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A NOVEL SYNTHESIS OF 2-BENZOTHIAZOLAMINE AND ITS DERIVATIVES BY A NICKEL(0)-CATALYZED REACTION OF 1,2-AMINOIODOARENES WITH THIOUREAS

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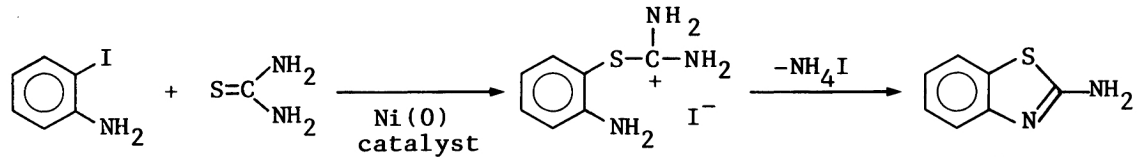
In the presence of a nickel(0) complex, 1,2-aminoiodoarenes underwent the reaction with thioureas to provide a facile, site-specific, and general synthetic procedure of 2-benzothiazolamine and its derivatives under non-oxidative conditions.

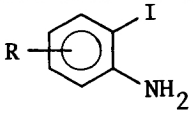
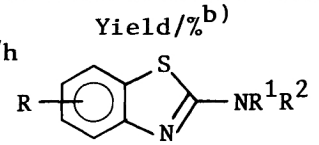
The application of transition organometallic compounds to a synthesis of heterocyclic compounds has been proved to be unequivocally useful.[1] As a constructive material of N-C-N, N-C-S, N-C, S-C, N, or S fragment of heterocycles, a versatility of thiourea (TU) is well established in heterocyclic chemistry: however, its utilization to a metal-promoted heterocyclic synthesis was scarcely undertaken, despite a propensity of TU to ligate to metals.[2,3] Therefore, a metal-assisted ring closure between TU and otherwise-inert bifunctional substrates is intrigues, if the latter are activated by metals. Here we will report a reaction of 1,2-aminoiodoarenes with TU or its derivatives (TUS) leading to 2-benzothiazolamine (3) and its derivatives with the aid of a nickel(0) complex.



1 2 3

In the presence of a catalytic amount of nickel(0) complex, generated in situ from bis(triethylphosphine)nickel(II) chloride and sodium cyanoborohydride as a reducing agent, o-iodoaniline (1) was reacted with TU in N,N-dimethylformamide (DMF) at 60 °C for 20 h to afford 3 in a 92% yield. Representative results are summarized in Table 1. It is to be noted that both alkenyl and ketonic groups were left intact under employed conditions.[4] Since this nickel(0) enables aryl halides to undergo a nucleophilic displacement with TU under cited conditions,[5] 3 was probably formed via an isothiuronium intermediate (2) in which an intramolecular nucleophilic addition of amino group onto imino group followed by a deamination might take place. The latter condensation step proceeded much faster than the proceeding step, judging from the fact that an interrupted solution contained only 1 and 3. Although steric hindrance decreased the rate of reaction considerably, TUS could be used instead of TU to produce a variety of N-substituted or N,N-disubstituted derivatives of 3 in good yields: symmetric TUS was suitable for the preparation of a N-alkyl or N,N-dialkyl derivative of 3, whereas asymmetric TUS was suitable for a N-phenyl derivative

Table 1. Synthesis of Benzothiazolamine and its Derivatives[a)]

Run	 R	$R^1R^2NC(S)CNR^3R^4$ R^1	R^2	R^3	R^4	Temp/°C	Time/h	Yield/%[b)] 
1	H	H	H	H	H	60	20	87 (93)
2	H	H	H	H	H	80	3	(74)[c)]
3	H	H	H	H	H	100	1	(84)
4	H	H	H	H	H	120	0.5	(81)
5	5-CH_3	H	H	H	H	60	90	89
6	5-Cl	H	H	H	H	60	20	94
7	H	CH_3	H	H	H	60	30	(54)[d)]
8	H	CH_3	H	CH_3	H	60	40	85
9	H	n-C_4H_9	H	n-C_4H_9	H	60	60	85
10	H	CH_3	CH_3	CH_3	CH_3	100	20	81
11	H	C_6H_5	H	H	H	60	24	69
12	5-CF_3	C_6H_5	H	H	H	60	40	93

a) Every runs were carried out under nitrogen. Molar ratio of each component (ArI/TUS/$NiCl_2(PEt_3)_2$/$NaBH_3CN$) was 1.0/1.5/0.02/0.03 (Runs 1–7) or 1.0/1.5/0.04/0.06 (Runs 8–12). The products were isolated by column chromatography on silica gel.
b) Isolated yields. Yields in parentheses were determined by GLC using internal standards.
c) The conversion was 91%.
d) The conversion was 88%. 3 was also obtained in a yield of 28%.

of 3. N,N-Diphenyl-TUS induced the decomposition of the nickel(0) complex and failed to give the desired product. Thus, the present nickel(0)-catalyzed reaction not only expands the utility of TUS in heterocyclic syntheses but also offers a facile and sitespecific synthetic procedure of 3 and its derivatives,[6)] which are widely used as starting materials for the synthesis of biologically active substances.[7)]

References

1) J. L. Davidson and P. N. Preston, Adv. Heterocyclic Chem., 30, 319 (1982).
2) T. S. Griffin, T. S. Woods, and D. L. Klayman, Adv. Heterocyclic Chem., 18, 99 (1975).
3) D. Neibecker and B. Castro, Tetrahedron Lett., 1977, 2351; T. F. Murray, E. G. Samsel, V. Varma, and J. R. Norton, J. Am. Chem. Soc., 103, 7520 (1981).
4) After 20 h, 97% of 1,1-diphenylethene or 96% of acetophenone was recovered from the reaction solution.
5) K. Takagi, Chem. Lett., 1985, 1307.
6) Hitherto, 3 and its derivatives were conveniently prepared by the oxidation of arylthioureas (A), the thiocyanation of *p*-substituted aniline (B), or the reaction of 2-aminothiophenol with isothiocyanates (C). However, each of these methods suffered such disadvantage as low chemoselectivity (A and B), low regio- or siteselectivity (A), lack of generality (B), and low yield (C).
7) See for example, R. A. Glennon, J. J. Gaines, and M. E. Rogers, J. Med. Chem., 24, 766 (1981).

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