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The Formation of Tin-Nitrogen Bonds. V. The Selective 1-Substitution Reaction of Tetrazoles by the Reaction of 5-Substituted 2-(Tri-*n*-butylstannyl)tetrazoles with Methyl Iodide, Methyl *p*-Toluenesulfonate, Dimethyl Sulfate, and Ethyl Bromoacetate

Tyûzô Isida, Tetsuo Akiyama, Kiyoshi Nabika, Keiiti Sisido, and Sinpei Kozima*
Department of Industrial Chemistry, Faculty of Engineering, Kyôto University, Sakyô-ku, Kyôto 606
**Department of Chemistry, College of Liberal Arts and Sciences, Kyôto University, Sakyô-ku, Kyôto 606*

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The selective 1-substitution reaction of tetrazole was developed by the treatment of 5-substituted 2-(tri-*n*-butylstannyl)tetrazoles with methyl iodide, methyl *p*-toluenesulfonate, dimethyl sulfate, or ethyl bromoacetate at room temperature. This selectivity was introduced by blocking the 2-nitrogen with the tri-*n*-butyltin group against the 2-substitution. In the case of 5-substituted 2-(trimethylstannyl)tetrazoles, a low selectivity was observed. The possible reaction pathways have been discussed.

In continuation of our research into the preparation and reaction of tetrazoles and their derivatives,[1] this paper will describe a highly selective 1-methylation method of tetrazoles.

The *N*-alkylation of 5-substituted tetrazoles has, until now, always been carried out by the reaction of tetrazole with either alkyl halide[2–10] or dialkyl sulfate[4,7,11,12] in the presence of a base, and also with diazomethane.[12–14] These reactions, in general, have provided the 2-alkyl isomers in a greater proportion than the 1-alkyl isomers.

It has now been found that the treatment of 5-substituted 2-(tri-*n*-butylstannyl)tetrazoles (I) with methyl iodide at room temperature for several hours afforded the 1-methyl isomer with a high selectivity (1-methyl-: 2-methyl isomer=90: 10). For the preparation of 5-substituted 1-methyltetrazole (III), this method is facile and comparable to the steady route of Harville, Herbst, Schreiner, and Roberts,[15] who prepared 1,5-disubstituted tetrazole from *N*-monosubstituted amide. Since the 2-(tri-*n*-butylstannyl)tetrazoles (I) can be prepared very easily by mixing free tetrazoles with bis(tri-*n*-butyltin) oxide,[1a] the 1-methylation can be carried out

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[1] a) K. Sisido, K. Nabika, T. Isida, and S. Kozima, *J. Organometal. Chem.*, **33**, 337 (1971). b) T. Isida, S. Kozima, K. Nabika, and K. Sisido, *J. Org. Chem.*, **36**, 3807 (1971). c) T. Isida, S. Kozima, S. Fujimori, and K. Sisido, This Bulletin, **45**, 246 (1972). d) T. Isida, S. Fujimori, K. Nabika, K. Sisido, and S. Kozima, *ibid.*, **45**, 1471 (1972).

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[3] R. A. Henry, *J. Amer. Chem. Soc.*, **73**, 4470 (1951).

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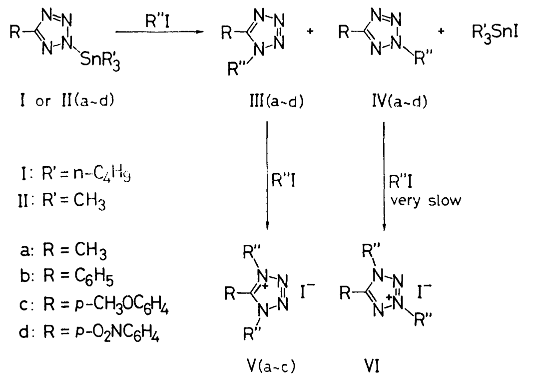
[15] E. K. Harville, R. M. Herbst, F. C. Schreiner, and C. W. Roberts., *ibid.*, **15**, 662 (1950).

by the simple procedure of dissolving a mixture of tetrazole and bis(tri-*n*-butyltin) oxide in methyl iodide. Additionally, the tri-*n*-butyltin iodide formed by the methylation process can be easily removed from the reaction mixture by extraction with light petroleum ether.



When 2-(tri-*n*-butylstannyl)-5-methyltetrazole (Ia) was dissolved in excess methyl iodide at room temperature and the solution was kept standing overnight, the *N*-methylation was completed. The ratio of 1,5-dimethyltetrazole (IIIa) and 2,5-dimethyltetrazole (IVa) was found to be 92: 8 by NMR analysis. Since 2,5-dimethyltetrazole (IVa) is much more volatile[1a,14] and far less reactive toward methyl iodide[1a] than IIIa, the evaporation of IVa and the surplus methyl iodide from the reaction products gave a mixture of IIIa and tri-*n*-butyltin iodide. Tri-*n*-butyltin iodide was also removed by simple extraction with light petroleum ether. Analytically pure 1,5-dimethyltetrazole (IIIa) was isolated in a good yield. 1,5-Dimethyltetrazole (IIIa) reacted gradually with excess methyl iodide at room temperature to give crystalline 1,4,5-trimethyltetrazolium iodide (Va), which began to precipitate after about 30 hr. When the reaction of Ia with excess methyl iodide was carried out at a higher temperature, a greater part of the IIIa was converted into the thermally stable tetrazolium iodide (Va).[1d]

A similar selective 1-methylation was also observed in the reactions of 5-phenyl and 5-(*p*-methoxyphenyl) analogues (Ib and Ic) with methyl iodide (Table 1). In the reaction of Ib with methyl iodide, the reaction temperature should be maintained at room temperature for the preparation of the 1-methyl isomer (IIIb), because on heating IIIb is easily converted into the 2-methyl isomer (IVb) in the presence of methyl iodide.[1b]

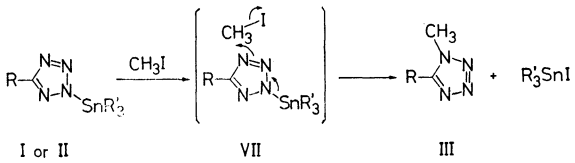
A less selective and much slower *N*-methylation was found in the reaction of 2-(tri-*n*-butylstannyl)-5-(*p*-nitrophenyl)tetrazole (Id) (Table 1). There occurred no further methylation of IIId to form the 1,4-dimethyltetrazolium salt (Vd). These results can be interpreted in terms of the electron-withdrawing character of the *p*-nitrophenyl group, which preferentially decreased the electron density of the 1- and 4-nitrogen atoms of the tetrazole ring, analogously to the reaction of potassium or sodium 5-substituted tetrazolate with methyl iodide.[4,6–8]

Table 1. Distribution of III and IV formed by the reaction of I with methyl iodide

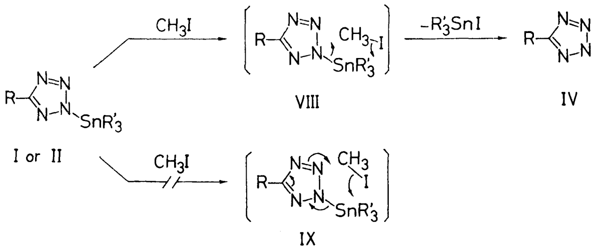
Compound	5-Substituent	Distribution (%) III	Distribution (%) IV
Ia	CH_3	92	8
Ib	C_6H_5	90	10
Ic	p-$CH_3OC_6H_4$	91	9
Id	p-$O_2NC_6H_4$	68	32

When the reaction of Ia—d with methyl iodide was carried out in the presence of methanol,[16] little change was found either in the isomer ratios of the products or in the reaction rate in comparison with the case of a reaction without methanol. This shows that the associative polymeric structure[1b] can not be involved in the selective 1-substitution reaction pathway.

It might be reasonable to consider that both the electron densities and steric requirements of the nitrogen atoms of tetrazole ring govern the site of the *N*-substitution. Since 2-substituted (or 2,5-disubstituted) tetrazoles react with methyl iodide[1b] or methyl *p*-toluenesulfonate[19] to yield exclusively 1,3-disubstituted (or 1,3,5-trisubstituted) tetrazolium salts, the 4-nitrogen of the 2-substituted tetrazole must be the most favorable site among the nitrogens to be attacked.[20] Analogously, it is probable that the *N*-methylation of 2-(trialkylstannyl)-5-substituted tetrazole (I or II) occurs preferentially on the 4-nitrogen.



The minor product, the 2-methyl isomer (IV), could be formed by the methylation of the 2- or 3-nitrogen of I (or II). Since the formation of 2,3,5-trisubstituted tetrazolium salt from 2,5-disubstituted tetrazole has never been observed by spectroscopic investigations,[1d] the *N*-methylation of the 3-nitrogen of I (or II) might



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[16] Addition of ligands such as alcohol to the toluene solution of tri-*n*-butylstannylimidazole has been reported to lower the viscosity, and hence the associative polymeric structure was fractured by the ligand to be the monomeric one.[17] Analogous fact has also been observed in the case of Ia—d.[18]

[17] M. J. Janssen, J. G. A. Luijten, and G. J. M. van der Kerk, *J. Organometal. Chem.*, **1**, 286 (1963).

[18] T. Isida, S. Kozima, and K. Sisido, unpublished results.

[19] W. P. Norris and R. A. Henry, *Tetrahedron Lett.*, **1965**, 1213.

[20] Formation of the 1,2,5-trisubstituted tetrazolium salts has never been reported and hence the 1-substitution of 2-substituted tetrazole can be excluded since the 1-nitrogen is sterically much more hindered than the 4-nitrogen.

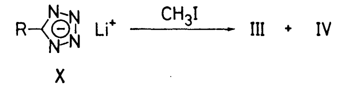
be much less probable; a possible process can be the direct methylation of the 2-nitrogen bonded to the tin atom *via* VIII.

In this selective methylation, consequently, the tri-*n*-butyltin group blocked the 2-nitrogen against the 2-methylation and led the methyl group into the 4-nitrogen. A comparable protection of the 1-nitrogen of 4-substituted imidazole by the benzoyl group has been reported for the specific preparation of 5-substituted 1-methylimidazole.[21,22]

Table 2. Distribution of III and IV formed by the reaction of II with methyl iodide

Compound	5-Substituent	Distribution (%) III	Distribution (%) IV
IIa	CH_3	40	60
IIb	C_6H_5	38	62
IIc	p-$CH_3OC_6H_4$	49	51
IId	p-$O_2NC_6H_4$	21	79

In the reaction of 5-substituted 2-(trimethylstannyl)-tetrazoles (II) with methyl iodide in methanol, the 2-methyl isomers (IV) have been produced in greater yields than the 1-methyl isomers (III) (Table 2). In the case of 2-(trimethylstannyl)-5-(*p*-nitrophenyl)tetrazole (IId), the distribution ratio of the 1-methyl *vs.* 2-methyl isomer was smaller than those in the case of the other homologs (IIa, IIb, and IIc). The electron-withdrawing *p*-nitrophenyl group apparently decreased the ratio of the 1-methylation, much as in the case of 2-(tri-*n*-butylstannyl) derivatives of tetrazoles with methyl iodide. In the presence of the electron-donating *p*-methoxyphenyl group in the 5-position, the 1-methyl isomer was obtained in a greater proportion than the cases of the phenyl and *p*-nitrophenyl groups. This is an additional case of how the electronic effect of the 5-substituent greatly influences the ratio of the 1-methylation *vs.* 2-methylation. The low selectivity in the *N*-methylation of 5-substituted 2-(trimethylstannyl)-tetrazoles (II) (Table 2), compared with the case of the 2-(tri-*n*-butylstannyl) analogues (I) (Table 1), is apparently correlated to the higher polarity of the tin-nitrogen bond in II. Because IIa is insoluble in non-polar solvents and is undistillable, while Ia is soluble and distillable,[1a] the trimethyltin-nitrogen bond in II is considered to be more polar than the tri-*n*-butyltin-nitrogen bond in I. As the polarity of the tin-nitrogen bond in II increases, the direct methylation of the 2-nitrogen atom *via* VIII could possibly increase. This trend has been supported by the predominant 2-methylation in the case of lithium salt of tetrazole (X), in which the lithium-nitrogen bond has a strongly ionic character (Table 3).



X

Table 3. Distribution of III and IV formed by the reaction of X with methyl iodide

Compound	5-Substituent	Distribution (%) III	Distribution (%) IV
Xb	C_6H_5	21	79
Xc	p-$CH_3OC_6H_4$	29	71
Xd	p-$O_2NC_6H_4$	19	81

Highly selective 1-methylation was also found in the reaction of 5-substituted 2-(tri-*n*-butylstannyl)tetrazole (I) with methyl *p*-toluenesulfonate or dimethyl sulfate (Table 4). In contrast to the easy removal of surplus methyl iodide from the products by evaporation, the use of these methyl esters as a methylating reagent is not preferred for the synthesis of III, since it is troublesome to remove the residual reagents and tri-*n*-butyltin salts from the product (III) by simple evaporation or extraction.

Table 4. Distribution of III and IV formed by the reaction of I with methyl *p*-toluenesulfonate, dimethyl sulfate, and ethyl bromoacetate

Compound	5-Substituent	Reagent	Distribution (%) III	Distribution (%) IV
Ia	CH_3	CH_3OTs[a]	79	21
Ib	C_6H_5	CH_3OTs	92	8
Ib	C_6H_5	$(CH_3O)_2SO_2$	93	7
Ia	CH_3	$BrCH_2CO_2C_2H_5$	90	10
Ib	C_6H_5	$BrCH_2CO_2C_2H_5$	91	9
Ie	$C_6H_5CH_2$	$BrCH_2CO_2C_2H_5$	94	6
Ib	C_6H_5	$ClCH_2CO_2C_2H_5$	No reaction	

a) Methyl *p*-toluenesulfonate.

A similar specific 1-substitution of tetrazole has also been achieved in the reaction of I with ethyl bromoacetate (Table 4). The synthesis of 5-substituted tetrazolylacetic acids and esters has been investigated for pharmaceutical purposes.[8,9,23,24] This method will provide a convenient route for the preparation of 5-substituted 1-tetrazolylacetic or -propionic acids and their esters.

Experimental

5-Substituted 2-(tri-*n*-butylstannyl)- and 2-(trimethylstannyl)tetrazoles (Ia—e and IIa—d) were prepared as has previously been described.[1a] The distribution of the 1-methyl and 2-methyl isomers was determined by studying the NMR spectrum, which was taken on a JEOL C-60HL spectrometer. All the melting points are uncorrected.

*Reaction of 2-(Tri-*n*-butylstannyl)-5-methyltetrazole (Ia) with Methyl Iodide.* A solution of 0.200 g of Ia in 0.25 ml of methyl iodide and 0.25 ml of $CDCl_3$ was kept in an NMR tube at room temperature for one day. The NMR spectrum of the reaction mixture was then measured. The distribution of the IIIa and IVa was determined to be 92:8 by

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21) R. A. Olofson and R. V. Kendall, *J. Org. Chem.*, **35**, 2246 (1970).

22) H. C. Beyerman, L. Meat, and A. Vauzor, *Rec. Trav. Chim. Pays-Bas*, **91**, 245 (1972).

23) R. T. Buckler, S. Hayao, O. J. Lorenzetti, L. F. Sancilio, H. E. Hartzler, and W. G. Strycker, *J. Med. Chem.*, **13**, 725 (1970),

24) A. K. Sorensen and N. A. Klitgaard, *Acta Chem. Scand.*, **26**. 541 (1972).

means of the integral ratio of the peak areas at δ 4.14 and 4.34 ppm respectively.[1c,d,14]

A mixture of 3.362 g (9.00 mmol) of Ia and 7 ml of methyl iodide was kept at room temperature for two days. The subsequent evaporation of the surplus methyl iodide and IVa from the reaction mixture gave a pasty liquid containing colorless crystals. To the residue was added 50 ml of light petroleum ether (bp 40—48 °C); fine crystals were then separated by filtration and rinsed twice with petroleum ether. The crystals were identified as IIIa; mp 70—71 °C (lit,[14] mp 71.8—72.6 °C), 0.515 g (58%).

*Reaction of 2-(Tri-*n*-butylstannyl)-5-phenyltetrazole (Ib) with Methyl Iodide.* A solution of Ib (4.009 g, 9.22 mmol) in 5.0 ml of methyl iodide was kept at room temperature for 3 days. The subsequent evaporation of the residual methyl iodide *in vacuo* gave 5.230 g of a liquid containing crystals. To the residue was then added three 20 ml portions of light petroleum ether to extract tri-*n*-butyltin iodide. The petroleum ether was then evaporated off to give 3.723 g (97%) of tri-*n*-butyltin iodide. The crystals (1.491 g), insoluble in petroleum ether, consisted of IIIb and IVb in a ratio of 90:10. The NMR peaks at δ 4.15 and 4.35 ppm were assigned to the *N*-methyl protons of IIIb and IVb respectively.[25] The recrystallization of the crystals from *n*-hexane gave 1.252 g (78%) of pure IIIb;[1b,15] mp 103—104 °C (lit,[15] mp 101—102 °C).

*Reaction of 2-(Tri-*n*-butylstannyl)-5-(*p*-methoxyphenyl)tetrazole (Ic) with Methyl Iodide.* A solution of 1.447 g (3.12 mmol) of Ic in 3 ml of methyl iodide was kept at room temperature for two days. The subsequent evaporation of the surplus methyl iodide gave 1.871 g of a liquid containing crystals. The proportional ratio of IIIc and IVc in the reaction mixture was determined to be 91:9; the peaks at δ 4.11 and 4.34 ppm were assigned to IIIc and IVc respectively. The reaction mixture was treated with two 20 ml portions of petroleum ether to remove the tri-*n*-butyltin iodide. The resulting crystals, 0.492 g (84.7%), were recrystallized from a mixture of diisopropyl ether and tetrahydrofuran (4:1) to give 1-methyl-5-(*p*-methoxyphenyl)tetrazole (IIIc); mp 121—122 °C.[26] NMR ($CDCl_3$): δ 3.84 (s, 3H, methoxy protons), 4.11 (s, 3H, 1-methyl protons), 7.24 (d, 2H, *meta*-protons with respect to the tetrazole ring, $J_{o,m}$ 8.7 Hz), 7.67 ppm (d, 2H, *ortho*-protons).

*Reaction of 2-(Tri-*n*-butylstannyl)-5-(*p*-nitrophenyl)tetrazole (Id) with Methyl Iodide.* A solution of 0.460 g (0.955 mmol) of Id in 5 ml of methyl iodide was kept at room temperature for 40 days. The subsequent evaporation of the surplus methyl iodide gave 0.587 g of solids. The NMR spectrum of the solids had two peaks, at δ 4.25 and 4.42 ppm, assignable to the *N*-methyl protons of IIId and IVd respectively.[25] The integral ratio of the two peaks showed the distribution of IIId and IVd to be 68:32. The reaction mixture was subsequently treated with 100 ml of diethyl ether to extract the tri-*n*-butyltin iodide, IVd, and the recovered Id. The resultant crystals, insoluble in ether, were treated with hot diisopropyl ether to isolate 0.107 g (55%) of IIId; mp 122—123 °C (lit,[25] mp 121—123 °C). The ether solution was then concentrated and treated with hot diisopropyl ether. From the insoluble part 0.048 g (25%) of IVd was isolated by column chromatography (Silica Gel, benzene–tetrahydrofuran 10:2); mp 173—174 °C (lit,[25] mp 171—172 °C).

Reaction of 2-(Trimethylstannyl)-5-methyltetrazole (IIa) with Methyl Iodide. A solution of 0.062 g (0.23 mmol) of IIa in 0.25 ml of methyl iodide and 0.1 ml of methanol was kept in an NMR tube at room temperature for 4 days. Long needles of Va were found in the reaction mixture. In the NMR spectrum of the mixture there were not the peaks at δ 4.14 and 0.74 ppm characteristic of IIIa and the starting ingredient, IIa respectively, but there were peaks at δ 4.34 and 0.87 ppm assignable to the 2-methyl protons of IVa and the methyl protons of trimethyltin iodide respectively. Methanol, IVa, and surplus methyl iodide were evaporated off from the reaction mixture *in vacuo* to leave crystalline Va and trimethyltin iodide. The iodide was then removed by extraction with ether. The resultant crystals were identified as Va, 0.0242 g (40%); mp 266 °C (dec).[1d] The distribution of IIIa and IVa was determined to be 40:60 on the basis of the following facts: the starting IIa was completely converted into IIIa and IVa, and the resultant IIIa reacted with methyl iodide quantitatively to give Va, while little reaction occurred between IVa and methyl iodide.[1d]

Reaction of 2-(Trimethylstannyl)-5-phenyltetrazole (IIb) with Methyl Iodide. A solution of 0.378 g (1.22 mmol) of IIb in 2 ml of methyl iodide and 5 ml of methanol was kept at room temperature for two days. Evaporation of methanol and surplus methyl iodide *in vacuo* gave 0.383 g of crystals, which were then treated with benzene to separate the insoluble IIb, which was recovered unchanged; 0.158 g (42%). From the benzene extract the trimethyltin iodide was removed by extraction with water. The resultant benzene solution was concentrated to give a mixture of IIIb and IVb; 0.085 g (44%); IIIb:IVb=38:62.

*Reaction of 2-(Trimethylstannyl)-5-(*p*-methoxyphenyl)tetrazole (IIc) with Methyl Iodide.* A solution of IIc (0.351 g) in 1 ml of methyl iodide and 2 ml of methanol was kept at room temperature for 5 days. Methanol and surplus methyl iodide were then evaporated off *in vacuo* to give 0.362 g of crystals, whose components were determined by NMR analysis to be IIc (49%) and IVc (51%).

*Reaction of 2-(Trimethylstannyl)-5-(*p*-nitrophenyl)tetrazole (IId) with Methyl Iodide.* A solution of 0.088 g (0.25 mmol) of IId in 0.25 ml of methyl iodide and 0.25 ml of methanol was kept at room temperature for 5 days. The subsequent evaporation of methanol and surplus methyl iodide gave yellowish crystals (0.076 g) which were then treated with chloroform to extract *N*-methyl isomers and leave the recovered IId (0.012 g, 14%). The chloroform solution was evaporated off to give 0.057 g of the yellowish crystals. The ratio of IIId and IVd in the crystals was determined by NMR analysis to be 21:79.

Reaction of Lithium 5-Phenyltetrazolate (Xb) with Methyl Iodide. The monohydrate of Xb (0.1062 g, 0.625 mmol), prepared from an equimolar mixture of lithium hydride and 5-phenyltetrazole, was dissolved in 1.0 ml of methyl iodide and 2.0 ml of methanol. The solution was kept at room temperature for 3 days. The subsequent evaporation of methyl iodide and methanol gave 0.226 g of a pasty liquid, which was then extracted with dry ether. The ether solution was evaporated off to give 0.106 g of a liquid. The distribution of IIIb and IVb was determined by NMR analysis to be 21:79.

*Reaction of Lithium 5-(*p*-Methoxyphenyl)tetrazolate (Xc) with Methyl Iodide.* A solution of 0.094 g (0.47 mmol) of Xc in 0.25 ml of methanol and 0.25 ml of methyl iodide was kept at room temperature for two days. The subsequent evaporation of methanol and methyl iodide *in vacuo* gave 0.216 g of brownish crystals which were dissolved in chloroform. The chloroform solution was evaporated off to give 0.081 g (91%) of crystals. The ratio of IIIc and IVc in the crystals was determined by NMR analysis to be 21:79. The separation of IVc from IIIc was carried out by column

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25) R. R. Fraser and K. E. Haque, *Can. J. Chem.*, **46**, 2855 (1968).

26) Although the melting point was different from the reported one (mp 93—94 °C),[15] not only the elemental analysis but also the NMR and mass spectra were consistent with the structure of IIIc.

chromatography (silica gel, benzene–chloroform 2: 1) to isolate 0.055 g of IVc; mp 86.5—87.5 °C, NMR: δ 3.86 (s, 3H, methoxy protons), 4.37 (s, 3H, 2-methyl protons), 7.02 (d, 2H, *meta*-protons with respect to the tetrazole ring, $J_{o,m}$ 9.0 Hz), 8.12 ppm (d, 2H, *ortho*-protons).

Found: C, 57.17; H, 5.19; N, 30.05%. Calcd for $C_9H_{10}N_4O$: C, 56.83; H, 5.30; N, 29.46%.

From the later fraction 0.015 g of IIIc was collected.

*Reaction of Lithium 5-(*p*-Nitrophenyl)tetrazolate (Xd) with Methyl Iodide.* A solution of 0.076 g (0.35 mmol) of the monohydrate of Xd in 0.25 ml of methanol and 0.25 ml of methyl iodide was kept at room temperature for two days. The subsequent evaporation of the methanol and surplus methyl iodide gave 0.176 g of brownish crystals, which were then dissolved in chloroform. The solution was treated with water to remove the lithium iodide and Xd. From the chloroform layer was obtained 0.060 g (83%) of brownish-yellow crystals in which IIId and IVd were present in a ratio of 19: 81.

Reaction of Ia with Methyl p-*Toluenesulfonate.* An equimolar solution of Ia and methyl *p*-toluenesulfonate in $CDCl_3$ was kept in an NMR tube at room temperature. After 21 days, the conversion of Ia into IIIa and IVa reached 42%. The distribution of IIIa and IVa was 79: 21.

Reaction of Ib with Methyl p-*Toluenesulfonate.* A solution of 0.870 g (2 mmol) of Ib and 0.372 g (2 mmol) of methyl *p*-toluenesulfonate in 5 ml of ether was kept at room temperature for one day. The subsequent purification of the reaction mixture by column chromatography (silica gel, benzene: ether= 1: 1) yielded 0.280 g (89%) of crystals, which contained IIIb and IVb (92: 8).

Reaction of Ib with Dimethyl Sulfate. A solution of 0.383 g of Ib and 0.200 g of dimethyl sulfate in 10 ml of ether was kept at room temperature for 8 days. After the evaporation of the ether, the reaction mixture was extracted with petroleum ether. The remaining crystals (0.087 g) were pure IIIb. From the extract, 0.015 g of a mixture of IIIb and IVb (1: 1) was obtained by column chromatography. Consequently, the ratio of IIIb and IVb was found to be 93: 7.

Reaction of Ib with Ethyl Bromoacetate. A solution of 0.671 g (1.5 mmol) of Ib and 0.259 g (1.5 mmol) of ethyl bromoacetate in 10 ml of benzene was refluxed for 10 days. The subsequent separation of the products by column chromatography (silica gel, benzene: ether= 1: 1) gave 0.327 g (91%) of crystalline ethyl 5-phenyl-1-tetrazolylacetate[8] and 0.033 g (9%) of ethyl 5-phenyl-2-tetrazolylacetate.[8] These esters were converted into the corresponding acids by alkali hydrolysis. 5-Phenyl-1-tetrazolylacetic acid, mp 169—170 °C (*n*-hexane) (lit,[8] mp 148—150 °C). Although the melting point is different from the reported one, the NMR and elemental analyses are consistent with the structure. NMR ($CDCl_3$: CF_3COOH= 1: 2): δ 7.70 (s, 5H, phenyl protons), 5.37 ppm (s, 2H, methylene protons). 5-Phenyl-2-tetrazolylacetic acid, mp 183—184 °C (*n*-hexane), (lit,[8] mp 182—184 °C). NMR ($CDCl_3$: CF_3COOH= 1: 2): δ 8.0 (m, 2H, *ortho*-protons), 7.55 (m, 3H, *meta*- and *para*-protons), 5.64 ppm (s, 2H, methylene protons).

Reaction of Ia with Ethyl Bromoacetate. An analogous treatment of Ia with ethyl bromoacetate for four days gave a mixture of the 1- and 2-substituted isomers. The NMR spectrum of the mixture showed that the ratio of the 1- and 2-substituted isomers was 90: 10. The peaks at δ 5.23 and 5.40 ppm were assigned to the methylene protons of the 1- and 2-substituents respectively.[8] 5-Methyl-1-tetrazolylacetic acid was isolated by the hydrolysis of the ester; mp 183—184 °C (dec) (*n*-hexane and ethyl acetate) (lit,[8] mp 184—186 °C (dec)).

*Reaction of 2-(Tri-*n*-butylstannyl)-5-benzyltetrazole (Ie) with Ethyl Bromoacetate.* An analogous treatment of Ie with ethyl bromoacetate gave a mixture of the 1- and 2-substituted isomers in a ratio of 94: 6. 5-Benzyl-1-tetrazolylacetic acid was isolated by the hydrolysis of the ester; mp 181—182°C (ethanol). NMR ($CDCl_3$: CF_3COOH= 1: 2): δ 7.6—7.0 (m, 5H, phenyl), 5.10 (s, 2H, $C\underline{H}_2COOH$), 4.43 ppm (broad s, 2H, $C_6H_5C\underline{H}_2$–).

Found: C, 54.95; H, 4.63; N, 25.43%. Calcd for $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.62; N, 25.68%.