# Synthesis of *gem*-Difluorocyclopropanes in a Phase-transfer Catalysed System[1]

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Reaction of $CH_2Br_2$ with $CBr_2F_2$ and alkenes **1a–e** in the presence of 60% aqueous KOH and tetrabutylammonium hydrogensulphate as a catalyst affords *gem*-difluorocyclopropanes **2a–e**.

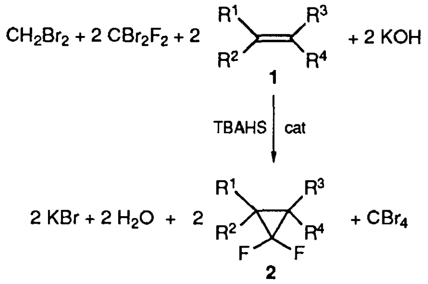
Application of phase-transfer catalysed systems[2,3] (alkali metal hydroxide and a quaternary onium salt as a catalyst) for generation of dihalogenocarbenes from the corresponding haloforms in the presence of alkenes provides a simple and efficient preparation of *gem*-dihalogenocyclopropanes, with the exception of the *gem*-difluoro-derivatives.[4] Starting from $HCClF_2$ and alkenes under the above conditions, the yields of *gem*-difluoro-derivatives did not exceed 10%.[2]

It is known that $:CF_2$ is formed by treating $HCClF_2$ with base *via* elimination of HCl.[5] This process, if carried out in a phase-transfer catalysed system, affords $:CF_2$ at the interphase, where it is destroyed owing to a fast reaction with $OH^-$ and/or $H_2O$, rather than reacting with an alkene to form a *gem*-difluorocyclopropane.[3]

In order to eliminate these undesired reactions, we tried to select suitable conditions which would ensure the generation of $:CF_2$ inside the organic phase of the two-phase system, where the concentration of $OH^-$ and $H_2O$ is negligible and thus greatly increasing the probability of reaction of this carbene with an alkene. To realize such an approach, our method[6] for the generation of $:CCl_2$ from $CH_2X_2$ ($X = Cl, Br$) and $CCl_4$ was adopted.

We found that simply stirring $CH_2Br_2$, $CBr_2F_2$ and alkenes **1a–e** with 60% aqueous KOH and tetrabutylammonium hydrogensulphate (TBAHS) as a catalyst afforded the expected *gem*-difluorocyclopropanes **2a–e**, according to the stoichiometry shown in Scheme 1. Under these, unoptimized, conditions the products **2** were formed in moderate to high yields (Table 1).

We presume that the lipophilic ion pair $H\bar{C}Br_2{}^+NBu_4$ present in the organic phase undergoes a halogenophilic reaction with $CBr_2F_2$ to form $HCBr_3$ and $^-CBrF_2{}^+NBu_4$,



a; $R^1 = R^2 = R^3 = R^4 = Me$
b; $R^1 = R^2 = R^3 = Me$, $R^4 = H$
c; $R^1 = MeO$, $R^2 = Me$, $R^3 = R^4 = H$
d; $R^1 = Ph$, $R^2 = Me$, $R^3 = R^4 = H$
e; $R^1 = Ph$, $R^2 = R^3 = R^4 = H$

**Scheme 1**

**Table 1** Synthesis of *gem*-difluorocyclopropanes **2** from $CH_2Br_2$, $CBr_2F_2$ and alkenes **1** in a phase-transfer catalysed system

| Alkene | Product[a] | Reaction time/h | Yield[b] (%) |
|---|---|---|---|
| **1a** | **2a** | 27 | 70[c] (96) |
| **1b** | **2b** | 27 | 60[c] (80) |
| **1c** | **2c** | 11 | 45[c] (—) |
| **1d** | **2d** | 30 | 30[d] (40) |
| **1e** | **2e** | 60 | — (31) |

[a] All products were characterized by NMR and/or mass spectra. [b] In parentheses are GLC yields. [c] Isolated by fractional distillation. [d] The reaction mixture was treated with bromine,[7] and **2d** was isolated by vacuum distillation.

which further splits into $:CF_2$ and $^-Br^+NBu_4$. Alternatively, $:CF_2$ may be formed *via* synchronous elimination of two bromine atoms from $CBr_2F_2$, during its reaction with $H\bar{C}Br_2{}^+NBu_4$. The side product of these transformations is $CBr_4$. In an independent experiment we have shown that it is formed in a halogenophilic reaction of $^-CBr_3$ with $CBr_2F_2$. The above reaction consumes the second molecule of $CBr_2F_2$ to generate $:CF_2$ (*via* a stepwise or synchronous process). Irrespective of the way $:CF_2$ is formed, its final reaction with **1** afforded **2** (Scheme 2).

The procedure for preparation of **2** is simple. Alkene **1** (0.02 mol), $CBr_2F_2$ (0.04 mol), $CH_2Br_2$ (0.04 mol or 0.02 mol for **1a**), 60% aqueous KOH (23 g) and TBAHS (0.34 g), were stirred at 18–20 °C for the time indicated in Table 1. The mixtures were worked-up by conventional procedures, and the products **2** were isolated as shown in Table 1.

$$H_2CBr_2 + 2NaOH + Q^+HSO_4^- \rightarrow H\bar{C}Br_2Q^+ + 2H_2O + Na_2SO_4$$

$$H_2CBr_2 + Q^+\,OH^- \rightarrow H\bar{C}Br_2Q^+ + H_2O$$

$$H\bar{C}Br_2Q^+ + CBr_2F_2 \rightarrow HCBr_3 + \bar{C}BrF_2Q^+$$

$$\bar{C}BrF_2Q^+ \rightarrow Br^-Q^+ + :CF_2$$

$$\text{or } H\bar{C}Br_2Q^+ + CBr_2F_2 \rightarrow HCBr_3 + :CF_2 + Br^-Q^+$$

$$HCBr_3 + 2\,NaOH + Q^+HSO_4^- \rightarrow \bar{C}Br_3Q^+ + 2H_2O + Na_2SO_4$$

$$HCBr_3 + Q^+\,OH^- \rightarrow \bar{C}Br_3Q^+ + H_2O$$

$$\bar{C}Br_3Q^+ + CBr_2F_2 \rightarrow CBr_4 + \bar{C}BrF_2Q^+$$

$$\bar{C}BrF_2Q^+ \rightarrow Br^-Q^+ + :CF_2$$

$$\text{or } \bar{C}Br_3Q^+ + CBr_2F_2 \rightarrow CBr_4 + :CF_2 + Br^-Q^+$$

$$:CF_2 + \mathbf{1} \rightarrow \mathbf{2}$$

**Scheme 2** $Q^+ = Bu_4N^+$

To summarize, we have described the first practical method for the synthesis of **2** in a phase-transfer catalysed system.[8]

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## References

1 For Part 171 of the series Reactions of Organic Anions, see Z. Wróbel and M. Mąkosza, *Org. Prep. Proc. Int.*, 1990, **22**, 575.
2 E. V. Dehmlow and S. S. Dehmlow, *Phase Transfer Catalysis*, 2nd edn., Verlag Chemie, Weinheim, 1983.
3 M. Mąkosza and M. Fedoryński, *Adv. Catal.* 1987, **35**, 375.
4 E. Dehmlow, in *Methoden der Organischen Chemie (Houben-Weyl)*, ed. M. Regitz, Georg Thieme, Stuttgart, 1989, vol. E19b (part 2), p. 1461.
5 J. Hine and P. B. Langford, *J. Am. Chem. Soc.*, 1957, **79**, 5497; W. Kimpenhaus and J. Buddrus, *Chem. Ber.*, 1976, **109**, 2370.
6 A. Jończyk and P. Balcerzak, *Tetrahedron Lett.*, 1989, **30**, 4697.
7 H. P. Fritz and W. Kornrumpf, *Z. Naturforsch., Teil B*, 1981, **36**, 1375.
8 P. Balcerzak, M. Fedoryński and A. Jończyk, Polish Pat. Appl. Nr P 282 376, 1989.