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BROMINATION OF ACTIVE HYDROGEN COMPOUNDS BY BROMOTRICHLOROMETHANE AND 1,8-DIAZABICYCLO[5.4.0]UNDECENE-7. A CONVENIENT SYNTHESIS FOR BROMIDES AND OLEFINS

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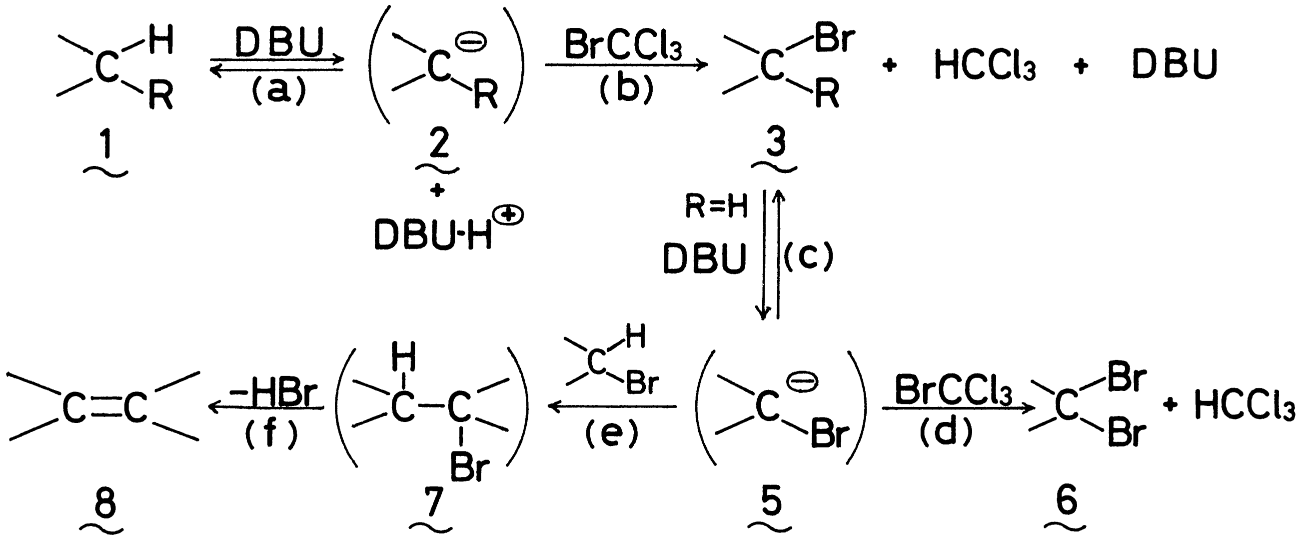
The DBU—$BrCCl_3$ reagent has been found to be an excellent reagent for bromination of active hydrogen compounds. The resulted bromides further afford dibromides and/or olefins in the case of active methylene compounds by controlling the reaction conditions.

Among the recent progress of various synthetic uses of 1,8-diazabicyclo[5.4.0]-undecene-7 (DBU),[1] we have found that the DBU—$BrCCl_3$ reagent can cause bromination of active hydrogen compounds to give bromides and/or olefins in good yields. This communication surveys the scope of the DBU—$BrCCl_3$-induced brominaton reaction of active hydrogen compounds, which we have developed.

Monoactive Hydrogen Compounds. In a representative procedure (Method A), to a mixture of phenylacetylene (5.1 g, 0.05 mol) and $BrCCl_3$ (13.9 g, 0.07 mol) in dry benzene (10 ml), there was added DBU (7.6 g, 0.05 mol) in dry benzene (10 ml) dropwise with stirring over 0.5 hr at 0°C under nitrogen atmosphere. The mixture was stirred for 3 hr at 0°C. After the mixture was acidified with dil. HCl, the solution was extracted with benzene. The organic layer was washed with water, dried over Na_2SO_4, and concentrated to afford pale yellow liquid (9.0 g, 99% yield) which was identified as phenylbromoethyne by comparison of its IR and NMR with those of authentic sample. From the recovered solvent, chloroform was detected by GLC. Similarly, diethyl butylmalonate gave diethyl butylbromomalonate in quantitative yield.

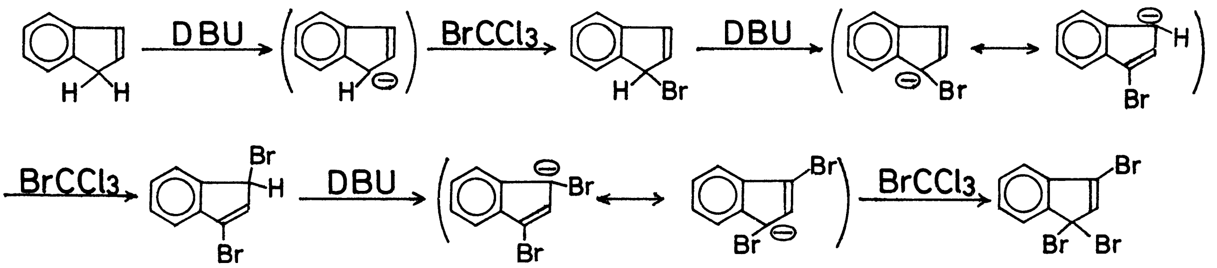
Active Methylene Compounds. Active methylene compounds reacted with the DBU—$BrCCl_3$ reagent to give mono- and dibromides and/or olefins depending on the reaction conditions. Reaction of fluorene and diethyl malonate with the DBU—$BrCCl_3$ reagent gave bromides, and in these cases, products distribution varies depending on the amount of $BrCCl_3$ used. Thus, 9,9-dibromofluorene was obtained as a sole product in 65% yield when fluorene was treated with 1.5 mol equivalent amounts of $BrCCl_3$ in Method A, and use of 3 mol equivalent amounts of $BrCCl_3$ resulted in the quantitative formation of the dibromide. On quenching with dil. HCl after 30 min, there was obtained the dibromide in 46% yield together with the starting fluorene, and no monobromide was detected. The reaction of diethyl malonate with 1.7 mol equivalent amounts of $BrCCl_3$

gave tetracarboethoxyethylene, a coupling product, in 86% yield. Quenching after 0.5 hr gave the coupling product and the monobromide, and no dibromide was detected in this case. However, the dibromide was obtained when large excess of $BrCCl_3$ was used. These results are summarized in Table, and can be explained best as shown in the following Scheme I.



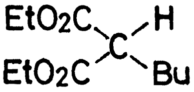
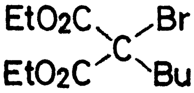
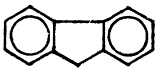
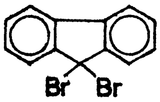
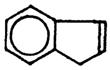
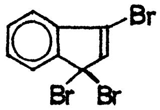
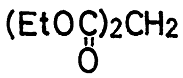
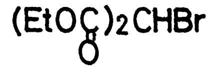
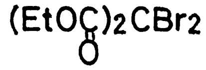
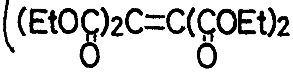
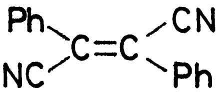
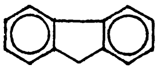
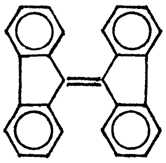
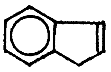
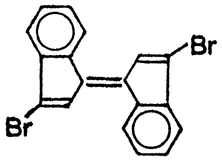
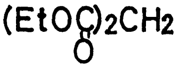
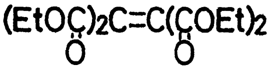
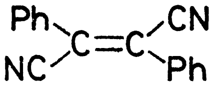
Scheme I

In the case of monoactive hydrogen compounds, an anion 2 which is formed via proton abstraction of 1 by DBU, reacts with $BrCCl_3$ to give monobromide 3. Here, formation of the anion 2 was confirmed by controlled experiment that addition of butylbromide to a mixture of diethyl malonate and DBU in benzene resulted in a quantitative formation of diethyl butylmalonate.$^{2)}$ In the case of diethyl malonate (R=H), the S_N2 type reaction of 3 with an anion 5, which is formed via proton abstraction of 3, gives the dimer 7, and subsequent elimination of HBr gives the olefin 8. In the case of fluorene, the concentration of the monobromide 3 (and 5) is low because equilibrium between 1 and 2 would lie so far to the left due to its lower acidity, and further structural factor would hinder the path e. Therefore, the anion 5 would favour to react with $BrCCl_3$ of which concentration is high, to give dibromide 6 (path d) rather than react with 3 to give 7. On reaction with 4 mol equivalent amounts of $BrCCl_3$, indene, which has similar acidity to that of fluorene, gave 1,1,3-tribromoindene in 80% yield. The reaction sequence is shown in Scheme II.



Scheme II

Table. The Reaction of Active Hydrogen Compounds by DBU–$BrCCl_3$

Substrate	pKa b)	DBU c)	$BrCCl_3$ c)	Temp. (°C)	Time (hr)	Product d)	Yield(%) e)
Method A a); Bromination of active hydrogen compounds.							
PhC≡CH	21	1	1.2	0	4	PhC≡CBr	99
		1.2	1.3	0	4		100
	25	2	3	0	4		99
	21	3	4	0	0.5		80
 $(EtO\underset{O}{\underset{\|}{C}})_2CH_2$	11	(3) 3	(1.7) 6	(0) 0	(0.5) 3	 $(EtO\underset{O}{\underset{\|}{C}})_2CHBr$	(45) 0
						 $(EtO\underset{O}{\underset{\|}{C}})_2CBr_2$	(0) 30
						 $(EtO\underset{O}{\underset{\|}{C}})_2C{=}C(\underset{O}{\underset{\|}{C}}OEt)_2$	(38) 50
PhCH$_2$CN	12	3	6	0	0.5	PhCHBrCN	5
							95
Method B a); Dimerization of active methylene compounds.							
	25	4	3	30	4		45
	21	2	4	0	4		65
 $(EtO\underset{O}{\underset{\|}{C}})_2CH_2$	11	1.5	1.7	-10	3	 $(EtO\underset{O}{\underset{\|}{C}})_2C{=}C(\underset{O}{\underset{\|}{C}}OEt)_2$	85
PhCH$_2$CN	12	1.5	1.7	-10	3		99

a) Method A; DBU was added dropwise into the mixture of substrate and $BrCCl_3$ in benzene. Method B; $BrCCl_3$ was added dropwise into the mixture of substrate and DBU in benzene.

b) The data of pKa were taken from W.K.McEwen [J. Am. Chem. Soc., 58, 1124 (1936)].

c) Mol ratio against the amount of substrate.

d) The structure of products were comfirmed by comparison of IR, NMR, and physical constants with those of authentic samples.

e) Yields were based on the starting substrates.

Reaction of phenylacetonitrile with the DBU–$BrCCl_3$ reagent gave the monobromide and the dimer in 5 and 95% yields, respectively, by 0.5 hr stirring, and prolonged reaction time (3 hr) resulted in exclusive formation of the dimer (99% yield) (Table).

It would be expected that the dimer could be obtained exclusively via path e in Scheme I, if concentration of $BrCCl_3$ is kept low during the reaction by its dropwise addition into a mixture of DBU and active methylene compounds in order to prevent the reaction of 5 with $BrCCl_3$ (path d). We have found that dropwise addition of $BrCCl_3$ (Method B) affords the olefin products exclusively in contrast to the former reaction in which $BrCCl_3$ is put initially in the reaction flask (method A). The results are summarized in Table. It can be seen that phenylacetonitrile, diethyl malonate, and indene give the corresponding olefins in good yields. In the case of fluorene, reaction at 0°C still affords the dibromide in 95% yield and raising reaction temperature to 30°C resulted in the formation of the olefin in 45% yield together with tarry substance. The difficulty with which the dimer is formed is due to its steric hindrance. Compounds with lower acidity such as xanthene (pKa=29), triphenylmethane (pKa=33), and diphenylmethane (pKa=35) resulted in no reaction.

These results clearly show that the DBU–$BrCCl_3$ reagent can be used as an excellent bromination agent for active hydrogen compounds, of which pKa is smaller than ca. 25, and that this provides a very convenient one-step synthetic method for bromides or olefins from appropriate active hydrogen compounds by controlling the reaction conditions.

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2) This was presented at the 34th Annual Meeting of the Chemical Society of Japan, Hiratsuka, April 1976. Monoalkylation of methyl cyanoacetate and acetylacetone using DBU was reported recently.[1-e)]

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