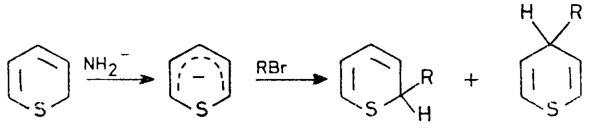
Unusual Reactivity of the 2*H*-Thiopyran Anion in Alkylation with t-Butyl Bromide and Cyclohexyl Bromide

By R. GRÄFING, H. D. VERKRUIJSSE, and L. BRANDSMA*
(*Department of Organic Chemistry of the University, Croesestraat* 79, *Utrecht, The Netherlands*)

Summary The anion of 2*H*-thiopyran (**2**) reacts with t-butyl bromide and cyclohexyl bromide in liquid ammonia to give 2-t-butyl-2*H*-thiopyran and a mixture of 2-cyclohexyl-2*H*-thiopyran and 4-cyclohexyl-4*H*-thiopyran in 53 and 82% yield, respectively.

IT is generally accepted that tertiary alkyl halides show great reluctance to undergo bimolecular attack by nucleophiles on the central carbon atom. Elimination of hydrogen halide is usually the predominant reaction and substitution products are formed, if at all, in very low yields. The low reactivity of t-butyl halides in S_N2 reactions is often mentioned as an example of steric hindrance.

We have observed a rapid reaction between the anion (**2**) of 2*H*-thiopyran (**1**), generated from (**1**) and excess of alkali amide in liquid ammonia, and t-butyl bromide, giving 2-t-butyl-2*H*-thiopyran (**3**; R = Bu^t) in up to 54% isolated yield. Even at −65 °C the t-butylation of (**2**) in liquid ammonia (K^+ cation) was complete within 2 min. Alkylation with cyclohexyl bromide ($c\text{-}C_6H_{11}Br$) resulted in a *ca.* 85:15 mixture of 2-cyclohexyl-2*H*-thiopyran (**3**; R = $c\text{-}C_6H_{11}$) and 4-cyclohexyl-4*H*-thiopyran (**4**; R = $c\text{-}C_6H_{11}$) in 82% yield.† Cyclohexyl halides often give low yields in reactions with nucleophiles, an effect which has been ascribed, *inter alia*, to *I* strain.[1]



(1) (2) (3) (4)

R = Bu^t or cyclohexyl

In tetrahydrofuran–hexamethylphosphoric triamide (THF–HMPA) (4:1) alkylation of the anion (**2**) [prepared by successive addition of butyl-lithium and (**1**) to a mixture of THF–HMPA and di-isopropylamine, cooled to −60 °C] with t-butyl bromide also proceeded smoothly at −60 °C. The yield of (**3**) was lower (31%) than in liquid ammonia, in part owing to decomposition of the 2*H*-thiopyran anion in the solvent mixture.

To our knowledge these extremely fast alkylations with t-butyl bromide and cyclohexyl bromide at very low temperatures are unique. A preliminary study in which a number of anions in liquid NH_3, *viz.* $^-CH_2C{\equiv}N$, $Ph\bar{C}H{-}C{\equiv}N$, $RC{\equiv}C^-$, Ph_2P^-, $H_2C{=}C{=}\bar{C}{-}SMe$, $(MeS)_2\bar{C}H$, $[MeS{-}\dot{C}H{-}\dot{C}H{-}\dot{C}H_2]^-$, and $[MeS{-}\dot{C}H{-}\dot{C}H{-}\dot{C}H{-}\dot{C}H{-}\dot{C}H_2]^-$ were allowed to react with t-butyl and cyclohexyl bromide showed that only the last anion [isoelectronic with the anion (**2**)] and cyclohexyl bromide reacted, to give a mixture of $MeS{-}CH(c\text{-}C_6H_{11})CH{=}CH{-}CH{=}CH_2$ and $MeS{-}CH{=}CH{-}CH(c\text{-}C_6H_{11}){-}CH{=}CH_2$ in *ca.* 30% yield.† The anion of indene (*cf.* ref. 2) and Bu^tBr reacted at −33 °C in liquid ammonia to give mixtures of 1- and 3-t-butylindene† (the latter resulting from base-catalysed isomerisation during the alkylation) in 48% yield, but this reaction required several hours.

We can only speculate on the mechanism. An S_N1 displacement in the reaction with the halides seems improbable because of the large difference between the rates of the reactions of (**2**) and other anions with Bu^tBr. The possibility of HBr-elimination and subsequent addition of the nucleophile to isobutene can be ruled out since no reaction was observed between (**2**) and isobutene in liquid NH_3 or in HMPA. If an S_N2-like mechanism is assumed, the high reactivity of (**2**) might be ascribed to a favourable combination of high polarisability and basicity.[3] 1 equiv. of lithium amide causes incomplete formation of (**2**) from (**1**), whereas in the case of potassium amide the deprotonation is almost complete. This fact suggests that the basicity of (**2**) is very near that of NH_2^-, being much higher than that of the indene anion.[4]

This investigation was supported by the Netherlands Organisation of Pure Research.

(*Received*, 20*th February* 1978; *Com.* 176.)

---

† Assignment of structures and determination of the composition are based on ^1H n.m.r. spectroscopy and g.l.c.

[1] H. C. Brown, R. S. Fletcher, and R. B. Johanneson, *J. Amer. Chem. Soc.*, 1951, **73**, 212; H. C. Brown, Special Publication No. 16, The Chemical Society, 1963.

[2] L. Meuring, *Acta Chem. Scand.*, 1974, **B28**, 295, claims a 45% yield of t-butylindene from the reaction of indenyl-lithium with Bu^t-Br in pentane–ether at 35 °C. We were unable to reproduce this result, our highest yield being only 7%.

[3] J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, 1962; **84**, 16; R. G. Pearson, H. Sobel, and J. Songstad, *ibid.*, 1968, **90**, 319.

[4] D. J. Cram, 'Fundamentals of Carbanion Chemistry,' Academic Press, New York, London, 1965.