693. *The Synthesis of Heterocyclic Alkenes by the Horner Reaction*

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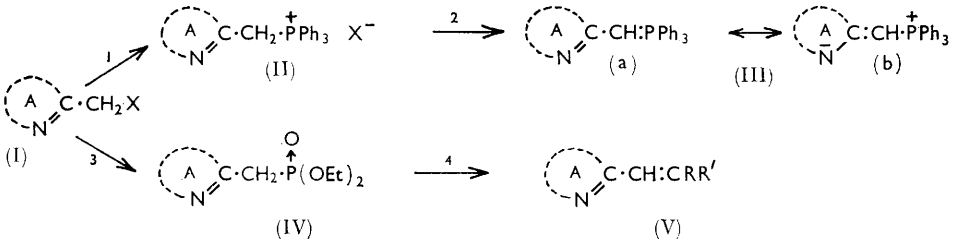
2-Bromomethylbenzothiazole and 2-chloromethylquinoline yield diethyl 2-benzothiazolyl- and 2-quinolyl-methylphosphonates, respectively, when heated with triethyl phosphite. The phosphonate anions react with aldehydes and ketones to give 2-benzothiazolyl- or 2-quinolyl-alkenes, many of which are useful for the preparation of cyanines.

Horner and his co-workers [1] first showed that phosphine oxides and phosphonates, containing a $CH_2P(:O)<$ group, condense, in the form of their anions, with carbonyl compounds to give alkenes. The scope of this reaction, and its superiority over the Wittig reaction in certain respects, has been demonstrated.[2-4]

The Wittig and Horner reactions have been principally applied in the aliphatic, aromatic, and alicyclic fields; little has appeared concerning heterocyclic alkenes. Non-basic heterocycles have been employed in Wittig reactions [5-7] and basic heterocyclic alkenes were obtained by the Horner reaction employing heterocyclic aldehydes [8] and heterocyclic methylphosphonates.[9]

The purpose of the present work was to obtain basic heterocyclic alkenes, of use in the synthesis of cyanines, which were inaccessible or difficulty accessible by other methods. Certain alkenes of this type in the benzothiazole series had previously been obtained [10] by



1, PPh_3; 2, –HX; 3, $P(OEt)_3$; 4, RR′C:O

the interaction of *o*-aminothiophenol and suitable ethylenic acid chlorides. The reaction sequences envisaged in applying the Wittig or Horner reactions to these syntheses both started from halogenomethyl-heterocycles (I).

2-Bromomethylbenzothiazole and triphenylphosphine in hot benzene yielded 2-benzothiazolylmethyltriphenylphosphonium bromide (cf. II) which, on treatment with base, gave the phosphorane (cf. III a ⟷ b) as a yellow, crystalline solid. Its resonance stabilisation is such, however, that it does not undergo Wittig condensation with either acetaldehyde or acetone. The same bromo-derivative reacted with triethyl phosphite at 140° to give diethyl 2-benzothiazolylmethylphosphonate (cf. IV), the anion of which readily underwent the Horner reaction with a number of aldehydes and ketones to yield

[1] L. Horner, H. Hoffmann, and H. G. Wippel, *Chem. Ber.*, 1958, **91**, 61; with G. Klahre, *ibid.*, 1959, **92**, 2499.
[2] H. Pommer, *Angew. Chem.*, 1960, **72**, 811, 911.
[3] W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1732.
[4] S. Trippett and D. M. Walker, *Chem. and Ind.*, 1961, 990.
[5] Yu. K. Yurev and D. Ekkardt, *Zhur. obshchei Khim.*, 1961, **31**, 3536.
[6] H. Saikachi, Y. Tamiguchi, and H. Ogawa, *J. Pharm. Soc. Japan*, 1963, **83**, 582.
[7] H. Heitman, J. H. S. Weiland, and H. O. Huisman, *Proc., k. ned. Akad. Wetenschap.*, 1961, **64**, *B*, 165.
[8] E. J. Seus and C. V. Wilson, *J. Org. Chem.*, 1961, **26**, 5243.
[9] P. Bednarek, R. Bodalski, J. Michalski, and S. Musierowicz, *Bull. Acad. polon. Sci.*, 1963, **11**, 507.
[10] P. de Smet and A. van Dormael, *Bull. Soc. chim. belges*, 1949, **58**, 472.

alkenes (cf. V). 2-Chloromethylquinoline also reacted with triethyl phosphite to yield diethyl 2-quinolylmethylphosphonate [9] the anion of which reacted with acetophenone to give 2-(2-phenylprop-1-enyl)quinoline.

The configuration of the above alkenes is not known. N.m.r. studies on 2-(2-phenylprop-1-enyl)benzothiazole by Professor J. Metzger favour a *trans*-configuration of the benzothiazolyl and phenyl groups, as would also be expected on steric grounds for a planar molecule.

Experimental

2-Benzothiazolylmethyltriphenylphosphonium Bromide (cf. II).—2-Bromomethylbenzothiazole [11] (2·28 g., 0·01 mole), triphenylphosphine (2·62 g., 0·01 mole), and benzene (10 ml.) were refluxed together for 15 min. A cream solid had then separated. It was collected after chilling and washed with cold benzene. From ethanol–ether it (4·15 g., 84%) formed fawn *needles*, m. p. 262—264° (Found: C, 63·5; H, 4·45; N, 2·75; S, 6·75. $C_{26}H_{21}BrNPS$ requires C, 63·7; H, 4·3; N, 2·85; S, 6·55%).

2-Benzothiazolylmethylenetriphenylphosphorane (cf. III).—The above phosphonium bromide (4·9 g., 0·01 mole) was added to a solution of sodium (0·23 g., 0·01 atom) in anhydrous ethanol (25 ml.). The solid dissolved, a little yellow tar formed, which crystallised rapidly, and a mass of crystals separated. The solids were collected after 15 min. From benzene–light petroleum the required *phosphorane* (2·05 g., 50%) formed orange prisms, m. p. 163° (Found: C, 76·5; H, 5·1; N, 3·2; P, 8·0; S, 8·05. $C_{26}H_{20}NPS$ requires C, 76·3; H, 4·9; N, 3·4; P, 7·55; S, 7·8%).

Diethyl 2-Benzothiazolylmethylphosphonate.—2-Bromomethylbenzothiazole (2·3 g.) and ethyl phosphite (1·75 ml.) were heated together at 140° for 45 min. Evolution of ethyl bromide had then ceased, leaving a residual brown oil. The *product* was obtained as a pale yellow oil, b. p. 170—176°/0·2 mm., in 80% yield (Found: C, 50·3; H, 5·6; N, 4·65; P, 10·7; S, 11·4. $C_{12}H_{16}NO_3PS$ requires C, 50·5; H, 5·6; N, 4·9; P, 10·85; S, 11·25%).

Alkene Formation from Phosphonate.—The phosphonate (0·01 mole) in anhydrous dimethoxyethane (20 ml.) was treated with sodium hydride (0·01 mole) at 20° with cooling and the aldehyde or ketone added at −10, 0, or 25°, depending on the carbonyl reactivity. The completion of slime separation was taken as an indication of reaction end-point. In some cases final heating was required. The temperature range of each experiment is given below. Products were isolated by dilution of the reaction mixture with water.

2-4′-Dimethylaminostyrylbenzothiazole (cf. V; R = H, R′ = C_6H_4·NMe_2) (20° then heat for 5 min. at 100°). From ethanol the product was obtained (92%) as soft yellow needles, m. p. 207—208° (lit.,[12] m. p. 206—208°) (Found: C, 72·6; H, 5·75; N, 10·1; S, 11·3. Calc. for $C_{17}H_{16}N_2S$: C, 72·8; H, 5·7; N, 10·0; S, 11·45%).

2-(4-p-Dimethylaminophenylbuta-1,3-dienyl)benzothiazole (cf. V; R′ = CH:CH·C_6H_4·NMe_2, R = H) (20° then heat for 5 min. at 100°). This *product* was obtained (91%) as a bright orange powder, m. p. 197—199° (from benzene) (Found: C, 74·5; H, 6·1; N, 8·95; S, 10·25. $C_{19}H_{18}N_2S$ requires C, 74·5; H, 5·9; N, 9·15; S, 10·45%). It fluoresces strongly orange-red in ultraviolet light.

2-(Penta-1,3-dienyl)benzothiazole (cf. V; R = H, R′ = CH:CHMe) (−10° to 0° for 10 min. then at 20° for 30 min.). From light petroleum (b. p. 40—60°) followed by an propan-2-ol rinse, this *product* (1·25 g., 62%) formed colourless plates, m. p. 72—73° (Found: C, 71·6; H, 5·6; N, 6·85; S, 16·0. $C_{12}H_{11}NS$ requires C, 71·6; H, 5·45; N, 6·95; S, 15·9%).

2-(2-Methylprop-1-enyl)benzothiazole (cf. V; R = R′ = Me) (25—37° then heat at 100° for 30 min.). From light petroleum (b. p. 60—80°) the product (0·95 g., 50%) formed flat yellow needles, m. p. 81—82° (lit.,[10] m. p. 79—80°) (Found: C, 70·1; H, 6·0; N, 7·2; S, 17·1. Calc. for $C_{11}H_{11}NS$: C, 69·8; H, 5·8; N, 7·4; S, 16·95%), $\lambda_{max.}$ 293 mμ in n-hexane.

2-(2-Methylbut-1-enyl)benzothiazole (cf. V; R = Me, R′ = Et) (0—25° during 2 hr.) was obtained as a colourless oil, b. p. 139—140°/5 mm. (lit.,[10] b. p. 138—139°/4·5 mm.) in 81% yield (Found: C, 71·5; H, 6·7; N, 7·0; S, 15·8. Calc. for $C_{12}H_{13}NS$: C, 71·0; H, 6·5; N, 6·9; S, 15·75%).

3-Ethoxycarbonylmethyl-5-[3-ethyl-4-(3-methylbenzothiazolin-2-ylidene)but-2-enylidene]-2-thiothiazolid-4-one. The compound (V; A = 2-Benzothiazolyl, R = Me, R′ = Et) (1·0 g.) and

[11] V. M. Zubarowski, *Zhur. obshchei Khim.*, 1951, **21**, 2055.
[12] L. G. S. Brooker and R. H. Sprague, *J. Amer. Chem. Soc.*, 1941, **63**, 3203.

dimethyl sulphate (0·5 ml.) were fused together in a steam-bath for 30 min. and the resulting tar was washed with ether. 3-Ethoxycarbonylmethyl-5-ethoxymethylenerhodanine [13] (1·4 g.), ethanol (10 ml.), and triethylamine (0·8 ml.) were added to the tar and the whole was refluxed for 15 min. The blue solution rapidly deposited the *dye*. It (1·7 g., 76%) was obtained as soft green flakes, m. p. 259° (from pyridine–ethanol) (Found: C, 56·9; H, 5·1; N, 5·95; S, 21·7. $C_{21}H_{22}N_2O_3S_3$ requires C, 56·5; H, 4·95; N, 6·3; S, 21·5%).

2-(2-*Phenylprop*-1-*enyl*)*benzothiazole* (cf. V; R = Me, R′ = Ph) (25—35° then heat for 15 min. at 100°) was obtained (1·6 g., 64%) as glistening cream flakes, m. p. 77 °(lit.,[10] m. p. 77—78°) (from ethanol) (Found: C, 76·5; H, 5·5; N, 5·75; S, 12·9. Calc. for $C_{16}H_{13}NS$: C, 76·4; H, 5·2; N, 5·6; S, 12·75%). It fluoresced weakly blue in ultraviolet light, $\lambda_{max.}$ 323 mμ in n-hexane.

2-(2-2′-*Naphthylprop*-1-*enyl*)*benzothiazole* (cf. V; R = Me, R′ = 2-$C_{10}H_7$) (20° then for 1 hr. at 100°). It (1·2 g., 40%) was obtained as glossy, white *flakes*, m. p. 151—155° (from ethanol) (charcoal) (Found: C, 79·7; H, 4·95; N, 4·45; S, 10·55. $C_{20}H_{15}NS$ requires C, 79·75; H, 5·0; N, 4·65; S, 10·6%). It fluoresced weakly blue in ultraviolet light. $\lambda_{max.}$ 336 mμ in n-hexane.

2-(2-2′-*Pyridylprop*-1-*enyl*)*benzothiazole* (V; R = Me, R′ = 2-C_5H_4N) (0° then for 30 min. at 100°). From light petroleum (b. p. 60—80°) (charcoal) it (1·4 g., 55%) formed short, pale yellow *needles*, m. p. 95—96° (Found: C, 71·2; H, 5·05; N, 11·2; S, 12·75. $C_{15}H_{12}N_2S$ requires C, 71·4; H, 4·75; N, 11·1; S, 12·7%). It fluoresced yellow to ultraviolet light, $\lambda_{max.}$ 330 mμ in n-hexane.

2-(2-3′-*Pyridylprop*-1-*enyl*)*benzothiazole* (cf. V; R = Me, R′ = 3-C_5H_4N) (0° then for 30 min. at 100°). It formed slender, pale yellow *needles*, m. p. 96—97° (from light petroleum) (67%) (Found: C, 71·6; H, 5·0; N, 11·3; S, 12·95). It fluoresced powerfully green-yellow in ultraviolet light, $\lambda_{max.}$ 328 mμ in n-hexane.

2-(2-4′-*Pyridylprop*-1-*enyl*)*benzothiazole* (cf. V; R = Me, R′ = 4-C_5H_4N) (0—15° for 30 min.). It (1·6 g., 64·5%) was obtained as cream *flakes*, m. p. 99—100° (from light petroleum) (Found: C, 71·6; H, 4·9; N, 11·1; S, 12·80). It fluoresced weakly blue to ultraviolet light, $\lambda_{max.}$ 325 mμ in n-hexane.

2-(2-2′-*Thienylprop*-1-*enyl*)*benzothiazole* (cf. V; R = Me, R′ = C_4H_3S) (0° then for 1 hr. at 100°). It (1·55 g., 60%) formed pale yellow *aggregates*, m. p. 85—86° (from ethanol, then light petroleum) (Found: C, 65·4; H, 4·4; N, 5·15; S, 24·75. $C_{14}H_{11}NS_2$ requires C, 65·4; H, 4·25; N, 5·45; S, 24·9%). It fluoresced blue in ultraviolet light, $\lambda_{max.}$ 350 mμ in n-hexane.

2-(4-*Phenylbut*-1-*en*-3-*ynyl*)*benzothiazole* (cf. V; R = H, R′ = C:CPh) (0° then set aside for 1 hr.). It was recrystallised from ethanol (charcoal) and obtained in 29% yield (0·75 g.) as soft, yellow *flakes*, m. p. 130—132° (Found: C, 78·3; H, 3·9; N, 5·35; S, 12·2. $C_{17}H_{11}NS$ requires C, 78·15; H, 4·2; N, 5·45; S, 12·25%). It fluoresced strongly yellow in ultraviolet light, $\lambda_{max.}$ 345 mμ in n-hexane.

2-(2-*Phenylprop*-1-*enyl*)*quinoline* (V; A = 2-quinolyl, R = H, R′ = Ph). Bromomethylquinoline [14] (3·15 g.) and triethyl phosphite (2·5 ml.) were heated together on a steam-bath for 10 min. Evolution of ethyl bromide had then ceased, but further heating for 20 min. at 140° caused slight further effervescence. The thick oil was dissolved in anhydrous 1,2-dimethoxyethane (20 ml.), and sodium hydride (0·7 g., 50%) was added while the temperature was kept below 20°. After completed hydrogen evolution at 23°, acetophenone (1·65 ml.) was added, the temperature being kept below 40° by cooling. After standing overnight, water (100 ml.) was added and the precipitated oil, which crystallised rapidly, was air-dried and recrystallised from benzene–light petroleum. It (0·85 g., 24·5%) formed cream *needles*, m. p. 102—103° (from ethanol) (Found: C, 88·35; H, 5·9; N, 5·7. $C_{18}H_{15}N$ requires C, 88·2; H, 6·1; N, 5·7%), $\lambda_{max.}$ 276, 339 mμ in n-hexane.

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[13] E. B. Knott, *J.*, 1954, 1482.
[14] B. R. Brown, D. Ll. Hammick, and B. H. Thewlis, *J.*, 1951, 1145.