Action of Carbon Tetrachloride on the Carbon Disulfied Adducts of Trimethyl- and Triethylphosphine.—Three grams each of the two carbon disulfide adducts were suspended in 50 ml. of carbon tetrachloride in a stoppered flask. During several hours standing the characteristic red color of the adduct disappeared and an oily product collected on the surface of the solvent. Evaporation of the solvent left an oil from which crystals formed slowly. The following quantitative observations were made: (1) The semisolid residue was completely soluble in water, (2) it was acidic to litmus, (3) silver nitrate gave a white precipitate, (4) no sulfide ions were detected with lead acetate, and (5) the characteristic odor of the phosphine (which exists in the carbon disulfide adduct) was no longer detectable.

The residue from the trimethylphosphine adduct was recrystallized from alcohol and produced a white solid melting at 154°. When an authentic sample of trimethylphosphine sulfide, prepared from methyllithium and thiophosphoryl chloride, was mixed with this solid, the melting point was not depressed.

When the residue from the triethylphosphine adduct was recrystallized from alcohol, a white solid melting at 94° was recovered. Although triethylphosphine sulfide has been reported[10] to melt at 94°, no authentic sample of this compound was available for comparison. Therefore, this compound was analyzed.

Anal. Calcd. for $C_6H_{15}PS$: C, 47.98; H, 10.06; P, 20.62. Found: C, 47.97, 48.09; H, 9.95, 10.20; P, 20.62, 20.62.

Acknowledgment.—We are appreciative of a grant from the Atomic Energy Commission which supported this work under Contact AT-(40-1)-2733. We also appreciate the helpful suggestions made by Dr. R. A. Zingaro.

Synthesis of Polyfluorinated Heterocycles by Indirect Fluorination with Silver Fluorides. I. Fluoro-*s*-triazines and Reactions of Cyanuric Fluoride[1]

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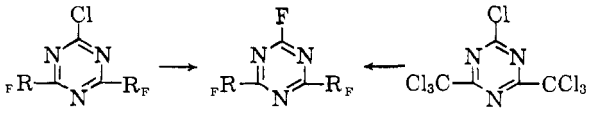
Received November 21, 1961

The conversion of chloro-*s*-triazines to the corresponding fluoro-*s*-triazines by means of several inorganic fluorinating agents was studied. Silver fluoride was found to be most useful for this purpose. Reactions of cyanuric fluoride with alcohols, amines, and diazomethane are described.

As part of a comprehensive study of the preparation of fluorinated heterocyclic compounds, possibilities for the conversion of chloro-*s*-triazines to the corresponding fluoro-*s*-triazines by means of inorganic fluorinating agents were investigated. At the time this study was undertaken, the conversion of cyanuric chloride into cyanuric fluoride by means of potassium fluorosulfinate[3] or sulfur tetrafluoride[4] had not been reported; however, this transformation had been achieved by means of antimony trifluoride dichloride (Swarts reagent).[5,6] The latter reagent converted 2,4-bis(trichloromethyl)-6-chloro-*s*-triazine (VI) easily into 2,4-bis(trifluoromethyl)-6-fluoro-*s*-triazine (III),[5] but when applied to the conversion of 2,4-bis(perfluoroalkyl)-6-chloro-*s*-triazines (I and II) into the perfluorinated triazines (IV and V), the reaction gave low yields.



I. $R_F = CF_2CF_3$ III. $R_F = CF_3$ VI
II. $R_F = CF_2CF_2CF_3$ IV. $R_F = CF_2CF_3$
V. $R_F = CF_2CF_2CF_3$

Therefore, other fluorinating agents were investigated for the preparation of the higher homologs of III from the readily accessible 2,4-bis(perfluoroalkyl)-6-chloro-*s*-triazines.[7] 2,4-Bis(pentafluoroethyl)-6-chloro-*s*-triazine (I) was selected as the prototype for this study.

With mercuric fluoride, only partial conversion of the chlorotriazine (I) to the desired perfluorinated triazine (IV) could be achieved, even when the reactants were heated for several hours. In contrast to this result, silver difluoride reacted vigorously with I to give IV in good yield, but it was difficult to control the very exothermic reaction. The reaction of I with silver fluoride required heating, proceeded smoothly, and gave an almost quantitative yield.

Lead difluoride, a very mild fluorinating agent, did not react at all with compound I even at reflux temperature, but was found to be very useful for the purification of 2,4-bis(perfluoro-

(1) This article is based on work performed during 1956 and 1957 under Project 116-B of The Ohio State University Research Foundation sponsored by the Olin Mathieson Chemical Corporation, New York, N. Y.

(2)(a) To whom inquiries should be directed. (b) Olin Mathieson Chemical Corporation, New Haven, Conn.

(3) D. W. Grisley, Jr., E. W. Gluesenkamp, and S. A. Heininger, *J. Org. Chem.*, **23**, 1802 (1958).

(4) C. W. Tullock, R. A. Carboni, R. J. Harder, W. C. Smith, and D. D. Coffman, *J. Am. Chem. Soc.*, **82**, 5107 (1960).

(5) E. Kober and Ch. Grundmann, *J. Am. Chem. Soc.*, **81**, 3767 (1959); U. S. Pat. 2,845,421, July 29, 1958.

(6) A. F. Maxwell, J. S. Fry, and L. A. Bigelow, *J. Am. Chem. Soc.*, **80**, 548 (1958).

(7) H. Schroeder, *J. Am. Chem. Soc.*, **81**, 5658 (1959).

alkyl)-6-chloro-*s*-triazines. Phosphoryl chloride, which is used in excess for the preparation of such chlorotriazines as I and II, is very difficult to separate from these products by fractional distillation. Treatment with lead difluoride, however, converts the small amounts of contaminating phosphoryl chloride into gaseous phosphoryl fluoride which is easily removed from the unaffected chlorotriazines I or II.

The conversion of 2,4-bis(pentafluoroethyl)-6-chloro-*s*-triazine (I) to the corresponding 6-fluoro-*s*-triazine (IV) by means of the fluorinating agents studied is illustrated by the following table. All reactions were conducted in the absence of solvent.

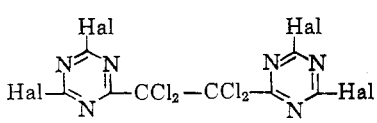
Fluorinating Agent	Reaction Time	Reaction Temp.	Yield, of IV, %
AgF_2	20 min.	20[a]	85
AgF	30 min.	90[a]	98
HgF_2	3 hr.	125	20
SbF_3Cl_2	12 hr.	150	14
PbF_2	1 hr.	125	No reaction

[a] The experiments were initiated at these temperatures, but the reactions were exothermic and led to considerable increase in temperature.

The fluorination of 2,4-bis(heptafluoropropyl)-6-chloro-*s*-triazine (II) by means of silver fluoride also gave a better yield of V than could be obtained with silver difluoride.

The fluorine atom in the 6-position of compounds IV and V appears to be less reactive than the corresponding chlorine atom in compounds I and II. This is indcated by the reaction of IV with toluene-*p*-sulfonyl hydrazide which gave only a 10% yield of 2,4-bis(pentafluoroethyl)-6-toluene-*p*-sulfonylhydrazino-*s*-triazine (VIII), even after refluxing for two days, whereas the chlorotriazine (I) was converted to VIII in nearly quantitative yield.[7]

1,2 - Bis(2,4 - dichloro - *s* - triazinyl - 6)tetrachloroethane (IX)[5] reacted with silver difluoride to give 1,2-bis(2,4-difluoro-*s*-triazinyl-6)tetrachloroethane (X); the chlorine atoms of the connecting aliphatic chain were not attacked.



IX. Hal = Cl
X. Hal = F

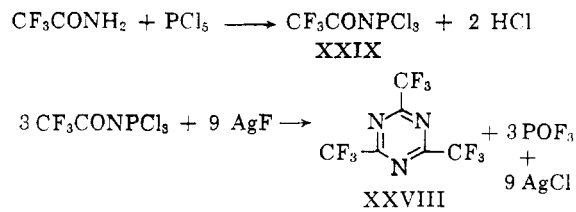
Silver fluoride was also successfully applied to the conversion of cyanuric chloride (XII) to cyanuric fluoride (XI), although the yield was not as high as had been obtained when Swarts reagent was used as the fluorinating agent.[8]

Although cyanuric fluoride (XI) is much more sensitive to hydrolysis than cyanuric chloride (XII),[3,5,6] comparable reactivity on aminolysis and alcoholysis was observed. In the latter reactions, either monosubstituted or disubstituted fluoro-*s*-triazines (XIII–XVIII) could be obtained by use of the appropriate molar ratio of cyanuric fluoride to the base. An attempt to prepare 2-*o*-chloroaniline-4,6-difluoro-*s*-triazine (XIX) from equivalent amounts of *o*-chloroaniline and triethylamine was not successful; the reaction product had the composition of the 2-*o*-chloroanilino - 4 - fluoro - *s* - triazine - (6) - triethylammonium fluoride (XX). Similar triazine ammonium salts have been described.[8]

The reaction of XI with excess ammonia in ether at 0° resulted in the formation of 2-amino-4,6-difluoro-*s*-triazine (XXII). Under identical conditions except for the use of tetrahydrofuran in place of ether, Grisley *et al.*[3] had obtained 2,4-diamino-6-fluoro-*s*-triazine (XXI).

By analogy to the reported formation of 2-diazomethyl-4,6-dichloro-*s*-triazine (XXIII)[9] from diazomethane and XII, the reaction of XI with diazomethane led to 2-diazomethyl-4,6-difluoro-*s*-triazine (XXIV) as the principal reaction product. This compound is much more unstable than XXIII and decomposes slowly at room temperature. XXIV reacted with hydrogen chloride and bromine, respectively, to give the expected products, 2-chloromethyl-4,6-difluoro-*s*-triazine (XXV) and 2 - dibromomethyl - 4,6 - difluoro - *s* - triazine (XXVI). Surprisingly, the reaction of XXIV with chlorine did not yield the 2-dichloromethyl-4,6-difluoro-*s*-triazine (XXVII) but gave a mixture of compounds. Elemental analysis indicated that not only the diazomethyl group, but also the fluorine atoms of XXIV had been attacked.

Finally, a new synthesis of 2,4,6-tris(trifluoromethyl)-*s*-triazine (XXVIII) is reported. Trifluoroacetamide reacted with an equivalent amount of phosphorus pentachloride to form trichlorophosphazotrifluoroacetyl (XXIX). Heating of XXIX with silver fluoride resulted in the formation of phosphoryl fluoride and a low boiling liquid which was identified as XXVIII.



We believe that this method can also be applied to the synthesis of other tris(perfluoroalkyl)-*s*-triazines.

(8) Austrian Patent 174,377.
(9) Ch. Grundmann and E. Kober, *J. Am. Chem. Soc.*, **79**, 994 (1957).

Experimental[10]

2,4-Bis(pentafluoroethyl)-6-fluoro-*s*-triazine (IV) and 2,4-Bis(heptafluoro-*n*-propyl)-6-fluoro-*s*-triazine (V).—(a) 2,4-Bis(pentafluoroethyl)-6-chloro-*s*-triazine (I) was added, with stirring, to a tenfold excess of Swarts reagent,[11] preheated to 150°. The liquid fluorination mixture became solid after a few minutes. The reaction mixture was kept at 150° for 12 hr. Distillation of the reaction product gave a mixture of the starting material I and the desired compound IV. Separation of compounds I and IV by fractional distillation was not possible. The yield of IV was calculated to be 14%.[12]

Compound V was obtained from 2,4-bis(heptafluoropropyl)-6-chloro-*s*-triazine (II) by the same procedure in a 21% yield.[12]

(b) 2,4-Bis(pentafluoroethyl)-6-chloro-*s*-triazine (I) was refluxed with mercuric fluoride for 3 hr. to give the fluorotriazine IV in 20% yield.[12]

(c) 2,4-Bis(pentafluoroethyl)-6-chloro-*s*-triazine (I, 7.5 g.) was added to silver difluoride (7.0 g.). The immediate vigorous reaction stopped after about three minutes. The mixture was refluxed for 20 min., then distilled at normal pressure, and redistilled *in vacuo* to give 6 g. (85%) of compound IV, b.p. 106° (760 mm), b.p. 73° (150 mm.); $n^{25}D$ 1.3160.

Anal. Calcd. for $C_7F_{11}N_3$: C, 25.09; F, 62.37; N, 12.54. Found: C, 25.07; F, 62.35; N, 12.58.

Compound V was obtained by the same procedure from II in a 85% yield; b.p. 131° (760 mm.), b.p. 98° (150 mm.); $n^{25}D$ 1.3165.

Anal. Calcd. for $C_9F_{15}N_3$: C, 24.84; F, 65.50; N, 9.69. Found: C, 24.86; F, 65.31; N, 9.63.

(d) 2,4-Bis(pentafluoroethyl)-6-chloro-*s*-triazine (I, 14 g.) was refluxed with silver fluoride (20 g.) for 30 min. The liquid was distilled to yield 13.3 g. (98%) of the perfluorinated compound IV; $n^{18}D$ 1.3200.

2,4-Bis(heptafluoropropyl-6-fluoro-*s*-triazine (V) was obtained by the same procedure from the corresponding 6-chloro derivative (II) in a 95% yield.

1,2-Bis(2,4-difluoro-*s*-triazinyl-6)-tetrachloroethane (X), —1,2-Bis(2,4-dichloro-*s*-triazinyl-6)-tetrachloroethane (IX. 35 g.) was added to silver difluoride (140 g.) in chloroform (100 ml.). The slightly exothermic reaction was completed by refluxing for 20 hr. After removing the chloroform *in vacuo*, the dry residue was sublimed at 1 mm. and a bath temperature up to 160° to yield 5.5 g. (18.2%) of compound X. Recrystallization from ligroin[13] yielded white prisms, m.p. 156.6°.

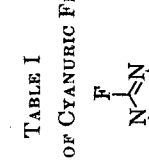
Anal. Calcd. for $C_8Cl_4F_4N_6$: C, 24.15; Cl, 35.64; F, 19.09; N, 21.12. Found: C, 24.24; Cl, 35.47; F, 18.78; N, 21.26.

2,4,6-Trisfluoro-*s*-triazine [Cyanuric Fluoride, (XI).].—Cyanuric chloride (XII, 16.6 g.) was added portionwise to silver fluoride (50 g.) at 100°. After refluxing for 1 hr., the cyanuric fluoride which formed (yield: 9.5 g. or 78.5%) was distilled through a small Widmer column. Repeated fractionation gave XI which was found to be identical with the product obtained by fluorination with Swarts reagent[8]; b.p. 70–72° (760 mm), $n^{24}D$ 1.3844.

Reactions of Cyanuric Fluoride (XI).—The reactions for the preparation of compounds XIII–XVIII, XX, and XXII were carried out in ether. Compounds XIII and XIV were prepared in the presence of one or two mole equivalents of triethylamine, respectively. Two or four mole equivalents

TABLE I

REACTIONS OF CYANURIC FLUORIDE



Compound	R^1	R^2	B.P. (mm.)	$n^{t}D$	t	Yield, %	Formula	—Carbon, %— Calcd.	Found	—Hydrogen, % Calcd.	Found	—Nitrogen, %— Calcd.	Found	—Chlorine, %— Calcd.	Found	—Fluorine, %— Calcd.	Found
XIII	OC_4H_9-*n*	F	66–68 (8)	1.4373	23	62.2	$C_7H_9F_2N_3O$	44.44	44.41	4.80	4.85	22.22	22.26			20.09	20.01
XIV	OC_4H_9-*n*	OC_4H_9-*n*	117–119 (1.3)	1.4607	24	96.5	$C_{11}H_{18}FN_3O_2$	54.30	54.14	7.45	7.39	17.28	17.55			7.71	7.92
XV	$N(C_2H_5)_2$	F	103–104[a]			55.4	$C_7H_{10}F_2N_4$	44.67	44.67	5.36	5.36	29.74	29.67			20.19	20.22
XVI	$N(C_2H_5)_2$	$N(C_2H_5)_2$	46–47[a]			99.5	$C_{11}H_{20}FN_5$	54.75	54.73	8.35	7.94	29.03	29.74			7.87	7.83
XVII	NHC_2H_5	NHC_2H_5	228–230[b]			100.0	$C_7H_{12}FN_5$	45.40	45.45	6.53	6.57	37.82	37.80			10.26	10.39
XVIII	NHC_6H_4Cl-*o*	NHC_6H_4Cl-*o*	142.5–144.5[c]			18.1	$C_{16}H_{10}Cl_2FN_5$	51.45	51.48	2.88	2.81	20.00	20.33	20.25	20.26	5.43	5.13
XX	NHC_6H_4Cl-*o*	$(C_2H_5)_3NF$				21.7	$C_{18}H_{29}ClF_2N_5$	52.40	52.06	5.86	5.94	20.37	20.48	10.31	9.57	11.05	12.35
XXII	NH_2	F	[d]			45.6	$C_3H_2F_2N_4$	27.28	27.20	1.52	1.43	42.43	42.64			28.77	29.19
XXIV	CHN_2	F	42–43[e]			100.0[f]	$C_4HF_2N_5$	31.18	30.58	0.64	1.48	44.59	42.25			24.19	24.48
XXV	CH_2Cl	F	63–64.5 (13)	1.4575	23	31.0	$C_4H_2ClF_2N_5$	29.02	29.11	1.22	1.37	25.38	25.01	21.41	20.96	22.94	22.64
XXVI	$CHBr_2$	F	83–86 (8)	1.5338	24	21.8	$C_4HBr_2F_2N_5$	16.63	16.54	0.35	0.51	14.55	14.61	55.32[g]	55.09[g]	13.15	12.94

[a] M.p. (from ligroin); XV is less soluble in ether or petroleum ether (b.p. 33–40°) than XVI; XV is only very slightly soluble in cold water. [b] M.p. (from dioxan); XVII is nearly insoluble in water. [c] M.p. (from ligroin). [d] See Experimental. [e] M.p. (from ligroin); distillation at 2.2 mm. (bath temperature 55–65°) yielded a yellow oil for which the analysis has been obtained; the same sample, analyzed a few days later, showed a nitrogen value of 32.88%. [f] Crude product. [g] Bromine.

(10) All melting points were taken with the Fisher-Johns apparatus; microanalyses were by the Galbraith Microanalytical Laboratories, Knoxville, Tenn., and by Spang Microanalytical Laboratory, Ann Arbor, Mich.

(11) A. Henne, *Org. Reactions*, 49 (1944).

(12) The yields are based on interpolation of analysis and refractive index.

(13) If not indicated otherwise, a fraction boiling from 90–97° was used.

of the appropriate amine were employed for the preparation of compounds XV and XVI, XVII, XVIII, respectively. Compound XX was obtained when equimolecular amounts of XI, *o*-chloroaniline, and triethylamine reacted at 0°. Crude XX was isolated by separation of the solids from the ethereal reaction mixture, evaporation of the ether, extraction of the residue with refluxing benzene, and addition of ligroin to the benzene extract. For the preparation of 2-amino-4,6-difluoro-*s*-triazine (XXII) ammonia was passed for 1 hr. into an ice-cold solution of 13.5 g. of cyanuric fluoride in 100 ml. of ether. The excess ammonia was removed by passing air through the ice-cold reaction mixture. The solid was then filtered by suction and the filter cake washed several times with ether. The dry filter cake (14.0 g.) consisted mainly of ammonium fluoride from which 3.1 g. of crude XXII was extracted with hot dioxane. Another crop of crude XXII (2.65 g.) was obtained when the solvent was removed from the ether filtrate, thus resulting in an over-all yield of 45.6%. Compound XXII was purified by sublimation under normal pressure at a bath temperature of 120–130°. XXII seems to split off hydrogen fluoride upon heating to give a polymeric material which does not melt up to 300°. If XXII is put on a plate, preheated to 270°, it first melts and then forms a white solid within a few seconds. XXII is a sternutator and produces burns on contact with the skin.

The synthesis of XXIV and the conversion of this compound into XXV and XXVI was accomplished according to the procedures described for the preparation of the corresponding 4,6-dichloro-*s*-triazines.[9]

Pertinent data for these compounds are listed in Table I.

Trichlorophosphazotrifluoroacetyl (XXIX).—Trifluoroacetamide (45.2 g.) was mixed with thoroughly powdered phosphorus pentachloride (83.4 g.) and heated. At 40°, evolution of hydrogen chloride started. The mixture was completely liquefied at 50°. Heating was continued for 4 hr. at 72° and the reaction mixture finally fractionated. After a small forerun, the principal product distilled at 146–149° (750 mm.); yield: 73.2 g. (73.6%); $n^{25}D$ 1.4341.

Anal. Calcd. for $C_2Cl_3F_3NPO$: N, 5.64; Cl, 42.83. Found: N, 5.03; Cl, 43.03.

Upon exposure to air, XXIX formed ***N*-trifluoroacetylphosphoramidic acid dichloride,** m.p. 76–77°.

Anal. Calcd. for $C_2HCl_2F_3NPO_2$: C, 10.45; H, 0.43; Cl, 30.84; N, 6.09; P, 13.48. Found: C, 10.45; H, 0.39; Cl, 29.50; N, 6.44; P, 13.45.

2,4,6-Tris(trifluoromethyl)-*s*-triazine (XXVIII).—Trichlorophosphazotrifluoroacetyl (XXIX, 24.85 g., 0.1 mole) was refluxed with 3 equivalents of silver fluoride (37.8 g.) for 2 hr. A considerable amount of low boiling material, consisting mainly of phosphoryl fluoride, was condensed in a carbon dioxide–acetone cooled trap which was connected with the reaction flask through the outlet of the reflux condenser. Fractionation of the reaction mixture yielded—besides 6.1 g. of unchanged XXIX—4.1 g. of XXVIII, b.p. 93° (lit.: 96–98°); $n^{28}D$ 1.3209.

Anal. Calcd. for $C_6F_9N_3$: C, 25.28; N, 14.74. Found: C, 24.91; N, 14.53.

Acknowledgment.—The authors are very much indebted to the Olin Mathieson Chemical Corporation for their generous support of this work.

Synthesis of Polyfluorinated Heterocycles by Indirect Fluorination with Silver Fluorides. II. Fluoropyrimidines[1-3]

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Received November 21, 1961

Tetrachloropyrimidine was converted with silver fluoride into 5-chloro-2,4,6-trifluoropyrimidine, but all attempts to replace the chlorine atom in 5-position with fluorine failed. 2,4,6-Trichloropyrimidine gave upon treatment with silver fluoride 2,4,6-trifluoropyrimidine which reacted with silver difluoride (AgF_2) in perfluorinated diluents to form tetrafluoropyrimidine. Numerous derivatives of the new halopyrimidines are described.

In the first paper of this series[2] the synthesis of certain perfluorinated derivatives of 1,3,5-triazine was described. It was demonstrated that silver difluoride and especially silver fluoride are excellent agents for the replacement of nuclear bound chlorine by fluorine in the *s*-triazine system.

The objective of the present investigation was the preparation of polyfluoropyrimidines, especially tetrafluoropyrimidine, and derivatives thereof. Based on our experience in the triazine series, the reaction of silver fluoride and silver difluoride with chloropyrimidines appeared to offer the most promising route of synthesis, especially since it had been shown that tetrachloropyrimidine was not affected at all by the "Swarts reagent" (SbF_3Cl_2).[5] Partial fluorination of 2,4,6-trichloropyrimidine by means of sulfur tetrafluoride has been reported recently.[6] This method gave a mixture of 4,6-dichloro-2-fluoropyrimidine and 2,6-dichloro-4-fluoropyrimidine when the reaction was carried out at 225°.

The perchlorinated pyrimidine, 2,4,5,6-tetrachloropyrimidine[7] (I), appeared to be the obvious

(1) This article is based on work performed during 1956 and 1957 under Project 116-B of The Ohio State University Research Foundation sponsored by the Olin Mathieson Chemical Corporation, New York, N. Y.

(2) Preceding communication: E. Kober, H. Schroeder, R. Rätz, H. Ulrich, and C. Grundmann, *J. Org. Chem.*, **27**, 2577 (1962).

(3) Preliminary publication: H. Schroeder, *J. Am. Chem. Soc.*, **82**, 4115 (1960).

(4) Present address: Olin Mathieson Chemical Corporation, New Haven, Conn.

(5) E. Kober and Ch. Grundmann, *J. Am. Chem. Soc.*, **81**, 3769 (1959).

(6) C. W. Tullock, R. A. Carboni, R. J. Harder, W. C. Smith, and D. D. Coffman, *J. Am. Chem. Soc.*, **82**, 5107 (1960).

(7) S. J. Childress and R. C. McKee, *J. Am. Chem. Soc.*, **72**, 4271 (1950).