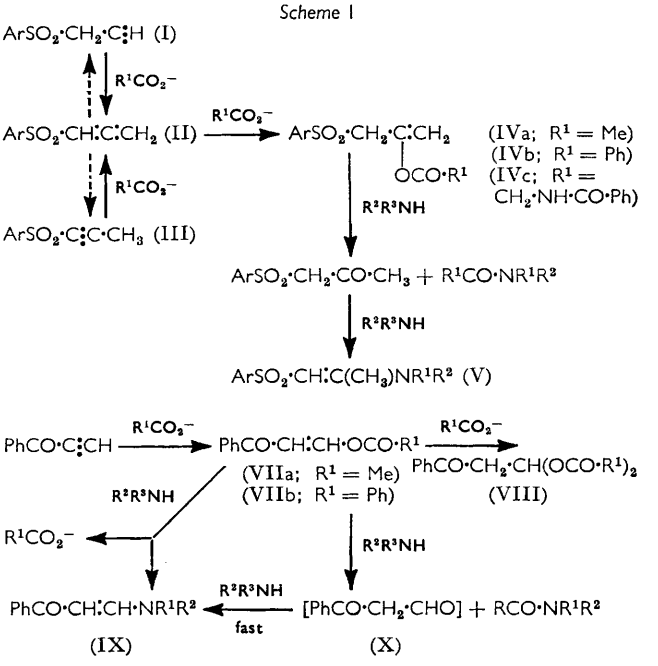
Conditions: (*a*) Acid 1·1 mole, Salt 5 mole, Dimethyl sulphoxide. (*b*) Acid 1·1 mole, Et_3N 1 mole, Dimethyl sulphoxide. (*c*) Acid 1·1 mole, Salt 0·1 mole, Dimethyl sulphoxide. (*d*) Acid 1·1 mole, Et_3N 1 mole, Methylene dichloride. (*e*) Acid 1·1 mole, Et_3N 1 mole, Benzene. (H = Hippuric acid).

yields reported are those of products with melting points not more than 5° lower than those of analytically pure samples; in most cases, much higher yields of crude products were obtained. Additions of hippuric acid were investigated because the adduct (IVc) is an activated ester of an acylamino-acid and acylations with this type of compound are of interest in connection with peptide coupling.

On addition of a carboxylic acid, each sulphone gives the same adduct (IV), whose structure is shown by proton magnetic resonance spectroscopy. This structure requires that, by analogy with reactions of methoxide ions,[3] isomerisation of sulphones (I) and (III) to the allene (II) occurs before nucleophilic addition. The allene is the most thermodynamically stable [2] as well as being the most reactive [6] member of the series. In these reactions, carboxylate ions show a much lower nucleophilicity : basicity ratio than, for example, benzenesulphinate ion which adds [2] directly to sulphone (III) without causing any isomerisation to the allene (II). When large excesses of sodium carboxylates are used in the addition reactions, a high-frequency carbonyl stretching band appears in the infrared spectrum of the crude product. We attribute this band to anhydride formed by subsequent acylation of carboxylate ion. This is discussed further below.

Additions to ethynyl phenyl ketone (VI) gave the adducts (VII) under conditions comparable with those used for the sulphones. Reactions were easily followed, as for those with the sulphones, by the appearance of the high-frequency infrared carbonyl stretching frequency characteristic of vinyl esters. The adducts obtained from additions of acetic acid and benzoic acid were identical with the esters obtained from treatment of the

Scheme 1



sodium salt of benzoylacetaldehyde with acetic anhydride [7] and benzoyl chloride [8] respectively. The ketone was more reactive in addition reactions than the sulphones, and the structures of the adducts were again confirmed by proton magnetic resonance spectroscopy. The configurations of the adducts are, however, uncertain; the ^1H n.m.r. coupling constant for the olefinic protons [9] (J = 12·5 c./sec.) is in the borderline region between *cis* and *trans* isomers.

Treatment of ethynyl phenyl ketone with excess of acetic acid in the presence of triethylamine gave the diacetate (VIII). Formation of this product indicates the greater activation of the carbon–carbon double bond caused by a carbonyl group when compared with a sulphonyl group. Formation [3] of a bis-adduct between the sulphones (I—III) and the much more reactive methoxide ion is incomplete even in concentrated solutions.

Reactions of Carboxylate Adducts with Nucleophiles.—The adducts produced by mono-addition to activated allenes and acetylenes are vinyl esters, and esters of this type are more reactive than simple alkyl esters because nucleophilic attack at the ester carbonyl group causes displacement of a relatively stable enolate anion. The principle has been employed in peptide coupling *via* vinyl esters of acylamino-acids [10] and it was expected that the adducts obtained in the present work should be particularly reactive towards nucleophiles because the leaving group is the exceptionally stable enolate anion

[7] L.-M. Roch, *Ann. Chim.* (*France*), 1961, **6**, 105.
[8] K. von Auwers and W. Schmidt, *Ber.*, 1925, **58**, 528.
[9] J. A. Elvidge, 'Nuclear Magnetic Resonance for Organic Chemists,' ed. D. W. Mathieson, Academic Press, London, 1967, p. 187.
[10] F. Weygand and W. Steglich, *Angew. Chem.*, 1961, **73**, 757.

of a β-sulphonyl ketone or β-keto-aldehyde. The two types of adduct behaved somewhat differently (Scheme 1) and will be considered separately.

Sulphone adducts. Reactions with amines have been given most attention (details in Table 2). These were

TABLE 2

Reactions of carboxylate adducts with amines *

Adduct	Amine	Reaction Time (hr.)/ Temp.	Yields (%) Acyl deriv.	Acid	Enamine
(IVa)	$CH_2(CH_2)_4NH$	18·5/20°	70	—	94 [a]
	$NH_2{\cdot}CH_2{\cdot}CO_2Et$	89/80	95	—	92 [b]
(IVb)	$PhCH_2{\cdot}NH_2$	23/20	100 [g]	—	92 [a]
	$PhCH_2{\cdot}NH_2$	64/80	88	—	73 [b]
	$(PhCH_2)_2NH$	288/80	78	—	39 [a]
	$CH_2(CH_2)_4NH$	25/20	100 [g]	—	92 [b]
	$NH_2{\cdot}CH_2{\cdot}CO_2Et$	89/80	78	—	91 [a]
	$NH_2{\cdot}CH_2{\cdot}CO_2Et$	168/20	92 [g]	—	88 [b]
(IVc)	$PhCH_2{\cdot}NH_2$	64/80	95	—	95
	$NH_2{\cdot}CH_2{\cdot}CO_2Et$	110/80	96	—	[c]
	$NH_2{\cdot}CH_2{\cdot}CO_2Et$	312/20	92 [g]	—	47 [a]
(VIIa)	$PhCH_2{\cdot}NH_2$	1/20	74	—	92
	$PhCH_2{\cdot}NH_2$	2·25/20	94 [e]	—	61
	$(PhCH_2)_2NH$	1·5/20		88 [e,j]	76
	$(PhCH_2)_2NH$	1/20		99 [f,j]	97
	$CH_2(CH_2)_4NH$	0·1/20	59 [d]	—	93
	$NH_2{\cdot}CH_2{\cdot}CO_2Et$	1/20	53	—	90
(VIIb)	$PhCH_2{\cdot}NH_2$	0·5/20		87 [h]	94
	$CH_2(CH_2)_4NH$	1·5/20		97	62

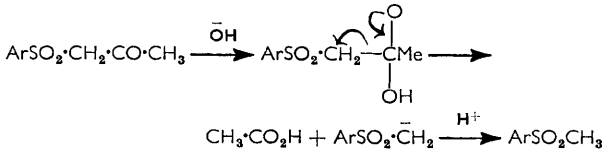
* Reactions were performed in benzene unless otherwise stated.

[a] As *p*-tolylsulphonylacetone. [b] As methyl *p*-tolyl sulphone. [c] Not isolated, shown by infrared spectroscopy to be a mixture of enamine and *p*-tolylsulphonylacetone. [d] 70% by v.p.c. [e] In methanol. [f] In dioxan. [g] In dimethyl sulphoxide. [h] As benzylamine benzoate. [j] By titration.

usually carried out in benzene and were followed by infrared spectroscopy. Disappearance of the high-frequency carbonyl band of the adduct was accompanied by appearance of the lower-frequency amide carbonyl band. Good yields of amides were obtained from both primary and secondary amines; change of solvent did not affect yields but in methanol and in dimethyl sulphoxide reactions were faster. The weakly basic [11] glycine ethyl ester reacted slowly under all conditions. When reactions were done with a slight excess of amine over adduct, the amide was obtained together with toluene-*p*-sulphonylacetone, but when an excess of amine was used, the complementary product was the β-sulphonylenamine (V) derived [3] from subsequent reaction with the ketone. The amide and β-sulphonylenamine are readily separated by mild acid hydrolysis of the latter to the β-sulphonyl ketone which is then removed as its enolate by alkaline extraction. Immediate acidification of the alkaline extracts regenerated the β-sulphonyl ketone. Otherwise, a slow subsequent reaction occurs and the product is methyl *p*-tolyl sulphone (Scheme 2). Yields of whichever product was isolated are given in Table 2. This procedure fails in reactions with ketone adducts (below) as enamino-ketones are not acid-labile.

The potential of these reactions for peptide coupling is indicated by the formation of benzoylglycylglycine ethyl ester in high yield from the hippurate adduct (IVc) and glycine ethyl ester. Addition of a carboxylic acid

Scheme 2



to an allenic or acetylenic sulphone thus constitutes a simple method for carboxyl activation similar in many respects to the use of dicyclohexylcarbodi-imide,[12] ketenimines,[13] and cyanamides.[14] Isolation of the vinyl esters is not essential for the acylation of amines by this procedure. Thus, for example, when the sulphone (I), benzoic acid, and triethylamine are allowed to react in dimethyl sulphoxide and benzylamine is subsequently added directly to the mixture, *N*-benzoylbenzylamine is obtained in 81% yield.

Other nucleophiles also react with the sulphone–carboxylate adducts. Methanolic sodium methoxide with the benzoate (IVb) gave a quantitative yield of methyl benzoate and toluene-*p*-sulphonylacetone. There was no reaction with methanol alone but in the presence of sodium benzoate, methyl benzoate was again obtained suggesting that benzoic anhydride is first formed by attack of benzoate anion on the adduct. Reaction of sodium phenoxide with the benzoate (IVb) in dimethyl sulphoxide gave phenyl benzoate, but in reactions with thiols, thiolesters were obtained only in low yields.

Ketone adducts. These adducts differ from the sulphone adducts in possessing three sites for nucleophilic attack, *viz.*, the ester and ketone carbonyl groups, and the carbon–carbon double bond. The last site is activated in these compounds by conjugation with the ketone carbonyl group. In reactions with amines, no attack at the ketone carbonyl group was observed, but choice between the other sites was dependent upon the structures of both ester and amine. The acetate (VIIa) gave acetamides (Table 2) on treatment with primary amines together with enamino-ketones (IX; $R^1 = H$), the structures of which have been described previously.[4,5] Two moles of amine per mole of ester are required for complete reaction, as the aldehyde (X) liberated by displacement at the ester carbonyl group reacts more rapidly with amines (to give enamino-ketones) than does the vinyl ester. With secondary amines, attack at the carbon–carbon double bond competes with acylation. Piperidine gives a moderate yield of *N*-acetylpiperidine but in reactions with dibenzylamine no acylation occurs and acetic acid is produced. This product probably

[11] V. H. Veley, *J. Chem. Soc.*, 1908, **93**, 652.
[12] F. Kurzer and K. Douraghi-Zadeh, *Chem. Rev.*, 1967, **67**, 107.
[13] C. L. Stevens and M. E. Munk, *J. Amer. Chem. Soc.*, 1958, **80**, 4069.
[14] G. Losse and H. Weddige, *Annalen*, 1960, **636**, 144.

arises from initial addition of the amine to the carbon–carbon double bond and subsequent elimination of carboxylate ion. This greater reactivity of secondary amines towards electrophilic olefins is in line with previous observations.[15] Neither piperidine nor benzylamine is benzoylated by the benzoate (VIIb). Alkyl benzoates are approximately ten times less reactive towards, *e.g.*, hydroxyl ion, than the corresponding acetates and this lower reactivity is evidently sufficient to divert reaction in the benzoate adduct from the carbonyl group to the carbon–carbon double bond.

Both types of carboxylate adduct considered here are much more reactive than simple esters. Comparison of the approximate half-times of reaction with piperidine in benzene of ethyl benzoate, vinyl acetate, the sulphone acetate (IVa), and the ketone acetate (VIIa) gives their relative reactivities as 1 : 100 : 8000 : 200,000.

Acids other than carboxylic acids also add to the acetylenic ketone and sulphones. These reactions and their application in, for example, phosphorylation will be the subject of a later Paper.

EXPERIMENTAL

General.—Solvents were anhydrous and solutions were evaporated at $\not>40°$. Extracts were dried over Na_2SO_4. 'AnalaR' benzene was dried over sodium and dimethyl sulphoxide was dried over Linde 5A molecular sieves. Triethylamine was purified as described in Part IV.[2] Light petroleum had b. p. 40—60°. Ethynyl phenyl ketone [16] and propadienyl, prop-1-ynyl, and prop-2-ynyl *p*-tolyl sulphones [6] were prepared by literature methods. Infrared spectra were determined on a Perkin-Elmer 237 instrument calibrated with polystyrene film. When reactions were followed by infrared spectroscopy, 5% w/v solutions of either acetylene or vinyl ester in benzene were used in 0·1 mm. path-length cells with NaCl windows. Proton magnetic resonance spectra were determined with a Perkin-Elmer R10 instrument operating at 60 Mc./sec.

General Procedures for Carboxylate Additions.—The following descriptions illustrate the procedures indicated by letters in Table 1.

(*a*) Prop-2-ynyl *p*-tolyl sulphone (3 g.) in dimethyl sulphoxide (40 ml.) was added to sodium acetate (5 mol.) and acetic acid (1·1 mol.) in dimethyl sulphoxide (20 ml.). After 5·5 hr., ether (400 ml.) was added and the solution was washed successively with water (3 × 500 ml.), saturated aqueous sodium hydrogen carbonate (2 × 250 ml.) and water (2 × 250 ml.). Evaporation of the solution gave crude *adduct* (IVa) (2·914 g., 74%), m. p. 80—83°, raised to 84—86° (64%) (from benzene–light petroleum) and to 90—91° (from methanol) (Found: C, 56·6; H, 5·4. $C_{12}H_{14}O_4S$ requires C, 56·7; H, 5·5%). The infrared spectrum showed $\nu_{C=O}$ 1755 cm.$^{-1}$ and the ^{1}H n.m.r. spectrum bands at τ 2—2·8 (m); 5·05 (q); 5·98 (s); 7·55 (s); 8·01 (s) with integrals in the ratio 4 : 2 : 2 : 3 : 3.

(*b*) Prop-1-ynyl *p*-tolyl sulphone (330 mg.) in dimethyl sulphoxide (5 ml.) was treated with benzoic acid (1·1 mol). and triethylamine (1 mol.). After 2·5 hr., ether (300 ml.) was added and the solution was washed successively with water (250 ml.), N-hydrochloric acid (2 × 100 ml.), and sodium hydrogen carbonate (2 × 100 ml.). Evaporation gave the crude *benzoate* (IVb) (87%), m. p. 130—133°, raised to 140—141° (from methanol) (Found: C, 64·5; H, 5·2. $C_{17}H_{16}O_4S$ requires C, 64·6; H, 5·1%), $\nu_{C=O}$ 1740 cm.$^{-1}$; ^{1}H n.m.r., τ 1·9—2·8 (m); 4·82 (q); 5·86 (s); 7·67 (s) with integrals in the ratio 9 : 2 : 2 : 3.

(*c*) Propadienyl *p*-tolyl sulphone (7 g.) in dimethyl sulphoxide (20 ml.) was treated with sodium hippurate (0·1 mol.) and hippuric acid (1·1 mol.) in dimethyl sulphoxide (15 ml.). After 67 hr., the working-up procedure in (*a*) (except that dichloromethane replaced ether) gave the *hippurate* (IVc) (67%), m. p. 118—121°, raised to 123—124° (from methanol) (Found: C, 60·7; H, 5·2. $C_{19}H_{19}NO_5S$ requires C, 61·1; H, 5·1%), $\nu_{C=O}$ 1770 cm.$^{-1}$ and 1660 cm.$^{-1}$; ^{1}H n.m.r., τ 1·8—3 (m); 4·92 (q); 5·75 (d); 5·92 (s); 7·58 (s) with integrals in the ratio 10 (including N–H) : 2 : 2 : 2 : 3.

(*d*) This procedure was similar to (*a*) except that the solvent was benzene. Application to ethynyl phenyl ketone gave the benzoate (VIIb) (77%), m. p. 64—68°, raised to 72—73° alone or mixed with a specimen (m. p. 72—73°) prepared [8] from the sodium enolate of benzoylacetaldehyde and benzoyl chloride; $\nu_{C=O}$ 1750 cm.$^{-1}$; ^{1}H n.m.r., τ 1·9—3·0 (m); 1·6 (d); 3·2 (d) (J = 12·5 c./sec.); with integrals in the ratio 10 : 1 : 1.

Acetic acid added to ethynyl phenyl ketone under similar conditions in dichloromethane. The acetate (VIIa) (91%), had m. p. 65—67°, raised to 69—70° (from light petroleum) alone or mixed with an authentic specimen obtained [7] from the sodium enolate of benzoylacetaldehyde and acetic anhydride; $\nu_{C=O}$ 1775 cm.$^{-1}$; ^{1}H n.m.r., τ 1·64 (d) (J = 12·5 c./sec.); 1·9—2·6 (m); 3·24 (d); 7·84 (s); with integrals in the ratio 1 : 5 : 1 : 3.

Repetition of this experiment with acetic acid (2 mol.) and triethylamine (0·2 mol.) gave the diacetate (VIII) (69%), m. p. 66—70°, raised to 78—79° (from benzene–light petroleum) (lit.,[17] m. p. 80°) (Found: C, 62·7; H, 5·6. Calc. for $C_{13}H_{14}O_5$: C, 62·4; H, 5·6%), $\nu_{C=O}$ 1755 and 1770 cm.$^{-1}$; p.m.r., τ 1·9—2·8 (m); 6·50 (d); 7·95 (s); with integrals in the ratio 6 (includes O–CH–O) : 2 : 6. Irradiation at 2·65 τ caused the doublet at 6·50 to collapse to a singlet and irradiation at 6·5 τ caused the triplet at 2·65 τ to collapse to a singlet.

In many instances, additions of acids to acetylenes and allenes were followed by use of infrared spectroscopy. In crude products, presence of weak bands with frequencies near 1800 cm.$^{-1}$ suggested the formation of small amounts of acid anhydride which result from attack of excess of carboxylate anion upon the vinyl ester produced by addition. The observation (below) that methanolysis of ester (IVb) is benzoate ion-catalysed, supports this suggestion.

Acylations with Acyloxy-sulphones (IV).—The following descriptions illustrate the general procedures. Results are summarised in Table 2.

Reactions with 2-Acetoxy-1-(toluene-p-sulphonyl)prop-2-ene.—(a) *Piperidine.* The ester (1 g.) in benzene (22·4 ml.) was treated with piperidine (338 mg., 1 mol). The reaction was followed by disappearance of the infrared carbonyl band at 1762 cm.$^{-1}$ (vinyl ester) and appearance of bands at 1655 cm.$^{-1}$ (amide) and 1720 cm.$^{-1}$ (ketone). It was complete after 18 hr. at *ca.* 25°. Evaporation of the solution gave a residue which was extracted with light petroleum

[15] S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1967, 343.

[16] K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 1946, 39.

[17] H. M. White, H. O. Colomb, and P. S. Bailey, *J. Org. Chem.*, 1965, **30**, 481.

(2 × 75 ml.). Distillation of the extracts gave *N*-acetylpiperidine (350 mg., 70%), b. p. 52°/0·6 mm., n_D^{20} 1·4818 (lit.,[18] n_D^{20} 1·4817). The residue from the distillation and from the light petroleum extraction was *p*-tolylsulphonylacetone (784 mg., 94%, in all), m. p. and mixed m. p. 47—50°.

(b) *Glycine ethyl ester.* The same procedure gave *N*-acetylglycine ethyl ester (95%), b. p. 140°/10 mm., m. p. and mixed m. p. 42—43°. Methyl *p*-tolyl sulphone was obtained in 92% yield.

Reactions with 2-*Benzoyloxy*-1-(*toluene*-p-*solphonyl*)*prop*-2-*ene*.—(a) *Benzylamine.* The ester (1 g.) in benzene (20 ml.) was treated with benzylamine (745 mg., 2·2 mol.). Reaction was complete (infrared spectrum) in 64 hr. at 80°. The solution was evaporated and the residue in tetrahydrofuran (20 ml.) was treated with 2N-hydrochloric acid (10 ml.). After 2 hr., the mixture was extracted with dichloromethane and the extract was washed with 2N-sodium hydroxide (3 × 50 ml.). The organic layer, on evaporation, gave *N*-benzylbenzamide (558 mg., 88%), m. p. and mixed m. p. 103—104°. Acidification of the alkaline washings after 16 hr. and extraction with dichloromethane gave methyl *p*-tolyl sulphone (375 mg., 73%), m. p. and mixed m. p. 85—85·5°.

(b) *Glycine ethyl ester.* The benzoate (1 g.) and glycine ethyl ester (2·2 mol.) were allowed to react in dimethyl sulphoxide (10 ml.) for 7 days at 25°. 2N-Hydrochloric acid (10 ml.) was added, and after 1 hr. the mixture was diluted with water and extracted with dichloromethane. The extracts were washed with 2N-aqueous sodium hydroxide and evaporation gave ethyl hippurate (92%), m. p. 52—55° alone or mixed with an authentic specimen, m. p. 57—58°, obtained by benzoylation of glycine ethyl ester with benzoyl chloride (Found: C, 63·6; H, 6·6. Calc. for $C_{11}H_{13}NO_3$: C, 63·8; H, 6·3%) (lit.,[19] m. p. 59—60°). Methyl *p*-tolyl sulphone (88%) was also obtained.

(c) *Dibenzylamine.* The product, *NN*-dibenzylbenzamide (78%), had m. p. and mixed m. p. 110—111°.

Reactions with 2-*Benzamidoacetyloxy*-1-(*toluene*-p-*sulphonyl*)*prop*-2-*ene*.—(a) *Glycine ethyl ester.* The hippurate (1 g.) in benzene (20 ml.) was refluxed with glycine ethyl ester (553 mg., 2 mol.). There was no further change in the infrared spectrum of the solution after 110 hr., and the mixture was set aside for 70 hr. Filtration gave *N*-benzoylglycylglycine ethyl ester (96%), m. p. 113·5—114·5° (from benzene–light petroleum) (Found: C, 59·2; H, 5·9. Calc. for $C_{13}H_{16}N_2O_4$: C, 59·1; H, 6·1%) (lit.,[20] m. p. 113—115°).

(b) *Benzylamine.* The product, *N*-(*N*-benzoylcarbamoyl)methylbenzamide (95%), had m. p. 158—159° raised to 159—160° (from benzene) (lit.,[21] m. p. 157—158°).

Reactions of 2-*Benzoyloxy*-1-*toluene*-p-*sulphonylprop*-2-*ene* (IVb) *with other Nucleophiles.*—(a) *Methanol.* The ester (500 mg.) was refluxed in methanol for 10 days. Evaporation of the solution and treatment of the residue with light petroleum gave recovered benzoate (80%), m. p. and mixed m. p. 134—138°. Evaporation of the light petroleum washings gave a residue (56 mg.) whose infrared spectrum showed it to be slightly impure methyl benzoate.

(b) *Sodium benzoate in methanol.* The ester (1 g.) and sodium benzoate (500 mg., 1·1 mol.) in methanol (15 ml.) were refluxed for 5 days. The mixture was diluted with dichloromethane and washed with aqueous 2N-sodium hydroxide (3 × 50 ml.). Evaporation of the organic extracts and addition of light petroleum to the residue precipitated methyl *p*-tolyl sulphone (31%), m. p. and mixed m. p. 84—85°. Distillation of the mother-liquors gave methyl benzoate (88%), b. p. 79—80°/11 mm., n_D^{25} 1·5145, whose infrared spectrum was identical with that of an authentic specimen.

The alkaline washings were acidified, saturated with sodium chloride, and extracted with dichloromethane. The extracts were washed with aqueous sodium hydrogen carbonate and evaporation gave *p*-tolylsulphonylacetone (63%), m. p. and mixed m. p. 50—51°. Acidification of the aqueous washings and extraction with dichloromethane gave benzoic acid (98%), m. p. and mixed m. p. 119—120°.

(c) *Sodium methoxide in methanol.* The ester (1 g.) in chloroform (5 ml.) was treated with methanolic 0·495N-sodium methoxide (7·03 ml., 1·1 mol.). After 10 min., the mixture was diluted with dichloromethane (50 ml.) and washed with aqueous 2N-sodium hydroxide (3 × 50 ml.). Evaporation of the organic layer gave a residue of crude methyl benzoate (97%), n_D^{25} 1·5159. Distillation gave the pure ester (84%), b. p, 82°/13 mm., n_D^{25} 1·5147. Acidification of the alkaline washings and extraction with dichloro-methane gave *p*-tolylsulphonylacetone (95%), m. p. and mixed m. p. 47—48·5°.

(d) *Sodium phenoxide.* The ester (500 mg.) and sodium phenoxide (20 mol.) were allowed to react in dimethyl sulphoxide (10 ml.) for 12 days. The mixture was diluted with dichloromethane and washed with aqueous sodium hydroxide as before. Evaporation of the organic layer gave phenyl benzoate (77%), m. p. 61—65°, raised to 68° (from light petroleum) alone or mixed with an authentic specimen. Methyl *p*-tolyl sulphone (48%) was recovered from the alkaline extracts.

(e) *Thiols.* (i) *Toluene-ω-thiol.* The ester (1 g.) in methanol (30 ml.) was added to toluene-ω-thiol (1·1 mol.) in methanolic 0·495N-sodium methoxide (6·4 ml., 1 mol.). After 6·5 hr., working up as in (c) gave methyl benzoate (71%) and methyl *p*-tolyl sulphone (54%).

(ii) Toluene-*p*-thiol. The ester (1 g.), sodium hydroxide (1 mol.), and toluene-*p*-thiol (1·1 mol.) were set aside in dimethyl sulphoxide (10 ml.) under nitrogen. After 9 days, the mixture was worked up as in (d). Evaporation of the organic layer and treatment of the residue with light petroleum precipitated recovered ester (60%), m. p. and mixed m. p. 138—139°. Evaporation of the light petroleum mother-liquors gave a residue which thin-layer chromatography on silica showed to be a mixture of di-*p*-tolyl disulphide, phenyl thiolbenzoate, and the benzoate (IVb). The presence of the thiol ester was also confirmed by the presence of an infrared carbonyl absorption at 1680 $cm.^{-1}$.

Reactions with 2-*Benzoylvinyl Acetate* (VIIa).—(a) *Benzylamine.* The acetate (250 mg.) was added to benzylamine (2·2 mol.) in methanol (7·5 ml.). After 2 hr., solvent was removed and the residue was stirred vigorously with water (50 ml.). Filtration gave a residue of 1-benzoyl-2-benzylaminoethylene (61%), m. p. 77·5—78°, alone or mixed with an authentic specimen (lit.,[4] 81·5—83°). The aqueous filtrates were saturated with sodium chloride and extracted with chloroform. Evaporation of the extracts gave *N*-acetylbenzylamine (94%), m. p. and mixed m. p. 55·5—58·5°.

[18] S. Komori, M. Okahara, and E. Shinsugi, *Technol. Reports Osaka Univ.*, 1958, **8**, 497.

[19] B. Sklarz and A. F. Al-Sayyab, *J. Chem. Soc.*, 1964, 1318.

[20] M. M. Bottvinik and S. M. Avaeva, *Zhur. obshchei Khim.*, 1958, **28**, 1534.

[21] R. Schwyzer, B. Iselin, and M. Feurer, *Helv. Chim. Acta*, 1955, **38**, 69.

(b) *Glycine ethyl ester*. The *N*-acetyl derivative (53%) was obtained in a similar way although continuous extraction of the aqueous solution was necessary. The *enaminoketone* (IX; $R^1 = H$; $R^2 = CH_2{\cdot}CO_2Et$) (90%) had m. p. 88·5—89° (from benzene–light petroleum) alone or mixed with an authentic specimen obtained by addition of glycine ethyl ester to ethynyl phenyl ketone (Found: C, 66·7; H, 6·4. $C_{13}H_{15}NO_3$ requires C, 67·0; H, 6·4%). The ^1H n.m.r. spectrum showed signals for olefinic protons with $J = 8$ c./sec. confirming the expected [4] *cis*-configuration.

(c) *Piperidine*. Vapour-phase chromatography (10% polyethylene glycol, 20M on Celite) of the product obtained as in (a) with the same proportions of reagents, showed a 70% yield of *N*-acetylpiperidine which was obtained (59%) directly from the reaction mixture by evaporation and distillation. It had b. p. 94°/12 mm., n_D^{20} 1·4815. The residue was 1-benzoyl-3-piperidinoethylene (93%), m. p. 89—89·5° (from benzene–light petroleum) (lit.,[22] m. p. 86—89°). The ^1H n.m.r. spectrum showed olefinic protons with $J = 13$ c./sec. confirming the expected *trans*-configuration.

(d) *Dibenzylamine*. The reaction was carried out as in (a) but with benzene as solvent. Infrared spectra and v.p.c. of the mixture showed that no amide was produced. The solution was washed with water and evaporation gave 1-benzoyl-2-dibenzylaminoethylene (IX; $R^1 = R^2 = CH_2{\cdot}Ph$) (97%), m. p. 108—109°, raised to 110—111° (from benzene–light petroleum) alone or mixed with an authentic specimen.[4] In a separate experiment in dioxan, liberated acetic acid (99·6%) was determined by titration of aliquot parts of the mixture against 0·1N-NaOH with phenolphthalein as indicator.

Relative Reactivities of Esters with Piperidine.—The ester in a 0·175M solution in benzene was allowed to react with piperidine (1·1 mol.). The half-time of each reaction was estimated by following the change in intensity of the ester carbonyl band with time. For the ketone acetate (VIIa), $t_{\frac{1}{2}} < 8$ min.; for the sulphone acetate (IVa), $t_{\frac{1}{2}} = ca.$ ·35 hr.; for vinyl acetate, $t_{\frac{1}{2}} = ca$ 12 days, and for ethyl benzoate, $t_{\frac{1}{2}}$ could not be estimated; no reaction was discernible after 66 days. As 5% of reaction would have been readily detectable, the rough value of 100 is assigned to the relative reactivity of vinyl acetate compared with ethyl benzoate.

Reactions with 2-Benzoylvinyl Benzoate (VIIb).—(a) *Benzylamine*. The benzoate (500 mg.) and benzylamine (2·2 mol.) were set aside in benzene (11·4 ml.) for 30 min. The infrared spectrum of the solution showed that no amide had been formed. Evaporation gave a residue which, on treatment with anhydrous ether, gave benzylamine benzoate (87%), m. p. 124·5—128°, alone or mixed with an authentic specimen (m. p. 127—128°). The ether solution was washed with saturated aqueous sodium hydrogen carbonate and N-hydrochloric acid. Evaporation gave a residue which, on addition of light petroleum, gave 1-benzoyl-2-benzylaminoethylene, (94·5%), m. p. and mixed m. p. 74—75°.

(b) *Piperidine*. When reaction as before was complete the mixture was washed with aqueous sodium carbonate and evaporation gave a residue which, on crystallisation from benzene–light petroleum gave 1-benzoyl-2-piperidinoethylene (62%), m. p. and mixed m. p. 88·5—89·5° (lit.,[22] 86—89°). Acidification of the alkaline extracts gave benzoic acid (97%).

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[22] A. N. Nesmeyanov and M. I. Rybinskaya, *Doklady Akad. Nauk S.S.S.R.*, 1958, **120**, 793.