Solid-Phase Synthesis of Quinazoline-2,4-Diones and Their Analogues from Resin-Bound Compounds with Primary Amines

Shingo Makino*

Pharmaceutical Research Laboratories, Ajinomoto Co. Inc., 1-1, Suzuki-cho, Kawasaki-ku, Kawasaki-shi, Kanagawa-ken, 210-0801, Japan

Abstract: Solid-phase organic synthesis of heterocyclic compounds on solid-support has been a focus of recent investigations because of the potential applicability of these compounds toward a variety of drug targets. Among the various heterocycles, we have been especially interested in quinazoline-2,4-diones because of the wide range of their bioactivities. Therefore, in this article we review methods for the solid-phase synthesis of quinazoline-2,4-diones and their analogues. Since all of these heterocycles can be speedily derivatized from resin-bound primary amines, incorporating the amines at the 3*N*-position of quinazoline-2,4-diones or corresponding positions of its analogues, it becomes possible to efficiently compare the bioactivities of these quinazoline-2,4-diones and their analogues. Various methods of solid-phase synthesis described herein should be practical and useful tools for the medicinal chemist in supporting drug discovery initiatives.

Keywords: Solid-phase synthesis, resin-bound, heterocycle, quinazoline, quinazoline-2,4-dione.

INTRODUCTION

Solid-phase organic synthesis of non-peptide compounds is emerging as an important tool for drug discovery [1]. The synthesis of heterocyclic compounds on solid-support [2], in particular, has been the focus of recent investigations because of the potential applicability of these compounds toward a variety of drug targets. Among various solid-phase syntheses of heterocycles, we are especially interested in syntheses starting from resin-bound compounds with primary amines, incorporating the amines in the rings of those heterocycles. There have been numerous reports of such syntheses as listed in Fig. **1** [3].

Therefore, in this review, we would like to specifically discuss the solid-phase synthesis of quinazoline-2,4-diones and their analogues from resin-bound compounds with primary amines, incorporating the amines at the 3*N*-position of quinazoline-2,4-diones or corresponding positions of their analogues [6-14] (Fig. **2**). As these quinazoline-2,4-diones and their analogues will likely possess comparable biological activities due to the similarity of their chemical structures, it would be interesting to compare the activities of variously substituted analogues once biological activity is found for one of these heterocycles. One can speedily synthesize these heterocycles once the methods for solid-phase synthesis of

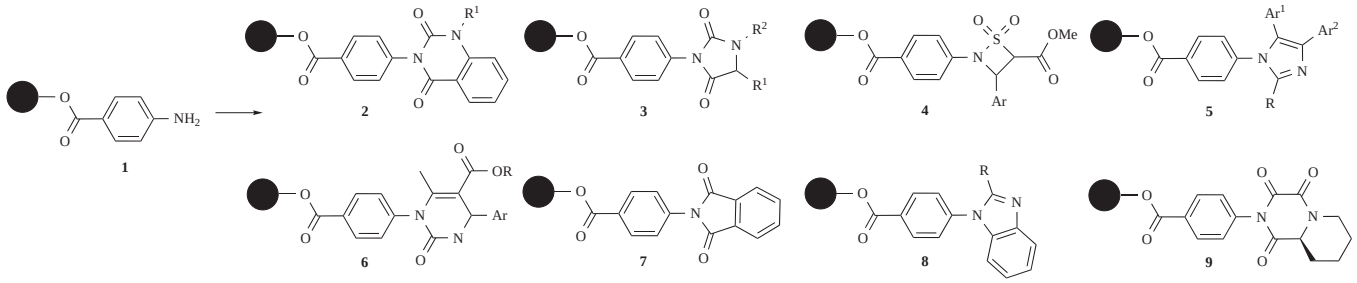


Fig. (1). Examples of solid-phase heterocycle syntheses from a resin-bound compound with primary amines, incorporating the amine as part of the derivatized heterocycles, according to previous reports. Note that various resin-bound compounds with primary amines in the original reports are simplified to 4-aminobonzoic acid ester for explanation. Not all the solid-phase syntheses have been tested with this resin-bound amine **1**.

These methods of solid-phase synthesis of heterocycles can be applied to a number of resin-bound compounds with primary amines. Among various heterocycles, solid-phase synthesis of quinazoline-2,4-diones [4] is particularly attractive because of the wide range of their bioactivities [5]. these heterocycles have been developed. Investigation of active compounds derived from different scaffolds is important in order to find compounds with better pharmacokinetic and toxicity profiles. Furthermore, investigation of a great number of substituents can be rapidly performed within the same class of scaffold by exploiting the efficiency of solid-phase synthesis.

*Address correspondence to this author at 6-14-9 Niitaka, Yodogawa-ku, Osaka-shi. 532-0033, Japan; Tel: +81-06-6350-0709; Fax: +81-06-6350-0709; E-mail: msmakino@aol.com

1389-5575/06 $50.00+.00

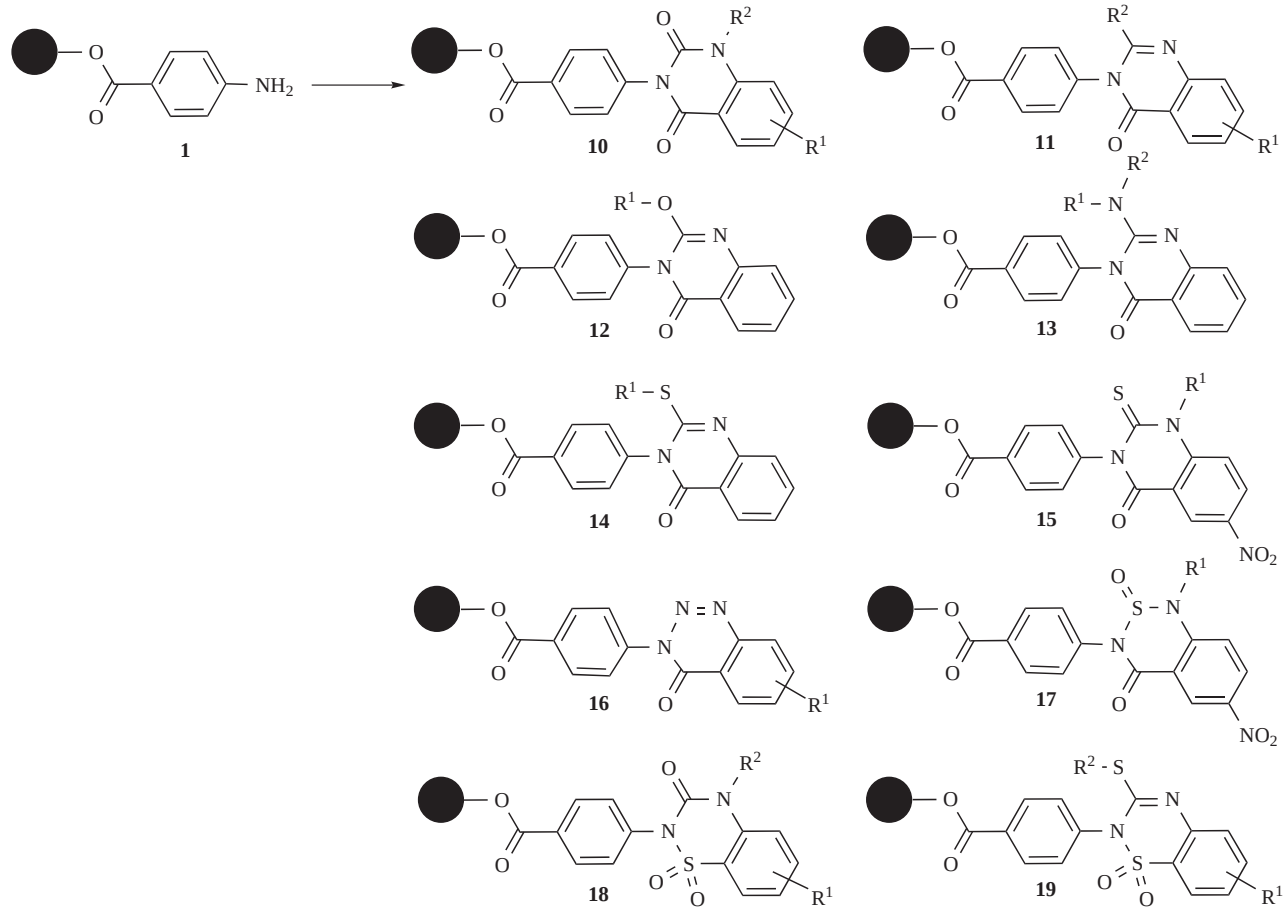


Fig. (2). Solid-phase syntheses of quinazoline-2,4-diones and their analogues from a resin-bound compound with a primary amine, incorporating the amine as part of the derivatized heterocycles. As in Fig. **1**, various resin-bound compounds with primary amines in the original reports are simplified to 4-aminobonzoic acid ester for explanation. Not all the solid-phase syntheses have been tested with this resin-bound amine **1**.

SOLID-PHASE SYNTHESIS OF QUINAZOLINE-2,4-DIONES

There have been numerous reports of the solid-phase syntheses of quinazoline-2,4-diones from resin-bound compounds with primary amines [6-14]. Construction of the quinazoline-2,4-dione skeleton on solid-support has been achieved either by urea bond formation followed by amide bond formation [6a,b], or vice versa [6c-e] (Fig. **3**). There are three different diversity points to be considered in the synthesis of quinazoline-2,4-diones. They are the substituents at the 1*N*- and 3*N*-positions and the substituents on the aromatic rings of quinazoline-2,4-diones. A substituent at the 3*N*-position comes from the starting material, a resin-bound compound with a primary amine. Substituents at the 1*N*-position and on the aromatic rings are derived from other reagents used in each synthesis. Here, the scope and limitations of the following quinazoline-2,4-dione syntheses will be discussed from the viewpoints of those substituents.

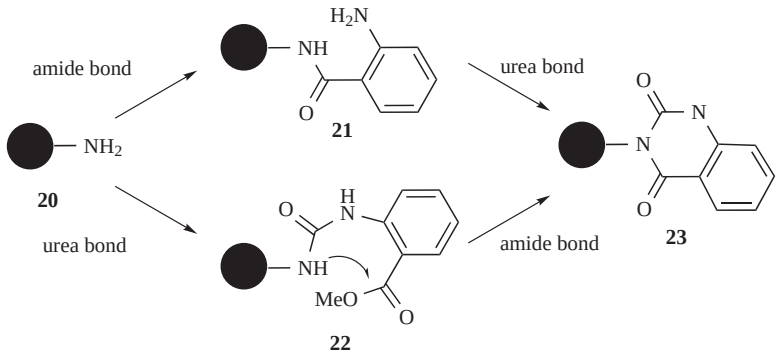
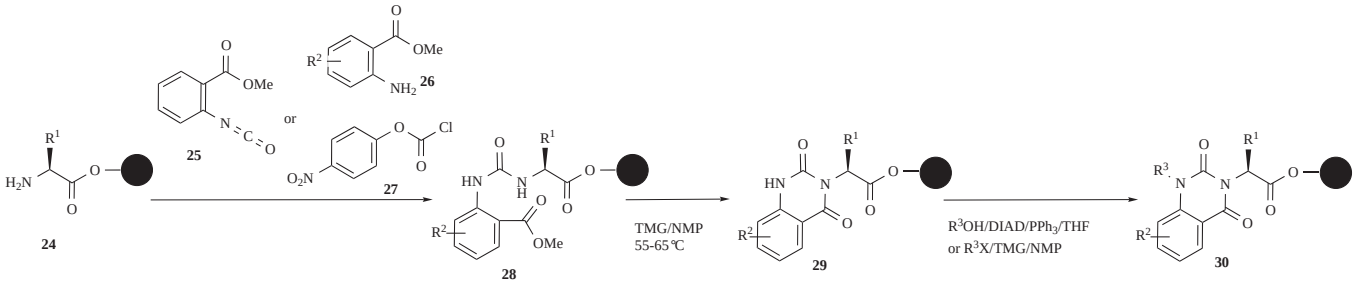


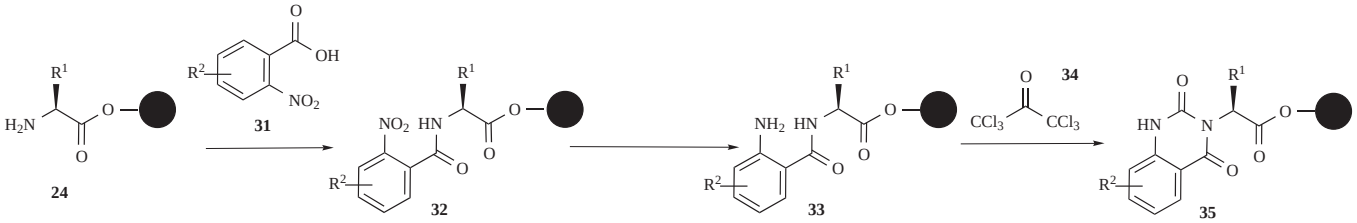
Fig. (3). Two different basic strategies for the synthesis of quinazoline-2,4-diones. The quinazoline-2,4-dione skeleton can be constructed either by the amide bond formation followed by the urea bond formation, or vice versa.



Scheme 1. Synthesis of quinazoline-2,4-diones by Gordeev.

Synthesis of Quinazoline-2,4-Dione: The Urea Bond Formation, then Amide Bond Formation

Gordeev *et al.* reported the synthesis of quinazoline-2,4-diones **29** by reacting resin-bound amino acids **24** with 2-methoxycarbonyl phenylisocyanate **25** [6a,b] (Scheme **1**). Although Gordeev *et al.* only described the use of resin-bound alkylamines **24** in their report, our investigation found that resin-bound anilines also worked excellently using this strategy. Subsequently, substituents at the 1*N*-position were easily introduced using alkyl halides or alcohols. Therefore, quinazoline-2,4-diones with a wide variety of substituents at the 1*N*- and 3*N*-positions can be prepared efficiently with this method. However, the synthesis of quinazoline-2,4-diones with many different substituents on the aromatic rings is limited by the commercial availability of 2-methoxycarbonyl phenylisocyanates. In the same report, they also described a similar strategy using the alternative reagents, methyl 2-aminobenzoates **26** and 4-nitrophenyl chloroformate **27** (Scheme **1**). However, we found the formation of the urea bond (**28**) was difficult due to the poor nucleophilicity of the amino group of methyl 2-aminobenzoates **26**, especially when electron-withdrawing substituents existed on the aromatic rings.

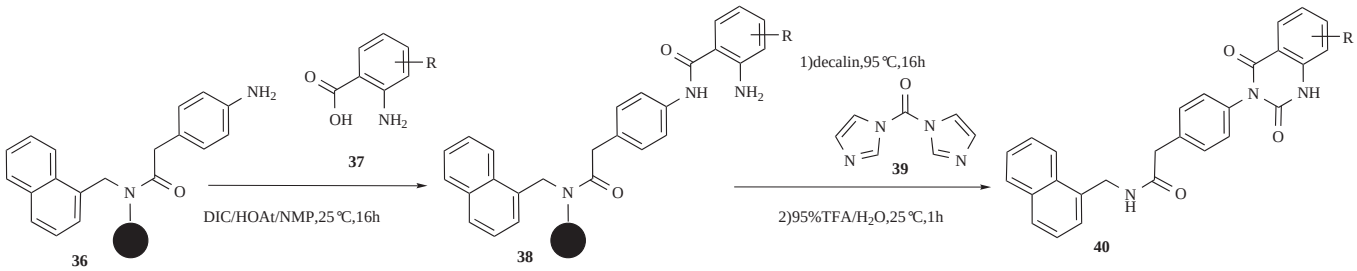


Scheme 2. Synthesis of quinazoline-2,4-diones by Puhl.

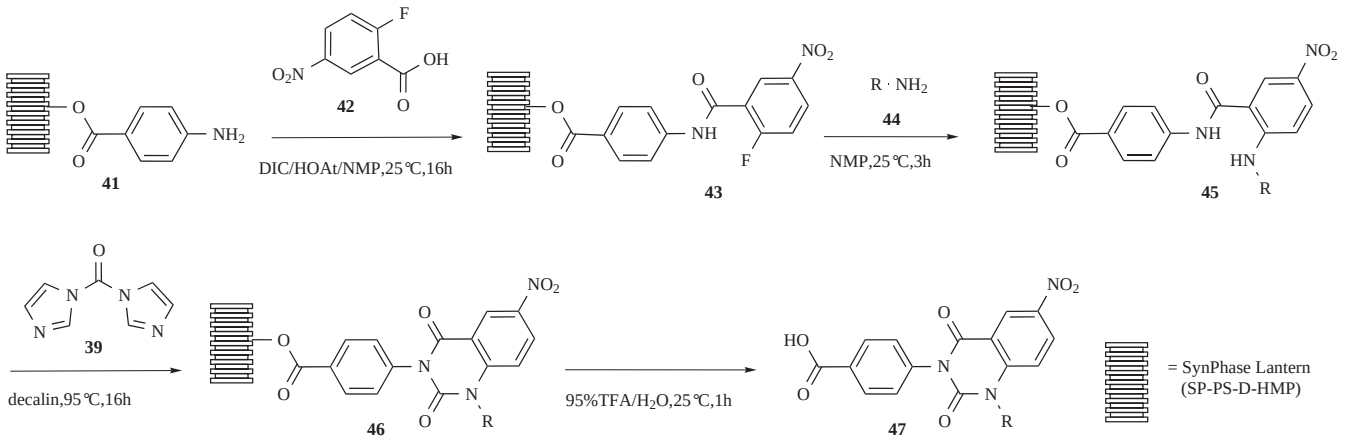
Synthesis of Quinazoline-2,4-Dione: The Amide Bond Formation, then Urea Bond Formation

Puhl *et al.* reported the synthesis of quinazoline-2,4-diones using 2-nitrobenzoic acids [6c] (Scheme **2**). Solid-supported 2-aminobenzamides **33** were prepared by coupling resin-bound amino acids **24** with 2-nitrobenzoic acids **31** and subsequent reduction of the nitro group of **32**. Cyclization of 2-aminobenzamides **33** with triphosgen **34** gave a range of quinazoline-2,4-diones **35**. As a wide range of 2-nitrobenzoic acids was commercially available, this synthesis was considered to be useful for the preparation of diverse quinazoline-2,4-diones. In our investigation, this synthesis worked not only with resin-bound alkylamines **24**, but also with resin-bound anilines; however, in many cases, various byproducts were found upon the reduction of the nitro group of **32**, limiting significantly the number of 2-nitrobenzoic acids that worked with this method. Protection of the amino group of 2-aminobenzoic acids [15] was investigated instead of using 2-nitrobenzoic acids **31**, though this protection was found to be difficult due to the poor nucleophilicity of the amino group of 2-aminobenzoic acids, especially when electron-withdrawing substituents existed on the aromatic rings.

Makino *et al.* reported the solid-phase synthesis of quinazoline-2,4-diones **40** with electron withdrawing-substituents by the coupling between resin-bound primary amines **36** and 2-aminobenzoic acids **37**, and subsequent cyclization of **38** using carbonyldiimidazole **39** [6d] (Scheme **3**). In fact, this coupling worked excellently without protecting the amines of 2-aminobenzoic acids **37** because of the poor nucleophilicity of the amino group. Ellman *et al.* also reported the coupling of 2-aminobenzoic acids without



Scheme 3. Synthesis of quinazoline-2,4-diones by Makino.



Scheme 4. Synthesis of quinazoline-2,4-diones by Makino.

protecting the amino group in the solid-phase synthesis of benzodiazepines [16].

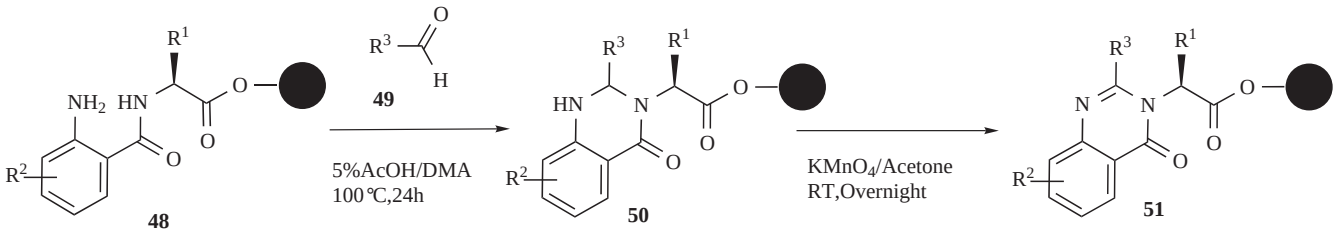
As an alternative way to introduce 1*N*-substituents, Makino *et al.* reported the solid-phase synthesis of quinazoline-2,4-diones **47** using 2-fluoro-5-nitrobenzoic acid **42** as a key building block [6e] (Scheme **4**). Instead of introducing 1*N*-substituents by alkylation, a variety of amines **44** were attached by S_NAr reaction with **43** to give **45**, thus allowing substituents that were not commercially available as alkylhalides or alcohols. In addition, quinazoline-2,4-diones with 1*N*-aryl substituents were easily synthesized using anilines as **44**. The preparation of 1*N*-aryl compounds has been difficult with previous methods [6a-d]. Subsequent carbonylation of **45** with carbonyldiimidazole **39** gave various quinazoline-2,4-diones **46**. However, introduction of other substituents on the aromatic ring of quinazoline-2,4-diones cannot be achieved with this method, because the usage of 2-fluoro-5-nitrobenzoic acid **42** was critical in this synthesis.

Solid-Phase Synthesis of Quinazolin-4-Ones with Various 2-Substituents

In this section, we discuss the solid-phase synthesis of quinazolin-4-ones with various 2-substituents, where the carbon, oxygen, nitrogen or sulfur atom is connected to the 2-position of quinazolin-4-ones. Even though these compounds possess a common skeleton, quinazolin-4-one, diverse strategies were necessary to introduce different atoms at the 2-position.

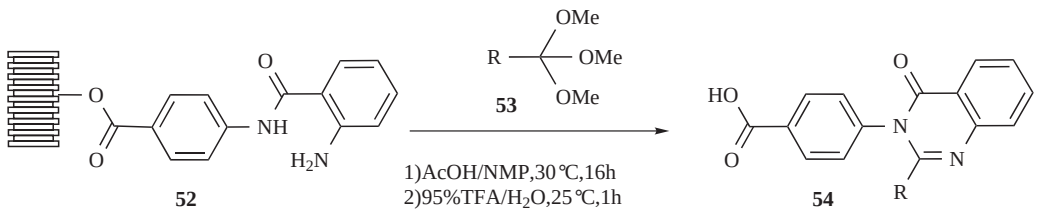
Synthesis of 2-Alkyl and Aryl Quinazolin-4-Ones: Carbon Atom Connected to the 2-Position

Mayer *et al.* reported the solid-phase synthesis of quinazolin-4-ones **51**, utilizing cyclocondensation between resin-bound 2-aminobenzamides **48** and aldehydes **49**, and subsequent oxidation of **50** with $KMnO_4$ [7a] (Scheme **5**). This method was effective for the synthesis of both 2-alkyl and 2-aryl quinazolin-4-ones. However, this synthesis is not applicable to compounds that are susceptible to oxidation, and the purity of these quinazolin-4-ones was not excellent according to their report.

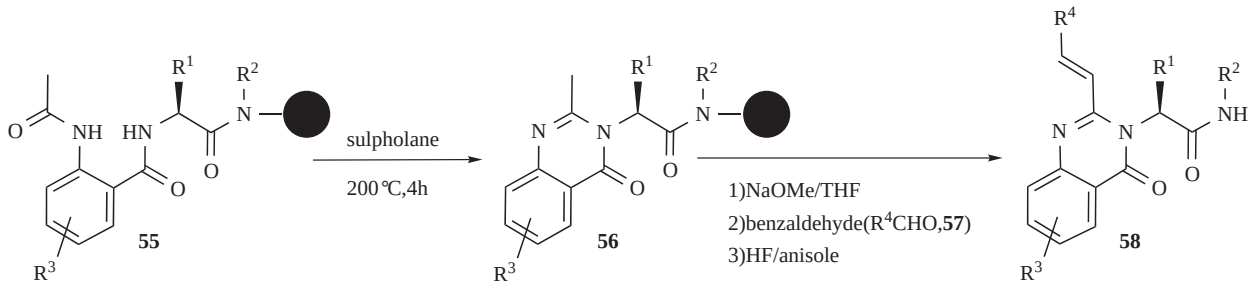


Scheme 5. Synthesis of quinazolin-4-ones by Mayer.

Makino *et al.* reported the synthesis of quinazolin-4-ones by reacting resin-bound 2-aminobenzamides **52** with orthoformates **53**, directly giving 2-alkyl and 2-aryl quinazolin-4-ones **54** with high purity [7b] (Scheme **6**). As orthoformates possess a higher oxidation state than aldehydes, the oxidation step after the cyclization was circumvented. In addition, orthoformates are more reactive



Scheme 6. Synthesis of quinazolin-4-ones by Makino.



Scheme 7. Synthesis of 2-styrylquinazolin-4-ones by Houghten.

equivalents of carboxylic acid. Hence, this cyclocondensation with orthoformates proceeded smoothly at 30°C, in contrast to the cyclization of N-acetyl-2-aminobenzamides **55** to quinazolin-4-ones **56** which required harsh reaction conditions (200°C, Scheme **7**) [7c].

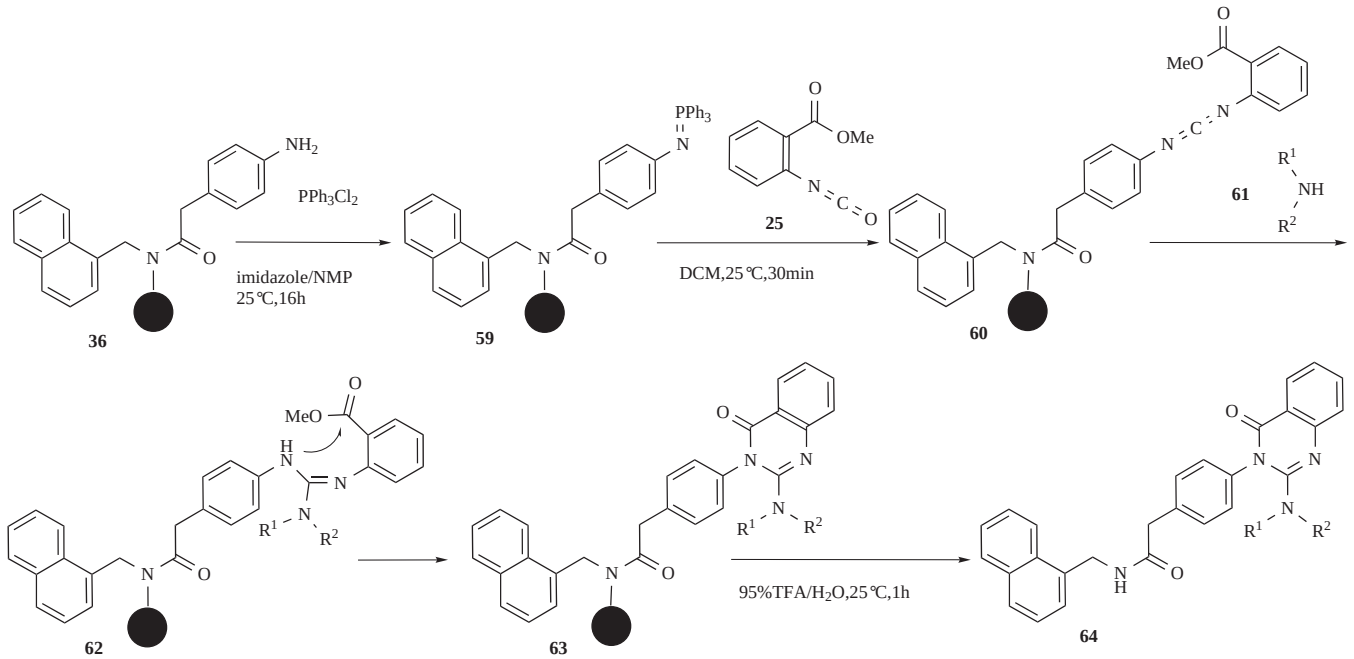
Houghten *et al.* reported the derivatization of resin-bound 2-methylquinazoline-2,4-diones **56** into various 2-styryl-quinazoline-2,4-diones **58** using benzaldehydes **57** [7c] (Scheme **7**). This solid-phase synthesis is considered to be an important complementary method for the preparation of quinazoline-2,4-diones, because solid-phase synthesis of 2-styrylquinazoline-2,4-diones is difficult with other strategies. However, this method is not applicable to compounds with ester moieties due to the usage of sodium methoxide.

Synthesis of 2-Alcoxyquinazolin-4-Ones: Oxygen Atom Connected to the 2-Position

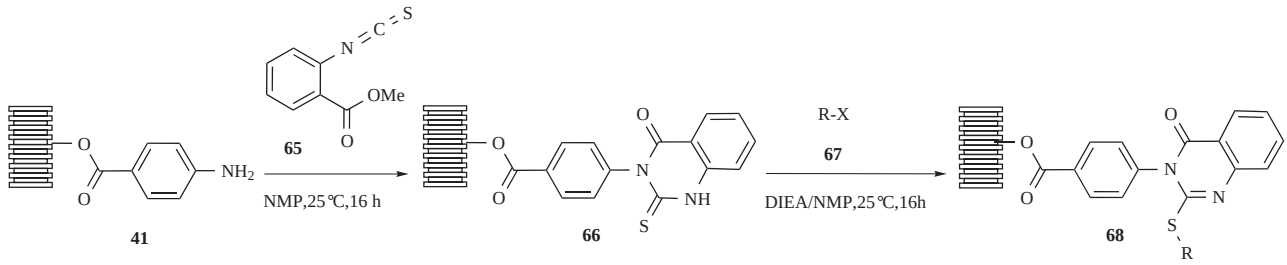
Makino *et al.* reported the solid-phase synthesis of 2-alcoxyquinazolin-4-ones using tetramethoxymethane as an "orthoformate" to obtain 2-methoxyquinazolin-4-ones [7b] (**54** in Scheme **6**, R=OMe). Note that 2-alcoxyquinazolin-4-ones cannot be prepared according to Scheme **5**. However, tetraalcoxymethanes were found to be less reactive than orthoformates. For example, 2-methoxyquinazolin-4-ones were obtained only when this set of reactions was performed at 50°C, while performing the reactions of Scheme **6** at 30°C was sufficient. The reaction with tetraethoxymethane gave only ca. 50% of the products. This lower reactivity of tetraalcokymethane than orthoformate is caused by higher electron density and less accessibility of the carbon atom at the reaction center due to the replacement of carbon by the larger oxygen atom. Further investigation of acidic catalysts and reaction temperature is necessary for the synthesis of 2-alcoxyquinazolin-4-ones.

Synthesis of 2-Aminoquinazolin-4-Ones: Nitrogen Atom Connected to the 2-Position

Makino *et al.* reported the solid-phase synthesis of 2-aminoquinazolin-4-ones **63** using aza *Wittig* reaction between resin-bound iminophosphorane **59** and 2-methoxycarbonylphenyl isocyanate **25** [8] (Scheme **8**). The iminophosphoranes **59** were prepared by the treatment of resin-bound anilines **36** with triphenylphosphindichloride/triazole. This synthetic strategy was attempted with various resin-bound anilines, but the derivatization of resin-bound alkylamines was not successful due to the failure of the iminophosphoranes. Several other methods for the solid-phase synthesis of 2-aminoquinazolin-4-ones have been proposed, although such synthetic strategies are not applicable when resin-bound primary amines are used as starting compounds.



Scheme 8. Synthesis of quinazolin-4-ones by Makino.



Scheme 9. Synthesis of quinazoline-2-thioxo-4-ones by Makino.

Synthesis of Quinazoline-2-Thioxo-4-Ones: Sulfur Atom Connected to the 2-Position

Makino *et al.* reported the synthesis of quinazoline-2-thioxo-4-ones **66** by reacting resin-bound anilines **35** with 2-methoxycarbonyl phenylisothiocyanate **65** [9] (Scheme **9**). Subsequent S-alkylation with alkylhalides **67** gave various S-substituted quinazoline-2-thioxo-4-ones **68** with high purity. Although S-alkylated thiourea usually reacts with various amines to give guanidines [17], these S-alkylated quinazoline-2-thioxo-4-ones **68** were found to be surprisingly stable, thus the attempts to convert these compounds into 2-aminoquinazolin-4-ones at high temperature were not successful.

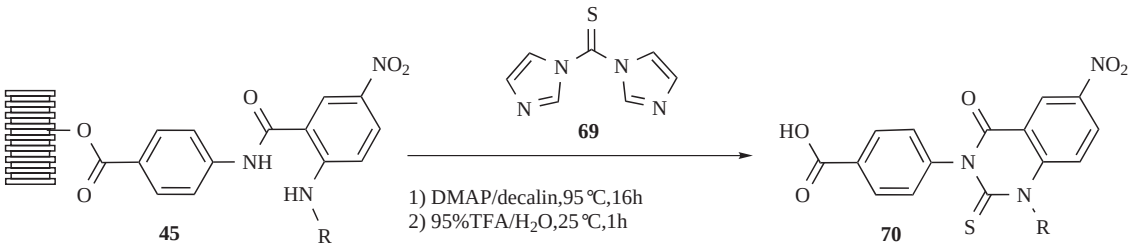
Although quinazoline-2-thioxo-4-ones with various S-substituents could be easily prepared according to Scheme **9**, introduction of 1*N*-substituents was not possible as S-alkylation proceeds faster than 1*N*-alkylation. Makino *et al.* successfully synthesized 1*N*-substituted 2-thioxoquinazolin-4-ones **70** by treating the intermediates **45**, which were prepared according to Scheme **4**, with thiocarbonyldiimidazole **69**, thus introducing 1*N*-substituents before the formation of the thiourea moiety [10].

SOLID-PHASE SYNTHESIS OF QUINAZOLINE-2,4-DIONE ANALOGUES: REPLACEMENTS OF THE 2- OR 4-CARBON ATOM ON THE QUINAZOLINE-2,4-ONE RING WITH HETEROATOMS

Finally, we discuss the solid-phase synthesis of quinazoline-2,4-dione analogues, where the 2- or 4-carbon atom on the quinazoline-2,4-one ring is replaced with heteroatoms.

Synthesis of 1,2,3-Benzotriazin-4-Ones: Replacement of the 2-Carbon Atom with Nitrogen Atom

Makino *et al.* reported the solid-phase synthesis of 1,2,3-benzotriazin-4-ones **73** by treating resin-bound 2-aminobenzamides **38** with t-butylnitrite **71** [11a] (Scheme **12**). Initially, $NaNO_2/AcOH/H_2O$ was used for diazotization, though the handling of the reaction was not easy in sealed vessels due to gas generation during the reaction [11b].

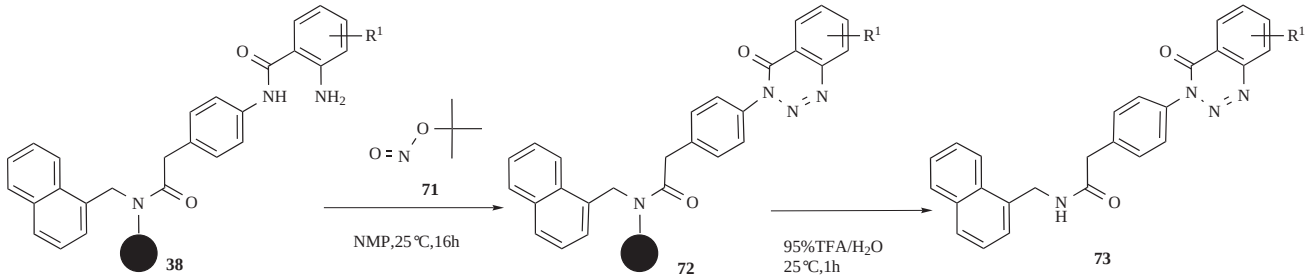


Scheme 10. Synthesis of quinazoline-2-thioxo-4-ones by Makino.

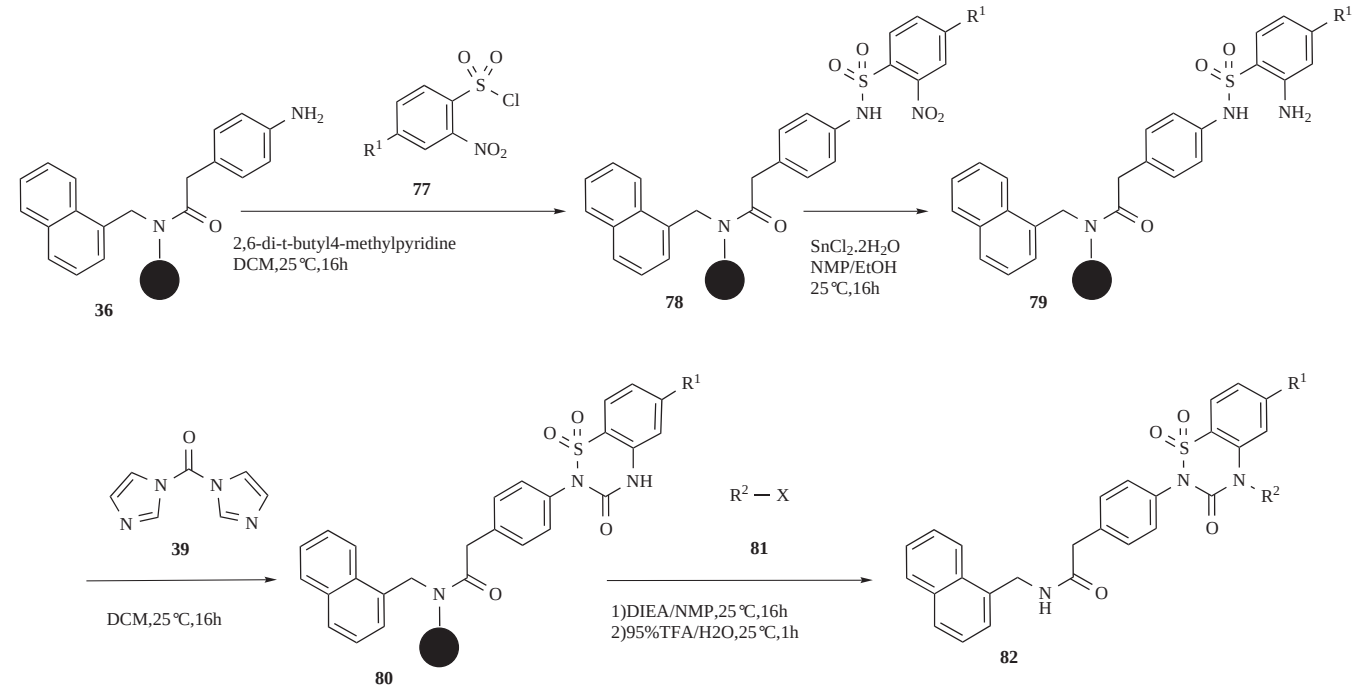
1,2,3-Benzotriazin-4-ones **73** with various substituents on the aromatic ring were synthesized because preparation of various 2-aminobenzamides **38** was possible according to Scheme **3**.

Synthesis of 2,1,3-Benzothiadiazin-4-One 2-Oxides: Replacement of the 2-Carbon Atom with Sulfur Atom

Makino *et al.* reported the synthesis of 2,1,3-benzothiadiazin-4-ones by treating **45** with thionylchloride **74**/ imidazole **75** [12] (Scheme **11**). This cyclization did not work with 2-aminobenzamides **38** in Scheme **3**, indicating a nitro substituent on the aromatic ring and/or a 1*N*-substituent was necessary for this cyclization. Since the intermediates **45** were prepared by S_NAr reaction of 5-nitro-2-fluorobenzamides **43** with amines **44** according to Scheme **4**, other substituents on the aromatic ring were not allowed.



Scheme 11. Synthesis of 1,2,3-benzotriazin-4-ones by Makino.



Scheme 13. Synthesis of 1,2,4-benzothiadiazin-3-one 1,1-dioxides by Makino.

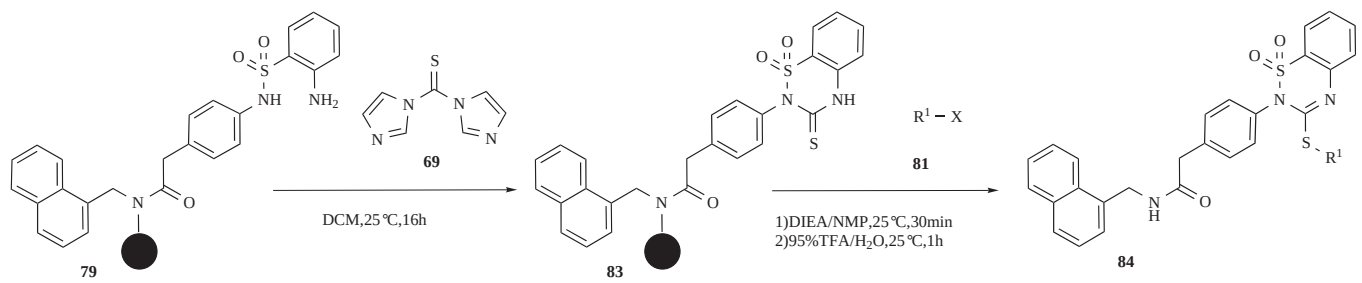
Synthesis of 1,2,4-Benzothiadiazin-3-One 1,1-Dioxides: Replacement of the 4-Carbonyl with Sulfur Atom

Makino *et al.* reported the solid-phase synthesis of 1,2,4-benzothiadiazin-3-one 1,1-dioxides **82** using 2-nitrobenzenesulfonyl chloride **77** [13] (Scheme **13**). 2-Nitrobenzenesulfonylamides have been often used for protection and activation of primary amines, and the 2-nitrobenzenesulfony group is usually removed by N-alkylation in the Fukuyama-Mitsunobu reaction. Instead of the removal of 2-nitrobenzenesulfonyl group, the reduction of the nitro group of **78** and subsequent cyclization of **79** with carbonyldiimidazole **39** gave successfully 1,2,4-benzothiadiazin-3-ones **80**. Furthermore, 1*N*-alkylation of **80** with alkylhalides **81** was also performed to give diverse 1,2,4-benzothiadiazin-3-one 1,1-dioxides **82**.

Makino *et al.* also reported the synthesis of 3-sulfanyl-1,2,4-benzothiadiazine 1,1-dioxides **83** *via* cyclization of the intermediates **79** in Scheme **13** using thiocarbonyldiimidazole **69** [14]. Subsequent S-alkylation of **83** with alkylhalides **81** gave various S-alkylated 3-sulfanyl-1,2,4-benzothiadiazine 1,1-dioxides **84** (Scheme **14**).

CONCLUSION

In this review, we summarized methods for the solid-phase synthesis of quinazoline-2,4-diones and their analogues from resin-bound compounds with a primary amine, incorporating the amine as parts of these heterocycles. These solid-phase syntheses are advantageous in the process of lead optimization for medicinal chemistry. When optimizing lead active compounds, it is important to be able to explore compounds with different classes of scaffolds, especially when problems associated with pharmacokinetics and toxicity are thought to be linked to the particular chemical scaffold of a lead compound. Needless to say, activity of a compound might be drastically increased or decreased upon modification of the scaffold. In addition, due to the efficiency of solid-phase synthesis, it is possible to investigate a great number of substituents attached to the same class of scaffold. We believe that the syntheses described in this review, combined with other knowledge of solid-phase synthesis reported so far, provide practical and useful tools for drug discovery in the pharmaceutical industry.



Scheme 14. Synthesis of 3-sulfanyl-1,2,4-benzothiadiazine 1,1-dioxides by Makino.

REFERENCES

[1] Review: (a) Thompson, L. A.; Ellman, J. A. *Chem. Rev*. **1996**, *96*, 555. (b) Booth, S.; Hermkens, P. H. H.; Ottenheijm, H. C. J.; Rees, D. C. *Tetrahedron* **1998**, *54*, 15385.

[2] Review: Bräse, S.; Gil, C.; Knepper, K. *Bioorg. Med. Chem.* **2002**, *10*, 2415.

[3] (a) Xiao, X.-Y.; Ngu, K.; Chao, C.; Patel, D. V. *J. Org. Chem.* **1997**, *62*, 6968. (b) Gordeev, M. F.; Gordon, E. M.; Patel, D. V. *J. Org. Chem.* **1997**, *62*, 8177. (c) Sarshar, S.; Siev, D.; Mjalli, A. M. M. *Tetrahedron Lett.* **1996**, *37*, 835. (d) Sarshar, S.; Zhang, C.; Moran, E. J.; Krane, S.; Rodarte, J. C.; Benbatoul, K. D.; Dixon, R.; Mjalli, A. M. M. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2599. (e) Wipf, P.; Cunningham, A. *Tetrahedron Lett.* **1995**, *36*, 7819. (f) Chandrasekhar, S.; Padmaja, M. B.; Raza, A. *Synlett* **1999**,1597. (g) Tumelty, D.; Schwarz, M. K.; Cao, K.; Needels, M. C. *Tetrahedron Lett.* **1999**, *40*, 6185. (h) Makino, S.; Nakanishi, E.; Tsuji, T. *Synlett*, 2003, *817*.

[4] (a) Buckman, B. O.; Mohan, R. *Tetrahedron Lett.* **1996**, *37*, 4439-4442. (b) Gouilleux, L.; Fehrentz, J. -A.; Winternitz, F.; Martinez, J. *Tetrahedron Lett*. **1996**, *37*, 7031. (c) Shao, H.; Colucci, M.; Tong, S.; Zhang, H.; Castelhano, A. L. *Tetrahedron Lett*. **1998**, *39*, 7235. (d) Villalgordo, J. M.; Obrecht, D.; Chucholowsky, A. *Synlett* **1998**, 1405. (e) Cobb, J. M.; Fiorini, M. T.; Goddard, C. R.; Theoclitou, M.-E.; Abell, C. *Tetrahedron Lett.* **1999**, *40*, 1045. (f) Zhang, W.; Mayer, J. P.; Hall, S. E.; Weigel, J. A. *J. Comb. Chem.* **2001**, *3*, 255. (g) Sun, Q.; Zhou, X.; Kyle, D. J. *Tetrahedron Lett.* **2001**, *42*, 4119. (h) Zhang, J.; Barker, J.; Lou, B.; Saneii, H. *Tetrahedron Lett.* **2001**, *42*, 8405. (i) O'Mahony, D. J. R.; Krchnak, V. *Tetrahedron Lett*. **2002**, *43*, 939. (j) Choo, H.-Y. P.; Kim, M.; Lee, S. K.; Kim, S. W.; Chung, I. K. *Bioorg. Med. Chem. Lett.* **2002**, *10*, 517.

[5] (a) de Laszlo S. E.; Quagliato, C. S.; Greenlee, W. J.; Patchett, A. A.; Chang, R. S. L.; Lotti, V. J.; Chen, T. -B.; Scheck, S. A.; Faust, K. A.; Kivlighn, S. S.; Schorn, T. S.; Zingaro, G. J.; Siegl, P. K. S. *J. Med. Chem*. **1993**, *36*, 3207-3210. (b) Hutchinson, J. H.; Cook, J. J.; Brashear, K. M.; Breslin, M. J.; Glass, J. D.; Gould, R. J.; Halczenko, W.; Holahan, M. A.; Lynch, R. J.; Sitko, G. R.; Stranieri, M. T.; Hartman, G. D. *J. Med. Chem*. **1996**, *39*, 4583-4591.

[6] (a) Gordeev, M. F.; Hui, H. C.; Gordon, E. M.; Patel, D. V. *Tetrahedron Lett.* **1997**, *38*, 1729. (b) Gordeev, M. F.; Luehr, G. W.; Hui, H. C.; Gordon, E. M.; Patel, D. V. *Tetrahedron*, **1998**, *54*, 15879. (c) Puhl, M.; Adida, S.; Klinge, D.; Kling, A. WO9856770, 1998, December 17. (d) Okuzumi, T.; Nakanishi, E.; Tsuji, T.; Makino, S. *Tetrahedron*, **2003**, *59*, 5603. (e) Makino, S.; Suzuki, N.; Nakanishi, E.; Tsuji, T. *Synlett.* **2001**, 333.

[7] (a) Mayer, J. P.; Lewis, G. S.; Curtis, M. J. Zhang, J. W. *Tetrahedron Lett.* **1997**, *38*, 8445. (b) Makino, S.; Suzuki, N.; Nakanishi, E.; Tsuji, T. *Synlett.* **2000**, 1670. (c) Theoclitou, M.-E.; Ostresh, J. M.; Hamashin, V.; Houghten, R. A. *Tetrahedron Lett*. **2000**, *41*, 2051.

[8] Makino, S.; Okuzumi, T.; Nakanishi, E.; Tsuji, T. *J. Comb. Chem.***2003**, *5*, 756.

[9] Makino, S.; Suzuki, N.; Nakanishi, E.; Tsuji, T. *Tetrahedron Lett.* **2000**, *41*, 8333.

[10] Makino, S.; Nakanishi, E.; Tsuji, T. *Tetrahedron Lett.* **2001**, *42*, 1749.

[11] (a) Okuzumi, T.; Nakanishi, E.; Tsuji, T.; Makino, S. *Tetrahderon Lett*. **2003**, *44*, 5539. (b) Makino, S.; Nakanishi, E.; Tsuji, T. *J. Brazil. Chem. Soc.* **2003**, *14*, 452-455.

[12] Makino, S.; Nakanishi, E.; Tsuji, T. *Bulletin of the Korean Chemical Society* **2003**, *24*, 3.

[13] Makino, S.; Nakanishi, E.; Tsuji, T. *J. Comb. Chem.* **2003**, *5*, 73.

[14] Makino, S.; Okuzumi, T.; Nakanishi, E.; Tsuji, T. *Tetrahedron Lett.* **2002**, *43*, 8402.

[15] Mayer, J. P.; Zhang, J.; Bjergarde, K.; Lenz, D. M.; Gaudino, J. J. *Tetrahedron Lett*. **1996**, *37*, 8081.

[16] Boojamra, C. G.; Burow, K. M.; Thompson, L. A.; Ellman, J. A. *J. Org. Chem.* **1997**, *62*, 1240.

[17] Schneider, S.; Bishop, P. A.; Salazar, M. A.; Bishop, O. A. Anslyn, E. V. *Tetrahedron* **1998**, *54*, 15063.

Received: May 26, 2005 **Revised: August 29, 2005** **Accepted: August 30, 2005**