BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 642—644 (1972)

Some Reactions of Tetrafluorobenzyne with Halogens and Ethers, and with Alcohols

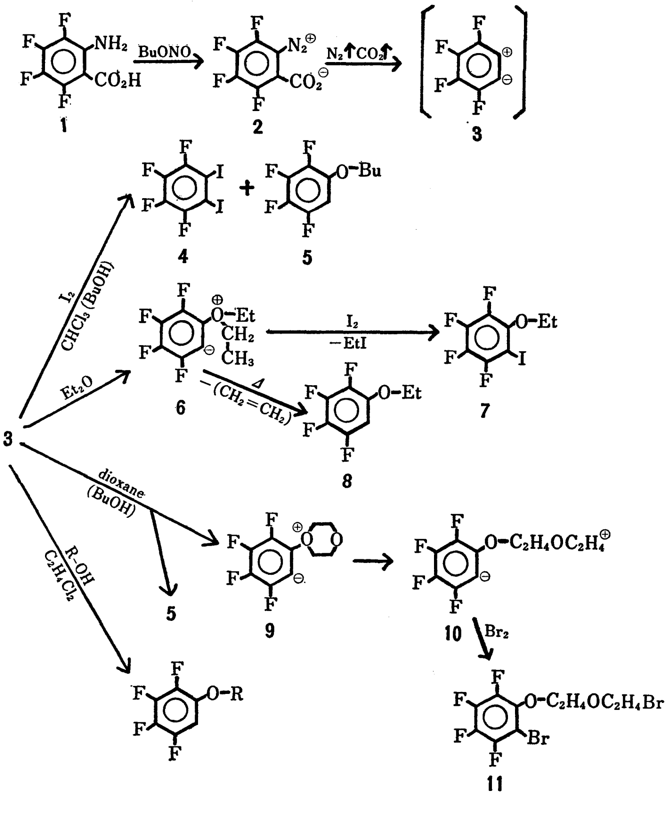
Seiichi Hayashi and Nobuo Ishikawa

Department of Synthetic Chemistry, Faculty of Engineering, Tokyo Institute of Technology, Meguro-ku, Tokyo

(Received August 11, 1971)

As reported previously,[1] tetrafluorobenzyne generated from tetrafluorobenzenediazonium-2-carboxylate behaved as a potential electrophile, and it reacted even with diethyl ether to give 1-ethoxy-2,3,4,5-tetrafluorobenzene(**8**). In our continued studies of this subject, we have found that the tetrafluorobenzyne reacts with halogens and ethers, such as iodine and diethyl ether, or with bromine and dioxane, to give *o*-halogenoalkoxytetrafluorobenzenes.

When tetrafluoroanthranilic acid (**1**) was diazotized with *n*-butyl nitrite in chloroform and the resulting tetrafluorobenzenediazonium-2-carboxylate (**2**) was decomposed in the presence of iodine, two products were obtained : one was the expected 1,2-diiodotetrafluorobenzene (**4**) (15% yield), while the other was 1-butoxy-2,3,4,5-tetrafluorobenzene (**5**) (25% yield). The latter compound was probably formed by the reaction of tetrafluorobenzyne and 1-butanol, which itself resulted from the diazotizing agent, *n*-butyl nitrite.



8 (R=Et)
5 (R=Bu)
12a (R=i-C_5H_{11})
12b (R=CH_2CH_2Cl)
12c (R=CH_2CH_2OH)
12d (R=CH_2CH_2OEt)

If the above reaction was carried out in diethyl ether, however, 1-ethoxy-2-iodo-3,4,5,6-tetrafluorobenzene (**7**) was obtained as the main product. In this case, it is evident that iodine reacted with the betaine intermediate **6**, prior to its intramolecular proton-withdrawing to ethoxytetrafluorobenzene (**8**) and ethylene.

Furthermore, if dioxane was used as the solvent and bromine was present in the reaction mixture, tetrafluorobenzyne reacted with both, thus affording 1-(β-(β'-bromoethoxy)ethoxy)-2-bromotetrafluorobenzene (**11**) as the main product. This reaction seemed to have started with the electrophilic attack of tetrafluorobenzyne on dioxane to form **9**, followed by the cleavage of dioxane molecule to **10** and the subsequent reaction of bromine on this betaine intermediate. This is probably the first example of the reaction of any benzyne with dioxane.

In the absence of bromine, however, the only product isolated was 1-butoxy-2,3,4,5-tetrafluorobenzene (**5**), which, as has been mentioned before, had been formed from tetrafluorobenzyne and butanol, which had itself come from *n*-butyl nitrite. In this case, no product which might be formed by the reaction between benzyne and dioxane was confirmed. We assume that this is because the intramolecular proton transfer in the betaine intermediate, **9** or **10**, is sterically more difficult than that in the case of **6**.

Our finding that, in the presence of halogen, dioxane is cleaved by tetrafluorobenzyne seems to be analogous to the facts, which have been reported recently, that tetrahydrofuran is cleaved by benzyne in the presence of water,[2] in the absence of it no product which might result from the cleavage of tetrahydrofuran is observed.[3]

As has been described above, tetrafluorobenzyne reacted with even a small amount of butanol present in the reaction mixture to give a considerable amount of butoxytetrafluorobenzene (**5**). Then, to generalize this reaction we effected the diazotization-decomposition of tetrafluoroanthranilic acid in various alcohols. As we had expected 1-alkoxy-2,3,4,5-tetrafluorobenzene was obtained in a rather good yield in every case. The structures of these compounds were clear from their ^1H and ^{19}F NMR spectra (Table 1).

---

[1] S. Hayashi and N. Ishikawa, *Nippon Kagaku Zasshi*, **91**, 1000 (1970).

[2] E. Wolthuis, B. Bouma, J. Modderman, and L. Sytsma, *Tetrahedron Lett.*, **1970**, 407.

[3] J. P. N. Brewer, H. Heaney, and J. M. Jablonski, *ibid.*, **1968**, 4455.

Table 1 Preparation and spectral properties of 1-alkoxy-2, 3, 4, 5-tetrafluorobenzene (**12**)

No.	Alcohol	Diazotizing agent	Product			
				R	Bp °C/mmHg	Yield %
1	ethanol	*n*-BuONO	[**8**]	Et	71—72/20	67
2	*n*-butanol	*n*-BuONO	[**5**]	*n*-Bu	92—93/20	77
3	isopentanol	*i*-$C_5H_{11}ONO$	[**12a**]	$CH_2CH_2CHMe_2$	110/24	76
4	2-chloroethanol	*n*-BuONO	[**12b**]	CH_2CH_2Cl	108—109/23	66
5	ethyleneglycol	*n*-BuONO	[**12c**]	CH_2CH_2OH	80—81/3	65
6	2-ethoxyethylalcohol	*n*-BuONO	[**12d**]	CH_2CH_2OEt	65—65.5/3	57

No.	Product									
	F Anal		IR		NMR					
					^1H τ (in CCl_4)		^{19}F ppm[a)] (in CCl_4, from ext. CF_3CO_2H)			
	Calcd.	Obsvd.	Ar-O-C	C-F	Ar-H	Alkyl-H	2-F	3-F	4-F	5-F
1	—	—	1204	1080	3.50	6.02 (CH_2) 8.56 (CH_3)	82.7	79.2	91.0	63.0
2	34.2	34.5	1198	1082	3.45	6.05 (αCH_2) 8.00—8.75 (βCH_2, γCH_2) 9.00 (CH_3)	82.2	78.2	90.0	62.3
3	32.2	32.0	1200	1076	3.50	6.04 (αCH_2) 8.15—8.60 (CH_2CH) 9.00 (CH_3)	82.1	78.1	90.0	62.3
4	33.2	33.0	1186	1086	3.40	5.78 (αCH_2) 6.25 (CH_2Cl)	81.2	77.4	88.7	61.5
5	36.2	36.6	1200	1080	3.39	6.00 (CH_2CH_2) 5.55 (OH)	82.3	78.3	89.3	61.8
6	31.9	31.5	1200	1080	3.33	5.92 (αCH_2) 6.32 (βCH_2) 6.49 (OCH_2) 8.82 (CH_3)	82.3	78.8	89.8	62.4

a) Values calculated according to Bruce's formula[4)] are: 2-F, 80; 3-F, 78; 4-F, 86; 5-F, 63 ppm.

Experimental

All the NMR spectra were run at room temperature, and CCl_4 was used as the solvent unless otherwise noted. The chemical shifts in ^{19}F NMR are shown by δ(ppm) from external CF_3CO_2H.

The Reaction of Tetrafluorobenzyne with Iodine in Chloroform. Into a solution of *n*-butyl nitrite (3.09 g, 0.030 mol) and iodine (7.62 g, 0.030 mol) in chloroform (20 m*l*), a solution of tetrafluoroanthranilic acid (**1**) (4.18 g, 0.020 mol) in chloroform (80 m*l*) was added drop by drop, at 50°C over a 40-min period. After refluxing for 6 hr, the solvent was distilled out in a vacuum and the residue was dissolved in diethyl ether. The ether solution was then treated with an aqueous solution of sodium sulfite to remove the excess iodine, and with a dilute aqueous sodium hydroxide solution to remove any alkaline-soluble matter. After subsequent washing with dilute hydrochloric acid and water, it was dried with magnesium sulfate. The solvent was evaporated, and the oily residue was distilled in a vacuum to give the following two products:

1) 1-*n*-butoxy-2,3,4,5-tetrafluorobenzene (**5**); bp 60—61°C/3 mmHg (1.1 g, 25% yield). Identified with **5** in Table 1 by means of its IR spectrum.

2) 1,2-diiodotetrafluorobenzene (**4**); bp 74°C/3 mmHg, mp 49—51°C (lit. mp 50—51°C[3)]). IR: 1110, 1023 cm^{-1} (C-F). ^{19}F NMR (in Me_2CO): +24.7 (3,6-F), +71.7 (4,5-F) ppm.

The Reaction of Tetrafluorobenzyne with Iodine and Diethyl Ether. Into a boiling mixture of *n*-butyl nitrite (2.48 g), iodine (5.08 g), dichloromethane (20 m*l*), and diethyl ether (20 m*l*), a solution of **1** (4.18 g) in diethyl ether (20 m*l*) was added, drop by drop, during the course of 3 hr. The reaction was then run and after-treated in the manner described above; 1-ethoxy-2-iodotetrafluorobenzene (**7**) (bp 65—66°C/3 mmHg, 1.75 g) was thus obtained in a 27% yield.

Found: F, 23.6%; I, 39.5%. Calcd for $C_8H_5F_4IO$: F, 23.7%; I, 39.7%. NMR: ^1H, τ 5.85 q (CH_2), 8.52 t (CH_3); ^{19}F, +38.8 (3-F), +74.9 (6-F), +75.7 (5-F), +82.1 (4-F).

The Reaction of Tetrafluorobenzyne with Bromine and Dioxane. Into a solution of *n*-butyl nitrite (2.60 g) and bromine (3.80 g) in dioxane (30 m*l*), we added a solution of **1** (4.18 g) in dioxane (30 m*l*) at 55—65°C over a 2-hr period. Stirring was continued for 8 more hr at 94°C, and then the reaction mixture was treated as usual, giving 1-(β-(β'-bromoethoxy)-ethoxy)-2-bromo-3,4,5,6-tetrafluorobenzene (**11**) (bp 124—125°C/2 mmHg, 2.2 g) in a 28% yield.

Found: Br, 40.8%; F, 19.3%. Calcd for $C_{10}H_8Br_2F_4O_2$: Br, 40.4%; F, 19.2%. NMR: ^1H, τ 5.78 t (α CH_2) 6.08—6.37 m (β CH_2 and $\alpha'CH_2$), 6.60 t (CH_2Br); ^{19}F,

---

4) M. I. Bruce, *J. Chem. Soc., A*, **1968**, 1459.

+52.8 (3-F), +75.6 (6-F), +77.6 (5-F), +83.0 (4-F). IR: 1190 (Ar-O-C), 1080 (C-F).

When the above reaction was carried out without bromine, **5** was obtained as the main product (bp 93—94°C/19 mmHg, 1.4 g, 32% yield), as was confirmed by a study of the IR spectrum. The other fraction isolated (bp 120—136°C/3 mmHg, 1.0 g) was a mixture of more than three components, as was shown by gas chromatography; they could not be separated from each other.

1-Ethoxy-2,3,4,5-tetrafluorobenzene (8). Into a mixture of *n*-butyl nitrite (1.3 g), ethanol (10 m*l*), and 1,2-dichloroethane (10 m*l*), we added a solution of **1** (2.1 g) in ethanol (10 m*l*) at 50—60°C over a 1 hr period. After refluxing for 3 hr with stirring, the solvent was evaporated in a vacuum, and the residue was dissolved in diethyl ether. On treating with an aqueous sodium hydroxide solution to remove the alkaline-soluble matter and washing with dilute hydrochloric acid and then with water, the ether solution was dried on magnesium sulfate. The ether was evaporated, and the residue was distilled to give **8** (1.3 g), which was identified with an authentic sample.[1]

The reactions with other alcohols were carried out in a similar manner (Table 1).