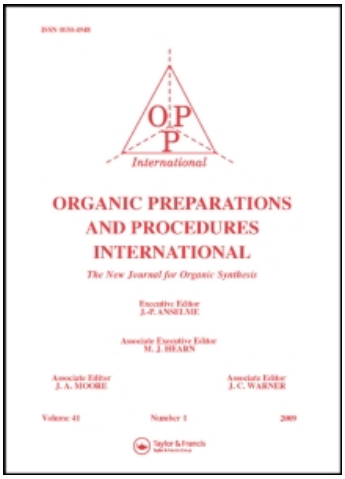


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

STUDIES ON POSITIONAL PROTECTIVE GROUPS ON AROMATIC RINGS I. A NEW PREPARATIVE METHOD FOR HALOPHENOLS WITH THE *t*-BUTYL OR BENZYL GROUP AS A PROTECTIVE GROUP

M. Tashiro[a]; H. Watanabe[a]; O. Tsuge[a]
[a] Research Institute of Industrial Science, Kyushu University, Hakozaki, Fukuoka, Japan

To cite this Article Tashiro, M. , Watanabe, H. and Tsuge, O.(1974) 'STUDIES ON POSITIONAL PROTECTIVE GROUPS ON AROMATIC RINGS I. A NEW PREPARATIVE METHOD FOR HALOPHENOLS WITH THE *t*-BUTYL OR BENZYL GROUP AS A PROTECTIVE GROUP', Organic Preparations and Procedures International, 6: 3, 107 — 115
To link to this Article: DOI: 10.1080/00304947409355082
URL: http://dx.doi.org/10.1080/00304947409355082

ORGANIC PREPARATIONS AND PROCEDURES INT. 6(3), 107-115 (1974

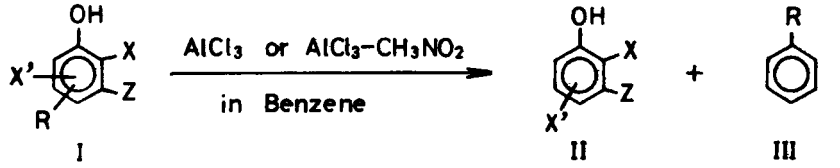
STUDIES ON POSITIONAL PROTECTIVE GROUPS ON AROMATIC RINGS I. A NEW PREPARATIVE METHOD FOR HALOPHENOLS WITH THE t-BUTYL OR BENZYL GROUP AS A PROTECTIVE GROUP

M. Tashiro*, H. Watanabe and O. Tsuge

Research Institute of Industrial Science,
Kyushu University, Hakozaki, Fukuoka 812, Japan

It has been previously reported that under the influence of Friedel-Crafts catalysts, the benzyl group in diphenylmethanes is easily transferred to aromatics such as benzene, toluene, and chlorobenzene.[1-3]

These results strongly suggested that the benzyl group might serve as a positional protective group in aromatic electrophilic substitution reactions.



I II III

	R	X	X'	Z
a:	4-benzyl	Br	6-Br	H
b:	4-t-butyl	Br	6-Br	H
c:	4-t-butyl	Br	6-Cl	H
d:	4-benzyl	Cl	6-Cl	H
e:	6-t-butyl	Br	4-Br	H
f:	6-benzyl	Cl	4-Cl	H
g:	4-t-butyl	Cl	6-Cl	H
h:	6-t-butyl	Br	4-Br	Me
i:	6-t-butyl	Cl	4-Cl	Me
j:	4-t-butyl	Br	H	H
k:	4-t-butyl	Cl	H	H

	X	X'	Z
a:	Br	6-Br	H
b:	Br	6-Cl	H
c:	Cl	6-Cl	H
d:	Br	4-Br	H
e:	Cl	4-Cl	H
f:	Br	4-Br	Me
g:	Cl	4-Cl	Me

a: R=benzyl
b: R=t-butyl

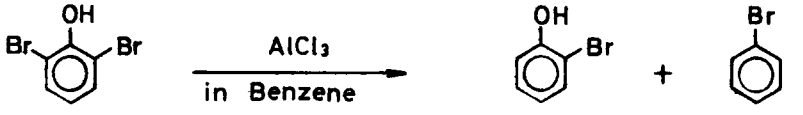
Hitherto, carboxyl,[4] amino,[5] sulfonic acid,[6] t-butyl,[7-9] and t-pentyl groups[10] have been used for this purpose.

We now report a new method for the preparation of chloro- and bromophenols by using benzyl and t-butyl groups as positional protective groups in the chlorination and bromination of phenols.

The transalkylation reactions of dihaloalkylphenols (Ia-Ii) and monohaloalkylphenols (Ij-Ik) were carried out under various conditions in order to prepare the corresponding dihalophenols (IIa-IIg) and monohalophenols like 2-chloro- and 2-bromophenol. The results are summarized in Table 1.

As is shown in Table 1, when aluminum chloride ($AlCl_3$) was used as the catalyst for the transalkylation of bromine-substituted I, the expected products, II and III were formed. In addition, by-products resulting from transbromination of benzene by II (Runs 1-4, 7 and 10) were isolated. Indeed, treatment of IIa with $AlCl_3$ catalyst under the same experimental conditions afforded 2-bromophenol and bromobenzene.

However, the transbromination reaction was repressed to some extent at lower reaction temperature (Runs 2,4 and 7).



IIa

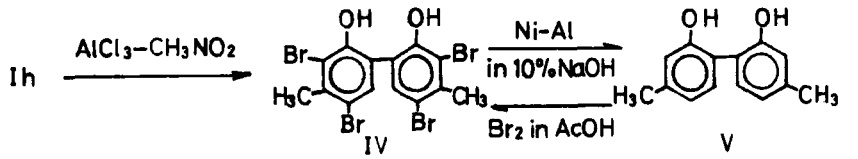
Table 1. The Transalkylation Reaction of Haloalkylphenols (I) in Benzene ($AlCl_3$ or $AlCl_3$-CH_3NO_2 Catalyst)[a]

		Product (%)			
Run	I	II	III	X-C_6H_4OH	PhBr
1[e]	a	a (58)	a (100)	2-Br- (24)	(28)
2[c,i]	a	a (70)	a (88)	2-Br- (14)	(16)
3[e]	b	a (78)	b (72)	2-Br- (25)	(23)
4[c]	b	a (79)	b (81)	2-Br- (9)	(9)
5[b,e]	b	a (15)	b (13)	—	—
6[b,i]	b	a (74)	b (85)	—	—
7[c]	c	b (97)	b (97)	2-Cl- (4)	(5)
8[b,i]	c	b (19)	b (27)	—	—
9[f]	d	c (78)	a (83)	—	—
10	e	d (64)	b (73)	2-Br- (15) 4-Br- (7)	(18)
11[b,i]	e	d (42)	b (49)	—	—
12[g]	f	e (52)	a (62)	—	—
13[d]	f	e (89)	a (82)	—	—
14	g	c (80)	b (70)	—	—
15[b,j]	h	f (95)	b (93)	—	—
16[b,h,k]	h	f (46)	b (45)	—	—
17	i	g (74)	b (52)	—	—
18[b]	j	—	b (81)	2-Br- (82)	—
19[b]	k	—	b (69)	2-Cl- (72)	—

a) Benzene/I = 30 mole/ 1 mole; catalyst/I = 1.2 mole/1 mole; catalyst is $AlCl_3$; temperature is 50° and time is 2 hrs unless otherwise indicated. b) $AlCl_3$-CH_3NO_2 catalyst.
c) Temp.: 30°. d) Temp.: 80°. e) Time: 1 hr. f) Time: 3 hrs.
g) Time: 5 hrs. h) Time: 6 hrs. i) Time: 10 hrs. j) IV ($C_{14}H_{10}Br_4O_2$) obtained 6.9% yield. k) IV obtained 16% yield.

It should also be noted that in contrast with $AlCl_3$, the $AlCl_3$-CH_3NO_2 catalyst[2,3,11,12] which is known to be an inactive catalyst for the transbenzylation reactions of diphenylmethanes, was an excellent catalyst for the transalkylation reactions of t-butylhalophenols but not for the transhalogenation as well as the transbenzylation reactions. This apparently suggests that the $AlCl_3$-CH_3NO_2 catalyst is the most suitable catalyst for the preparation of bromophenols by using t-butyl group as the positional protective group.

Although the $AlCl_3$-CH_3NO_2 catalyzed transalkylation reaction of Ih and of other substrates afforded the expected IIf in good yield, small amounts of a by-product IV, (mp. 243-245°) was obtained. The yield of IV increased with reaction time, while the yield of IIf decreased (Runs 15 and 16). Compound IV was easily reduced by Raney Ni-Al alloy in 10% sodium hydroxide solution to a debrominated compound (V, mp. 117-118°) which could be brominated with bromine in acetic acid to IV in good yield; IV was also formed by the treatment of IIf with $AlCl_3$-CH_3NO_2 catalyst under the same conditions as those used for the transalkylation reaction of Ih.



These observation coupled with elemental analyses and spectral data showed IV and V to be 3,3', 5,5'-tetrabromo-4,4'-dimethyl-2,2'-dihydroxydiphenyl and 4,4'-dimethyl-2,2'-dihydroxydiphenyl respectively and suggest that this catalyst acts as an oxidizing agent for the oxidative coupling reaction of IIf to IV.

Further investigation concerning to the oxidative coupling reaction is in progress and the result will be published in the near future.

EXPERIMENTAL

All the melting points are uncorrected. The haloalkylphenols were prepared by the reported method and were purified by fractional distillation and/or recrystallization. Ia:[13] bp. 195-198°/3mm, mp. 62-63°. Ib:[14] bp. 128-136°/5mm, mp. 77-79°. Ic: mp. 49-50°. Id:[15] mp. 64-65°. Ie:[16] mp. 62-63°. If:[15] bp. 150-152°/20mm, mp. 81-82°. Ig:[9] bp. 95-105°/3mm, mp. 44-45°. Ih:[17] mp. 53-54°. Ii:[17] bp. 114-115°/5mm. Ij:[18] bp. 180-188°/130mm. Ik:[19] bp. 100-105°/7mm.
Ic was unknown in literature.

Anal. Calcd. for $C_{10}H_{12}BrClO$: C, 45.54; H, 4.59
Found: C, 45.87; H, 4.40

IR cm^{-1}: 3560(νOH).

Aluminum chloride was purified by sublimation just prior to use, and aluminum chloride - nitromethane catalyst was prepared as reported previously.[20]

Analytical Procedure.- The analyses were carried out by gas chromatography using a Yanagimoto Gas Chromatography, Yanaco YR-101: column, 30% high vacuum silicon grease, 75 cm; increase rate of column temperature, 12°/min, carrier gas, hydrogen, 30 ml/min.

From the areas of individual peaks, mole % figure were calculated for each product after the relative response data had been determined by the internal standard method. Nitrobenzene was used as an internal standard. The data in the Table 1 are given as the average of at least three parallel determinations.

General Procedure.- After a mixture of 30 equivalents of benzene, 1.2 equivalents of the catalyst per equivalent of I and 1 mole of I had been maintained at a desired, constant temperature and a specified reaction time with shaking (120 cycle/min), the reaction mixture was quenched with 10% hydrochloric acid. The organic layer was separated and dried over sodium sulfate. A definite amount of nitrobenzene was added into the organic layer as an internal standard substance for the gas chromatographic analyses. After the analyses, the products were isolated and purified by distillation and/or recrystallization respectively.

Typical Procedures.-

a) The $AlCl_3$ catalyzed transalkylation reaction of Ig.- To a solution og 69g of Ig in 820 ml of benzene, was added gradually 51g of $AlCl_3$. After the mixture had been shaken at 30° for 3hrs, it was quenched with 100 ml of 10% hydrochloric acid. The separated organic layer was extracted with 10% sodium hydroxide solution and the extract was acidified with 10% hydrochloric acid. After extraction with ether and drying the ethereal extract over sodium sulfate, distillation

afforded 46.8g (91%) of IIc, bp. 115-120°/25mm; mp. 64-65°, Lit.[4] mp. 64.5-65.5°.

Distillation of the residual organic layer extracted with 10% sodium hydroxide gave IIIb (60%).

b) The $AlCl_3$-CH_3NO_2 Catalyzed Transalkylation Reaction of Ih.- A mixture of 50g of Ih, 400 ml of benzene and $AlCl_3$-CH_3NO_2 (25g/46g) catalyst was shaken at 50° for 2 hrs, the reaction mixture was then treated and worked up as described above. The ethereal extract upon evaporation, afforded 42.4g of colorless crystals which upon addition of 100 ml of petroleum ether disolved almost completely. Filteration of the insoluble crystals gave 3.4g (6.9%) of colorless crystals which upon recrystallization from petroleum benzine gave 3.0g (6.1%) of IV, mp. 243-245° as colorless needles.

Anal. Calcd. for $C_{14}H_{10}Br_4O_2$: C, 31.70; H, 1.89.
Found: C, 31.71; H, 1.74.

IR cm^{-1}: 3480 (νOH). Mass spectrum m/e; 526, 528, 530, 532, and 534 (M^+).

Compound IIf (38g, 92%) was obtained by evaporating of the filtrate as colorless needles, mp. 41-43°.

The Oxidative Coupling Reaction of IIf with $AlCl_3$-CH_3NO_2 Catalyst.- After a mixture of 5.0g of IIf, 50 ml of benzene and $AlCl_3$-CH_3NO_2 catalyst (3g/5.5g) was shaken at 50° for 6 hrs, the reaction mixture was treated as described above, to give 1.6g (32.4%) of IV.

Reduction of IV.- To a solution of 1g of IV in 20 ml of 10% sodium hydroxide solution, was gradually 6.0g of Raney Ni-Al

alloy. After addition of the alloy, the reaction mixture was acidified with 10% hydrochloric acid, and 0.35g (87%) of V precipitated as colorless crystals. Recrystallization from petroleum ether afforded colorless needles, mp. 117-118°.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59.
Found: C, 78.40; H, 6.28.

IR cm^{-1}: 3200 (νOH). Mass spectrum m/e: 214 (M^+).

REFERENCES

* To whom inquiries should be sent.

1. O. Tsuge and M. Tashiro, The Coal Tar (Koru Taru), 14, 513 (1962).
2. O. Tsuge and M. Tashiro, Bull. Chem. Soc. Japan, 38, 185 (1965); 40, 115, 199, 125 (1967).
3. G. A. Olah, S. Kobayashi, and M. Tashiro, J. Am. Chem. Soc., 94, 7488 (1972).
4. D. S. Tarbell, J. W. Wilson, and P. E. Fanta, Org. Syn. Coll. Vol. III, 267 (1955).
5. L. A. Bigelow, J. R. Johnson, and L. T. Sandborn, ibid., Coll. Vol. I, 133 (1948).
6. R. C. Huston and M. N. Ballard, ibid., Coll. Vol. II, 97 (1950).
7. M. J. Schlatter, J. Am. Chem. Soc., 76, 4952 (1954).
8. M. Kulka, ibid., 76, 5469 (1954).
9. D. R. Stevens, U.S. Patent, 2,403,748; C.A., 47, 8093 (1953).
10. J. F. Olin, U.S. Patent, 2,403,748; C.A., 40, 6100 (1946).
11. G. A. Olah, S. J. Kuhn, and S. H. Flood, J. Am. Chem. Soc., 84, 1688 (1962).

12. G. A. Olah, S. J. Kuhn and S. H. Flood, ibid., 84, 1695 (1962).
13. R. C. Huston, A. Neeley, B. L. Fayerweather, H. M. D'Arcy, F. H. Maxfield, M. M. Ballard and W. C. Lewis, ibid., 55, 2146 (1933).
14. M. Tsubota, Nippon Kagaku Zasshi, 89, 602 (1968); C.A., 69, 106083 (1968).
15. R. C. Huston and E. F. Eldridge, J. Am. Chem. Soc., 53, 2260 (1931).
16. I. Brown, G. Eglinton, and M. Martin-Smith, Spectrochimica Acta, 18, 1593, 1601 (1962).
17. L. E. Forman and W. C. Sears, J. Am. Chem. Soc., 76, 4977 (1952).
18. R. H. Rosenwald, ibid., 74, 4602 (1952).
19. L. E. Mills, U.S. Patent, 2,221,807; C.A., 35, 1936 (1941).
20. O. Tsuge, M. Tashiro, and A. Torii, Kogyo Kagaku Zasshi, 70, 2287 (1967); C.A., 68, 104304 (1968).

(Received January 26, 1974; in revised form March 19, 1974)