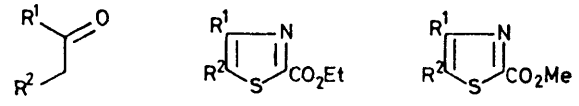
An Infrared Study of Rotational Isomerism in Thiazole-2-carboxylates

By **Perry T. Kaye, G. Denis Meakins,* Charles Willbe,** and **Peter R. Williams,** Dyson Perrins Laboratory, Oxford University, South Parks Road, Oxford OX1 3QY

A series of alkyl thiazole-2-carboxylates containing a range of substituents at the 4- and 5-positions has been prepared. Solutions of these esters (mostly new compounds) show well resolved doublets in the i.r. C=O region which arise from rotational isomers. The higher wavenumber components are assigned to the more polar carbonyl *O,S-anti-s-trans*-rotamers and the lower wavenumber components to the carbonyl *O,S-syn-s-trans*-forms. Small, but systematic, differences between the methyl esters are noted.

As already discussed,[1a] rotational isomerism in esters is more effectively studied by i.r. spectrometry than by n.m.r. methods, and in previous work the rotamers of furan-,[1b] thiophen-,[1c] and pyrrole-2-carboxylates [1a] were identified by examining their C=O stretching bands. In thiazole-2-esters the planar forms produced by rotating the ester function have the CO group in the proximity of either the nitrogen or the sulphur atom of the heterocyclic system, and it was conjectured that this might lead to doublet absorptions with an appreciable separation between the components.

Few thiazole-2-carboxylates are described in the literature.[2] In the present work a series of ethyl esters with a range of functional groups at the 4- and 5-positions was readily obtained by the Hantzsch method (see the Scheme); from these the corresponding methyl esters and one t-butyl ester were prepared, care being taken to avoid decarboxylation of the intermediate thiazole-2-carboxylic acids. To facilitate interpretation of the spectrometric results it was important [3] to have available esters with deuterium and bromine substituents at position 5. A 5-deuterio-ester (2m) was synthesised directly from the deuteriated bromo-ketone (5). The 5-bromo-esters (2n), (3n), and (3o) were obtained by routes in which 2-amino-groups were used to facilitate bromination at position 5 and the products were then converted into 2-esters by standard methods. In 2,5-dibromo-4-trifluoromethylthiazole (7) the bromine atoms appear to be of similar reactivity towards butyllithium since the carboxylation sequence gives both the 2-, and 5-bromo-esters (3-) and (8) and the diester (9).



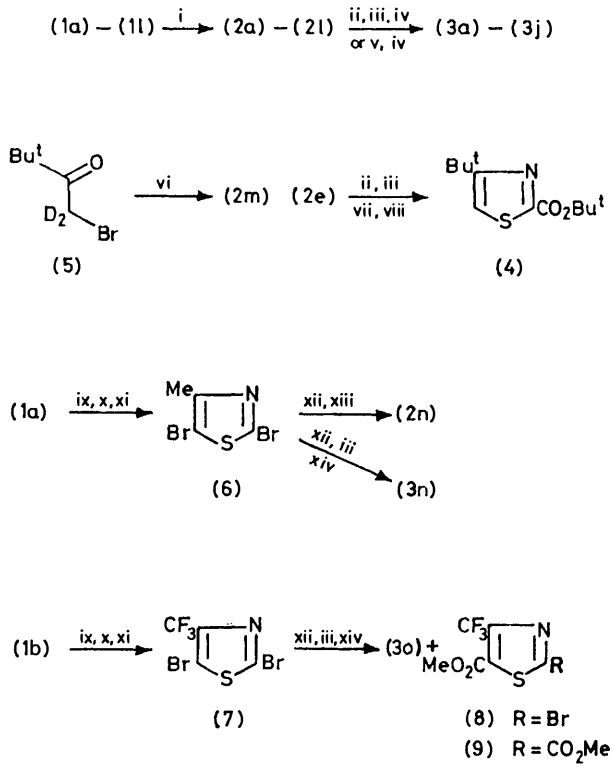
(1) (2) (3)

	R^1	R^2		R^1	R^2		R^1	R^2
a;	Me	H	f;	Ph	H	k;	Me	Et
b;	CF_3	H	g;	C_6H_4Br-*p*	H	l;	1-Ad	H
c;	Et	H	h;	H	Me	m;	Bu^t	D
d;	Pr^n	H	i;	H	Et	n;	Me	Br
e;	Bu^t	H	j;	Me	Me	o;	CF_3	Br

1-Ad = 1-Adamantyl

The i.r. bands of the esters in the 1 800—1 700 and 3 600—3 400 cm^{-1} regions are recorded in Table 1. Apart from the three 4-trifluoromethyl compounds (2b), (3b), and (3o), which have three bands, solutions of the esters in carbon tetrachloride show doublets in the CO fundamental region, the components being so well separated (*ca.* 30 cm^{-1}) that there is little overlap. The persistence of these doublets in (i) solutions in carbon tetrachloride of different concentrations, (ii) a solvent (acetonitrile) of much higher polarity, (iii) the overtone region, and (iv) esters with a variety of substituents (notably those which afford a comparison between a 5-protio-ester and its deuterio- or bromo-analogue) establishes [3] that they arise from rotational isomers.

By the reasoning set out earlier [1b] the rotamers generat-



SCHEME *Reagents:* i, $H_2N{\cdot}CS{\cdot}CO_2Et$; ii, KOH–$H_2O$; iii, aqueous HCl, 20 °C; iv, H_2SO_4–MeOH, 10 d at 20 °C; v, KOH–MeOH; vi, $H_2N{\cdot}CS{\cdot}CO_2Et$–EtOD; vii, $[COCl]_2$; viii, $LiOBu^t$; ix, $[H_2N]_2CS$; x, Br_2–Et_2O; xi, HNO_2–NaBr–$CuSO_4$; xii, Bu^nLi, then CO_2; xiii, H_2SO_4–EtOH, 10 d at 20 °C; xiv, CH_2N_2.

TABLE 1

I.r. of alkyl thiazole-2-carboxylates

Esters were examined as described previously [a] at a spectral slit-width of 1.5 cm^{-1} on a spectrometer purged continuously with dry air. Solutes and solvents were dried immediately before use, and solutions were made up in a dry box. The experimental traces of $\nu(cm^{-1})$ *vs.* absorbance were resolved into symmetrical components using an analogue computer, and the components' positions (in cm^{-1} at 303K) are followed, in parentheses, by their percentage areas. Weak bands (areas <5%) were neglected and are not shown here. Enthalpy differences (ΔH^0, J mol^{-1}) between the forms giving rise to the doublets, obtained using solutions in CH_2Cl_2 over the range 213–308K, are in the direction (form with higher ν)→(form with the lower ν); the statistical errors in ΔH^0 vary between ±300 and ±600 J mol^{-1} according to the correlation coefficients of the regressions of $1/T$ *vs.* ln (area of lower ν component/area of higher ν component).

	CO Fundamental region				CO Overtone region		
	CCl_4		MeCN		CCl_4		
Ester							ΔH^0
(3a)	1 751(35)	1 723(65)	1 741(52)	1 719(48)	3 485(40)	3 427(60)	300
(2a)	1 748(30)	1 716(70)	1 737(49)	1 713(51)	3 478(35)	3 414(65)	−1 200
(3b) [b]	1 758(23)	1 728(70)	1 747(56)	1 726(44)	3 502(33)	3 440(67)	−200
(2b) [b]	1 755(14)	1 722(76)	1 744(53)	1 719(47)	3 492(29)	3 426(71)	−800
(3c)	1 748(35)	1 721(65)	1 739(52)	1 717(48)	3 479(43)	3 424(57)	
(2c)	1 746(31)	1 714(69)	1 734(57)	1 710(43)	3 473(33)	3 412(67)	−600
(3d)	1 750(34)	1 722(66)	1 740(52)	1 718(48)	3 481(40)	3 428(60)	
(2d)	1 746(31)	1 716(69)	1 736(49)	1 712(51)	3 473(44)	3 414(56)	−1 400
(3e)	1 748(34)	1 721(66)	1 740(54)	1 718(48)	3 481(42)	3 428(58)	200
(2e)	1 744(34)	1 715(66)	1 736(56)	1 712(44)	3 471(40)	3 413(60)	−800
(2m)	1 743(33)	1 715(67)	1 735(55)	1 711(45)	3 470(37)	3 412(63)	
(4)	1 740(42)	1 708(58)	1 730(65)	1 704(35)	3 460(46)	3 398(54)	−500
(2l)	1 745(31)	1 714(61)	1 735(52)	1 711(48)	3 470(36)	3 411(64)	−1 200
(3f)	1 750(37)	1 722(63)	1 741(46)	1 719(54)	3 483(41)	3 428(59)	−800
(2f)	1 746(36)	1 715(64)	1 737(49)	1 713(51)	3 474(40)	3 413(60)	−1 600
(3g)	1 752(35)	1 723(65)	1 742(49)	1 719(51)	3 484(40)	3 428(60)	−100
(2g)	1 749(33)	1 717(67)	1 737(47)	1 713(53)	3 480(35)	3 416(65)	−200
(3h)	1 749(35)	1 720(65)	1 739(54)	1 716(46)	3 481(36)	3 422(64)	0
(2h)	1 746(31)	1 714(69)	1 735(51)	1 710(49)	3 472(34)	2 410(66)	−100
(3i)	1 748(34)	1 720(66)	1 739(55)	1 717(45)	3 480(43)	3 424(57)	
(2i)	1 744(33)	1 714(67)	1 735(54)	1 711(46)	3 472(39)	3 412(61)	−1 600
(3j)	1 746(34)	1 719(64)	1 737(56)	1 715(44)	3 473(37)	3 422(63)	
(2j)	1 743(32)	1 713(68)	1 733(55)	1 709(45)	3 466(35)	3 408(65)	−800
(2k)	1 742(32)	1 712(68)	1 731(54)	1 708(46)	3 465(43)	3 407(57)	−1 400
(3n)	1 752(32)	1 724(68)	1 743(48)	1 720(52)	3 488(39)	3 426(61)	−400
(2n)	1 748(30)	1 717(70)	1 739(46)	1 714(54)	3 478(35)	3 417(65)	−1 600
(3o) [b]	1 758(14)	1 729(71)	1 748(57)	1 726(43)	3 501(33)	3 439(67)	−200

[a] D. J. Chadwick, J. Chambers, G. D. Meakins, and R. L. Snowden, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1959. [b] Third bands (CCl_4 solutions, CO fundamental region) of appreciable intensity are given at 1 765(7) by the ester (3b), 1 761(10) by the ester (2a), and 1 765(15) by the ester (3o).

ing the doublets may be taken to be the carbonyl *O,S-anti-s-trans-* and the carbonyl *O,S-syn-s-trans-forms* (see the Figure). From Table 1 it is seen that both the higher- and the lower-wavenumber components of each doublet (termed for brevity the *h* and *l* bands) move to lower wavenumber with increasing solvent polarity, but that the decrement is much greater for the *h* band. Further, while the *l* band is the stronger in carbon tetrachloride the bands are of approximately equal intensity in acetonitrile. Thus the rotamer giving the *h* band is the more polar form. Dipole moment considerations, even at the simple level illustrated in the Figure, suggest that the *anti*-rotamer (10a) is the more polar form and, hence, gives the *h* band.

While neither rotamer is likely to be planar, repulsion arising from the proximity of the nitrogen and carbonyl oxygen-atom lone pairs in the *anti*-rotamer (10a) should lead to a greater twisting between the heterocyclic ring and the ester function in this form; the contribution of the dipolar canonical (10b) will then be less than that of the corresponding canonical (11b) to the *syn*-rotamer (11a). This feature not only supports the attribution of the *h* band to the *anti*-rotamer, reached by considering band intensities, but also explains the larger shift in position of this band as the solvent polarity is changed. (With the doublets of somewhat similar esters, the quinoxaline-2-carboxylates, the *h* components have been ascribed to carbonyl *O,N-syn*-rotamers, corresponding to the present *anti*-forms [4]).

Comparison of the results obtained with corresponding methyl and ethyl esters reveals effects which, although small, occur with all the pairs of thiazole-2-esters. As expected, the ethyl esters absorb at lower wavenumber than the methyl esters. However, for the *h* and *l* bands of the carbon tetrachloride solutions the decrease is larger for the *l* band; the effect applies also to the solutions in acetonitrile, but is there attenuated by the more polar solvent. This difference may stem from an electrostatic attraction between the carbonyl-oxygen and ring-sulphur atoms in the *syn*-form, giving a system (12) in which the inductive effect of an alkyl group on the double-bond character of the carbonyl system would be accentuated. A larger decrease in wavenumber of the *l* band would result, especially in the non-polar solvent.

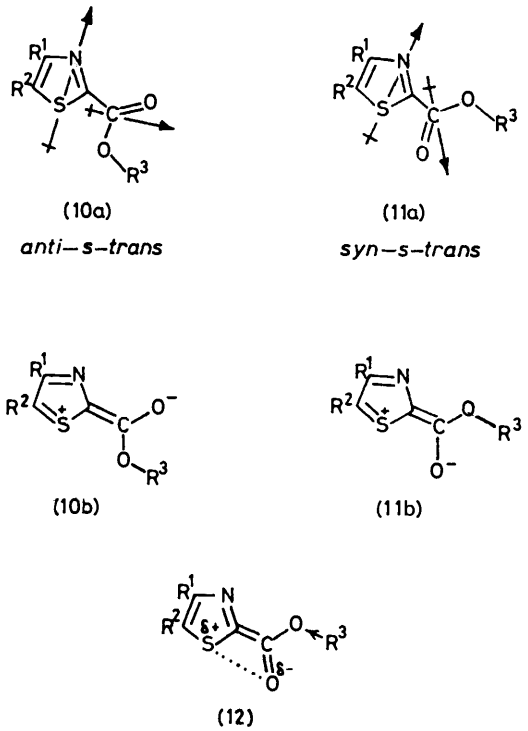


FIGURE Rotational isomers

In order to compare investigation by different techniques the esters were examined over a range of temperatures using, as solvent, deuteriomethylene chloride for ^1H and ^{13}C n.m.r. measurements and methylene chloride for i.r. work. The lack of significant variation in the n.m.r. spectra confirms the expectation [1a] of a very low barrier to rotation between the forms of the esters. Although systematic changes in the relative intensities of the i.r. bands (*l* and *h*) occurred these are so small that most of the derived enthalpy differences (Table 1) are no bigger than the possible errors associated with them. It appears that the *syn*-rotamers of the ethyl esters are the thermochemically more stable forms, but detailed discussion is unwarranted.

EXPERIMENTAL

The general procedures for preparing the esters (2a)—(2l) and (3a)—(3l) are illustrated by examples. The characterisation of all new esters is shown in Table 2. The constants of the known esters agreed with the literature values [references cited in ref. 2(*a*) for esters (2a), (3a), and (2h) and ref. 2(*b*) for ester (2f)].

4-t-Butylthiazole-2-carboxylates (2e), (2m), (3e), *and* (4).—1-Bromo-3,3-dimethylbutan-2-one (16.8 ml) was added during 15 min to a solution of ethyl thiocarbamoylformate (16.6 g) in EtOH (100 ml) which was boiling under reflux. The solution was boiled for a further 30 min, poured into ice–water (250 ml), basified with 18M NH_3, and extracted with EtOAc. The EtOAc solution was washed with aqueous NaCl, dried, and treated with activated charcoal. Evaporation of the solvent and distillation of the residue gave *ethyl 4-t-butylthiazole-2-carboxylate* (2e) (13.6 g), b.p. 102—104 °C at 0.4 mmHg, which crystallised from MeOH.

A mixture of 3,3-dimethylbutan-2-one (15 ml), dry Et_2O (15 ml), D_2O (25 ml), and 9M NaOD in D_2O (5 ml) was stirred vigorously in a sealed flask for 1 d at 20 °C. The layers were separated and the Et_2O solution was treated with more D_2O (25 ml) and 9M NaOD (5 ml). The Et_2O solution was dried over molecular sieves (previously washed with D_2O and dried at 80 °C under reduced pressure) and

TABLE 2

Characterisation of new esters

Ester	M.p. (°C)	B.p. (°C) bath temp./ mmHg	Analyses (%) found C	H	N	Molecular formula	Required (%) C	H	N
(2b)	33—35		37.3	2.5	6.2	$C_7H_6F_3NO_2S$	37.1	2.5	6.2
(3b)	27—29		34.2	1.9	6.5	$C_6H_4F_3NO_2S$	34.1	1.9	6.6
(2c)		129—130/1.5	52.1	6.0	7.4	$C_8H_{11}NO_2S$	51.9	6.0	7.6
(3c)		58—61/0.7	48.9	5.3	8.1	$C_7H_9NO_2S$	49.1	5.3	8.2
(2d)		66—68/0.3	54.1	6.6	7.1	$C_9H_{13}NO_2S$	54.25	6.6	7.0
(3d)		55—58/0.2	51.8	6.0	7.4	$C_8H_{11}NO_2S$	51.9	6.0	7.6
(2e)	40—41		56.4	7.1	6.5	$C_{10}H_{15}NO_2S$	56.3	7.1	6.6
(2m)	39—40		56.1		6.6	$C_{10}H_{14}CNO_2S$	56.05		6.5
(3e)	48—49		54.4	6.6	6.9	$C_9H_{13}NO_2S$	54.2	6.6	7.0
(4)	113—114		59.8	7.9	5.9	$C_{12}H_{19}NO_2S$	59.7	7.9	5.8
(2l)	147—148		66.1	7.3	4.8	$C_{16}H_{21}NO_2S$	66.0	7.3	4.8
(3f)	77—78		60.0	4.2	6.5	$C_{11}H_9NO_2S$	60.3	4.1	6.4
(2g)	106—107		46.1	3.1	4.5	$C_{12}H_{10}BrNO_2S$	46.15	3.2	4.5
(3g)	149—151		44.0	2.6	4.8	$C_{11}H_8BrNO_2S$	44.3	2.7	4.7
(3h)	56—57		45.8	4.6	8.7	$C_6H_7NO_2S$	45.9	4.5	8.9
(2i)		104—105/0.8	51.8	6.1	7.6	$C_8H_{11}NO_2S$	51.9	6.0	7.6
(3i)		65—67/0.1	49.3	5.2	8.1	$C_7H_9NO_2S$	49.1	5.3	8.2
(2j)		118—120/1.1	52.1	5.9	7.3	$C_8H_{11}NO_2S$	51.9	6.0	7.6
(3j)		94—96/0.7	49.2	5.3	8.1	$C_7H_9NO_2S$	49.1	5.3	8.2
(2k)		102—104/0.8	54.3	6.8	6.9	$C_9H_{13}NO_2S$	54.2	6.6	7.0
(2n)		85—87/0.1	33.9	3.3	5.5	$C_7H_8BrNO_2S$	33.6	3.2	5.6
(3n)	68—70		30.6	2.6	5.9	$C_6H_6BrNO_2S$	30.5	2.6	6.0
(3o)	35—37		25.1	1.0	4.6	$C_6H_3F_3NO_2S$	24.8	1.0	4.8
(8)	37—39		24.8	0.9	4.9	$C_6H_3F_3BrNO_2S$	24.8	1.0	4.8
(9)	41—42		35.8	2.2	5.2	$C_8H_6F_3NO_4S$	35.7	2.2	5.2
			C	N	S		C	N	S
(7)		30—32	15.4	4.6	10.5	$C_4Br_2F_3NS$	15.5	4.5	10.3

was then evaporated. Distillation gave 1,1,1-trideuterio-3,3-dimethylbutan-2-one (8.7 g), b.p. 104—106 °C; τ 8.88 (s, Bu^t); *m/e* 103 (M^+, 11%) and 57 (100), containing less than 3% protium in the CD_3·CO group. Bromine (4.1 ml) was added in drops during 25 min to a stirred mixture of the deuterio-ketone (8.2 g), $AlCl_3$ (0.2 g), and dry Et_2O (50 ml) at 5 °C. (The reaction was initiated by warming the mixture briefly to 18 °C.) After a further 15 min the mixture was cooled to −5 °C and D_2O (15 ml) was added cautiously. The Et_2O layer was separated, washed with D_2O, dried over molecular sieves, and evaporated to give an oil (12.1 g) estimated by ^{1}H n.m.r. to contain 97% of 1-bromo-1,1-dideuterio-3,3-dimethylbutan-2-one; τ 8.77 (s, Bu^t); $\nu_{max.}$ 1 726 cm^{-1}, *m/e* 182 and 180 (M^+, ^{81}Br and ^{79}Br, 1%) and 57 (100). Condensation of this material (4.7 g) with ethyl thiocarbamoylformate (3.33 g) in EtOD (10 ml) and subsequent work-up by dilution with D_2O (10 ml), basification with anhydrous K_2CO_3, and extraction with Et_2O gave *ethyl 4-t-butyl-5-deuteriothiazole-2-carboxylate* (2m) (1.95 g), b.p. 105—107 °C at 0.4 mmHg; *m/e* 214 (M^+, 40%) and 153 (100), estimated by ^{1}H n.m.r. to be 97% deuteriated at the 5-position.

A mixture of the ethyl ester (2e) (3 g) and KOH (1.5 g) in H_2O (10 ml) was boiled under reflux for 5 min, diluted with H_2O (15 ml), cooled, washed with Et_2O, made slightly acidic with 2.7M HCl, and extracted with Et_2O. Evaporation at 15 °C gave 4-t-butylthiazole-2-carboxylic acid (2.1 g), m.p. 92—95 °C (with evolution of CO_2). The acid (1.2 g) was added to a solution, cooled to 20 °C, of H_2SO_4 (5.2 ml) in MeOH (50 ml) and the mixture was kept at 20 °C, with occasional shaking, for 10 d. Neutralisation with aqueous $NaHCO_3$ and extraction with Et_2O gave a material which was absorbed from light petroleum onto a column of SiO_2 (30 g). Elution with Et_2O–light petroleum (1 : 1) gave an oil which sublimed at 1 mmHg to give *methyl 4-t-butylthiazole-2-carboxylate* (3e) (0.85 g).

In an alternative procedure a solution of KOH (0.68 g) in MeOH (16 ml) was added to the ethyl ester (2e) (1.1 g) in MeOH (5 ml) at 40 °C. After 30 min at 40 °C the solvent was removed at 20 °C and 15 mmHg. Treatment of the residue with H_2SO_4–MeOH and work-up as before gave the methyl ester (3e) (0.75 g).

Oxalyl chloride (1.14 ml) was added to a stirred suspension of 4-t-butylthiazole-2-carboxylic acid (1.2 g) in dry C_6H_6 (25 ml) under an atmosphere of N_2. The mixture was warmed gradually and then boiled under reflux for 15 min. The solvent was removed under reduced pressure, dry tetrahydrofuran (THF) (5 ml) was added, and the solution was added as drops to a solution of LiOBu^t, prepared by adding 1.52M Bu^{n}Li in hexane (4 ml) as drops to a stirred solution of dry Bu^{t}OH (0.45 g) in THF (8 ml) under N_2. The mixture of solutions was boiled under reflux for 1 h and then cooled to 0 °C. Water (11 ml) was added slowly and the mixture was stirred for a further 10 min. Extraction with EtOAc and crystallisation from MeOH gave *t-butyl 4-t-butylthiazole-2-carboxylate* (4) (0.72 g).

5-Bromo-4-methylthiazole-2-carboxylates (2n) *and* (3n).—Condensation of bromoacetone with thiourea gave 2-amino-4-methylthiazole, b.p. 96—98 °C at 0.7 mmHg (lit.,[5] 130—133 °C at 18 mmHg). Bromine (124 g) was added during 2 h to a vigorously stirred solution of the 2-amine (79 g) in Et_2O (700 ml) at 15 °C. Collection of the precipitate and crystallisation from EtOH gave 5-bromo-4-methylthiazol-2-ylammonium bromide (141 g), m.p. *ca.* 165 °C (decomp.) (lit.,[6] 128 °C). Solutions of the bromide (27.4 g) in 9M H_2SO_4 (950 ml) and of $CuSO_4$ (30 g) and NaBr (26 g) in H_2O (300 ml) were mixed and stirred at 0 °C. A solution of $NaNO_2$ (16 g) in H_2O (50 ml) was added slowly beneath the surface of the reaction mixture at such a rate that the temperature did not exceed 3 °C. After a further 30 min at 3 °C and 30 min at 20 °C the mixture was diluted with brine (800 ml) and extracted with Et_2O to give a material which was distilled in steam. Extraction of the distillate with Et_2O gave 2,5-dibromo-4-methylthiazole (6) (13.5 g), b.p. 80—81 °C at 15 mmHg (lit.,[7] 110 °C at 27 mmHg).

A solution of the dibromo-compound (6) (1.3 g) in hexane (20 ml) was added as drops to a solution of Bu^{n}Li (0.83 g) in hexane (110 ml), stirred under N_2 at −60 °C. The solution was stirred for 1 h at −60 °C, then poured into a slurry of solid CO_2–Et_2O. Water (200 ml) was added, the H_2O layer was separated, washed with Et_2O, made slightly acidic with 5M HCl, and extracted with EtOAc. The dried EtOAc solution was treated with CH_2N_2 in Et_2O [prepared from *N*-nitrosomethylurea (5.2 g)] and, after 5 min, the solvents were removed and the residue was sublimed at 1 mmHg to give *methyl 5-bromo-4-methylthiazole-2-carboxylate* (3n) (0.91 g).

The preceding experiment was repeated as far as the treatment with solid CO_2–Et_2O. The mixture was filtered, and the precipitate was washed with Et_2O, then dissolved in a solution, cooled to 20 °C, of H_2SO_4 (12 ml) in EtOH (120 ml). After 10 d at 20 °C the solution was worked up to give *ethyl 5-bromo-1-methylthiazole-2-carboxylate* (2n) (0.75 g).

4-Trifluoromethylthiazole-2-carboxylates (3o), (8), *and* (9).—Condensation of 3-bromo-1,1,1-trifluoropropane with thiourea gave 2-amino-4-trifluoromethylthiazole, m.p. 67—68 °C (lit.,[8] 68—69.5 °C). This amine (15 g) was treated with Br_2 as in the preceding section to give *5-bromo-4-trifluoromethylthiazol-2-ylammonium bromide* (18.3 g), m.p. 240—243 °C (from EtOH) (Found: C, 14.6; H, 0.7; N, 8.5. $C_4H_3Br_2F_3N_2S$ requires C, 14.6; H, 0.9; N, 8.4%); *m/e* 246 (81%) and 167 (100), a portion (12.6 g) of which was converted into *2,5-dibromo-4-trifluoromethylthiazole* (7) (7.8 g). A solution of this dibromo-compound (2.8 g) in hexane (30 ml) was added to 1.53M Bu^{n}Li in hexane (15 ml), and the resulting mixture was treated with solid CO_2, acidified, extracted with ethyl acetate, and treated with CH_2N_2 as in the preceding experiment. The resulting oil (4.3 g) was heated gradually to 120 °C at 0.05 mmHg and the volatile material was subjected to preparative g.l.c. on a Pye R105 Chromatograph (15-in column of 15% OV17 on Embacel, N_2 flow of 60 ml min^{-1}). The products emerged in the following order: *methyl 2-bromo-4-trifluoromethylthiazole-5-carboxylate* (8) (510 mg), *methyl 5-bromo-4-trifluoromethylthiazole-2-carboxylate* (3o) (444 mg), and *dimethyl 4-trifluoromethylthiazole-2,5-dicarboxylate* (9) (668 mg).

We thank the S.R.C. for a studentship (to C. W.).

[0/1971 *Received*, 23*rd December*, 1980]

REFERENCES

[1] (*a*) P. T. Kaye, R. Macrae, G. D. Meakins, and C. H. Patterson, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1631; (*b*) D. J. Chadwick, J. Chambers, R. Macrae, G. D. Meakins, and R. L. Snowden, *ibid.*, 1976, 597; (*c*) D. J. Chadwick, J. Chambers, G. D. Meakins, S. E. Musgrave, and R. L. Snowden, *J. Chem. Res.*, 1977, (*S*) 26; (*M*) 0385.

[2] (*a*) R. Meyer in ' Thiazole and Its Derivatives,' Part 1, Ch. IV, ed. J. V. Metzger, John Wiley and Sons, New York, 1979, lists six thiazole-2-carboxylates in Table IV–2, p. 540; (*b*) G. Kempler, H. Schafer, and G. Sarodnick, *Z. Chem.*, 1970, **10**, 460, prepared ethyl 4-phenylthiazole-2-carboxylate.

[3] D. J. Chadwick, J. Chambers, G. D. Meakins, and R. L. Snowden, *J. Chem. Soc., Perkin Trans. 2*, 1975, 13.

[4] W. F. Gun and M. M. Jouille, *J. Org. Chem.*, 1965, **30**, 3982.

[5] J. R. Byers and J. B. Dickey, *Org. Synth.*, 1943, **2**, 31.

[6] Y. Garreau, *Bull. Soc. Chim. Fr.*, 1954, 1048.

[7] H. Minato, E. Sakamoto, K. Shinmoni, and K. Takeda, *J. Pharm. Soc. Jpn.*, 1947, **67**, 193.

[8] J. B. Dickey, E. B. Towne, and G. F. Wright, *J. Org. Chem.*, 1955, **20**, 499.